Glycaemic Control, Complications, and Well-Being among People with Type 2 Diabetes in Saudi Arabia

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Glycaemic Control, Complications, and Well-Being among People with Type 2 Diabetes in Saudi Arabia

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Monash University in 2019

Department of Epidemiology and Preventive Medicine

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Declaration

This thesis contains no material which has been accepted for the award of any other degree or diploma at any university or equivalent institution and that, to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

Print Name: Mohammed Jassim A. Alramadan

Date: 5/9/2019

Dedication

This thesis is dedicated to my family

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Acknowledgements

Above all, I thank Allah the Almighty for giving me this opportunity and providing me the strength to complete my PhD thesis successfully.

My deepest appreciation and gratitude go to my supervisors, Dr Billah and Prof. Magliano for their invaluable help, support, guidance and advice throughout the time of research and writing of this thesis. I am especially appreciative to Dr Billah for his promptness in reviewing my work and answering my questions despite his busy schedule. It was indeed a privilege to work with you.

Special thanks are given to my PhD colleagues, especially Afsana Afroz, Nazmul Karim, Farwa Rizvi, and Nassif Hossain, with whom I established lifelong friendships as we supported each other in our research and worked together on several projects. I have learned a lot from them, and they have made my PhD a happy journey on which to reflect.

My PhD would not have been possible without all the support I received from the School of Public Health and Preventive Medicine, and Monash University. I also must acknowledge the Saudi Ministry of Health, Ministry of Education, and The Saudi Cultural Mission in Australia for providing me with a postgraduate scholarship and generously supporting me during my PhD.

I also would like to thank the people with type 2 diabetes in Saudi Arabia who contributed data to this study. My appreciation is also given for the dedication of the people who collected data for me during the period of patients' recruitment.

My heartfelt thanks to my beloved wife and daughters for their love, help, and encouragement. This journey would not have been possible without their support and patience. A heartfelt thanks, also, to my father, mother, brothers, and sisters for their continuous support and encouragement.

Abstract

Background

Type 2 diabetes mellitus (T2DM) is highly prevalent in Saudi Arabia. A large proportion of the affected people have poor blood glucose control, diabetes comorbidities and complications, and poor quality of life. The effect of lifestyle and other factors on glycaemic control and their association with diabetes comorbidities, complications and poor quality of life has not been adequately explored in existing literature for the Saudi population with T2DM.

Aims

This project has five main objectives: 1) to examine factors related to glycaemic control; 2) to explore factors correlated to diabetes complications; 3) to develop a risk scoring system to predict diabetes complications; 4) to explore the issues of obesity, hypertension, and dyslipidaemia as comorbidities of diabetes; and 5) to assess the health-related quality of life and its associated factors for people with T2DM in Saudi Arabia.

Methods

A survey was conducted among adults with T2DM attending diabetes centres in three regions in Saudi Arabia. Participants were interviewed face-to-face, their anthropometrics were measured in a standardised way, and their medical records were reviewed for lab test results, prescribed medications, and documented diagnosis of diabetes comorbidities and complications. Univariate and multiple linear and logistic regression analysis and bootstrapping methods were used for data analysis.

Results

A sample of 1121 participants was recruited. The mean age was 57.6 ±11.1 years, 65.2% of the participants were females, and 75.9% of the participants had inadequate glycaemic control (haemoglobin A1c ≥7%). The modifiable risk factors for inadequate control were a low intake of fruits and vegetables, physical inactivity, lack of knowledge about target haemoglobin A1c, high waist-hip ratio, and low adherence to medication.

The prevalence of coronary artery disease was 17.0%; diabetic foot, 13.1%; stroke, 3.7%; neuropathy, 20.3%; renal impairment, 14.5%; and retinopathy was 42.8%. Lifestyle and modifiable factors associated with one or more of these complications were physical inactivity, longer sitting time, obesity, smoking, hypertension, poor glycaemic control, and dyslipidaemia.

Six to ten of the following variables appeared as significant in each of the six risk scoring tools developed for type 2 diabetes related complications: age ≥60 years, gender, low education level, obesity, physical inactivity, long sitting time, smoking, long duration of diabetes, insulin use, low adherence to treatment, family history of diabetes, haemoglobin A1c ≥9%, hypertension, and dyslipidaemia. The area under the receiver operating characteristic curves ranged from 71.2% to 80.5%, and slope calibration ranged from 93.7% to 99.3%.

The prevalence of obesity, hypertension, and dyslipidaemia was 62.5%, 70.0% and 70.7%, respectively. The modifiable risk factors of these comorbidities include physical inactivity, longer sitting time, body mass index ≥30 Kg/m², and the use of insulin. Age, gender, lower education level, low income, renal impairment, and longer diabetes duration were the other associated factors. Obesity, hypertension, and dyslipidaemia substantially increased the risk of cardiovascular complications especially when they coexisted.

The mean utility index of the quality of life was 0.739 ±0.261 (0.795 ±0.197 for males and 0.709 ±0.285 for females), which dropped to 0.566 ±0.339 in the presence of micro- and macro-vascular complications. Among

the study participants, 51.0% had problems with mobility, 12.3% with self-care, and 30.5% with usual activity, while 51.6% had problems with pain-discomfort and 45.8% with anxiety-depression. Factors associated with poor health-related quality of life were lower education level, physical inactivity, longer sitting time, anxiety, depression, and diabetes complications.

Conclusion

Inadequate glycaemic control, diabetes comorbidities, and complications are highly prevalent among people with type 2 diabetes in Saudi Arabia. The overall health-related quality of life is low, especially among those who have diabetes complications. Eating healthy food, reducing sitting time, increasing exercise, maintaining normal body weight, and avoiding smoking will give people better control of their diabetes. A healthy lifestyle should reduce the risk of diabetes related comorbidities and complications and improve the quality of life. The developed risk scoring tools for diabetes related complications will help healthcare providers to raise the awareness of people with type 2 diabetes about their risk, and to identify people at high risk.

Publications during enrolment

I hereby declare that this thesis contains no material which has been accepted for the award of any other degree or diploma at any university or equivalent institution and that, to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

This thesis includes a published methodology and systematic review papers, as well as five original papers (two published and three submitted). The core theme of the thesis is to examine the determinants of poor glycaemic control, diabetes complications, diabetes comorbidities, and poor quality of life for people with type 2 diabetes in Saudi Arabia. The ideas, development and writing up of all the papers in the thesis were the principal responsibility of myself, the student, working within the School of Public Health and Preventive Medicine under the supervision of Dr Baki Billah.

The inclusion of co-authors reflects the fact that the work came from active collaboration between researchers and acknowledges input into team-based research.

Thesis Chapter	**Publication Title**	**Status** *(published, in press, accepted or returned for revision, submitted)*	**Nature and % of student contribution**	**Co-author name(s) Nature and % of Co-author's contribution***	**Co-author(s), Monash student Y/N***
Chapter 2	Patient-Related Determinants of Glycaemic Control in People with Type 2 Diabetes in the Gulf Cooperation Council Countries: A Systematic Review	Published	Concept, design, data collection, literature search, data extraction, data analysis, results interpretation, and drafting the manuscript (62%)	Afsana Afroz 4% Concept, design, literature search, data extraction, and critically reviewed the manuscript Sultana Monira Hussain 4% Concept, design, and critically reviewed the manuscript Mohammed Ali Batais 4% Concept, design, and critically reviewed the manuscript Turky H. Almigbal 4% Concept, design, and critically reviewed the manuscript Hassan Ahmad Al-Humrani 4% Concept, design, and critically reviewed the manuscript Ahmed Albaloshi 4% Concept, design, and critically reviewed the manuscript Lorena Romero 4% Concept, design, search strategy, and critically reviewed the manuscript Dianna J Magliano 4% Concept, design, and critically reviewed the manuscript Baki Billah 6% Concept, design, data analysis, results interpretation, and drafting the manuscript	Yes No No No No No No No
Chapter 3	A Study Protocol to Assess the Determinants of	Published	Concept, design, data collection, data analysis, results interpretation,	Afsana Afroz 4% Concept, design, and critically reviewed the manuscript	Yes

	Glycaemic Control, Complications and Health Related Quality of Life for People with Type 2 Diabetes in Saudi Arabia		drafting the manuscript (65%)	Mohammed Ali Batais 4% Concept, design, and critically reviewed the manuscript Turky H. Almigbal 4% Concept, design, and critically reviewed the manuscript Hassan Ahmad Alhamrani 4% Concept, design, and critically reviewed the manuscript Ahmed Albaloshi 4% Concept, design, and critically reviewed the manuscript Fatimah A Alramadan 4% Concept, design, data collection, and critically reviewed the manuscript Dianna J Magliano 5% Concept, design, and critically reviewed the manuscript Baki Billah 6% Concept, design, data analysis, results interpretation, and drafting the manuscript	No No No No No No No
Chapter 4	Glycaemic control for people with type 2 diabetes in Saudi Arabia – an urgent need for a review of management plan	Published	Concept, design, data collection, data analysis, results interpretation, drafting the manuscript (64%)	Dianna J Magliano 5% Concept, design, data analysis, and critically reviewed the manuscript Turky H. Almigbal 4% Concept, design, results interpretation, and critically reviewed the manuscript Mohammed Ali Batais 4% Concept, design, results interpretation, and critically reviewed the manuscript Afsana Afroz 4% Concept, design, data analysis, and critically reviewed the manuscript Hesham J. Alramadhan 4% Concept, design, data collection, and critically reviewed the manuscript Waad Faozi Mahfoud 4% Concept, design, data collection, and critically reviewed the manuscript Adel Mehmas Alragas 4% Concept, design, data collection, and critically reviewed the manuscript Baki Billah 7% Concept, design, data analysis, results interpretation, and drafting the manuscript	No No No Yes No No No No
Chapter 5 part 1	Lifestyle Factors and Macro- and Micro-Vascular Complications among People with Type 2	Published	Concept, design, data collection, data analysis, results interpretation, drafting the manuscript (64%)	Dianna J Magliano 5% Concept, design, results interpretation, and critically reviewed the manuscript Hassan Ahmad Alhamrani 4%	No

	Diabetes in Saudi Arabia			Concept, design, results interpretation, and critically reviewed the manuscript Ameerah J Alramadan 4% Concept, design, data collection, and critically reviewed the manuscript Sara M. Alameer 4% Concept, design, data collection, and critically reviewed the manuscript Ghada Mohammed Amin 4% Concept, design, data collection, and critically reviewed the manuscript Wed A. Alkharras 4% Concept, design, data collection, and critically reviewed the manuscript Nour A. Bayaseh 4% Concept, design, data collection, and critically reviewed the manuscript Baki Billah 7% Concept, design, data analysis, results interpretation, and drafting the manuscript	No No No No No No No
Chapter 5 part 2	Risk Scoring System for Macro- and Micro-Vascular Complications Related to Type 2 Diabetes in Saudi Arabia	Submitted	Concept, design, data collection, data analysis, results interpretation, drafting the manuscript 62%	Mohammed Ali Batais 4% Concept, design, results interpretation, and critically reviewed the manuscript Turky H. Almigbal 4% Concept, design, results interpretation, and critically reviewed the manuscript Md Nazmul Karim 4% Concept, design, data analysis, results interpretation, and critically reviewed the manuscript Dianna J Magliano 4% Concept, design, analysis results interpretation, and drafting the manuscript Basmah J. Al Ramadhan 4% Concept, design, data collection, and critically reviewed the manuscript Nouf A. Alzaid 4% Concept, design, data collection, and critically reviewed the manuscript Noor A. Alabdullah 4% Concept, design, data collection, and critically reviewed the manuscript Manzur Ashraf 4%	No No No No No No No

				Concept, design, online risk calculator development, and critically reviewed the manuscript	No
				Baki Billah 6% Concept, design, data analysis, results interpretation, and drafting the manuscript	No
Chapter 6	Obesity, Hypertension, and Dyslipidaemia among People with Type 2 Diabetes in Saudi Arabia	Submitted	Concept, design, data collection, data analysis, results interpretation, drafting the manuscript (69%)	Ahmed Albaloshi 4% Concept, design, results interpretation, and critically reviewed the manuscript	No
				Hassan Ahmad Alhamrani 4% Concept, design, results interpretation, and critically reviewed the manuscript	No
				Hawra Alramadhan 4% Concept, design, data collection, and critically reviewed the manuscript	No
				Ayat Alabdullah 4% Concept, design, data collection, and critically reviewed the manuscript	No
				Nawaf Almogaible 4% Concept, design, data collection, and critically reviewed the manuscript	No
				Waad Faozi Mahfoud 4% Concept, design, data collection, and critically reviewed the manuscript	No
				Baki Billah 7% Concept, design, data analysis, results interpretation, and drafting the manuscript	No
Chapter 7	Health Related Quality of Life for People with Type 2 Diabetes in Saudi Arabia	Submitted	Concept, design, data collection, data analysis, results interpretation, drafting the manuscript (61%)	Afsana Afroz 4% Concept, design, data analysis, and critically reviewed the manuscript	No
				Bodrun Siddiquea 4% Concept, design, results interpretation, and critically reviewed the manuscript	No
				Noor A. Alabdullah 4% Concept, design, data collection, and critically reviewed the manuscript	No
				Sara M. Alameer 4% Concept, design, data collection, and critically reviewed the manuscript	No
				Adel Mehmas Alragas 4% Concept, design, data collection, and critically reviewed the manuscript	No
				Ghada Mohammed Amin 4% Concept, design, data collection, and critically reviewed the manuscript	No
				Nour A. Bayaseh 4%	No

				Concept, design, data collection, and critically reviewed the manuscript Fatimah A Alramadan 4% Concept, design, data collection, and critically reviewed the manuscript Baki Billah 7% Concept, design, data analysis, results interpretation, and drafting the manuscript	 No No

I have renumbered sections of submitted or published papers in order to generate a consistent presentation within the thesis.

Student: Mohammed Alramadan **Date:** 1/9/2019

The undersigned hereby certify that the above declaration correctly reflects the nature and extent of the student's and co-authors' contributions to this work. In instances where I am not the responsible author I have consulted with the responsible author to agree on the respective contributions of the authors.

Main Supervisor: Baki Billah **Date:** 2/9/2019

Communications arising from this research

Publications

- **Alramadan MJ**, Afroz A, Hussain SM, Batais MA, Almigbal TH, Al-Humrani HA, et al. Patient-Related Determinants of Glycaemic Control in People with Type 2 Diabetes in the Gulf Cooperation Council Countries: A Systematic Review. Journal of Diabetes Research. 2018.
- **Alramadan MJ**, Afroz A, Batais MA, Almigbal TH, Alhamrani HA, Albaloshi A, et al. A Study Protocol to Assess the Determinants of Glycaemic Control, Complications and Health Related Quality of Life for People with Type 2 Diabetes in Saudi Arabia. Journal of Health Education Research & Development. 2017;5(2):1-6.
- **Alramadan MJ**, Magliano DJ, Almigbal TH, Batais MA, Afroz A, Alramadhan HJ, et al. Glycaemic control for people with type 2 diabetes in Saudi Arabia–an urgent need for a review of management plan. BMC endocrine disorders. 2018;18(1):62.
- **Alramadan MJ**, Magliano DJ, Alhamrani HA, Alramadan AJ, Alameer SM, Amin GM, et al. Lifestyle factors and macro-and micro-vascular complications among people with type 2 diabetes in Saudi Arabia. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2018;13(1):484-91.

Manuscript under review

- **Alramadan MJ**, Batais MA, Almigbal TH, Nazmul MK, Dianna MJ, Al Ramadhan BJ, et al. Risk Scoring System for Macro- and Micro-Vascular Complications Related to Type 2 Diabetes in Saudi Arabia
- **Alramadan MJ**, Albaloshi A, Alhamrani HA, Alramadhan HH, Alabdullah AS, Almogaible N, et al. Obesity, Hypertension, and Dyslipidaemia among People with Type 2 Diabetes in Saudi Arabia.
- **Alramadan MJ,** Afroz A, Magliano DJ, Alabdullah NA, Alameer SM, Alragas AM, et al. Health Related Quality of Life for People with Type 2 Diabetes in Saudi Arabia

Presentations

- Patient-Related Determinants of Glycaemic Control in People with Type 2 Diabetes in the Gulf Cooperation Council Countries: A Systematic Review. International Diabetes Federation Congress Abu, December 2017, Dhabi, UAE. (Poster)
- Diabetes in Saudi Arabia: Prevalence, Glycaemic Control and Complications – a Systematic Review. The 15th International Diabetes Epidemiology Symposium, December 2017, Abu Dhabi, UAE. (Poster)
- Lifestyle Factors and Macro- and Micro-Vascular Complications among People with Type 2 Diabetes in Saudi Arabia. IDF Diabetes Complication Congress, October 2018, Hyderabad, India. (Oral presentation)
- Risk Scoring System for Macro- and Micro-Vascular Complications Related to Type 2 Diabetes in Saudi Arabia. Alfred Health Week Research Poster Display, June 2019, Melbourne, Australia. (Poster)

Glossary of Abbreviations

ANOVA	Analysis of variance
BMI	Body mass index
CAD	Coronary artery disease
EQ-5D-5L	EuroQol 5-Dimension 5-Level
FBG	Fasting blood glucose
GAD-2	Generalized Anxiety Disorder Scale-2
GFR	Glomerular filtration rate
GPAQ	Global Physical Activity Questionnaire
HbA1c	haemoglobin A1c (Glycated haemoglobin)
HDL	High density lipoprotein
HRQoL	Health related quality of life
LDL	Low density lipoprotein
OGTT	Oral glucose tolerance test
PHQ-2	Patient Health Questionnaire-2
RUDAS	Rowland Universal Dementia Assessment Scale
RBG	Random blood glucose
T2DM	Type 2 diabetes mellitus
VAS	Visual Analogue Scale
WHO	World Health Organization

Chapter 1:

Introduction and Research Aims

1.1 Introduction

1.1.1 Diabetes Mellitus

Insulin, which is a hormone secreted from the beta cells of the pancreas, is one of the most important hormones responsible for controlling the glucose levels in the blood stream. Diabetes Mellitus is a serious chronic disease that occurs when the body cannot produce a sufficient amount of insulin, or cannot use insulin effectively, which results in high blood glucose levels (1). Symptoms of diabetes include increased thirst, frequent urination, hunger, fatigue and blurred vision. However, many people have no symptoms at the time of diagnosis. The chronically elevated glucose in the bloodstream (hyperglycaemia) can damage many of the body's organs, resulting in disabling and life-threatening diabetes-related complications. Early diagnosis and effective treatment can prevent or delay these complications.

The three main types of diabetes are type 1, type 2, and gestational diabetes (GDM). Type 1 diabetes is caused by autoimmune destruction of the beta cells of the pancreas, resulting in insulin deficiency. The etiology of the autoimmune destruction of the beta cells is not completely understood, but genetic susceptibility and environmental factors are thought to play a role (2, 3). Type 1 diabetes usually occurs before adulthood, and the affected person needs insulin to maintain normal blood glucose levels.

When elevated blood glucose levels are first detected during pregnancy, it is classified as gestational diabetes. This type of diabetes occurs when hormones produced by the placenta reduce the responsiveness of the body to the action of insulin. If this is not treated, high blood glucose in pregnancy can cause a variety of adverse pregnancy outcomes. In addition, half of the women who have gestational diabetes will develop type 2 diabetes within five to ten years, and babies born to women with gestational diabetes have a higher risk of developing type 2 diabetes (1). Gestational diabetes is treated by diet, exercise, and insulin.

Type 2 diabetes mellitus (T2DM) is the most common type, accounting for 90% of all the cases of diabetes (1). T2DM usually begins with a reduction in the responsiveness of the body's cells to the action of insulin (insulin resistance), resulting in a high blood glucose levels. The pancreas responds to the elevated blood glucose by increasing the secretion of insulin. However, over time, the insulin production decreases and many patients require externally administered insulin. Lifestyle factors, including sedentary lifestyle, unhealthy eating habits, and obesity, are key risk factors for T2DM (4, 5), and this type of diabetes can be prevented by eating a healthy diet, regular physical activity, and the maintenance of normal body weight (6).

1.1.2 The prevalence of diabetes globally and in the Middle East

Diabetes mellitus is one of the most common chronic noncommunicable diseases in the world (7, 8). In 2017, it was estimated that 451 million adults had diabetes worldwide, with a prevalence of 8.8% (9). According to the International Diabetes Federation, North America and the Caribbean had the highest prevalence of diabetes (11.1%) followed by the Middle East and North Africa (10.8%) (1) where there were an estimated 38.7 million adults with this disease, of whom over 49% were undiagnosed (1). It was predicted that the number of people with diabetes in these regions would reach 82 million by 2045 (1).

1.1.3 The risk of Diabetes related complications

Long-term abnormally high glucose levels in the blood stream place people with diabetes at high risk of developing diabetes complications (10). Diabetes complications can be classified as micro- or macro-vascular. The main macrovascular complications are coronary artery disease, cerebrovascular disease (stroke), and peripheral vascular disease; they are due to damage to the large blood vessels. The main microvascular complications, which occur due to damage to the small vessels, include diabetes

retinopathy, nephropathy (renal disease) and neuropathy. People with diabetes have a two to four times higher risk of developing macrovascular complications and a 10 to 20 times higher risk of developing microvascular complications than people without diabetes (10). Apart from the micro- and macro-vascular complications, diabetes is also linked to cataracts, liver disease, sleep apnoea, anxiety, depression, and cancer (11, 12). It is possible to prevent or delay diabetes complications by ensuring good control of blood glucose, blood lipids, and blood pressure.

1.1.4 The importance of good glycaemic control for diabetes

It is well established that elevated blood glucose levels increase the risk of diabetes complications and mortality among people with diabetes (13, 14). Intensive glycaemic control, on the other hand, substantially lowers this risk (15, 16). Therefore, the corner stone of the management of diabetes is to maintain blood glucose levels within, or close to, a normal range (17). This is achieved by adequate adherence to medication administration, as well as lifestyle modification, including healthy eating, regular physical activity, and maintaining a healthy body weight.

Diabetes medications can be divided into insulin or noninsulin. Insulin is the main treatment for those with type 1 diabetes; it is also frequently prescribed for people with T2DM and gestational diabetes. Currently, there are many types of insulin in use, and these are categorised according to the time period of action (18). Various noninsulin medications are available at present. Their mechanisms of action include increasing sensitivity to insulin, increasing secretion of insulin from the pancreas, decreasing glucose absorption from the intestine, or blocking the reuptake of glucose in the renal tubules.

Glycated haemoglobin or haemoglobin A1c (HbA1c) is the preferred test to monitor the level of glycaemic control. Compared to fasting and random blood glucose tests that measure the glucose level over a very short period of time, HbA1c measures glycaemic control over a number of weeks (17). For a person with diabetes, it is highly recommended to maintain HbA1c below 7%, with a more relaxed cut-off for older people with comorbidities and complications (17).

1.1.5 Obesity, hypertension and dyslipidaemia among people with diabetes

People with diabetes are at increased risk of developing diabetes complications and mortality. This risk increases further when a person with diabetes has comorbidities, such as obesity, hypertension, and an abnormal blood lipid profile (dyslipidaemia). A study reported that among people with T2DM, a 5-unit increase in body mass index (BMI) increased the risk of cardiovascular disease and total mortality by 13% and 27%, respectively (19). Another study showed that people with T2DM and hypertension have 4.7-fold higher odds of developing cardiovascular disease compared with people with T2DM only (20). People with T2DM and dyslipidaemia were also found to have a 1.54-fold and 2.13-fold higher hazard ratio for coronary artery disease and stroke, respectively, compared with people with T2DM and no dyslipidaemia (21). Unfortunately, people with T2DM are predisposed to have, or acquire, these comorbidities. The prevalence of hypertension, obesity, and dyslipidaemia among people with T2DM can exceed 75%, 50%, and 75%, respectively (22-24). Preventing or controlling these comorbidities is key to reducing the risk of diabetes complications, and has been prioritised in the management of diabetes guidelines (17).

1.1.6 Diabetes and the quality of life

Diabetes and its comorbidities and complications can have a detrimental effect on health and quality of life of those affected. Global studies have reported that people with diabetes have a lower quality of life compared with people without diabetes (25-27). Among this high-risk population, hyperglycaemia, hypoglycaemia, insulin use, and the use of multiple medications were linked to a lower quality of life

(28-32). Diabetes complications, however, were found to have the highest impact (25, 28, 29). The main aim of the management of diabetes is to control the disease and prevent, or manage, diabetes complications such that affected people can have a quality of life similar or close to that of people without diabetes. Nevertheless, maintaining good quality of life for people with diabetes is a challenge, especially in the long term of the disease.

1.1.7 Diabetes in Saudi Arabia

Similar to other Arabian Gulf Cooperation Council countries, Saudi Arabia has witnessed enormous economic and lifestyle changes over the past few decades. Vast changes in lifestyle, and the rising rate of obesity among all age groups, have led to a rapid increase in the prevalence of diabetes in Saudi Arabia. Compared with studies conducted in the 1990s that reported Saudi Arabia to have a prevalence of diabetes between 5.0% and 10.4% (33-35), studies published after 2000 reported a prevalence of between 11.9% and 31.6% (36-40). Furthermore, it is projected that the prevalence of diabetes in the country will continue to increase rapidly (41).

Disease control among people with diabetes in Saudi Arabia is not optimal. Previous studies showed that half to two-thirds of people with T2DM in the country had poor glycaemic control (42-44), and the prevalence of obesity, hypertension, and dyslipidaemia was high amongst them (45-53). Furthermore, the prevalence of diabetes complications is high (50, 54-63), and the quality of life of the affected people is low (27, 64). This adds further problems to the heavy burden of diabetes in Saudi Arabia. It is estimated that Saudi Arabia spends around 25 billion Saudi Riyals (13.9% of total health expenditure) annually for the treatment of people with diabetes and its complications (65, 66).

Risk factors for poor glycaemic control, diabetes comorbidities, and complications were not adequately explored among the Saudi population. The majority of the studies that explored these issues in Saudi Arabia were limited to a single centre and had a small sample size, which may have affected the reliability and generalisation of their findings. Moreover, these studies have mainly focused on traditional demographics and clinical characteristics. International studies, however, reported strong associations between lifestyle factors and poor glycaemic control, as well as diabetes comorbidities and complications (67-69). The evidence regarding the association between life style factors and glycaemic control, diabetes comorbidities and complications is scarce for the Saudi population with diabetes. In order to improve glycaemic control and prevent diabetes comorbidities and complications, all important risk factors must be identified. Once identified, these risk factors should be the main target in the patients' management plans and national population preventive strategies.

The high prevalence of diabetes related complications in Saudi Arabia, according to previous studies, warrants the use of a risk prediction tool. This tool helps clinicians to identify patients with a high risk of diabetes complications and manage them so as to lower their risk. This tool can also be used in counselling and education of the patient to raise their awareness of their risk of complications, and its use has been recommended in the diabetes management guidelines (70, 71). A risk prediction tool for diabetes complications for the Saudi population has not yet been developed. Currently, clinicians in Saudi Arabia use the Framingham risk score calculator for predicting coronary artery disease (72), which was developed in the United States of America. However, the Framingham risk scoring tool is not specific for people with diabetes. A number of diabetes complications risk prediction tools have been developed for western and other populations; however, these may not work accurately for the Saudi population due to variations in genetic, environmental, and lifestyle factors (73, 74). Therefore, a Saudi Arabian T2DM-population-specific tool is preferable to tools developed for other populations.

The quality of life of people with diabetes in Saudi Arabia is another area that needs further exploration. Other than the methodological limitation of the previous studies, risk factors for poor quality of life were not explored adequately. The person's knowledge, beliefs, experiences, and expectations can affect their quality of life and influence how other factors affect it. Therefore, factors that affect quality

of life may vary between different populations, and it is crucial to identify population-specific factors in order to maintain the quality of life for people with diabetes.

1.2 Gaps in the knowledge and study aims

T2DM is a major public health issue in Saudi Arabia. This chronic disease is highly prevalent in the country and a large proportion of the affected people have poor control of the disease, are at high risk of diabetes comorbidities and complications, and have a poor quality of life. Potentially important risk factors of poor glycaemic control, diabetes comorbidities, complications, and low quality of life were not explored adequately for people with diabetes in Saudi Arabia. Thus, the general aim of this study was to assess the status of glycaemic control, diabetes comorbidities, complications, and quality of life among people with T2DM in Saudi Arabia, and to explore factors related to them with a special focus on lifestyle and other modifiable risk factors.

The specific objectives are as follows:

1. To measure the prevalence of poor glycaemic control and its correlated factors among people with T2DM in Saudi Arabia.
2. To determine the prevalence of major micro- and macro-vascular complications and their correlates among people with T2DM in Saudi Arabia.
3. To develop risk-prediction tools for major diabetes complications for people with T2DM in Saudi Arabia.
4. To measure the prevalence of obesity, hypertension, and dyslipidaemia, and explore their associated factors for people with T2DM in Saudi Arabia.
5. To assess the health-related quality of life and the factors affecting it among people with T2DM in Saudi Arabia.

In order to achieve these objectives, a multi-centre, cross-sectional survey was conducted to assess glycaemic control, diabetes comorbidities, complications, and health-related quality of life among people with T2DM in Saudi Arabia. The methodology is described in detail in chapter 3.

1.3 Thesis overview and structure

Chapter 2 of this thesis describes a systematic review that was conducted to explore factors that affect glycaemic control for people with T2DM in the Gulf Cooperation Council Countries. This review summarises the results of the available literature with regards to the risk factors of poor glycaemic control, and provides recommendation based on those findings. The review also identifies gaps in the knowledge that require addressing in future research.

Chapter 3 of this thesis describes the study protocol to generate the data that was used in chapters 4 to 7. This chapter also summarises the data analysis methods used in the following chapters.

Chapter 4 of this thesis assesses the prevalence of poor glycaemic control and its determining factors among people with T2DM in Saudi Arabia. The chapter shows the importance of lifestyle factors in controlling blood glucose level.

Chapter 5 of this thesis investigates the prevalence of major macro- and micro-vascular diabetes complications and explores their correlated factors. The findings of this chapter highlight the major risk factors that should be controlled to lower the risk of diabetes complications among the Saudi population. **Chapter 5** also describes the development and validation of a risk-scoring system to predict major diabetes complications for people with T2DM in Saudi Arabia.

Chapter 6 explores the prevalence of diabetes comorbidities, including obesity, hypertension, and dyslipidaemia, and their associated factors, for people with T2DM in Saudi Arabia. This chapter also explores the individual, as well as the combined, effect of these comorbidities on the risk of cardiovascular disease.

Chapter 7 examines the health-related quality of life of people with T2DM in Saudi Arabia. Factors associated with low health-related quality of life are also identified and a number of recommendations are made.

Chapter 8 summarises the findings of this thesis, discusses limitations and gaps in the knowledge, and provides a conclusion.

1.4 Conference presentation

Poster presented at the International Diabetes Federation 2017 Congress behold in Abu Dhabi, UAE from 8 to 10 December 2017

MONASH University
School of Public Health & Preventive Medicine

DIABETES IN SAUDI ARABIA: PREVALENCE, GLYCAEMIC CONTROL AND COMPLICATIONS – A SYSTEMATIC REVIEW

Mohammed J Alramadan, Nassif Hossain, Mohammed Ali Batais, Turky H. Almigbal, Hassan Ahmad Al-Humrani, Ahmed Albaloshi, Dianna J Magliano, Baki Billah

OBJECTIVE:

The aim of this review was to summarise the findings of previous studies that investigated the prevalence of diabetes mellitus (DM), its complications and the status of glycaemic control in Saudi Arabia.

METHOD:

- MEDLINE, EMBASE, PSYCINFO and PubMed databases were searched using the terms "Saudi Arabia" and "diabetes".
- Studies were included if they assessed one of the following among adults living in Saudi Arabia :
  - DM prevalence (national or reginal);
  - glycaemic control; and/or
  - DM micro/macrovascular complications.

RESULTS:

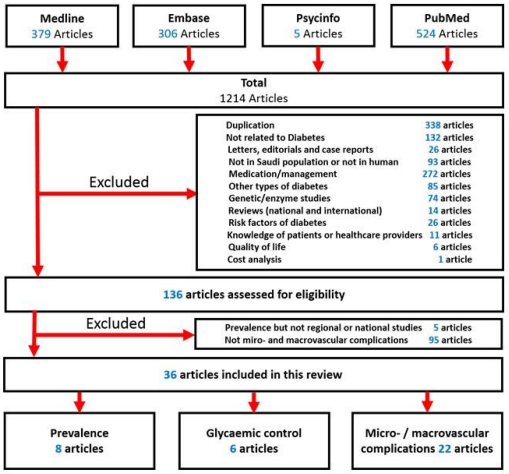

Figure 1: Flow chart of the systematic literature search

Table 1: Prevalence of diabetes and its complications

Prevalence	Saudi Arabia	Global	Regional* Middle East
Diabetes	11.9% - 31.6%	8.8%	10.7%
Coronary artery disease	23.1% - 24.0%	-	15.0%-20.0%
Retinopathy	31.3% - 36.8%	27.2%	-
Peripheral Neuropathy	17.8% - 65.3%	15.0%	-

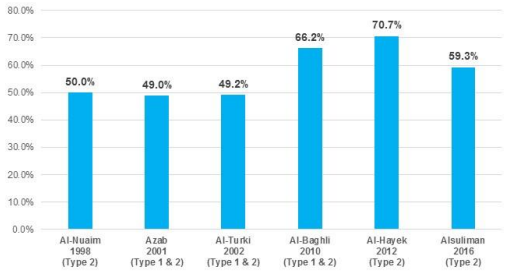

Figure 2: Prevalence of poor glycaemic control in Saudi Arabia

The majority of studies included in this review:

- had small sample size;
- were confined to a small geographical location;
- varied in the type of sampled populations, study methods and findings; and
- Did not adequately explore the association between lifestyle-related factors, cognitive function and family support and diabetes control and complications.

CONCLUSION:

- Diabetes and its complications are a major public health burden in Saudi Arabia.
- There is an urgent need to explore the effect of lifestyle factors, family support and cognitive function on glycemic control and complications.

Chapter 2:

Literature Review: Factors Related to Glycaemic Control in People with Type 2 Diabetes in the Gulf Cooperation Council Countries

2.1 Introduction

The Gulf Cooperation Council (GCC) consists of six countries: Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and the United Arab Emirates (UAE). These countries share boundaries and similar climates, cultures, and lifestyle. With the discovery of oil, all of the GCC countries have undergone vast economic changes that have been accompanied by changes in the lifestyle of people living in these countries. Consequently, the prevalence of diabetes, T2DM in particular, has increased rapidly over the past few years. Currently, GCC countries are among the countries with the highest prevalence of diabetes in the Middle East and worldwide（1）.

The cornerstone of the management of diabetes is maintaining the blood glucose level within or very close to the normal ranges. A HbA1c higher than 7% substantially increases the risk of diabetes complications and mortality (13, 14). Various factors can affect glycaemic control in a person with diabetes and these risk factors vary among different populations. A number of studies have explored the status of glycaemic control among people with T2DM in GCC countries. Their results showed that 65% to 88.8% of people with T2DM have poor glycaemic control (43, 44, 75-81).

Identifying the risk factors for poor glycaemic control among a specific population is vital. It helps clinicians and patients to improve glycaemic control by controlling these risk factors. Knowing these risk factors is also essential for the development of strategies to improve glycaemic control at a population level. A number of studies concerning GCC countries examined the factors that increase the risk of poor glycaemic control. This chapter of this thesis provides a systematic review of patient-related factors that affect glycaemic control in people with T2DM in GCC countries. The aim of this systematic review was to summarise the available literature to make it more accessible to clinicians and policy makers, as well as to identify gaps in the literature and provide guidelines for future research.

2.2 Article:

Alramadan MJ, Afroz A, Hussain SM, Batais MA, Almigbal TH, Al-Humrani HA, et al. Patient-Related Determinants of Glycaemic Control in People with Type 2 Diabetes in the Gulf Cooperation Council Countries: A Systematic Review. Journal of Diabetes Research. 2018.

At: https://www.hindawi.com/journals/jdr/2018/9389265/

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Volume 2018, Article ID 9389265, 14 pages
https://doi.org/10.1155/2018/9389265

Review Article

Patient-Related Determinants of Glycaemic Control in People with Type 2 Diabetes in the Gulf Cooperation Council Countries: A Systematic Review

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The aim of this systematic review is to assess patient-related factors affecting glycaemic control among people with type 2 diabetes in the Arabian Gulf Council countries. MEDLINE, Embase, PsycINFO, CINAHL, and Cochrane CENTRAL databases were searched from their date of inception to May 2016. Two researchers independently identified eligible studies and assessed the risk of bias. A total of 13 studies met the inclusion criteria. One study was population based, six recruited participants from multiple centres, and the remaining were single centred. The majority of the studies were of low to moderate quality. Factors associated with poor glycaemic control include longer duration of diabetes, low level of education, poor compliance to diet and medication, poor attitude towards the disease, poor self-management behaviour, anxiety, depression, renal impairment, hypertension, and dyslipidaemia. Healthcare providers should be aware of these factors and provide appropriate education and care especially for those who have poor glycaemic control. Innovative educational programs should be implemented in the healthcare systems to improve patient compliance and practices. A variation in the results of the included studies was observed, and some potentially important risk factors such as dietary habits, physical activity, family support, and cognitive function were not adequately addressed. Further research is needed in this area.

1. Introduction

Diabetes mellitus is one of the major public health issues of the 21st century [1–3]. Globally, 8.8% (415 million) of adults suffered from diabetes in 2015, and it is estimated that 652 million people (10.4%) will have diabetes by 2040 [2]. The World Health Organization (WHO) reported that high blood glucose level due to diabetes is the third highest risk factor for premature mortality after high blood pressure and tobacco use [4]. Diabetes is attributed to 14.5% of all-cause mortality among adults, and half of these deaths occur in adults under the age of 60 years [2]. Nonetheless, diabetic complications are a major cause of disability and reduced quality of life. The estimated total global health expenditure due to diabetes is $673 billion in 2015, and it will reach $802 billion in 2030 [2].

A recent International Diabetes Federation (IDF) report suggests that the Middle East and North Africa regions, which include the Gulf Cooperation Council (GCC) countries (Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and

the United Arab Emirates (UAE)), have the highest prevalence of diabetes (10.7%) in the world next to North America and the Caribbean region (11.5%) [2]. An estimated 35.4 million adults in the Middle East and North Africa regions had diabetes in 2015, of whom over 40.6% were undiagnosed [2]. The number of people with diabetes in this region is anticipated to reach 72.1 million by 2040 [2]. The GCC countries share boundaries and similar climates, cultures, lifestyles, and economic development. These countries are among those with the highest prevalence of diabetes in the Middle East and North Africa regions and globally, with the prevalence of the disease ranging from 14.8% (Oman) to 20% (Saudi Arabia, Kuwait, and Qatar) [2].

Diabetes management involves strictly maintaining a person's blood glucose level close to the normal range. There is a strong relationship between an elevated blood glucose level and the risk of complications and mortality in people with diabetes [5, 6]. Poor glycaemic control is defined as a glycated haemoglobin (HbA1c) equal to or above 7% or a fasting plasma sugar (FPS) above 7.2 mmol/l for adults who are not pregnant [7]. Poor glycaemic control (HbA1c > 7%) among people with type 2 diabetes mellitus (T2DM) in the GCC countries is common, ranging between 59% and 70.7% in Saudi Arabia [8, 9], 68% and 69% in the UAE [10, 11], 86.5% and 88.8% in Bahrain [12, 13], and 54% and 65% in Oman [14, 15], while a study reported that 55% of people with T2DM in Kuwait have HbA1c > 9% [16].

A number of studies have assessed factors associated with poor glycaemic control among people with T2DM in GCC countries sporadically. A systematic approach is needed to summarise their findings in order to identify gaps in the literature and provide guidelines for future research. Thus, the aim of this systematic review is to assess patient-related factors that affect glycaemic control among people with type 2 diabetes in the GCC countries.

2. Methods

2.1. Literature Search Strategy. A senior librarian (LR), with input from the research team, developed and implemented a comprehensive search using Embase, CINAHL, Cochrane Library, MEDLINE, and PsycINFO from the date of their inception to the 31 of May 2016. The search covered three concepts: T2DM, glycaemic control, and the Arabian Gulf Council countries. For T2DM, the following terms were used in the search combined by "OR": "diabetes mellitus, type 2" (subject headings [SH]), Hyperglycaemic (SH), "adult-onset diabet*," "ketosis-resistant diabet*," "maturity-onset diabet*," "non-insulin-dependent diabet*," "noninsulin-dependent diabet*," "slow-onset diabet*," "type 2 diabet*," "type ii diabet*," "insulin resistance," "insulin resistant," and "T2D." For glycaemic control, the following terms were used in the search combined by "OR": "glucose," "blood sugar," "glyco*," "glyca*," "glyce*," "hb a1*," "hba1*," "haemoglobinA1*," "hemoglobinA1*," "haemoglobin A1*," and "hemoglobin A1*." For searching the Arabian Gulf countries, the following terms were used combined by "OR": "Saudi*," "Kuwait*," "Bahrain*," "Qatar*," "Arab*," "Emirat*," "Oman*," "Middle East*," "Gulf cooperation," and "gulf co-operation." The final search was then conducted after having combined the three concepts using "AND." The search was not limited by language. Relevant articles were also sought by searching the reference lists of articles retrieved for full-text review.

2.2. Selection of Studies. Two reviewers (MJA and AA) independently screened the retrieved articles by title, then by abstract, and finally by reviewing the full text of eligible articles. Any disagreement between the two reviewers was resolved by discussion with a third reviewer (BB).

2.3. Studies Inclusion and Selection Criteria. All observational studies that examined the effect of patient-related factors affecting glycaemic control among adults with T2DM living in the GCC countries were considered for inclusion. Because the majority of people in the GCC countries have T2DM, studies that assessed the level of control among people with diabetes in general (types 1 and 2) were included. Studies were excluded if they did not include adults with T2DM, if the sample was recruited from outside of the GCC countries, and/or if the study did not examine the association between patient-related factors and glycaemic control. Studies that focused only on type 1 diabetes, children with T2DM, gestational diabetes, or adults with impaired glucose tolerance or impaired fasting glucose were excluded. Studies investigating the effectiveness of antidiabetic medications only were also excluded. In addition, articles were excluded if they were reviews or conference presentations.

2.4. Data Extraction. Two reviewers (MJA and AA) independently extracted the data using a data extraction form. The extracted data include the first author, the year of publication, the name of the country, the sampled population, the number of participants, participants' gender, participants' age, the method of assessing glycaemic control, the data collection tool, the risk factors investigated, and the factors found to be associated with glycaemic control.

2.5. Assessment of Quality. Two reviewers (MJA and AA) independently assessed the risk of bias of the included studies using the National Heart Lung and Blood Institute (NHLBI) quality assessment tool for observational studies (Tables 1 and 2) [17]. The tool assesses the internal validity and risk of bias using 14 criteria for cohort and cross-sectional studies and 12 criteria for case-control studies. Each criterion was rated as "yes," "no," "cannot determine," "not applicable," or "not reported." An overall judgment of the quality of the study was then rated as high (low risk of bias), fair (moderate risk of bias), or low (high risk of bias). Any disagreement between the two reviewers regarding the assessment of risk of bias was settled by discussion.

3. Results

3.1. Search Results. Figure 1 shows a flow chart of the search results and the number of studies included in this review. A total of 1788 articles were retrieved from the five databases (MEDLINE = 460, Embase = 1076, PsycINFO = 10,

Table 1: Quality assessment tool for observational cohort and cross-sectional studies.

Criteria	Yes	No	Others (CD, NR, and NA)*
(1) Was the research question or objective in this paper clearly stated?			
(2) Was the study population clearly specified and defined?			
(3) Was the participation rate of eligible persons at least 50%?			
(4) Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?			
(5) Was a sample size justification, power description, or variance and effect estimates provided?			
(6) For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?			
(7) Was the time frame sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?			
(8) For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure or exposure measured as continuous variable)?			
(9) Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
(10) Was the exposure(s) assessed more than once over time?			
(11) Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
(12) Were the outcome assessors blinded to the exposure status of participants?			
(13) Was loss to follow-up after baseline 20% or less?			
(14) Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?			
Quality rating (good, fair, or poor) (see guidance)			
Rater no. 1 initials:			
Rater no. 2 initials:			
Additional comments (if poor, please state why):			

*CD: cannot determine; NA: not applicable; NR: not reported.

CINAHL = 149, and Cochrane = 93). After the removal of duplicates, 1211 articles remained. After having screened article titles and abstracts, 1161 articles were removed as these were letters, editorials, case reports, review articles, animal/cell studies, not from the GCC countries, did not include adult participants with T2DM, did not cover glycaemic control, or did not assess factors affecting glycaemic control. Thus, 50 full-text articles were screened for further eligibility. Of these 50 articles, 37 articles were excluded. Eight articles did not evaluate glycaemic control, four studies were not conducted in the GCC countries, one study did not include people with T2DM, and 16 did not evaluate patient-related factors affecting glycaemic control. In addition, eight articles were conference papers and were therefore excluded. A total of 13 studies met the inclusion criteria of this review.

3.2. Characteristics of Included Studies. The characteristics of the included studies are described in Table 3. Five studies were from Saudi Arabia [8, 18–21], four from Oman [14, 15, 22, 23], three from the UAE [10, 11, 24], and one from Bahrain [25]. Only one study was population based [20], while three studies recruited participants from multiple primary healthcare centres regulated by one hospital (including the participants of this hospital) [10, 11, 24] and three studies recruited participants from a number of primary healthcare centres [22, 23, 25]. Of the remaining six studies, four recruited participants from a single hospital [8, 15, 18, 19], and two recruited participants from a single primary healthcare centre [14, 21]. All studies were cross-sectional [8, 10, 11, 14, 15, 19–25] except for one which was case-control in design [18]. Three studies extracted data from medical records regarding sociodemographic factors, medical history (duration of diabetes, comorbidities, complications, and modality of treatment), and biochemical data related to glycaemic control [14, 21, 22]. In nine studies, data on sociodemographic and medical history were collected using an interviewer-administered questionnaire [8, 10, 11, 15, 18–20, 24, 25], while one study used self-administered questionnaire [23]. In these 10 studies, data regarding glycaemic control were collected by laboratory investigation. Five studies recruited participants with type 1 and 2 diabetes [10, 18–20, 24], while the eight other studies included participants with T2DM only [11, 14, 15, 21–23, 25]. The number of participants per study ranged from 103 to 1266, with a median of 300 participants. Most of the studies included both males and females [8, 10, 11, 14, 15, 18, 20–25], while one study included only female participants [19]. Mean age of participants was reported in nine studies that ranged between 42.6 ± 9.1 and 57.3 ± 14.4 years [8, 10, 11, 14, 19–22, 25]. Two studies reported age as

Table 2: Quality assessment of case-control studies.

Criteria	Yes	No	Others (CD, NR, and NA)*
(1) Was the research question or objective in this paper clearly stated and appropriate?			
(2) Was the study population clearly specified and defined?			
(3) Did the authors include a sample size justification?			
(4) Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same time frame)?			
(5) Were the definitions, inclusion and exclusion criteria, algorithms, or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?			
(6) Were the cases clearly defined and differentiated from controls?			
(7) If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			
(8) Was there use of concurrent controls?			
(9) Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?			
(10) Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			
(11) Were the assessors of exposure/risk blinded to the case or control status of participants?			
(12) Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?			
Quality rating (good, fair, or poor) (see guidance)			
Rater no. 1 initials:			
Rater no. 2 initials:			
Additional comments (if poor, please state why):			

*CD: cannot determine; NA: not applicable; NR: not reported.

categories: in one study, the age categories ranged from 20 years to +59 years [23], and in the other study, the age categories ranged from 30 years to +60 years [15]. Two other studies did not report the age of the participants [18, 24]. Glycaemic control was assessed using haemoglobin A1c (HbA1c) in 10 studies [8, 10, 11, 14, 15, 18, 19, 22, 23, 25], while two studies used fasting blood glucose (FBG) [21, 24] and one used random blood glucose (RBG) [20].

3.3. Quality Assessment (Risk of Bias). Of the 13 studies included, seven (53.8%) were of low quality, four (50.8%) were of moderate quality, and two (15.4%) were of high quality (Table 4). Seven studies (53.8%) recruited a small sample size with no justification or calculation of power [8, 14, 18, 19, 21, 23, 25]. The sampling was not random in 10 studies (76.9%) [8, 14, 15, 18, 19, 21–25]. The majority of the studies (69.2%) did not adjust for possible confounding factors of the association between glycaemic control and the assessed risk factors [8, 11, 14, 15, 18, 19, 23–25]. In addition, the results were not generalisable in six studies (46.1%) because they were single centred [8, 14, 15, 18, 19, 21].

3.4. Key Findings

3.4.1. Nonmodifiable Factors. The results of the 13 studies included in this review are detailed in Table 5. D'Souza et al. found that among elder participants (50–59 years and ≥60 years), larger proportions had poor control compared to younger participants (p value <0.001) [15], while Al-Kaabi et al. reported that age was negatively associated with HbA1c level (adjusted beta coefficient −0.023, p value 0.047) [10]. In the study by Al-Lawati et al., it was found that, compared to those aged 20–39 years, the adjusted odds ratio (OR) of good glycaemic control was 1.7-fold (p value: 0.01) and 2.5-fold (p value: 0.001) higher for those aged 40–59 years and ≥60 years, respectively [22]. On the other hand, the remaining seven studies did not find any association [8, 11, 14, 18, 20, 21, 24].

The association between gender and glycaemic control was evaluated in 10 studies. Of these, one study reported that female gender was associated with poor glycaemic control compared to male gender (adjusted OR: 2.84, p value <0.05) [21]. In contrast, Al-Lawati et al. showed that female gender was associated with good glycaemic control (adjusted OR: 1.5, p value: 0.001) [22]. No association was found between gender and glycaemic control in the other eight studies [8, 10, 11, 14, 15, 18, 20, 24].

Three out of eight studies that assessed the association between the duration of diabetes and glycaemic control have found an association. Binhemd et al. have reported a positive correlation between the duration and HbA1c level ($p < 0.001$) [19]. In the study by Al-Lawati et al., the adjusted OR of good glycaemic control for people with a duration of diabetes ≥5 years was 0.8 (p value: 0.041) compared to those with a duration of <5 years [22]. D'Souza et al. reported that the people with poor control were 49.1%, 52.8%, and 70.5% for diabetes duration groups 0–9 years, 10–19 years, and ≥20 years, respectively

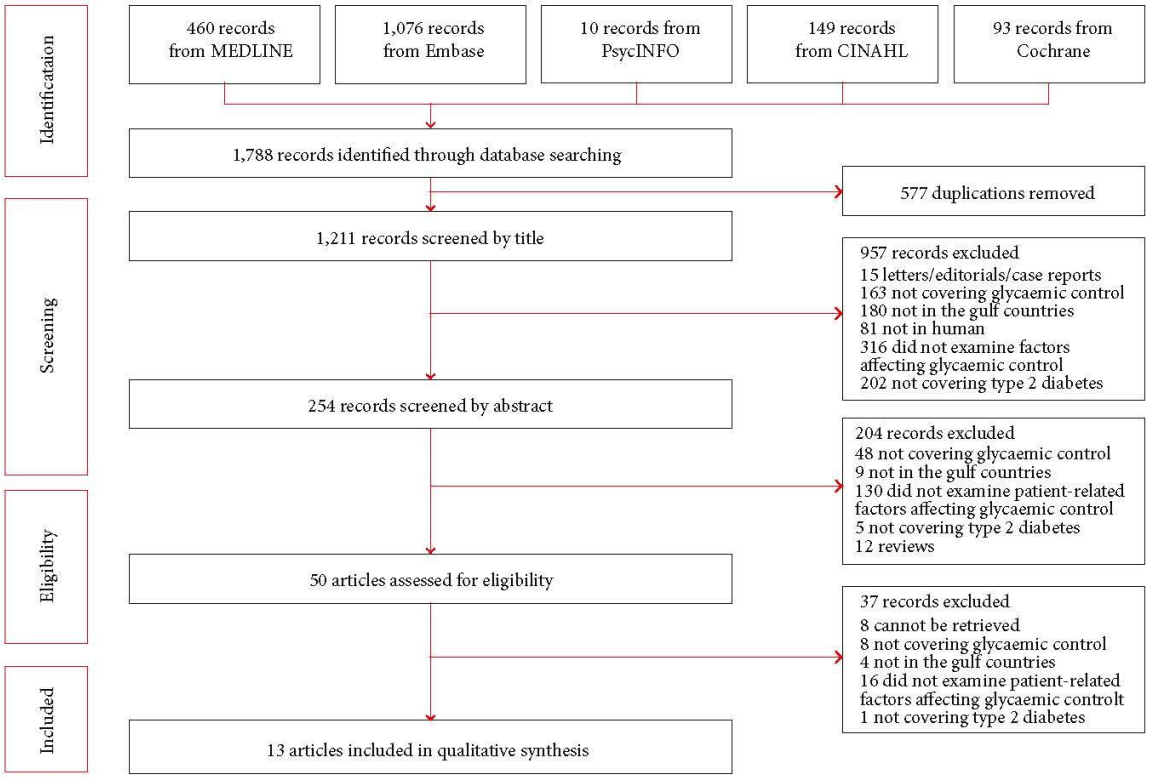

Figure 1: Flow chart of the systematic literature search.

(p value <0.001) [15]. In the other five studies, no association was found [11, 14, 18, 19, 21].

Two studies assessed the effect of family history of diabetes on glycaemic control. In one study, no significant association was found [21]. Meanwhile, in the other study, a family history of diabetes was found to be associated with lower risk of poor glycaemic control (OR: 0.39, p value: 0.001) [24]. This study also assessed the effect of ethnicity on glycaemic control, but no association was found.

3.4.2. Modifiable Factors. A number of modifiable factors were found to be associated with glycaemic control. Binhemd et al. reported a negative correlation between HbA1c and patient compliance to management as well as the attitude towards the disease (p value < 0.001 and 0.01, resp.) [19]. Al-Hayek et al. showed that compared to participants with HbA1c < 7%, those with HbA1c ≥ 7% had lower mean score of adherence to medication (5.4 ± 1.2 compared to 7.4 ± 1.4, p value < 0.001), higher mean score of anxiety (10.3 ± 1.7 compared to 7.9 ± 1.3, p value < 0.001), and higher mean score of depression (9.8 ± 1.3 compared to 6.9 ± 0.9, p value < 0.001) [8]. Malik et al. found that individuals who were followed up in primary healthcare centres were more likely to have poor glycaemic control (OR: 2.4, p value: 0.001) compared to those who were followed up in hospital [24]. Al-Kaabi et al. reported that the number of carbonated drinks (sugar sweetened and sugar free) consumed was positively associated with HbA1c level (adjusted beta coefficient: 0.20, p value: 0.029) [10]. Shamsi et al. showed that the mean HbA1c level increases progressively from 5.97% ± 1.34% for those with very good dietary practice to 10.95% ± 1.6% for those with very poor dietary practice (p value: 0.006) [25]. Al-Lawati et al. reported that compared to estimated glomerular filtration rate (eGFR) below 60 ml/min/1.73 m^2, the OR of good glycaemic control was 1.9 (p value 0.013) for those who have eGFR ≥ 60 ml/min/1.73 m^2 [22]. Al Balushi et al. showed that compared to participants with HbA1c ≤ 7%, those with HbA1c > 7% had higher mean diastolic blood pressure (84 ± 9 mmHg compared to 80 ± 8 mmHg, p value: 0.006), higher total cholesterol (5.2 ± 1.3 mmol/l compared to 4.7 ± 0.8 mmol/l, p value: 0.002), and higher low-density lipoprotein (LDL) (3.8 ± 1.0 mmol/l compared to 3.0 ± 1.2 mmol/l, p value: 0.38) [14]. D'Souza et al. reported that a large proportion of those who completed diploma/technical degree had poor glycaemic control (67.4%) compared to those who completed high school (45.7%) and lower than high school (52.1%) (p value < 0.001) [15]. Two other studies did not find an association between education level and glycaemic control [10, 11]. The study by D'Souza et al. has also reported that patient perception of empowerment for self-management increased the likelihood of good glycaemic control (beta coefficient: 0.66, p value 0.001) [15].

Table 3: Included studies and their general features.

Author Publication year Country	Study design population	Population	Number of participants (male and female)	Age (mean age ± SD)	Glycaemic control measurement method(s)	Risk factors examined	Instrument used to measure risk factors
Ajabnoor 1987 [18] Saudi Arabia	Case-control	Diabetics attending King Abdulaziz University Hospital diabetic clinic	Cases 73 (23, 50) Controls 30 (19, 11)	—	HbA1c	Age, gender, FPG, and treatment modality	Questionnaire and lab test
Binhemd 1992 [19] Saudi Arabia	Cross-sectional	Females attending Diabetes and Endocrine Centre in Dammam	300 (0, 300)	42.6 ± 9.1	HbA1c	KAP (knowledge, attitude and practice), diabetes type, and diabetes duration	Interview using a questionnaire, anthropometric measures, and lab test
Al-Nuaim 1998 [20] Saudi Arabia	Cross-sectional	National (different regions of SA)	613 (320, 293)	Good control 47.0 ± 14.8 Poor control 51.5 ± 13.8	RBG	Age, BMI, region, residency, gender, and treatment modalities	Interview using a questionnaire, anthropometric measures, and lab test
Malik 1999 [24] United Arab Emirates	Cross-sectional	Patients attending Mafraq Hospital in Abu Dhabi and its surrounding health clinics	696	—	FPG	Age, gender, ethnicity, diabetes duration, family history, treatment modalities, and follow-up location	Interview using a questionnaire and lab test
Abdelmoneim 2002 [21] Saudi Arabia	Cross-sectional	Patients attending diabetic clinic in a primary healthcare centre	198 (90, 108)	Males 59.5 ± 8.9 Females 53.8 ± 8.1	FPG	Age, gender, family history, diabetes duration, BMI, cholesterol level, complications, number of health education session, and crowding index	Review of medical records
Al-Kaabi 2008 [10] United Arab Emirates	Cross-sectional	Diabetic patients attending outpatient clinic at Tawam Hospital and primary healthcare centres in Al Ain district	409 (158, 251)	51.4 ± 11.2	HbA1c	Age, gender, marital status, level of education, occupation, smoking, eating practice, BMI, abdominal circumference, blood pressure, and lipid profile	Interviewer-administered questionnaire and anthropometric measures. Blood tests from medical records
Al-Kaabi 2009 [11] United Arab Emirates	Cross-sectional	Diabetic patients attending outpatient clinic at Tawam Hospital and primary healthcare centres in Al Ain district	309 (68, 241)	52 ± 9.9	HbA1c	Age, gender, nationality, marital status, level of education, employment, income, diabetes duration, smoking, diabetes complications, physical activity, BMI, abdominal circumference, and blood pressure	Interviewer-administered questionnaire and anthropometric measures. Blood tests from medical records

Table 3: Continued.

Author Publication year Country	Study design population	Population	Number of participants (male and female)	Age (mean age ± SD)	Glycaemic control measurement method(s)	Risk factors examined	Instrument used to measure risk factors
Al-Lawati 2012 [22] Oman	Cross-sectional	Multicentred (different regions of Oman)	1266 (570, 696)	53.3 ± 11.5	HbA1c	Age, gender, duration of diabetes, treatment modalities, BMI, eGFR, smoking, and healthcare index	Data collected from patients' medical records
Al-Hayek 2012 [8] Saudi Arabia	Cross-sectional	Patients attending Sultan Bin Abdulaziz Humanitarian City, Riyadh	147 (99, 48)	57.3 ± 14.4	HbA1c	Age, gender, marital status, employment, BMI, self-care management behaviour, self-monitoring of blood glucose, medication adherence, anxiety, and depression	Interviewer-administered questionnaire and anthropometric measures. Blood tests from medical records
Shamsi 2013 [25] Bahrain	Cross-sectional	Patients attending 5 healthcare centres in Bahrain	400 (192, 208)	54.7 ± 9.95	HbA1c	Dietary practice	Interviewer-administered uestionnaire. Anthropometric measures and blood tests results were collected from medical records
Al Balushi 2014 [14] Oman	Cross-sectional	Type 2 patients attending Al Dakhliya region primary healthcare centre	177 (71, 106)	53 ± 12	FBG HbA1c	Age, gender, diabetes duration, BMI, blood pressure, creatinine, and lipid profile	Data collected from patients' medical records
Alrahbi 2014 [23] Oman	Cross-sectional	Patients attending 35 healthcare centres in Muscat and Al Dakhliya	266 (121, 145)	—	HbA1c	Diabetes self-management	Self-administered questionnaire and blood test for HbA1c
D'Souza 2015 [15] Oman	Cross-sectional	Patients attending diabetic clinic at a public hospital in Oman	300 (143, 157)	—	HbA1c	Age, gender, education, diabetes duration, diabetes education, medication, and BMI	Interviewer-administered questionnaire and patient's medical records for HbA1c

HbA1c: haemoglobin A1c; FPS: fasting plasma sugar; eGFR: estimated glomerular filtration rate; TTT: treatment.

Table 4: Risk of bias for the included studies.

Study	Criteria 1	Criteria 2	Criteria 3	Criteria 4	Criteria 5	Criteria 6	Criteria 7	Criteria 8	Criteria 9	Criteria 10	Criteria 11	Criteria 12	Criteria 13	Criteria 14	Overall quality
Case-control															
Ajabnoor 1987 [18]	Yes	Yes	No	No	NR	Yes	No	NR	Yes	Yes	No	No	—	—	Low
Cross-sectional															
Binhemd 1992 [19]	Yes	Yes	NR	Yes	No	NA	NA	No	Yes	NA	Yes	NA	NA	No	Low
Al-Nuaim 1998 [20]	Yes	Yes	NR	Yes	No	NA	NA	Yes	Yes	NA	Yes	NA	NA	Yes	High
Malik 1999 [24]	Yes	No	NR	Yes	No	NA	NA	Yes	Yes	NA	Yes	NA	NA	No	Low
Abdelmoneim 2002 [21]	Yes	Yes	NR	Yes	No	NA	NA	No	Yes	NA	Yes	NA	NA	Yes	Moderate
Al-Kaabi 2008 [10]	Yes	Yes	NR	Yes	No	NA	NA	No	No	NA	Yes	NA	NA	Yes	Moderate
Al-Kaabi 2009 [11]	Yes	Yes	NR	Yes	No	NA	NA	Yes	Yes	NA	Yes	NA	NA	No	High
Al-Lawati 2012 [22]	Yes	Yes	NR	Yes	No	NA	NA	Yes	Yes	NA	Yes	NA	NA	Yes	Moderate
Al-Hayek 2012 [8]	Yes	Yes	NR	Yes	No	NA	NA	Yes	Yes	NA	Yes	NA	NA	No	Low
Shamsi 2013 [25]	Yes	Yes	NR	Yes	No	NA	NA	Yes	Yes	NA	Yes	NA	NA	No	Moderate
Al Balushi 2014 [14]	Yes	Yes	NR	Yes	No	NA	NA	Yes	Yes	NA	Yes	NA	NA	No	Low
Alrahbi 2014 [23]	Yes	Yes	NR	Yes	No	NA	NA	Yes	Yes	NA	Yes	NA	NA	No	Low
D'Souza 2015 [15]	Yes	Yes	NR	Yes	Yes	NA	NA	Yes	Yes	NA	Yes	NA	NA	No	Low

NR: not reported; NA: not applicable.

Table 5: Results of the included studies.

Author Year	Risk factors examined	Risk factors associated with glycaemic control	Statistical analysis of positive results			Main conclusion
Ajabnoor 1987 [18]	Age, gender, duration of diabetes, FPG, and treatment modality	FPG and treatment modalities	FPG/HbA1c correlation $r = 0.19$, $p < 0.005$			HbA1c is associated with FBG and treatment modality but not with age, gender, and duration of diabetes
			Treatment modality	Mean HbA1c	p value	
			Insulin	14.3 ± 1.3		
			Oral	17.0 ± 0.0	<0.001	
			Diet	16.3 ± 1.8	0.02	
Binhemd 1992 [19]	Knowledge, attitude and practice (KAP), diabetes type, and diabetes duration	KAP and diabetes duration	Positive correlation between HbA1c and diabetes duration ($p < 0.001$). Negative correlation between HbA1c and the practice (p : 0.03) and the attitude (p : 0.01)			The positive correlation between HbA1c and the patients' practice and attitude reflects the need for continuous patient education, follow-up, and support
Al-Nuaim 1998 [20]	Age, BMI, region, residency, gender, and treatment modalities	TTT modalities	Adjusted odds ratio and 95% confidence interval (95% CI) of poor glycaemic control			There is a significant relation between glycaemic control and treatment modalities
			TTT modality (ref: diet regimen)			
				Odds ratio	95% CI	p value
			Oral agent	1.7	1.1–2.6	0.005
			Insulin	2.6	1.4–5.0	
Malik 1999 [24]	Age, gender, ethnicity, diabetes duration, family history, treatment modalities, and follow-up location	Duration of diabetes, follow-up location, and family history	Control		Odds ratio (p value)	Improvements are needed in primary care and in the community-based approach to diabetes control
					Fair	Poor
			Diabetes duration (years)		1.03 (0.329)	1.08 (0.007)
			Follow-up at health centres (ref: hospital)		1.86 (0.036)	2.47 (0.001)
			Family history (ref: none)		0.62 (0.095)	0.39 (0.001)
Abdelmoneim 2002 [21]	Age, gender, family history, diabetes duration, BMI, cholesterol level, complications, number of health education session, and crowding index	Gender and health education	Odds ratio (p value) (ref: good control)			Female sex is a significant predictor of poor glycaemic control, and among females, the lower the number of education sessions, the poorer the diabetes control
			Gender (ref: male)	2.84 (<0.05)		
			Health education among females	0.28 (<0.05)		
			Health education among males	1.39 (<0.05)		

Table 5: Continued.

Author Year	Risk factors examined	Risk factors associated with glycaemic control	Statistical analysis of positive results				Main conclusion
Al-Kaabi 2008 [10]	Age, gender, marital status, level of education, occupation, smoking, eating practice, BMI, abdominal circumference, blood pressure, and lipid profile	Carbonated drinks age	Regression analyses of HbA1c level (adjusted beta coef. (p value))				The dietary practice of people with diabetes in the UAE is inadequate and needs improvement
			Number of carbonated drinks	0.201 (0.029)			
			Age	0.023 (0.047)			
Al-Kaabi 2009 [11]	Age, gender, nationality, marital status, level of education, employment, income, diabetes duration, smoking, diabetes complications, physical activity, BMI, abdominal circumference, and blood pressure	No significant association	Multiple regression analysis of HbA1c in relation to age, gender, education, duration of diabetes, and physical activity did not reveal any significant association				The physical activity practice of people with diabetes in the UAE is largely inadequate to meet the recommendations
Al-Lawati 2012 [22]	Age, gender, duration of diabetes, treatment modalities, BMI, eGFR, smoking, and healthcare index	Age, gender, eGFR, diabetes duration, and TTT modalities	Adjusted odds ratio and p value of good glycaemic control				Younger Omani adults exhibit worse glycaemic levels compared to older adults
			Age (ref: 20–39 yrs)	40–59 yrs	1.7	0.01	
				60+ yrs	2.5	0.0001	
			Sex (ref: men)	Women	1.5	0.001	
			Diabetes duration (ref: <5 yrs)	≥5 yrs	0.8	0.041	
			Treatment type (ref: diet)	Oral	0.2	0.001	
				Insulin ± oral	0.1	0.001	
			eGFR (ref: <60 ml/min/1.73 m^2	≥60 ml/min	1.9	0.001	
Al-Hayek 2012 [8]	Age, gender, marital status, employment, BMI, self-care management behaviour, self-monitoring of blood glucose, medication adherence, anxiety, and depression	Medication adherence, anxiety, and depression		HbA1c < 7%	HbA1c ≥ 7%	p value	Poor diabetes self-care management behaviour, low adherence to medicine, and higher level of anxiety and depression are associated with poor glycaemic control
			Medication adherence	7.4 ± 1.4	5.4 ± 1.2	0.0007	
			Anxiety	7.9 ± 1.3	10.3 ± 1.7	0.0005	
			Depression	6.9 ± 0.9	9.8 ± 1.3	0.0002	
			Total hospital anxiety and depression scale (HADS)	14.8 ± 1.8	20.1 ± 2.1	0.0001	
Shamsi 2013 [25]	Dietary practice	Dietary practice	Dietary practice	HbA1c (mean ± SD)		p value	There is a significant relation between the dietary practice and the HbA1c level
			Very poor	10.95 ± 1.56		0.006	
			Poor	7.46 ± 1.74			
			Average	7.46 ± 1.97			
			Good	7.31 ± 2.07			
			Very good	5.97 ± 1.36			

Table 5: Continued.

Author Year	Risk factors examined	Risk factors associated with glycaemic control	Statistical analysis of positive results					Main conclusion
					HbA1c < 7%	HbA1c ≥ 7%	p value	
Al Balushi 2014 [14]	Age, gender, diabetes duration, BMI, blood pressure, creatinine, and lipid profile	Total cholesterol, diastolic blood pressure, and LDL	Diastolic blood pressure, mmHg (mean ± SD)		80 ± 8	84 ± 9	0.006	There is a significant association between HbA1c and diastolic blood pressure, total cholesterol, and LDL
			Total cholesterol, mmol/l (mean ± SD)		4.7 ± 0.8	5.2 ± 1.3	0.002	
			LDL, mmol/l (mean ± SD)		3.0 ± 1.2	3.8 ± 1.0	0.034	
Alrahbi 2014 [23]	Diabetes self-management	No association between diabetes self-management and glycaemic control was found	No association was found					There is no association between diabetes self-management and glycaemic control
					HbA1c < 7%	HbA1c ≥ 7%	p value	
D'Souza 2015 [15]	Age, gender, education, diabetes duration, diabetes education, medication, BMI, and patient empowerment	Age, education, diabetes duration prior to diabetes education, TTT modalities empowerment, effect of diabetes on activities of daily living	Age (no. (%))	30–39 yrs	24 (51.1)	23 (48.9)	0.000	Interventions to increase the empowerment of people with T2DM should be made for better glycaemic control
				40–49 yrs	52 (50.5)	51 (49.5)		
				50–59 yrs	36 (39.1)	56 (60.9)		
				≥60 yrs	26 (44.8)	32 (55.2)		
			Education (no. (%))	Until 8th grade	56 (47.9)	61 (52.1)	0.000	
				High school	51 (54.3)	43 (45.7)		
				Diploma/tech	31 (10.3)	58 (67.4)		
			Duration of diabetes (no. (%))	0–9 yrs	57 (50.9)	55 (49.1)	0.000	
				10–19 yrs	68 (47.2)	76 (52.8)		
				≥20 yrs	13 (29.5)	31 (70.5)		
			Diabetes education program (no. (%))	No	54 (47.0)	61 (53.0)	0.000	
				Yes	84 (45.4)	101 (54.6)		
			Medications (no. (%))	Oral	109 (50.5)	107 (49.5)	0.000	
				Insulin and oral	29 (34.5)	55 (65.5)		
			Regression analysis					
			Empowerment and glycaemic control		Beta coef.	p value		
					0.657	0.001		

HbA1c: haemoglobin A1c; FPS: fasting plasma sugar; eGFR: estimated glomerular filtration rate; TTT: treatment; ref: reference.

In regard to the effect of modality of treatment on glycaemic control, Al-Nuaim et al. found that compared to participants on diet regimen, only the adjusted OR of poor control was 1.65 and 2.64, respectively, for those on oral agent and insulin [20]. Similarly, Al-Lawati et al. reported that the likelihood of good control was lower for those on oral agent (adjusted OR: 0.2, p value: 0.001) and for those on insulin (adjusted OR: 0.1, p value: 0.001) compared to diet regimen only [22]. Ajabnoor et al. reported, however, that participants on insulin had lower mean HbA1c (14.3 ± 1.0) compared to diet only (16.3 ± 1.8) and oral agent (17.0 ± 0.0) (p value < 0.001) [18].

4. Discussion

This systematic review summarises patient-related factors affecting glycaemic control among adults with T2DM in the GCC countries. Using a reproducible search strategy and prespecified inclusion/exclusion criteria, we identified 13 articles for inclusion in this review. The quality of the included studies is low to moderate in general, and the effect of some potentially important risk factors (including diet, physical activity, family support, and cognitive impairment) was not adequately investigated.

One cross-sectional study reported that age was associated with poor glycaemic control [15]. With advancing age, there might be a waning of the function of the β-cells of the pancreas, and some people develop other comorbidities that may affect glycaemic control. Similar to the findings of a previous systematic review [26], however, two of the included studies have found that elderly people with diabetes had better glycaemic control than young people [10, 22]. Elderly people are more likely to adhere to the management plan compared to young people who are more likely to be affected by the change in lifestyle and urbanisation [22, 27].

The duration of the disease is another important nonmodifiable risk factor of poor glycaemic control that was identified in three cross-sectional studies [15, 19, 22]. With longer duration of diabetes, the function of the pancreas further deteriorates because of the failure of the β-cells [28]. In addition, individuals with longer duration of diabetes are at a higher risk of developing diabetes-related complications, which can have a substantial effect on glycaemic control. With regard to the effect of gender on glycaemic control, two cross-sectional studies found an association but with contradicting results. One study reported that female gender was associated with poor glycaemic control [21], while another reported that females had better glycaemic control compared to males [22]. The inconsistency in the results of these studies may be explained in part by a variation in the methodology and heterogeneity between patients across the study population. In the systematic review undertaken by Sanal et al., however, it was found that the female gender was a risk of poor glycaemic control [26].

Compliance to diabetes management including adherence to diet, physical activity, medications, and self-monitoring of blood sugar is crucial in the management of diabetes. This current review shows that compliance to management and adherence to medications were significantly associated with good glycaemic control [19]. There is a gap in the knowledge, however, regarding barriers to compliance and adherence to management for people with diabetes in the GCC countries.

Two recent studies included in this review have found that compared to people with diet regimen only, those who were on oral agent and insulin had higher risk of poor control after adjustment for other risk factors [20, 22]. These findings may emphasize the potentially important role of lifestyle modification on the glycaemic control. In this review, however, we have found that the effect of lifestyle factors, including dietary habit and physical activity, on glycaemic control has not been studied adequately in the context of the GCC countries. Well-planned healthy eating habits with the supervision of a dietician can reduce HbA1c by 0.5 to 2.0% for people with T2DM [29–32]. There is also strong evidence of the effect of regular exercise on lowering HbA1c for people with T2DM [33–35]. Of the 13 studies included in this review, only two cross-sectional studies explored the association between dietary habits and glycaemic control [10, 25]. One study that assessed the association between various dietary practices and glycaemic control reported that consumption of carbonated (soda) drinks was the only associated factor [10]. The other study showed that participants who followed healthier dietary practices had a lower mean HbA1c [25]. Similarly, only two studies evaluated the association between physical activity and glycaemic control and reported no association [11]. In the latter four studies [10, 11, 25], however, the recruited sample was relatively small, no adjustment for confounders was done in most of them [11, 25], and the majority were of low to moderate [10, 25] quality.

Other modifiable risk factors that were found to be associated with glycaemic control in this review include patients' attitude to diabetes, the location of scheduled follow-up visits (hospital or primary healthcare centres), eGFR, anxiety, depression, diastolic blood pressure level, cholesterol level, LDL level, and patient empowerment for self-management [10, 14, 15, 19, 22, 24]. Studies included in this review, however, have assessed different sets of these risk factors; hence, a comparison of their findings was not possible.

In the GCC countries, wives are usually responsible for preparing meals for the whole family, including members with diabetes. For cultural reasons, on the other hand, some women prefer to be accompanied by a relative when they go out for exercise or when they visit healthcare centres. Therefore, it is likely that family support has an important role in the management of diabetes, which should be taken into account when evaluating glycaemic control. This is supported by the results of a systematic review showing a potential importance role of family support in the management of T2DM [36]. In addition, poorly controlled diabetes has been associated with a decline in cognitive function [37, 38], and impaired cognitve function is likely to have a negative effect on glycaemic control. That is because people with impaired cognition is less likely to be compliant to diabetes treatment plan.

Family support and cognitive function are potentially important risk factors for glycaemic control, which have not been explored in any of the included studies in this systematic review. Thus, the relationship of these factors with control needs a comprehensive investigation in future studies. Further, some of the modifiable risk factors such as the attitude towards the disease, barriers to compliance, anxiety, depression, and patient empowerment were not addressed adequately; hence, they need re-evaluation to build a stronger evidence. Future researchers should also reassess the association between glycaemic control and lifestyle factors using methodologically sound study design.

The strength of this review lies in the systematic, comprehensive, and unbiased approach taken during the literature search, data extraction, and assessment of the risk of bias. As the identified studies were either cross-sectional or case-control studies, a causal relationship between the risk factors and glycaemic control cannot be established. Moreover, because the studies in this review used different statistical methods, it was neither possible to generalise the magnitude of the effect of risk factors on glycaemic control nor possible to conduct a meta-analysis.

No studies assessing the factors affecting glycaemic control in Qatar or Kuwait were identified. Nevertheless, the results of this systematic review can be useful to all of the GCC countries. The populations of the GCC countries share similar cultures and lifestyles, and the healthcare services and medications are free of charge to all citizens.

5. Conclusion

This systematic review identified the following variables as the risk factors for poor glycaemic control in the GCC countries: low level of education, longer duration of diabetes, poor compliance to diet and medication, poor attitude towards the disease, poor self-management behaviour, anxiety, depression, renal impairment, hypertension, and dyslipidaemia. The policymakers should introduce large-scale awareness program and educational models to improve patient compliance and practices and to support patient empowerment for self-management. Healthcare providers should be aware of these risk factors and provide optimal care and guidelines for enriching self-management of the disease. The existing studies from the GCC have heterogeneity in their methodology, which may be related to the variation in their findings. In addition, some risk factors that may affect glycaemic control such as lifestyle, social support, and cognitive function have not been investigated adequately. Future research should address these issues.

Conflicts of Interest

All authors declare that they have no conflicts of interest.

Authors' Contributions

All authors were involved in the conception and design of the study. Mohammed J. Alramadan and Afsana Afroz researched the literature, extracted the data, and assessed the risk of bias. Mohammed J. Alramadan drafted the manuscript. All authors critically reviewed the manuscript and approved the final version.

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2.3 Conference presentation

Poster presented at the International Diabetes Federation Congress, December 2017, Abu Dhabi, UAE.

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Patient-Related Determinants of Glycaemic Control in People with Type 2 Diabetes in the Gulf Cooperation Council Countries: A Systematic Review

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Background and Objective:
The aim of this systematic review was to summarise patient-related factors that affect glycaemic control among people with type 2 diabetes in the Arabian Gulf Council Countries.

Methods
- Embase, CINAHL, Cochrane Library, Medline, and PsycINFO were searched comprehensively.
- All observational studies were considered for inclusion if they:
  - examined factors affecting glycaemic control, and
  - included adults with type 2 diabetes living in the Arabian Gulf Council Countries.

Results
- A total of 13 studies met the inclusion criteria (see **Figure 1**); five studies were from Saudi Arabia, four from Oman, three from the United Arab Emirates and one from Bahrain.
- All studies were cross-sectional except one which was a case-control.
- One study was population based, six recruited participants from multiple centres, while the remaining were single centred.
- Factors associated with glycaemic control were age, gender, duration of diabetes, family history, compliance to management, attitude to diabetes, location of scheduled follow up visits (hospital or primary healthcare), consumption of carbonated drinks, renal impairment, anxiety, depression, adherence to medication, diastolic blood pressure, cholesterol level, low density lipoprotein level, education level and perception of empowerment.

Discussion
- The quality of the majority of the reviewed studies was low to moderate.
- There was inconsistency in the findings of the included studies.

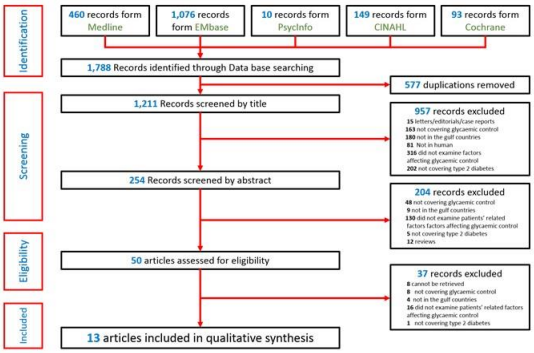

Figure 1: flow chart of the systematic literature search

- The association between glycaemic control and dietary habit and physical activity has not been studied adequately.
- No studies has evaluated the association between glycaemic control and family support or cognitive function.
- The heterogeneity in the methodology and findings across the studies made it difficult to compare their findings or to conduct a meta-analysis.

Conclusion
- A number of patient related factors associated with glycaemic control were identified.
- There was a wide variation in the findings of the current studies.
- The relationship of glycaemic control with some potential important risk factors including dietary habit, physical activity, family support, and cognitive function were not addressed adequately.
- Further research is needed in this area.

Keywords: Type 2 diabetes, glycaemic control, Gulf Countries, Saudi Arabia, Kuwait, Bahrain, Qatar, United Arab Emirates, Oman

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Chapter 3:

Research Methodology

3.1 Introduction

This chapter describes the methods that were used to collect data for the following studies:

- Glycaemic Control for People with Type 2 Diabetes in Saudi Arabia (Chapter 4)
- Lifestyle Factors and Macro- and Micro-Vascular Complications among People with Type 2 Diabetes in Saudi Arabia (Chapter 5)
- Risk Scoring System to Predict Diabetes Macro- and Micro-vascular Complications for People with Type 2 Diabetes in Saudi Arabia (Chapter 5)
- Obesity, Hypertension, and Dyslipidaemia among People with Type 2 Diabetes in Saudi Arabia (Chapter 6)
- Health Related Quality of Life for People with Type 2 Diabetes in Saudi Arabia (Chapter 7)

After the methodology was published, some changes were made to the objectives of this thesis, as well as to the data analysis methods. This chapter describes in detail the data analysis methods used in chapters 4 to 7.

3.2 Study design and data collection procedure

The following published article describes the study design, population, sample, recruitment procedure, data collection instrument, and data management.

3.3 Article:

Alramadan MJ, Afroz A, Batais MA, Almigbal TH, Alhamrani HA, Albaloshi A, et al. A Study Protocol to Assess the Determinants of Glycaemic Control, Complications and Health Related Quality of Life for People with Type 2 Diabetes in Saudi Arabia. Journal of Health Education Research & Development. 2017;5(2):1-6.

At: https://www.omicsonline.org/open-access/a-study-protocol-to-assess-the-determinants-of-glycaemic-controlcomplications-and-health-related-quality-of-life-for-people-with-t-2380-5439-1000219.php?aid=90359

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Research Article OMICS International

A Study Protocol to Assess the Determinants of Glycaemic Control, Complications and Health Related Quality of Life for People with Type 2 Diabetes in Saudi Arabia

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Abstract

Background: The prevalence of type 2 diabetes mellitus is high in Saudi Arabia, and a large proportion of those affected by the disease are not controlling their blood sugar, which exposes them to diabetes complications. The aim of this study is to evaluate factors associated with poor glycaemic control, complications and poor quality of life among people with type 2 diabetes in Saudi Arabia.

Methodology: Using a cross-sectional study design, 1082 participants with type 2 diabetes attending diabetes centres in Riyadh, Jeddah and Hofuf will be recruited in the study. They will be interviewed to complete a pre-tested electronic questionnaire. The questionnaire collects information related to socio-demographics, medical history, lifestyle, family support, utilisation of healthcare services, anxiety, depression, quality of life, cognitive function, independence in daily living activity, neuropathy, anthropometric measures, up-to-date documented lab test results and current medication. Data will be summarised and presented as mean ± standard deviation (or median and percentiles) for numerical data and frequency and percentage for categorical data. T-test, ANOVA and chi-square tests will be used to explore associations between risk factors and outcomes. Any association will be evaluated further using regression analysis.

Discussion: Knowledge of the risk factors pertaining to poor glycaemic control, diabetes complications and poor quality of life for people with type 2 diabetes is crucial. This knowledge will assist healthcare providers to identify and provide more intensive care plans to those who need it, as well as guide the development of new strategies to improve management of the disease. This will improve the health of people with type 2 diabetes and lower their risk of complications, and reduce the burden of this highly prevalent disease on families and the community.

Keywords: Type 2 diabetes; Saudi Arabia; Glycaemic control; Complication; Quality of life

Introduction

Diabetes mellitus is one of the most common chronic non-communicable diseases [1,2]. An estimated 415 million adults had diabetes worldwide in 2015 and this number is expected to rise to 642 million by 2040 [3]. In 2015, approximately five million individuals between the age of 20 and 79 years died because of diabetes [3]. Furthermore, roughly 14.5% of global all-cause mortality among adults is attributed to diabetes and half of these deaths occur among those aged below 60 [3].

Similar to other countries in the Middle East, modernisation has taken its toll on the population of Saudi Arabia. The vast lifestyle changes of Saudis over the last few decades, accompanied by rising rates of obesity, have led to a rapid and progressive increase in the prevalence of diabetes. A recent study showed that 13.4% of Saudis aged 15 years and above have diabetes, which is significantly higher than both the global prevalence (8.8%) and the prevalence in the Middle East (10.7%) [3,4].

The control of blood glucose levels is the cornerstone of diabetes management. Studies have shown that there is a strong association between an elevated blood glucose level and the risk of diabetes-related complications and mortality for people with diabetes [5,6]. Of particular concern is that between 50% and 70% of people with type 2 diabetes mellitus (T2DM) in Saudi Arabia have uncontrolled blood glucose levels [7-9], and the prevalence of diabetes-related complications among them is high [10-13].

A few studies that have examined factors affecting glycaemic control for people with T2DM in Saudi Arabia have indicated poor control to be associated with increasing age, insulin use, smoking, lower levels of physical activity, poor diabetes self-care behaviour, low adherence to medicine, anxiety and depression [7-9]. A number of other factors that may have an impact on glycaemic control, diabetes complications and quality of life-such as the duration of diabetes, family support, cognitive function and lifestyle factors (diet and physical activity)-were not investigated adequately in existing studies from Saudi Arabia [14-16].

Furthermore, it is well-established that haemoglobin A1c (HbA1c) is a more accurate measure of blood sugar control, compared to fasting

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and random blood sugar measurements, because HbA1c reflects the level of glycaemic control over several weeks [17]. However, some of the studies from Saudi Arabia used random blood sugar for determining the level of control, which was a limitation to these studies. In addition, the majority of studies from Saudi Arabia involved a single centre, or were hospital-based [8-10,13,18-26] and may not accurately represent the large and diverse population of the country.

To address the above gaps, a multi-centre study is required which will comprehensively investigate the effect of all possible risk factors. Thus, the aim of this proposed study is to conduct a multi-centre study in Saudi Arabia to explore the effect of lifestyle factors, family support and cognitive impairment, as well as other risk factors for glycaemic control, diabetes complications and quality of life for people with T2DM mellitus (T2DM). The knowledge of these risk factors will help healthcare providers, the individuals with the disease, and society as a whole. Understanding the burden of the associated risk factors is also important for public health policymakers who develop healthcare priorities that yield the greatest benefits.

Objectives

This study has three main objectives. Firstly, to evaluate the determinants of poor glycaemic control among people with T2DM in Saudi Arabia. Secondly, to investigate the prevalence of coronary artery disease, neuropathy, nephropathy and cognitive impairment, as well as their associated factors among people with T2DM. Thirdly, to examine factors associated with poor health-related quality of life for people with T2DM. Furthermore, secondary objectives of this study is to examine factors associated with poor control of blood pressure as well dyslipidaemia among people with T2DM.

Methodology

Ethical approval

Both the Monash University Human Research Ethics Committee and the Research Ethics Committee of the Ministry of Health in Saudi Arabia approved this project. The approval of the College of Medicine Institutional Review Board at Kind Saud University was also obtained.

Study design

A cross-sectional study will be conducted to address the research questions. Cross-sectional study design has the advantage of being inexpensive and less time-consuming compared to other epidemiological study designs. Moreover, in using this study design, the prevalence of outcomes such as poor glycaemic control and complications, as well as the prevalence of risk factors, can be measured.

Study population

The study population will consist of people with T2DM in Saudi Arabia attending diabetes centres in the cities of Hofuf, Riyadh and Jeddah (Figure 1). These cities are among the top most populated in the country and their diabetic centres serve a mixture of people who come from urban, as well as rural settings. Inclusion criteria include confirmed diagnosis of T2DM, age 18 years and above and duration of diabetes of one year and more. Participants will be excluded if they have other types of diabetes (type 1 or gestational), or if there is no HbA1c test results in their medical records for the past 6 months. Pregnant women will also be excluded.

Sample size

A total of 1082 subjects with T2DM will be recruited for the study which was calculated based on 90% power, 5% significance level and a margin of error of 2.5% for prevalence of glycaemic control. A back calculation of power shows that a sample size of 1082 participants will maintain a power of 90% or above for all other primary and secondary objectives of this study.

Recruitment

A systematic random-sampling method will be used to recruit participants. The number of participants recruited each day is expected to be 10. Every day during the data-collection period, the data collectors will begin by randomly selecting a participant with T2DM from the first K participants attending the diabetes centre and invite them to participate. The value of K will depend on the number of people attending the centre every day, which varies between centres. Following on, every K-th patient will be approached. If the K-th person declines or does not have T2DM, the next person will be invited. The recruitment will be continued for a period of six months or until data have been collected from 1082 patients, whichever comes first.

Informing participants about the study and obtaining the consent

Data collectors will fully inform each of the participants about the purpose of the study, how the data will be collected and how the collected information will be used while maintaining participants' confidentiality. Then, participants will be given an explanatory statement and allowed some time to read and ask questions. Upon their agreement to participate, they will be required to read and sign a consent form.

Data collection instrument

A pre-tested questionnaire will be used to collect data. The original English version of the questionnaire has been translated into Arabic. The Arabic version was then translated into English to check that the Arabic and the original English versions have exactly the same meanings. Prior to collecting the data, data collectors will be trained by the primary investigator on how to approach participants, inform participants about the study, fill in the electronic questionnaire and take the anthropometric measurements.

Research Electronic Data Capture (REDCap) will be used to collect and manage the data [27]. REDCap is a secure web-based application

Figure 1: Map of Saudi Arabia showing the main cities and the cities where the research will be conducted (red arrows).

for constructing electronic surveys and collecting data for research studies. It provides a user-friendly interface with validated data entry, audit trails for tracking data manipulation, and an automated export procedure for seamless data downloads to common statistical software packages.

Using a standard questionnaire, the following information will be collected for all participants:

- Diabetes centre and data collector details.
- Participant's socio-demographics data, including name, age, gender, marital status, education, nationality, work status and household income.
- Medical history: duration of diabetes, place of follow-up, frequency of follow-up, diabetes treatment, self-monitoring blood glucose, hypoglycaemic events, medical history of other diseases, diabetes complications and medication adherence (Morisky Medication Adherence questionnaire).
- Family support for diabetes, utilisation of healthcare services, knowledge of HbA1c.
- Lifestyle data including smoking status, dietary habits (UK diabetes and diet questionnaire at: https://sps.onlinesurveys.ac.uk/the-uk-diabetes-and-diet-questionnaire-ukddq) and physical activity (WHO STEPS questionnaire for diet at: http://www.who.int/chp/steps/STEPS_Instrument_v2.1.pdf).
- Psychological aspect data that include depression (the Patient Health Questionnaire-2 (PHQ-2)) [28] and anxiety (Generalized Anxiety Disorder Scale (GAD-2)) [29].
- Patient's quality of life (EQ-5D-5L) [30] and independence regarding activities in daily life (Katz Index) [31].
- Rowland Universal Dementia Assessment Scale (RUDAS) [32].
- Neuropathy screening tool (the Michigan Neuropathy Screening Instrument [33]).
- Anthropometrics: height, weight, blood pressure and waist and hip circumference.
- Materials and equipment: digital scale, measuring tape, and digital automatic blood pressure monitor
- Height: height will be measured for all participants using a portable stadiometer. Standing height is measured with the subject in bare feet, back-square against the wall and eyes looking straight ahead. A set square resting on the scalp and a tape measurement from the wall/bed is used to measure height to the nearest 0.5 cm. This will be done twice and if the measurement varies more than 2 cm, a third measurement will be taken. A stool will be used where necessary.
- Weight: participant will be instructed to remove their shoes and outer layers of clothing (such as jackets or jumpers). Weight will be recorded to the nearest 0.1 kg.
- Waist circumference: will be measured against thin clothing (for cultural reasons), on exhalation, midway between the lower rib margin and the anterior superior iliac spine (hip bone) or narrowest abdominal point. Subject should be relaxed with arms held loosely at sides. The tape measure must be kept horizontal for standing measurement. This will be done twice and if the measurement varies by more than 2 cm, a third measurement will be taken. The waist circumference will be recorded to the nearest 0.5 cm.
- Hip circumference: measure at the widest circumference around the hip bones, so that the tape passes over the greatest protrusion of the gluteal muscles. The tape measure must be kept horizontal for standing measurement. This will be done twice and if the measurement varies more than 2 cm, a third measurement will be taken. The hip circumference will be recorded to the nearest 0.5 cm.
- Blood pressure: participants should be seated for at least five minutes, legs uncrossed, feet flat on the floor and any excess clothing items that may interfere with measurement must be removed. Three systolic and diastolic blood pressure readings will be taken using an automated blood pressure monitor machine.
- Information from patients' medical records, including the three most recent blood pressure measures, fasting blood sugar measures, HbA1c, serum creatinine, albumin/creatinine ratio, eGFR, lipid profile, current prescribed medications and documented diagnosis of hypertension, coronary artery disease and stroke.

Data management and analysis

During the data-collection period, the data will be saved in the secure REDCap web-based application hosted by Monash University. The application is accessible only by the research team. When the data collection is completed the data will be exported to the IBM SPSS statistical package and will be saved on the secure School of Public Health and Preventive Medicine at Monash University allocated network storage (Monash (S:) drive). Participants' names will be removed from the database and each participant will be identified by a numeric code generated by REDCap. The database containing all information will be saved in a separate secure electronic folder, which will not be used for data analysis. Only the research team will have access to the identified and de-identified electronic databases.

Data will be summarised and presented as either mean ± standard deviation or median and percentiles for numerical data and frequency, and percentage for categorical data. Depending on the type of data, t-test, ANOVA, nonparametric tests or chi-square tests will be used to examine for associations between risk factors and outcomes. Any association will be further evaluated using simple and multiple logistic regression analysis.

Outcomes assessment

Definitions of the main study outcomes that will be considered:

- Glycaemic control: the proportion of the glycosylated haemoglobin (HbA1c) measured as a percentage and categorised as good control (HbA1c<7.0%), reasonable control (HbA1c 7%-8%) and poor control (HbA1c>8.0%).
- Nephropathy: documented eGFR (calculated by the CKD EPI formula) below 90 ml/min (categorised as mild renal impairment (60-89 ml/min), moderate renal impairment (30-59 ml/min), severe renal impairment (15-29 ml/min) and renal failure (<15 ml/min).
- Coronary artery disease: documented diagnosis of coronary artery disease (CAD).

- Neuropathy: a score of 7 or more using the Michigan Neuropathy Screening Instrument.
- Quality of life: EQ-5D-5L health states scores will be converted into a single index value between 0 and 1, and the quality of life will be categorised as Good quality of life (0.67-1.00), fair quality of life (0.34-0.66) and poor quality of life (≤ 0.33).
- Hypertension: either a documented diagnosis of hypertension, on antihypertension medications or three previous high blood pressure readings (systolic ≥ 140 and diastolic ≥ 90). Persons with poor blood pressure control are defined as having hypertension and their current systolic blood pressure as ≥ 140 mm Hg or diastolic ≥ 90 mm Hg.
- Dyslipidaemia: Documented total cholesterol>4.0 mmol/L, low density lipoproteins (LDL)>2.0 mmol/L, high density lipoprotein (HDL)<1.0 mmol/L, triglycerides>2.0 mmol/L or taking lipid lowering medication.
- Impaired cognitive function is defined as a score of ≤ 22 in the Rowland Universal Dementia Assessment Scale (RUDAS).

Pilot Study

The questionnaire was piloted on 29 participants attending diabetes centre in Hofuf over a period of two weeks. The sociodemographic characteristics of the participants in the pilot study are presented in Table 1. Mean age was 55.7 (± 11.6) years. Approximately 38% of participants were female and the majority of participants were married (93.1%). Roughly a quarter (24.1%) of participants was illiterate and 41.4% had only achieved primary school. The majority of participants (82.8%) reside in Hofuf city, while the rest lived in remote villages. With regard to work status, 17.2% worked and 34.5% were homemakers (house-wives). The rest of the participants were either retired (27.6%) or not working (20.7%). A large proportion of participants (41.4%) had a total household income between 3000 and 6000 Saudi Riyals.

A summary of some disease characteristics and main study outcomes is presented in Table 2. Participants had a mean duration of diabetes of 17.7 (± 10.5) years. Mean HbA1c was 9.6% (± 2.0%). The majority of participants (69.0%) had poor glycaemic control (HbA1c>8), while 10.3% had good glycaemic control (HbA1c ≤ 7%) and 17.2% had reasonable control (HbA1c 7.1%-8.0%). More than half of the participants (58.6%) had dyslipidaemia and close to half (48.3%) had hypertension, while the diagnosis of CAD was documented in 31.0% of participants. Using the Michigan Neuropathy Screening Instrument, 31.0% of participants had a score (≥ 7), suggestive of neuropathy. eGFR calculated from most recent serum creatinine showed that 55.2% of participants had some renal impairment. Of those, 27.6% had mild impairment, 24.1% had moderate impairment, and 3.4% had severe impairment. Cognitive function was impaired in about half (51.7%) of participants using the Six-item Cognitive Impairment Test (6CIT) [34]. The quality of life was fair for 34.5% and poor for 3.4% of participants, while the majority (62.1%) had good quality of life. There were some missing values in some important investigations including HbA1c, cholesterol and triglycerides. The range of missing values was between 3.4% for HbA1c and 5.0% for triglycerides.

The questionnaire was found to be acceptable by most of the participants and practical by data collectors. However, the average time required to complete data collection for one participant was more than one hour. In order to ensure the collection of data from the planned number of participants, the length of the questionnaire was reduced after the completion of the pilot study. The STOP-BANG Sleep Apnea and the chest pain (Rose) questionnaires were removed [35,36]. Questions related to the duration of complications reported by participants were also removed.

Based on our findings in the pilot study that a relatively large proportion of people were illiterate, a decision was made to use the Rowland Universal Dementia Assessment Scale (RUDAS) instead of the Six-item Cognitive Impairment Test (6-CIT) to evaluate cognitive function. RUDAS is a multicultural cognitive assessment tool that is not affected by literacy level, and has been validated among Arabic-speaking people [32,37]. Approval to use the amended questionnaire was obtained from all ethical committees that have approved this project.

Discussion

This project is a comprehensive multi-centre study that will improve our understanding of the factors associated with poor control of blood glucose level, the factors that increase risk of diabetes complications and the factors associated with poor quality of life among people with T2DM in Saudi Arabia. The anticipated valuable information that will be obtained from this study will help healthcare providers to identify people with diabetes who are at risk of poor control and complications,

Variable	Descriptive statistics	Variable	Descriptive statistics
Age in years (mean ± SD)	55.7 ± 11.6	**Work status %**	
Gender %		Working	5(17.2%)
Female	11(37.9%)	Not working (able to work)	2(6.9%)
Male	18(62.1%)	Not working (unable to work)	4(13.8%)
Marital status %		Homemaker (house-wife)	10(34.5%)
Married	27(93.1%)	Retired	8(27.6%)
Divorced (separated)	1(3.4%)		
Widowed	1(3.4%)		
Highest education level achieved %		**Total household monthly income %**	
None (illiterate)	7(24.1%)	≤ 3000 Saudi Riyals	3(10.3%)
Primary school	12(41.4%)	3000–6000 Saudi Riyals	12(41.4%)
Intermediate school	1(3.4%)	6001–9000 Saudi Riyals	4(13.8%)
Tertiary school	8(27.6%)	9001–12000 Saudi Riyals	7(24.1%)
University degree	1(3.4%)	≥ 12001 Saudi Riyals	3(10.3%)
Home location %			
Inside the city	24(82.8%)		
Remote village	5(17.2%)		

Table 1: Pilot study participants' sociodemographic characteristics.

Variable	Descriptive statistics	Variable	Descriptive statistics
Diabetes duration in years (mean ± SD)	17.7 ± 10.5	**Hypertension %** No Yes	15(51.7%) 14(48.3%)
HbA1c % (mean ± SD)	9.6 ± 2.0		
Glycaemic control % Good Reasonable Poor	3(10.3%) 5(17.2%) 20(69.0%)	**CAD %** No Yes	20(69.0%) 9(31.0%)
Quality of life % Good Fair Poor	18(62.1%) 10(34.5%) 1(3.4%)	**Neuropathy %** No Yes	20(69.0%) 9(31.0%)
Cognitive impairment % No Yes	14(48.3%) 15(51.7%)	**Nephropathy %** No Mild Moderate Severe	13(44.8%) 8(27.6%) 7(24.1%) 1(3.4%)
Dyslipidaemia % No Yes	12(41.4%) 17(58.6%)		

Table 2: Characteristics related to diabetes, complications and health related quality of life.

and provide them with more intensive care plans. It will also identify priority issues that will guide the development and implementation of new national strategies to promote the health of people with T2DM in Saudi Arabia.

The strength of this study lies on the relatively large number of participants and the recruitment from three highly populated cities in three different regions of Saudi Arabia. The evaluation of a wide range of risk factors and outcomes using validated tools also provide strength to this study. Since this study is cross-sectional, we will be assessing association; no causal relation can be inferred. Observational study designs are also prone to bias. Nevertheless, this study will not only provide valuable information that will be used by healthcare providers and health policy makers, but will also generate hypotheses that will guide future advance research projects in the field of diabetes in Saudi Arabia, in the Middle East region and globally.

Competing Interests

All authors declare that they have no competing interests.

Author Contributions

All authors were involved in the conception and design of the study. MJA and AA reviewed the literature and MJA drafted the manuscript. All authors critically reviewed the manuscript and approved the final version.

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3.4 Data analysis methods

Stata SE version 15.0 was used for data analysis in chapters 4 to 7. A p-value of 0.05 or less was considered as statistically significant.

3.4.1 Data analysis methods for Chapter 4:
Factors Associated with Poor Glycaemic Control among People with T2DM in Saudi Arabia

Here, the outcome was glycaemic control that was based on participants' HbA1c level. Glycaemic control was categorised into controlled (HbA1c < 7%), partially controlled (HbA1c 7% to < 8%), and poorly controlled (HbA1C ≥ 8%) (82). A HbA1c cut-off value of ≥ 9% was also used to represent very poor control (83). The following were considered as potential risk factors: age, gender, level of education, location of residency, region, household income, active smoking, eating habit score, eating fruits and vegetables per week, physical activity per week, sitting time per day, diabetes duration, family history of diabetes, modality of treatment, adherence to medication, main follow up centre, glucometer use, hypoglycaemia, family support with diet, family support with physical activity, knowledge about HbA1c, BMI, waist-hip ratio, depression, anxiety, cognitive function, hypertension, dyslipidaemia, and macro- and micro-vascular complications. The data was summarised and presented as a mean (± standard deviation) for numerical data and a frequency and percentage for categorical data. ANOVA and chi-square tests were used to examine univariate associations between the risk factors and the level of glycaemic control. The potential risk factors with a p-value of 0.2 in the univariate analysis were entered into a multivariable logistic regression with stepwise variable selection (84). In the regression analysis, glycaemic control (the dependent factor) was categorised into controlled (HbA1c < 7%) and inadequately controlled (HbA1c ≥ 7%). The determinants were also examined for very poor glycaemic control (HbA1c ≥ 9%).

3.4.2 Data analysis methods for Chapter 5:
Macro- and Micro-vascular Complications among People with T2DM in Saudi Arabia

Part 1: Prevalence and factors related to macro- and micro-vascular diabetes complications

Macrovascular complications, including CAD, stroke, and diabetic foot, and microvascular complications, including retinopathy, neuropathy, and nephropathy, were the study outcomes. CAD was defined as the documented diagnosis of CAD, taking medication for CAD, or underwent a procedure for CAD. Stroke was defined as the documented diagnosis of an irreversible cerebrovascular accident. Diabetic foot was defined as a history of lower extremity ulcers or amputations. Retinopathy was defined as the documented diagnosis of retinopathy, or the participant had been told by an ophthalmologist that he or she had retinopathy. Diabetes peripheral neuropathy was defined as a score of seven or more using the Michigan Neuropathy Screening Instrument (85). Renal impairment was defined as estimated glomerular filtration rate ≤ 60 ml/min/1.73m², which was calculated from serum creatinine using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (86, 87). The data was summarised and presented as a mean (± standard deviation) for the numerical data and a frequency and percentage for the categorical data. A T-test or chi-square test was used to examine the univariate associations between the potential risk factors and each of the diabetes complications. The potential risk factors that were considered in the study were age, gender, level of education, location of residency, region, household income, active smoking, passive smoking, physical activity per week, sitting time per day, diabetes duration, family history of diabetes, modality of treatment, adherence to medication, hypertension, BMI, waist-hip ratio, glycaemic control (based on HbA1c), total cholesterol, LDL, HDL, and triglycerides. The risk factors with a p-value of 0.1 in the univariate analysis were entered into a multivariable logistic regression analysis with stepwise removal (84).

Part 2: Risk prediction system for diabetes complications

The outcomes of this chapter were CAD, stroke, diabetic foot, retinopathy, neuropathy, and nephropathy. These diabetes complications are defined as in Chapter 5. The risk factors that were considered were age, gender, education, smoking, physical activity per week, sitting time per day, duration of diabetes, family history of diabetes, treatment modality, adherence to medications, BMI, haemoglobin A1c (HbA1c), dyslipidaemia, and hypertension. For each complication as an outcome, the remaining complications were also considered as plausible risk factors. Simple logistic regression analysis was used to examine the univariate association of individual complications with each of the plausible risk factors. Missing data was imputed five times using the chained equation method (88, 89), creating five imputed samples. The bootstrap-receiver operating characteristic method (90) was used to develop the prediction models. The steps were as follows:

1. Bootstrap resampling with replacement was used to select 5,000 random samples from each of the imputed samples. This resulted in 25,000 bootstrap samples, each the same size as the original sample.
2. In each sample, a multiple logistic regression was run and the variables that appeared as significant were identified.
3. The percentage of times each variable appeared as significant was calculated and then ranked.
4. Variables were added to the multiple logistic regression model one by one, starting with the most to the least selected in the bootstrap analysis. Thus, the first model had only one variable, the second model had two variables, and so on. Variables that had a percentage appearance of less than 20% were dropped from the model development.
5. The area under the receiver operating characteristic (ROC) for each model was recorded.
6. A trade-off between the parsimony of the model and the optimisation of ROC was made in order to select the variables for the final prediction model (90).
7. The selected variables were then entered into multiple mixed-effect logistic regression models in order to account for variations in the locations of diabetic centres (Hofuf, Riyadh, and Jeddah).
8. First order interaction effect and multicollinearity between the risk factors were investigated.

The calibration of the selected model for each complication was tested using the decile-decile plot. A linear regression model was fitted with the deciles of the observed (dependent) and predicted (independent) outcomes to measure the amount of variation in the observed outcome explained by its predicted value (R^2). The model's discrimination was evaluated using 1,000-fold bootstrap validation, where 1,000 random samples were drawn, each of which were 90% the size of the original sample. The ROC was calculated for each sample and then averaged.

3.4.3 Data analysis methods for Chapter 6:
Obesity, Hypertension, and Dyslipidaemia among People with Type 2 Diabetes in Saudi Arabia

BMI was categorised according to the current World Health Organization (WHO) guidelines into normal (< 25.0 kg/m²), pre-obesity (25.0 – 29.9 kg/m²), and obesity (class I, II and II ≥ 30.0 kg/m²). Hypertension was defined as either the documented diagnosis of hypertension, taking antihypertension medications, or three previous high blood pressure measures (systolic ≥ 140 mmHg or diastolic ≥ 90 mmHg) (82). Dyslipidaemia was defined as taking lipid lower drugs or any of the following: cholesterol > 4.0 mmol/L, low density lipoprotein lipase (LDL) > 2.0 mmol/L, triglycerides > 2.0 mmol/L, or high density lipoprotein lipase (HDL) < 1.0 mmol/L (91). The following were considered as risk factors for all of the study's outcomes: age, gender, level of education, location of residency, region, household

income, ever smoked, physical activity per week, sitting time per day, diabetes duration, using insulin, and HbA1c ≥7.0%. BMI and high waist/hip ratio were also considered as risk factors for hypertension and dyslipidaemia, while renal impairment was considered as a risk factor for hypertension. The data was summarised and presented as a frequency and percentage and a chi-square test and a simple logistic regression were used to examine the univariate associations between potential risk factors and the comorbidities. In the regression analysis, obesity as an outcome was defined as BMI ≥ 30.0 kg/m². Missing data was imputed five times using the chained equation method, creating five imputed samples (89). Multiple logistic regression with bootstrap resampling with replacement (84, 92) was used to identify the factors associated with each of the outcomes. From each imputed sample, 5,000 samples each of the same sample size of the original sample were randomly drawn with replacements (a total of 25,000 samples). Multiple logistic regression was run in each of these samples and the percentage of times each variable appeared as a significant predictor in all of the 25,000 samples was calculated. Along with age and gender, the variables with the percentage of appearance as a significant predictor of 50% and higher were added to a multilevel mixed-effect logistic regression model that accounted for regional variation. In addition, the separate and combined effect of obesity, hypertension, and high triglycerides combined with low HDL (atherogenic dyslipidaemia) on the risk of cardiovascular complications was examined using multilevel mixed-effect logistic regression adjusted for age, gender, smoking, and duration of diabetes and accounts for regional variation.

3.4.4 Data analysis methods for Chapter 7:
Health Related Quality of Life for People with Type 2 Diabetes in Saudi Arabia

The health-related quality of life (HRQoL) was assessed using the EuroQol 5-Dimension 5-Level (EQ-5D-5L). The EQ-5D-5L is a generic preference-based health status measuring tool (93). It provides information on health status in five dimensions, namely mobility, self-care, usual activities, pain-discomfort, and anxiety-depression. Each dimension has five possible responses: no problems, slight problems, moderate problems, serious problems, and inability or extreme problems. The Visual Analogue Scale (VAS) is another part of the EQ-5D instrument in which respondents use a 20-centimetre VAS to subjectively rate their health status on that day between zero (worst imaginable health status) and 100 (best imaginable health state).

The United Kingdom scoring algorithm was used to convert the scores in the EQ-5D-5L dimensions to a single index-based utility score. The original five responses to the EQ-5D-5L dimensions were dichotomised to ‘no problems’ and ‘any problems’. The mean and standard deviation or frequency and percentages were used to summarise the data and the univariate association between the potential risk factors and the EQ-5D dimensions, utility index, and VAS score was assessed using a Chia square, t-test, or ANOVA. Based on a literature review and clinical judgment age, gender, education, household income, location of residence, smoking, physical activity per week, length of sitting time per day, duration of diabetes, number of medications, hypoglycaemia events, insulin use, BMI, HbA1c, hypertension, diabetes complications, anxiety, depression, and cognitive impairment were identified as the potential risk factors for poor HRQoL. Missing data was imputed five times using the Ice Chained Equation method (89).

To identify factors associated with the EQ-5D-5L dimensions, multiple logistic regression with bootstrap resampling with replacement was used, while multiple linear regression with bootstrap resampling with replacement was used for the utility index and VAS score (84, 92). The steps of the multiple regression with bootstrap resampling analysis were as follows: from each of the five imputed samples, 5,000 samples each of the same size as the original sample were randomly drawn with replacement, a total of 25,000 bootstrap samples were drawn for each of the study outcomes. Multiple regression was run for each of the bootstrap samples and variables that appeared as significantly associated with each of the outcomes (p-value ≤ 0.05) were recorded. The percentage of times each

variable appeared as significant in all of the 25,000 samples was calculated. The variables with a percentage of appearance as significant of 50% and higher were added to a multiple (logistic or linear) regression model along with age and gender. The adjusted odds ratio or beta coefficient, their 95% confidence interval, and the p-values for the risk factors were reported.

3.5 Definition of common risk factors

- Using the Global Physical Activity Questionnaire (GPAQ) (94), the total number of minutes of physical activity per week was categorised into ≥ 150 minutes and < 150 minutes (82).
- The number of hours spent in sitting position per day were categorized into < 10 hours and ≥ 10 hours (95).
- BMI was categorised according to the current World Health Organization guidelines into normal (< 25.0 kg/m²), pre-obesity (25.0 – 29.9 kg/m²), and obesity (class I, II and II ≥ 30.0 kg/m²)
- High waist-hip ratio was defined as a ratio > 0.96 for men and > 0.98 for women (96).
- Renal impairment was defined as estimated glomerular filtration rate (eGFR) ≤ 60 ml/min/1.73m² which was calculated from serum creatinine using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (86)
- Using the Morisky Medication Adherence questionnaire (97) medication adherence was categorized into adequate (a score of zero), and inadequate (a score of one or more)
- Based on HbA1c level, glycaemic control was categorised into good control (HbA1c < 7.0%) and poor control (HbA1c ≥ 7.0%).
- High cholesterol was defined as cholesterol > 4.0 mmol/L, high LDL was defined as LDL > 2.0 mmol/L, and high triglycerides was defined as triglycerides > 2.0 mmol/L, while low HDL was defined as HDL < 1.0 mmol/L (91).
- Hypoglycaemia symptoms last month was defined as any symptoms of mild or severe hypoglycaemia including feeling hungry, trembling or shakiness, sweating, confusion, difficulty concentrating, and loss of consciousness.
- Depression was defined as a score of three and more using the Patient Health Questionnaire-2 (PHQ-2)) (98).
- Anxiety was defined as a score of three and more using the Generalized Anxiety Disorder Scale (GAD-2)) (99).
- Impaired cognitive function was defined as a score of ⩽ 22 in the Rowland Universal Dementia Assessment Scale (RUDAS) (100).
- Macrovascular complications were defined as having one of the following: documented diagnosis of stroke (irreversible cerebrovascular accident), documented diagnosis of coronary artery disease, taking medication for coronary artery disease, underwent a procedure for coronary artery disease, or self-reported lower extremity ulcers or amputations.
- Microvascular complication was defined as having one of the following: documented diagnosis of retinopathy, the participant had been told by an ophthalmologist that he or she had retinopathy, a score of seven or more using the Michigan Neuropathy Screening Instrument (85).

Chapter 4:

Factors Associated with Poor Glycaemic Control among People with Type 2 Diabetes in Saudi Arabia

4.1 Introduction

Poor control of blood glucose level among people with diabetes is a strong independent risk factor for diabetes complications and mortality (13, 14, 101). In contrast, intensive glycaemic control can substantially lower the risk of the development and progression of diabetes complications (15, 16). The recommended target of HbA1c for adults with no pregnancy is below 7% (17). The current guidelines, however, advise that a more stringent goal of below 6.5% should be set for selected individuals, including those on lifestyle modifications and metformin only. On the other hand, a less stringent target of less than 8% is appropriate for people with limited life expectancy who have had a history of sever hypoglycaemia and advanced diabetes complications (17). Many factors can affect glycaemic control. These include age, level of education, duration of diabetes, type of medications, adherence to medication, and glucometer use, to mention a few.

Lifestyle factors also have a strong effect on glycaemic control. A healthy diet and regular physical activity lower blood glucose level and reduce the risk of cardiovascular disease, which is a leading cause of death among patients with T2DM (102-104). The current guidelines recommend the consumption of eight to 8-10 servings of fruit and vegetables daily and the performance of at least 150 minutes of moderate to vigorous intensity physical activity per week (82).

Recent studies from Saudi Arabia reported that 59.3% to 70.7% of people with T2DM had poor glycaemic control (43, 44, 105). However, the risk factors concerning this poor glycaemic control were not explored adequately in the current literature. A few studies from Saudi Arabia have focused on demographics and clinical risk factors, while lifestyle factors have been given less attention. This chapter describes a study that was conducted to examine factors associated with poor glycaemic control among people with T2DM in Saudi Arabia with an emphasis on lifestyle and other modifiable factors.

4.2 Article:

Alramadan MJ, Magliano DJ, Almigbal TH, Batais MA, Afroz A, Alramadhan HJ, et al. Glycaemic control for people with type 2 diabetes in Saudi Arabia–an urgent need for a review of management plan. BMC endocrine disorders. 2018;18(1):62.

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Glycaemic control for people with type 2 diabetes in Saudi Arabia – an urgent need for a review of management plan

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Abstract

Background: The aim of this study was to assess inadequate glycaemic control and its associated factors among people with type 2 diabetes in Saudi Arabia.

Methods: A cross-sectional study design was used. Adults with type 2 diabetes attending diabetes centres in Riyadh, Hofuf and Jeddah cities were interviewed and their anthropometrics were measured. Their medical records were also reviewed to collect information related to recent lab tests, medications, and documented comorbidities. Multivariable logistic regression were used for data analysis.

Results: A total of 1111 participants were recruited in the study. Mean age was 57.6 (±11.1) years, 65.2% of the participants were females, and mean HbA1c was 8.5 ± 1.9%. About three-fourths of participants had inadequate glycaemic control (≥ 7%). Multivariable analysis showed that age ≤ 60 years, longer duration of diabetes, living in a remote location, low household income, low intake of fruits and vegetable, low level of physical activity, lack of knowledge about haemoglobin A1c, high waist-hip ratio, low adherence to medication, and using injectable medications were independent risk factors for inadequate glycaemic control.

Conclusions: Inadequate glycaemic control is prevalent among people with type 2 diabetes in Saudi Arabia. In order to improve glycaemic control diabetes management plan should aim at controlling the modifiable risk factors which include low intake of fruits and vegetable, low level of physical activity, lack of knowledge about haemoglobin A1c, high waist-hip ratio, and low adherence to medications.

Keywords: Saudi Arabia, Diabetes, Glycaemic control

Background

Diabetes mellitus is a major worldwide public health issue. A recent study showed that the prevalence of diabetes mellitus in Saudi Arabia was 13.4% [1], which is higher than the global prevalence of 8.8% and the prevalence in the Middle East of 10.7% [2]. In fact, Saudi Arabia is among the countries with the highest prevalence of diabetes regionally and globally [2], and the prevalence of diabetes in the country is on the rise [3].

The primary goal of the management of diabetes is to maintain blood glucose levels within or close to normal ranges [4]. It is well established that elevated blood glucose level increases the risk of diabetes complications and mortality [5, 6], while intensive glycaemic control substantially lower the risk [7, 8]. Unfortunately, studies from Saudi Arabia showed that half to two-thirds of people with type 2 diabetes mellitus (T2DM) have poor glycaemic control [9–13], and the prevalence of diabetes complications is higher than the global and regional prevalence [14–16].

A few studies have examined risk factors of poor glycaemic control among people with T2DM in Saudi Arabia [9, 10, 12, 13, 17]. Many of these studies were limited to a small geographical location and included a relatively small cohort of participants. In addition, some of these studies used random or fasting blood sugar test

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to assess glycaemic control which is not as accurate as the glycated haemoglobin A1c (HbA1c) level that measures the control over a number of weeks [4]. Moreover, not all potential risk factors of poor control were explored in the previous studies. A systematic review and meta-analysis showed that among other factors, diet and physical activity were significantly associated with glycaemic control [18]. Studies from Saudi Arabia, however, did not adequately explore the effect of physical activity and eating habits.

To achieve glycaemic control goals among people with T2DM, all possible associated risk factors of inadequate control must be identified and considered in the management. The aim of this study was to assess the current status of glycaemic control and to identify risk factors for inadequate control among people with T2DM in Saudi Arabia.

Methods

This study was conducted as a part of a research project that examined the status of glycaemic control, diabetes complications and quality of life for people with T2DM in Saudi Arabia. The study methodology has been described in detail in another article [19]. Ethical approval was obtained from the Monash University Human Research Ethics Committee in Australia and the Research Ethics Committee of the Ministry of Health in Saudi Arabia. All the study procedures were carried out in accordance with the principles of the Declaration of Helsinki as revised in 2013.

Participants

The study population were people with T2DM aged 18 years and over who were followed up at diabetes centres in three major cities (Hofuf, Riyadh, and Jeddah) in Saudi Arabia. The plan was to recruit 1082 participants based on a sample size calculation with 90% power, 5% significance level, a margin of error of 2.5%, and a prevalence of poor glycaemic control of 50% [9, 20]. Inclusion criteria include documented diagnosis of T2DM, aged 18 years and above, and duration of diabetes of at least 1 year. Pregnant women and participants who did not have a HbA1c test within 1 year were excluded.

Data collection

Participants were selected randomly from consecutive attendees of the diabetic centres between May 15 and November 30, 2017. After explaining the study and obtaining informed consent in writing, participants were interviewed using a pre-tested structured electronic questionnaire through Research Electronic Data Capture (REDCap) application [19, 21]. The questionnaire collects information related to socio-demographics, lifestyle, medical history, cognitive function, anxiety and depression. Socio-demographic data include gender, date of birth, marital status, education, and income. Lifestyle data include smoking status, physical activity (Global Physical Activity Questionnaire (GPAQ) [22]), and dietary habits. The dietary habit section included 10 questions selected from the UK diabetes and diet questionnaire (UKDDQ) [23] with some modifications to make some points more suitable for the eating habits of the Saudi population. The dietary questions include the frequency of consuming fruits, vegetables, red meat, desserts, date, sugary drinks, butter, bread, and rice and the fat content of consumed milk. The dietary habit variable was measured as a scale between zero and 48, where high score means the individual is following healthy eating habits. Medical history data include the duration of diabetes, modality of treatment, follow-up centre, other comorbidities, medication adherence (the 4-item Morisky Medication Adherence questionnaire) [24], family support in regards to diet and physical activity, and peripheral neuropathy (the Michigan Neuropathy Screening Instrument) [25]. Mental status data include anxiety (Generalized Anxiety Disorder Scale (GAD-2)) [26], depression (the Patient Health Questionnaire-2 (PHQ-2)) [27], and cognitive function (Rowland Universal Dementia Assessment Scale (RUDAS)) [28]. The establishers' permission to use the above-mentioned tools was obtained.

After interviewing participants, their anthropometrics were measured and recorded. Blood pressure was measured three times after sitting for at least 10 min using the Omron BP742N5 Series Upper Arm Blood Pressure Monitor with a cuff that fits standard and large arms. Weight was measured after instructing participants to remove their shoes and outer layers of clothing. Height, waist circumference, and hip circumference were measured twice and if the measurement varied by more than 2 cm, a third measurement was taken. Waist and hip circumference were measured against thin clothing. Participants' medical records were reviewed for most recent lab test results, namely HbA1c, creatinine, cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL), and triglycerides. Information regarding currently prescribed medication, and documented diagnosis of hypertension, coronary artery disease, retinopathy, and stroke was also collected from medical records.

Operational definitions

Glycaemic control was categorised into controlled (HbA1c < 53 mmol/mol (< 7%)), partially controlled (HbA1c 53–63 mmol/mol (7% to < 8%)), and poorly controlled (HbA1C ≥ 64 mmol/mol (≥ 8%)) [4]. A HbA1c cut-off value of > 68 mmol/mol (≥ 9%) was also used to represent very poor control [29]. Using the Global Physical Activity Questionnaire (GPAQ) [22], the total number

of minutes of physical activity per week was categorised into ≥150 min and < 150 min [4]. Treatment modalities was categorized as oral tablets only, injectable medications (insulin and glucagon-like peptide-1 receptor agonists) only, and combined (oral tablets and injectable medications). Using the Morisky Medication Adherence questionnaire [24] medication adherence was categorized into adequate (a score of zero), and inadequate (a score of one or more). Hypoglycaemia was defined as episodes of mild or severe hypoglycaemia symptoms including hunger sweating, light headedness, headache, shaking, trembling, weakness, dizziness, confusion, loss of consciousness, and seizures. Family support in regards to healthy diet and physical activity was categorised as good support if healthy diet and physical activity were encouraged all the time, inadequate support if encouragement was sometimes, and poor support if family members rarely or never encouraged healthy diet or physical activity. Participants were considered unaware of HbA1c if they had not heard of HbA1c before or they did not know the recommended HbA1c target for people with diabetes. Body Mass Index (BMI) was categorised according to the current World Health Organization guidelines into normal (< 25.0 kg/m^2), pre-obesity (25.0–29.9 kg/m^2), and obesity (class I, II and II ≥ 30.0 kg/m^2). High waist-hip ratio was defined as a ratio of > 0.96 for men and > 0.98 for women [30]. Hypertension was defined as either a documented diagnosis of hypertension, taking antihypertension medications, or three previous high blood pressure readings (systolic ≥140 or diastolic ≥90) [4]. Dyslipidaemia was defined as any of the following: total cholesterol > 4.0 mmol/L (154.7 mg/dl), LDL > 2.0 mmol/L (77.3 mg/dl), triglycerides > 2.0 mmol/L (177.1 mg/dl), or HDL < 1.0 mmol/L (38.7 mg/dl) [31]. Impaired cognitive function was defined as a score of ≤22 in the Rowland Universal Dementia Assessment Scale (RUDAS) [28]. Depression was defined as a score of three and more using the Patient Health Questionnaire-2 (PHQ-2)) [27]. Anxiety was defined as a score of three and more using the Generalized Anxiety Disorder Scale (GAD-2)) [26]. Macrovascular complications were defined as having one of the following: documented diagnosis of stroke (irreversible cerebrovascular accident), documented diagnosis of coronary artery disease, taking medication for coronary artery disease, underwent a procedure for coronary artery disease, or self-reported lower extremity ulcers or amputations. Microvascular complication was defined as having one of the following: documented diagnosis of retinopathy, the participant had been told by an ophthalmologist that he or she had retinopathy, a score of seven or more using the Michigan Neuropathy Screening Instrument [25], or estimated glomerular filtration rate ≤ 60 ml/min/1.73m^2 calculated from serum creatinine using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [32, 33].

Data analysis

Stata SE version 15.0 was used for data analysis. Data were summarised and presented as a mean (± standard deviation) for numerical data and frequency and percentage for categorical data. ANOVA and chi-square tests were used to examine univariate associations between risk factors and levels of glycaemic control. Potential risk factors with a *p*-value of 0.2 from univariate analysis were entered into multivariable logistic regression with step wise variable selection [34]. In the regression analysis, glycaemic control was categorised into controlled (HbA1c < 53 mmol/mol (< 7%)) and inadequately controlled (HbA1c ≥ 53 mmol/mol (≥ 7%)). The determinants were also examined for very poor glycaemic control (HbA1c > 68 mmol/mol (≥ 9%)). A *p*-value of 0.05 or less was considered as statistical significant.

Results

A total of 1111 participants were recruited in this study; 624 participants (56.2%) were from Riyadh, 239 (21.5%) were from Hofuf, and 248 (22.3%) were from Jeddah. Four hundred and-fifty participants (40.5%) were followed up at diabetes centres only, while 125 participants (11.3%) were followed up at both diabetes centres and hospitals and 535 participants (48.2%) were followed up at both diabetes centres and primary healthcare centres. Mean age was 57.6 (±11.1) years, mean duration of diabetes was 13.9 (±8.4) years, and 65.2% (724) of the participants were females, while 34.8% (387) were males. Mean body mass index was 32.9 (±8.1) kg/m^2. Mean HbA1c was 69.4 (±15.5) mmol/mol (8.5% (±1.9%)), and 24.1% of participants had good glycaemic control (HbA1c < 53 mmol/mol (< 7%)), 21.7% had partial control (HbA1c 53–63 mmol/mol (7–7.9%)), and 54.2% had poor control (HbA1C ≥ 64 mmol/mol (≥ 8%)). None of the study participants were on insulin pump or continuous glucose monitoring.

Table 1 summarises participants' demographic and lifestyle characteristics by different levels of glycaemic control. There was a higher prevalence of poor glycaemic control among those with lower levels of education (*p*-value: < 0.001), living in a remote place (*p*-value: 0.002), and not working including house-wives (*p*-value: 0.005). A higher proportion of those aged 60 years and younger had poor glycaemic control, however, the association was not statistically significant in univariate analysis. Similarly, gender, nationality, household income, and region were not significantly related to glycaemic control. Regarding lifestyle factors, there was no difference in the mean of healthy eating habit score among different categories of glycaemic control. However, higher proportions of those with less than daily intake of fruits and vegetables had poor glycaemic control (*p*-value: 0.011). Similarly, higher proportions of those with physical activity less than

Table 1 Demographic and lifestyle characteristics by level of glycaemic control

Variable	Glycaemic control			*P*-value
	Good (HbA1c < 7.0%) *n* = 263	Partial (HbA1c 7.0% - 7.9) *n* = 237	Poor (HbA1c ≥ 8%) *n* = 592	
Age % (n)				
> 60 years	28.4 (109)	22.4 (86)	49.2 (189)	0.106
46–60 years	21.4 (123)	21.6 (124)	57.0 (327)	
< 46 years	23.1 (31)	20.2 (27)	56.7 (76)	
Gender: female % (n)				
Female	22.9 (162)	20.9 (148)	56.3 (399)	0.173
Male	26.4 (101)	23.2 (89)	50.4 (193)	
Nationality % (n)				
Saudi	23.6 (246)	21.7 (226)	54.7 (570)	0.207
Non-Saudi	34.0 (17)	22.0 (11)	44.0 (22)	
Education level % (n)				
University/college	30.9 (60)	28.9 (56)	40.2 (78)	< 0.001
Lower education level	22.6 (203)	20.2 (181)	57.2 (514)	
Location of residency % (n)				
Urban	24.3 (229)	22.9 (216)	52.8 (497)	0.002
Rural	30.4 (28)	15.2 (14)	54.4 (50)	
Remote	10.3 (6)	12.1 (7)	77.6 (45)	
Working status % (n)				
Working	23.9 (55)	20.4 (47)	55.7 (128)	0.005
Not working / house-wife	21.6 (141)	21.0 (137)	57.4 (374)	
Retired	31.9 (67)	25.2 (53)	42.9 (90)	
Household income % (n)				
≥ 6001 SAR	25.2 (148)	23.7 (139)	51.1 (300)	0.074
< 6001 SAR	22.8 (115)	19.4 (98)	57.8 (292)	
Region % (n)				
Riyadh	26.4 (161)	22.5 (137)	51.1 (311)	0.125
Jeddah	22.7 (56)	21.5 (53)	55.9 (138)	
Hofuf	19.5 (46)	19.9 (47)	60.6 (143)	
Active smoking % (n)				
Never	24.6 (230)	21.9 (205)	53.5 (501)	0.563
In the past (> 1 year)	20.7 (19)	17.4 (16)	62.0 (57)	
Current smoker	22.2 (14)	25.4 (16)	52.4 (33)	
Eating habit score (mean ± SD)	30.2 ± 4.4	29.6 ± 5.1	29.8 ± 5.1	0.451
Fruits and vegetables % (n)				
Daily	31.3 (76)	20.2 (49)	48.6 (118)	0.011
Less frequent	21.9 (186)	22.2 (188)	55.9 (474)	
Physical Activity % (n)				
≥ 150 min/week	29.0 (94)	21.9 (71)	49.1 (159)	0.032
< 150 min/week	22.0 (169)	21.6 (166)	56.4 (433)	
Sitting hours (mean ± SD)	6.1 ± 3.6	5.8 ± 3.5	6.2 ± 3.8	0.380

150 min per week had poor control (*p*-value: 0.032). Mean number of sitting hours and smoking did not differ significantly among the categories of glycaemic control.

The association between various clinical characteristics and glycaemic control are presented in Table 2. Higher proportions of poor control were among people with longer duration of diabetes (*p*-value: < 0.001), and who were taking injectable medications (*p*-value: < 0.001), followed up mainly at primary health care or diabetes centres (*p*-value: 0.019), used glucometer twice or more a week (*p*-value: 0.017), and were not aware of HbA1c or the recommended HbA1c target for people with diabetes (*p*-value: 0.016). Similarly, higher proportions of poor control were among those who had less frequent hypoglycaemia events (*p*-value: 0.016), macrovascular complications (*p*-value: 0.019), microvascular complications (*p*-value < 0.001), and high waist-hip ratio (*p*-value: 0.001). Other clinical characteristics including family history of diabetes, family support, hypertension, adherence to medication, depression, anxiety, cognitive function, dyslipidaemia, and body mass index, did not appear to have an association with glycaemic control.

Figure 1 summarises the results of the multivariable logistic regression analysis. A total of 379 participants (34.1%) had very poor glycaemic control (HbA1c > 68 mmol/mol (> 9%)). Less than daily intake of fruits and vegetables increased the risk of inadequate and very poor control by 60% and 79% respectively. Low level of physical activity was associated with 48% and 62% higher risk of inadequate and very poor control respectively. Inadequate knowledge of HbA1c was associated with 1.9-fold and 2.5-fold higher risk of inadequate and very poor control respectively. High waist-hip ratio increased the risk of very poor control by 72%, while frequent episodes of hypoglycaemia is associated with lower risk of both inadequate and very poor control. Other risk factors that were associated with inadequate and very poor control include younger age, longer duration of diabetes, remote location of residence, and using injectable medications with or without oral tablets.

Figure 2 illustrates the adjusted association between risk factors and inadequate control (HbA1c ≥ 7%) for people who were on oral tablets only as well as for those on injectable medications (with or without oral tablets). Among people on oral tablets the risk of inadequate control was higher by: 56% for low intake of fruits and vegetables, 50% for high waist-hip ratio, and by 55% for inadequate adherence to medication. Inadequate knowledge of HbA1c was associated with 2.1-fold increased risk among those on oral tablets, while frequent hypoglycaemia reduced the risk by 58%. Other risk factors of inadequate control among those on oral tablets include younger age and longer diabetes duration. For participants who were on injectable medications, low level of physical activity increased the risk of inadequate control by 2.1-folds, while high waist-hip ratio reduced the risk by 61%. Other risk factors of inadequate control among those on injectable medications were lower household income and followed up mainly at diabetes centres, while people from Jeddah appeared to have lower risk.

Discussion

In this current multi-centre study we have assessed the status of glycaemic control and its associated factors among people with T2DM attending diabetes centres in Saudi Arabia. One important finding was that only 24.1% of people with T2DM achieved the recommended HbA1c level of less than < 53 mmol/mol (< 7%), while the majority (75.9%) did not attained this target. Our findings, however, were comparable to the findings of recent studies from Saudi Arabia and other Arabian Gulf Countries [10–13, 35–39]. Despite quality health care services and various antidiabetic medications that are available for people with diabetes at no cost, the majority of people with T2DM in Saudi Arabia continue to have inadequate glycaemic control. A possible explanation could be the embracing of unhealthy lifestyle.

Sedentary lifestyle and the consumptions of processed, energy condensed, and fat-rich food have led to the increased prevalence of obesity and diabetes, and have made it difficult for people with diabetes to control their blood sugar. Recent studies showed that more than half of the Saudi population consumed less than one serving of fruits and vegetables per day [40], and 96.1% of them were physically inactive [41]. Furthermore, 51.0% of the adult Saudi population were either overweight or obese [42] and the prevalence of overweight and obesity among people with diabetes was significantly higher than the general population in the country [43, 44]. In addition, studies from Saudi Arabia found an association between low physical activity and poor glycaemic control [10, 13, 35], while a study from Bahrain [45], a country that shares boundaries and similar culture with Saudi Arabia, showed an association between unhealthy eating habits and higher HbA1c among people with T2DM.

Healthy eating habits and regular physical activity are key components in the management of T2DM. The current guidelines for people with diabetes recommend 8–10 servings of fruits and vegetables every day [4]. A serving of fruits is equal to a medium-size apple, orange, or banana, while a serving of vegetables is half a cup of corn, carrot or leafy vegetables. The guidelines also recommend at least 150 min of moderate to vigorous intensity physical activity per week [4]. The majority (77.5%) of participants in this study, however, did not eat fruits and vegetables daily, which has increased their risk of

Table 2 Clinical characteristics by level of glycaemic control

Variable	Glycaemic control			*P*-value
	Good (HbA1c < 7.0%) *n* = 263	Partial (HbA1c 7.0% - 7.9) *n* = 237	Poor (HbA1c ≥ 8%) *n* = 592	
Diabetes Duration % (n)				
≤ 10 years	34.7 (143)	25.5 (105)	39.8 (164)	< 0.001
> 10 years	17.5 (119)	19.4 (132)	63.0 (428)	
Family history of diabetes % (n)				
Yes	22.9 (187)	22.2 (181)	54.9 (447)	0.325
No	27.2 (75)	20.3 (56)	52.5 (145)	
Modality of treatment				
Oral tablets	36.4 (219)	25.8 (155)	37.9 (228)	< 0.001
Injectable	9.9 (22)	18.5 (41)	71.6 (159)	
Oral and injectable	7.9 (21)	15.4 (41)	76.8 (205)	
Main follow up centre % (n)				
Hospital	34.2 (42)	22.0 (27)	43.9 (54)	0.019
Primary care centre	24 (125)	23.0 (120)	53.0 (276)	
Diabetes centre	21.3 (95)	20.1 (90)	58.6 (262)	
Glucometer use % (n)				
Once or more a week	21.4 (145)	21.7 (147)	57.0 (387)	0.017
Less than once a week	28.6 (118)	21.8 (90)	49.6 (205)	
Hypoglycaemia events % (n)				
None	26.9 (170)	21.1 (133)	52.0 (328)	0.016
1–5 times	18.2 (71)	22.8 (89)	59.1 (231)	
6 times and more	30.4 (21)	21.7 (15)	47.8 (33)	
Medication adherence % (n)				
Adequate	26.0 (165)	22.4 (142)	51.7 (328)	0.110
Inadequate	21.4 (98)	20.8 (95)	57.8 (264)	
Family support with diet % (n)				
Good	23.5 (103)	22.2 (97)	54.3 (238)	0.621
Inadequate	23.0 (73)	23.9 (76)	53.1 (169)	
Poor	25.9 (87)	19.1 (64)	55.1 (185)	
Family support with physical activity % (n)				
Good	21.4 (66)	21.0 (65)	57.6 (178)	0.460
Inadequate	23.2 (74)	23.2 (74)	53.6 (171)	
Poor	26.5 (123)	21.1 (98)	52.4 (243)	
knowledge about HbA1c % (n)				
Aware	29.5 (103)	20.3 (71)	50.1 (175)	0.016
Not aware	21.5 (160)	22.3 (166)	56.1 (417)	
Body mass index % (n)				
Underweight/normal	22.7 (25)	20.9 (23)	56.4 (62)	0.075
Pre-obesity	26.4 (78)	26.4 (78)	47.1 (139)	
Obesity (class I – III)	23.3 (158)	20.0 (136)	56.7 (385)	
Waist-hip ratio % (n)				
Normal	26.4 (144)	24.8 (135)	48.8 (266)	0.001
High (male: > 0.96, female: > 0.98)	22.1 (96)	17.5 (76)	60.5 (263)	

Table 2 Clinical characteristics by level of glycaemic control *(Continued)*

Variable	Glycaemic control			*P*-value
	Good (HbA1c < 7.0%) *n* = 263	Partial (HbA1c 7.0% - 7.9) *n* = 237	Poor (HbA1c ≥ 8%) *n* = 592	
Depression % (n)				
No	24.1 (220)	22.3 (203)	53.6 (489)	0.563
Yes	23.9 (43)	18.9 (34)	57.2 (103)	
Anxiety % (n)				
No	24.2 (224)	22.4 (207)	53.4 (493)	0.328
Yes	23.2 (39)	17.9 (30)	58.9 (99)	
Cognitive function % (n)				
Intact	24.3 (169)	21.4 (149)	54.2 (377)	0.709
Impaired	22.1 (59)	23.2 (62)	54.7 (146)	
Dyslipidaemia % (n)				
No	29.6 (45)	23.0 (35)	47.4 (72)	0.142
Yes	23.2 (218)	21.5 (202)	55.3 (520)	
Hypertension % (n)				
No	22.8 (74)	20.3 (66)	56.9 (185)	0.503
Yes	24.6 (189)	22.3 (171)	53.1 (407)	
Macrovascular complications				
No	25.3 (199)	23.1 (182)	51.6 (406)	0.019
Yes	21.0 (64)	18.0 (55)	61.0 (186)	
Microvascular complication				
No	29.4 (146)	23.7 (118)	46.9 (233)	< 0.001
Yes	19.7 (117)	20.0 (119)	60.3 (359)	

inadequate and very poor glycaemic control. Similarly, more than two-thirds of participants (70.5%) did not achieve the recommended length of time of physical activity per week even though walking for transportation and physical activities at work were included in measuring it. Results of this current study also showed that a low level of physical activity was an independent risk factor for inadequate and very poor glycaemic control. Continuous education programs emphasising the role of lifestyle modification in controlling blood glucose level will be of great benefit for people with T2DM in Saudi Arabia.

Previous studies have shown that the more knowledge of diabetes a person has the more likely that he or she will have lower HbA1c level [17, 46]. Though the participants' knowledge of the disease was not evaluated in this study, their awareness of HbA1c and its recommended level for people with diabetes was assessed as a proxy for knowledge of the disease. Only 31.9% of participants were aware of HbA1c and knew the recommended target (< 53 mmol/mol (< 7%)). The remaining participants either have not heard of HbA1c before (32.0%) or did not know the recommended HbA1c target (36.1%), which was associated with increased risk of inadequate and very poor control after adjustment for other risk factors. This finding is supported by the results of randomised control trials which showed that knowledge of actual and target HbA1c was associated with a significant reduction in HbA1c levels [47, 48]. In order to improve glycaemic control, physicians and health educators should ensure that people with diabetes are fully aware of their actual as well as the target HbA1c they should achieve.

Similar to studies conducted in the Arabian Gulf [49, 50] and other countries [18, 51] we found that younger age groups (≤60 years) were at higher risk of inadequate glycaemic control. Younger people are more likely to be affected by the change in lifestyle and less likely to be adherent to a management plan because of active occupational and social life [52]. Old people, in contrast, are less likely to be affected by the change in lifestyle and more likely to adhere to a management plan because they might be more concerned about their health, especially when they start to have comorbidities and complications [49]. Because of the beneficial effect of optimal glycaemic control on delaying complications, improving quality of life, and extending life expectancy among young

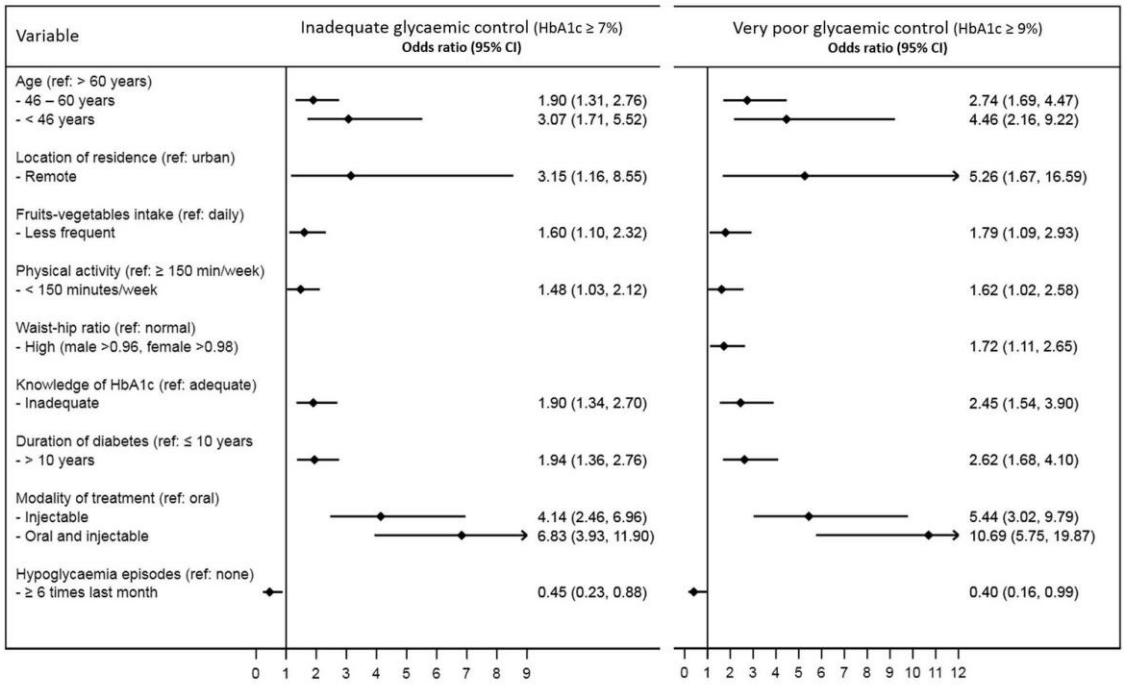

Fig. 1 Adjusted association between risk factors and inadequate (HbA1c ≥ 7%) and very poor (HbA1c ≥ 9%) glycaemic control. Variables introduced in the multivariable analysis were age, gender, education level, location of residence, work status, income, region, intake of fruits and vegetables, physical activity, duration of diabetes, treatment modality, glucometer use frequency, hypoglycaemia, follow-up location, adherence to medication, awareness of HbA1c, BMI, waist-hip ratio, macrovascular complications, microvascular complications and dyslipidaemia

people with diabetes [53], the management should aim at tight control once the diagnosis is made.

Another concerning finding of this study is that while the mean age of participants was 57.6 (±11.1) years (median: 57.8, 25th percentile: 51.8, 75th percentile: 63.9 years), they have a relatively long mean duration of diabetes of 13.9 (±8.4) years (median: 13.0, 25th percentile: 6.0, 75th percentile: 20 years). This indicates that the majority of people acquired diabetes in their early 40s. Early onset T2DM is associated with poor glycaemic control and a higher risk of comorbidities and complications [54]. With longer duration of T2DM, on the other hand, there is usually further deterioration of the function of the pancreas and the body's resistance to insulin increases, which makes it more difficult to control blood glucose level. The likelihood of acquiring diabetes complications also increases with longer duration, and complications can negatively affect the control either directly through inflammation and disturbance of the body's metabolism and indirectly through the effect of poly-pharmacy, anxiety, depression and stress. To prevent or delay diabetes and its complications, the healthcare system in Saudi Arabia should fully activate the screening programs and establish an intensive management protocols to identify and treat people at risk of diabetes.

Though BMI did not appear to affect glycaemic control, we found that a high waist-hip ratio was an independent risk factor for inadequate and very poor control. Similar findings were also observed in studies from Japan and the United States [55, 56]. In addition, compared to BMI, a high waist-hip ratio was found to have stronger association with cardiovascular disease among people with type 2 diabetes [57]. Waist-hip ratio is a more accurate measure of central obesity which is strongly linked with T2DM, poor glycaemic control, and cardiovascular disease [58]. Therefore, similar to BMI, waist-hip ratio should be measured and recorded for people with diabetes with every follow up visit, and health care providers should raise the awareness of people with diabetes about high waist-hip ratio and the risk associated with it.

We found that living in a remote village was a strong predictor of inadequate and very poor glycaemic control. People living in remote villages are likely to have a low level of formal education and are likely to have less access to fresh healthy food options. Because of accessibility issues, they limit their follow-up to the local primary health care centre and may not visit a specialised diabetes clinic

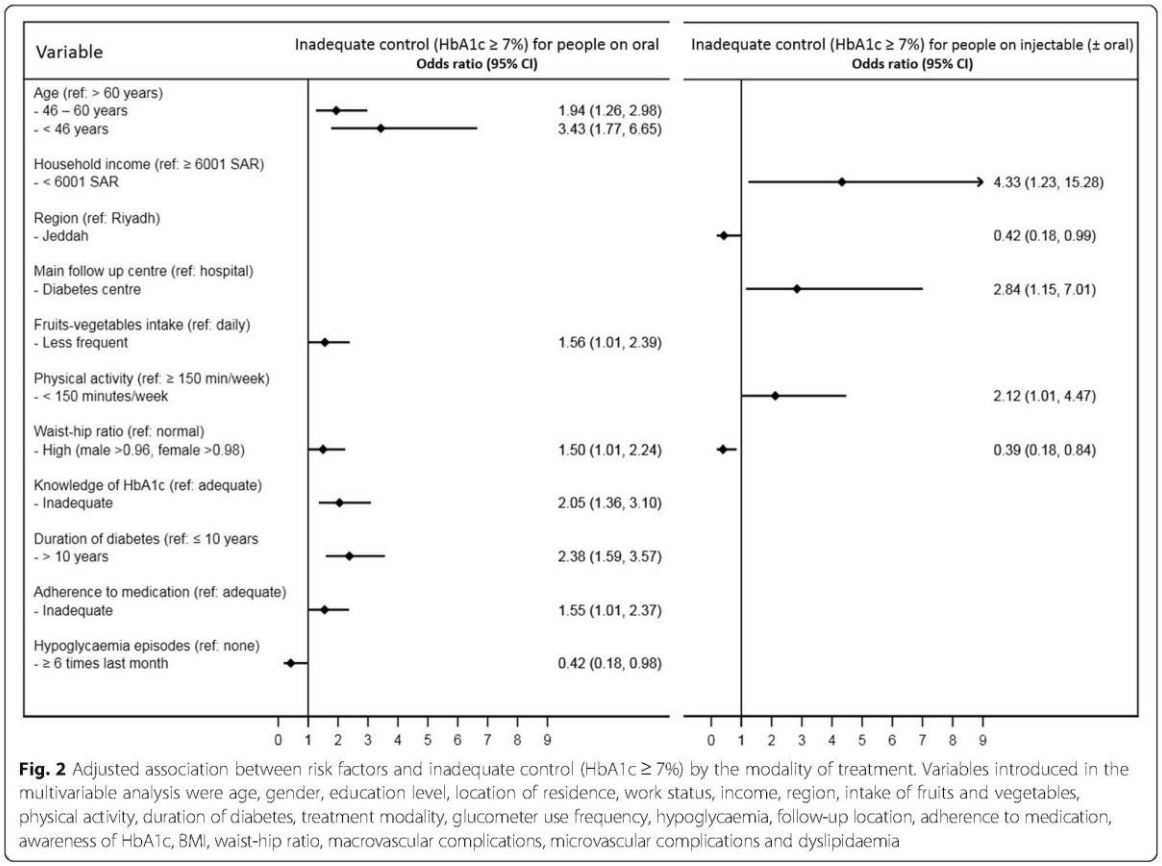

Fig. 2 Adjusted association between risk factors and inadequate control (HbA1c ≥ 7%) by the modality of treatment. Variables introduced in the multivariable analysis were age, gender, education level, location of residence, work status, income, region, intake of fruits and vegetables, physical activity, duration of diabetes, treatment modality, glucometer use frequency, hypoglycaemia, follow-up location, adherence to medication, awareness of HbA1c, BMI, waist-hip ratio, macrovascular complications, microvascular complications and dyslipidaemia

or centre until the disease has progressed and they acquire complications. To improve the control among this susceptible group, the healthcare system should provide special diabetes education programs for healthcare providers working at remote places, and motivate them to use the online continuous education programs that are currently available and accredited by the Saudi Health System. General physicians working on remote sittings should also be provided with timely hotline or email access to specialists including endocrinologists, ophthalmologist and podiatrist. Patients, on the other hand, should have frequent teleconference or phone calls by diabetes educators, dietitians and other allied health professionals if these healthcare professionals are not assigned to the remote place where patients live.

Similar to other previous studies [18, 49, 50], our results showed that the use of injectable medications was a strong predictor for inadequate control. It is of concern that even after management with insulin, which is highly effective modality of treatment [59], a large proportion of people continued to have high blood glucose level. Low adherence to injectable medication regimen because of social stigmata, interference with daily activity, and fear of hypoglycaemia, have been suggested to increase the risk of poor control among people using injectable medications [60]. In Addition, the progression of the disease, weight gain related to insulin use, and polypharmacy can also contribute to poor glycaemic control among people with T2DM who are on injectable medications [61].

Our findings support the previous study that showed an association between inadequate glycaemic control and low income as well as low adherence to medications [18, 52, 62]. Low income decreases the likelihood of adherence to lifestyle modifications and treatment regimen [62], and low adherence to management plan is a known risk factors for poor glycaemic control [18, 52].

The association between hypoglycaemia and glycaemic control is of interest. Our findings showed that people with infrequent symptoms of hypoglycaemia were at higher risk of poor glycaemic control compared to those who had frequent symptoms of hypoglycaemic. This may indicate that while an intensive treatment regimen improve glycaemic control, it may come at the cost of frequent hypoglycaemia symptoms. Severe hypoglycaemia is associated with lower productivity, reduced quality of life, and a higher risk of anxiety, depression and mortality [63, 64]. Therefore,

hypoglycaemia should be prevented, and the treatment should aim at achieving the lowest HbA1c level without severe hypoglycaemia episodes and a minimum number of mild hypoglycaemia symptoms [65].

The strength of this study lays on the relatively large sample size that was recruited from multiple centres from different regions of Saudi Arabia. The consideration of several potential risk factors and the use of a validated electronic questionnaire, which reduce data errors, also add strength to this study. This study, however, has some limitations. Cross-sectional study design lack temporality and causality cannot be inferred. Another limitation is that information regarding individualised glycaemic control targets could not be collected because it was not documented in participants' medical records. Therefore, a HbA1c cut off point of 7% was selected to categorise adequate control which is too strict for old people with longer duration of the disease and those who have advanced cardiovascular disease [4]. In addition, we could not investigate the effect of new anti-hyperglycaemic agents such as the glucagon-like peptide-1 (GLP-1) receptor agonists on glycaemic control because only a very small number of participants in our database were using them. Nonetheless, this study clearly revealed the burden of inadequate glycaemic control among people with T2DM in Saudi Arabia and its associated risk factors.

Conclusion

Inadequate glycaemic control is a common and widespread problem among people with T2DM in Saudi Arabia. Healthcare providers should undertake a patient-centred approach and individualise management strategies with consideration to all identified risk factors for inadequate control. Continuous education programs should also be implemented to raise the awareness of the disease and the importance of lifestyle modification. The healthcare system should prioritise diabetes prevention strategies through active screening and intensive management of people at risk. The health system should also take special measures to improve glycaemic control for people with diabetes living at remote locations. Future research should investigate the effectiveness of education programs targeting people with diabetes and barriers to adhering to lifestyle modifications.

Abbreviations

BMI: Body Mass Index; eGFR: Estimated glomerular filtration rate; HbA1c: Glycated haemoglobin A1c; HDL: High density lipoprotein; LDL: Low density lipoprotein; T2DM: Type 2 diabetes mellitus

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Author contributions

All authors were involved in the conception and design of the study. MJA, HJA, WFM, and AMA contributed to the acquisition of data. MJA, DJM, AA, BB, THA and MAB contributed to data analysis and interpretation of results. MJA and BB drafted the manuscript. All authors critically reviewed the manuscript and approved the final version.

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Availability of data and materials

The datasets generated during and analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Ethical approval was obtained from the Monash University Human Research Ethics Committee in Australia and the Research Ethics Committee of the Ministry of Health in Saudi Arabia. Written informed consent was obtained from all the study participants.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Chapter 5:

Macro- and Microvascular Complications among People with T2DM in Saudi Arabia

5.1 Part 1: Prevalence and factors related to macro- and micro-vascular diabetes complications

5.1.1 Introduction

People with diabetes are at high risk of developing a number of diabetes related complications. Among these complications, macro- and micro-vascular complications are a leading cause of morbidity, reduced quality of life, and mortality. Diabetes retinopathy is the main cause of loss of vision in working-age adults (1) and diabetic nephropathy is a leading cause of renal failure (106). Diabetic foot is a leading cause of lower limb amputation (106) and cardiovascular disease is the leading cause of death in people with diabetes (1).

Lifestyle modifications play an important role in preventing diabetes complications. It is well established that regular physical activity improves glycaemic control and lowers blood lipids, blood pressures, and body weight, thus indirectly lowering the risk of diabetes complications (107-109). Studies also showed that physical activity has a direct effect on lowering the risk of diabetes complications that is independent of its effect on cardiovascular disease risk factors (68, 110). This is why all diabetes management guidelines recommend that people with diabetes undertake regular physical activity (1, 17).

According to previous studies from Saudi Arabia, macro- and micro-vascular complications are prevalent in people with T2DM in the country (50, 54-63). However, the risk factors of these major diabetes complications were not explored adequately and little attention was paid to behavioural lifestyle factors. In this chapter, the aim was to reassess the prevalence of diabetes macro- and micro-vascular complications in people with T2DM in Saudi Arabia and to explore their correlated factors, including physical inactivity and longer sitting time.

5.1.2 Article:

Alramadan MJ, Magliano DJ, Alhamrani HA, Alramadan AJ, Alameer SM, Amin GM, et al. Lifestyle factors and macro-and micro-vascular complications among people with type 2 diabetes in Saudi Arabia. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2018;13(1):484-91.

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Original Article

Lifestyle factors and macro- and micro-vascular complications among people with type 2 diabetes in Saudi Arabia

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ABSTRACT

Aims: The aim of this study is to identify lifestyle factors that place people with type 2 diabetes in Saudi Arabia at a greater risk of macro- and microvascular complications.
Methods: A survey was conducted among adults with type 2 diabetes who attended diabetes centres in three major cities in Saudi Arabia. Participants were interviewed and their medical files were reviewed for lab test results and documented comorbidities. Associations between complication and lifestyle factors were assessed using multiple logistic regression analysis.
Results: A total of 1121 participants were recruited. Mean age was 57.6 (±11.1) years. The prevalence of coronary artery disease, diabetic foot, and stroke was 17.0%, 13.1% and 3.7%, and that of neuropathy, renal impairment, and retinopathy was 20.3%, 14.5%, and 42.8% respectively. Lifestyle factors associated with one or more of the complications were inadequate physical activity, longer sitting time, obesity, current or past smoking, passive smoking, hypertension, poor glycaemic control, low HDL and high triglycerides.
Conclusions: Diabetes complications are common among people with type 2 diabetes in Saudi Arabia. Life style factors such as inadequate physical activity, longer sitting time, obesity, smoking, hypertension, and poor control of blood glucose and lipids should be assimilated into complications prevention program.

1. Introduction

Saudi Arabia has experienced enormous economic and lifestyle changes over the past few decades. Along with these changes there was a rapid increase in the prevalence of diabetes mellitus which is currently a major public health issue in the country. A recent report estimated that the prevalence of diabetes among adults in Saudi Arabia was 17.7%, which was considerably higher than the global (8.8%) and the regional (10.7%) prevalence and it places Saudi Arabia among the countries with the highest prevalence of the disease [1].

Diabetes complications is another concerning issue in Saudi Arabia. Even though, people with diabetes in Saudi Arabia have free access to both good quality healthcare services and medications, the prevalence of microvascular (retinopathy, neuropathy, and nephropathy) and macrovascular complications (coronary artery disease (CAD), stroke, and peripheral vascular disease) were high among them [2–9]. Diabetes complications reduces the quality of life and life expectancy of the affected people and creates an economic, emotional and social disease burden. A study from Saudi Arabia estimated that in 2014 the annual cost of treating a person with diabetes with complications was US$11,706.9 which is four-fold higher than the cost of treatment for a person without

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complications (US$2746.7) [10]. Prevention or delay of complications can be achieved by early detection and changing of lifestyle risk factors. Thus, it is important to identify lifestyle risk factors for complications for people with type 2 diabetes in Saudi Arabia.

A number of studies from Saudi Arabia investigated traditional risk factors for macro- and micro-vascular diabetes complications [2,4–9,11,12]. The majority of these studies found that gender, older age, longer duration of diabetes, use of insulin, and poor glycaemic control were associated factors [2,4–9,11,12], while a few of them showed an association of diabetes complications with uncontrolled hypertension, smoking and dyslipidaemia [8,9,12]. Some of these studies, however, were underpowered and limited to a single centre or a small geographical location. Moreover, studies outside Saudi Arabia reported an association between complications and lifestyle factors such as physical inactivity as well as longer sitting periods [13,14]. None of the previous studies from Saudi Arabia, however, have evaluated this association.

Given that the prevalence of type 2 diabetes and its related complications are high in Saudi Arabia, do these patients have some specific traditional risk factors which could explain the observed increase in the individual macro- and microvascular complications. Thus, the aim of this study was two-fold. Firstly, to measure the prevalence of macro- and micro-vascular complications among people with Type 2 diabetes mellitus (T2DM) in Saudi Arabia. Secondly, to identify the lifestyle and other modifiable risk factors for these complications. The finding of this study will be useful for patients, healthcare providers and health policy makers in developing individual patient level management plan.

2. Methods

2.1. Participants

The study population consisted of adults 18 years and above with T2DM who were followed up at diabetes centres in Hofuf, Riyadh, and Jeddah cities in Saudi Arabia. A sample size of 1082 participants was calculated for another outcome in this study [15]. Based on the reported prevalence of macro- and microvascular complications in the previous studies [2,5,7,9], a sample size of 1082 participants maintains a power higher than 90% with a significance level of 0.05. Inclusion criteria of participants includes documented diagnosis of T2DM, aged 18 years and above, and a duration of diabetes of at least one year. Pregnant women and participants who did not have haemoglobin A1c (HbA1c) test within the past one year were excluded. Both the Monash University Human Research Ethics Committee in Australia and the Research Ethics Committee of the Ministry of Health in Saudi Arabia approved this research project. All the study procedures were carried out in accordance with the principles of the Declaration of Helsinki as revised in 2013.

2.2. Data collection

Full description of the data collection tool and procedure were detailed in a previous article [15]. A systematic random sample of participants were recruited from the attendees of diabetes centres between May 15 and November 30, 2017. Informed consent was obtained from all participants, and they were surveyed by trained data collectors using interview administer questionnaire. The questionnaire was filled online through Research Electronic Data Capture (REDCap) application [16]. The collected data include socio-demographics, smoking, physical activity (Global Physical Activity Questionnaire (GPAQ) [17]), medical history, adherence to medication [18] and neuropathy (Michigan Neuropathy Screening Instrument [19]). The establishers' permission to use the above-mentioned tools was obtained. After interviewing participants, their blood pressure, weight, height, waist circumference, and hip circumference were measured in a standardized way [15]. Medical records were reviewed for most recent HbA1c, creatinine, cholesterol, high density lipoprotein lipase (HDL), low density lipoprotein lipase (LDL), and triglycerides. Information regarding currently prescribed medication, and documented diagnosis of hypertension, CAD, stroke and retinopathy was also collected from medical records.

2.3. Data analysis

Data analysis was carried out using Stata SE version 15.0. Data were summarised and presented as a mean (±standard deviation) for numerical data and frequency and percentage for categorical data. T-test and chi-square test were used to examine univariate associations between potential risk factors and CAD, diabetic foot, stroke, neuropathy, retinopathy, and renal impairment. Risk factors with a p-value of 0.1 in univariate analysis were entered into multivariable logistic regression analysis with stepwise removal [20]. A p-value of 0.05 or less was considered as statistical significant. Definitions of outcomes and risk factors are available in the appendix.

3. Results

3.1. General characteristics

Out of 1121 participants, 10 (0.9%) were excluded as they had substantially incomplete records. Thus, the records of 1111 participants were used in the analysis. Mean age was 57.6 (±11.1) years, and mean duration of diabetes was 13.9 (±8.4) years. 65.2% (724) of the participants were female and 34.8% (387) were male. Mean body mass index was 32.9 (±8.1) kg/m^2. The overall prevalence of macrovascular complication was 28%, and that of microvascular complication was 54.6%. The prevalence of CAD, stroke and diabetic foot was respectively 17%, 13.1% and 3.7%, and that of diabetic neuropathy, renal impairment, and retinopathy was 20.3%, 14.5% and 42.8% respectively.

3.2. Univariate association between risk factors and complications

Table 1 summarises participants' demographic and lifestyle characteristics for each of the macro- and micro-vascular complications. Longer sitting time was significantly associated with higher prevalence for all complications. Similarly, physical activity less than 150 min per week was associated with all complications except CAD. Other risk factors that were associated with one or more diabetes complications include older age, male gender, lower level of education, lower household income, region of living, and active as well as passive smoking (defined as no current smoking but exposed to the smoking of others).

Clinical characteristics for each macro- and micro-vascular complications are summarised in Table 2. Longer duration of diabetes was associated with all complications. With the exception of stroke, all other complications were more prevalent among those who were taking insulin. The prevalence of CAD, stroke, renal impairment and retinopathy was higher among people with hypertension. Other risk factors that were associated with one or more of the complications include positive family history of diabetes, low adherence to medications, high body mass index, high waist-hip ratio, poor glycaemic control, low HDL, and high triglycerides. Normal cholesterol and LDL were associated with higher prevalence of CAD, stroke and renal impairment.

Table 1
Demographic characteristics by type of macro- and micro-vascular complications.

Variables	CAD 17.0% (n = 189)		Diabetic foot 13.1 (n = 145)		Stroke 3.7% (n = 41)		Neuropathy 20.3% (n = 202)		Renal impairment 14.5% (n = 161)		Retinopathy 42.8% (n = 476)	
	%	p-value	%	%	%	%	p-value	p-value	p-value	p-value	%	p-value
Age % (n)												
<60 years	13.0	<0.001	12.8	0.847	2.8	0.146	20.5	0.995	8.8	<0.001	38.5	<0.001
61–70 years	23.9		14.0		4.7		19.9		20.3		46.8	
>71 years	21.6		12.2		5.8		20.3		29.5		55.4	
Gender: % (n)												
Female	15.6	0.088	13.1	0.924	4.1	0.566	12.8	<0.001	14.2	0.732	44.6	0.103
Male	19.6		12.9		3.5		25.0		15.0		39.5	
Education level % (n)												
University/college	13.1	0.064	10.6	0.111	1.5	0.031	9.9	<0.001	13.1	0.037	30.8	<0.001
Intermediate/secondary	15.1		11.1		2.6		16.2		11.1		39.0	
Illiterate/primary	19.5		15.1		5.1		26.8		17.1		49.4	
Region												
Hofuf	30.5	<0.001	23.9	<0.001	5.9	0.107	28.3	0.003	20.9	0.006	46.4	0.397
Jeddah	10.5		12.9		2.4		17.8		12.9		43.2	
Riyadh	14.4		9.0		3.4		17.9		12.7		41.4	
Location of residence % (n)												
Urban	16.1	0.154	12.3	0.102	3.9	0.280	19.4	0.086	14.6	0.973	42.1	0.231
Rural	23.2		15.8		4.2		22.6		13.7		43.2	
Remote	21.0		21.0		0.0		31.5		14.5		53.2	
Household income % (n)												
6000 SAR and less	19.1	0.115	17.5	<0.001	4.5	0.381	29.3	<0.001	11.0	0.085	36.1	0.003
6001–9000 SAR	17.4		7.7		3.5		14.6		16.2		41.7	
9001 SAR and over	13.6		10.4		2.7		11.6		16.0		47.9	
Active smoking % (n)												
Never	15.8	0.013	12.0	0.006	3.6	0.507	21.0	0.080	14.1	0.409	43.2	0.573
In the past (>one year)	27.7		16.0		3.2		11.7		19.2		43.6	
Current smoker	19.1		25.4		6.4		23.8		14.3		36.5	
Passive smoking % (n)												
No	17.0	0.915	12.2	0.027	3.7	0.569	19.1	0.020	14.9	0.376	42.5	0.581
Yes	17.3		18.6		44.5		27.7		12.2		44.9	
Physical Activity % (n)												
Active (>150 min/week)	13.7	0.059	8.5	0.004	1.8	0.033	12.5	<0.001	10.1	0.007	31.4	<0.001
Inactive (<150 min/week)	18.4		14.9		4.5		23.7		16.4		47.6	
Sitting hours (mean ± SD)	No: 5.8 ± 3.4 Yes:7.3 ± 3.6	<0.001	No: 5.9 ± 3.4 Yes: 7.2 ± 4.7	<0.001	No: 6.0 ± 3.5 Yes: 7.7 ± 5.5	0.004	No: 5.7 ± 3.2 Yes: 6.6 ± 4.4	<0.001	No: 5.8 ± 3.4 Yes: 7.7 ± 4.4	<0.001	No: 5.8 ± 3.4 Yes: 6.5 ± 3.9	0.001

3.3. Multivariable association between risk factors and macrovascular complications

Table 3 shows the results of the multivariable logistic regression analysis with stepwise selection for the association between each of the macrovascular complications and different risk factors. Hypertension and obesity increased the odds of CAD by 3.4-fold and 1.7-fold respectively, while every one hour of sitting per day increased the odds by 10%. The odds of CAD was also higher for male gender, older age, longer duration of diabetes, while using insulin alone or insulin with oral tablets increased the odds by 2.2-fold and 1.9-fold respectively. The adjusted odds of diabetic foot was 2.7-fold and 2-fold higher for current smoking and past smoking respectively, while passive smoking increased the odds by 1.9-fold. Low level of physical activity was associated with 90% increased odds of diabetic foot. Other risk factors of diabetic foot include use of insulin, and low household income. For both CAD and Diabetic foot, increased odds was observed among people living in the Hofuf region. In regards to stroke, hypertension increased the odds by 4.9-fold, while lower level of education was associated with 2.6-fold higher odds. The odds of stroke was also 2.2-fold higher for male gender, while for every one hour of sitting per day the risk increased by 10%.

3.4. Multivariable association between risk factors and microvascular complications

The results of the multivariable logistic regression analysis for microvascular complications of neuropathy, retinopathy and renal impairment and various risk factors are presented in Table 4. The adjusted odds of neuropathy was 2.7-fold higher for current smokers, 1.5-fold higher for low physical activity, and 1.1-fold higher for every one hour of sitting. Both obesity and very poor glycaemic control (HbA1c ≥ 9%) were associated with 50% increase in the odds of neuropathy, while Low household income increased the odds by 2.4-fold. Other risk factors of neuropathy include male gender, family history of diabetes and use of insulin. In regards to renal impairment, hypertension increased the odds by 2.2-fold, while low HDL and high triglycerides increased the odds by 1.9-fold and 1.8-fold respectively. Every one hour of sitting increased the risk of renal impairment by 10% and use of insulin alone increased the odds by 80%. Older age was also a strong predictor of renal impairment and patients living in Hofuf region and with household income between 6001 and 9000 Saudi Riyals had higher odds. Longer duration of diabetes increased the odds of retinopathy by 2.3–fold, and the risk was 1.5-fold higher for age above 70 years. The odds of retinopathy was also increased by 40% for patients with hypertension, 60% for low level of physical activity, and 90% for insulin users. Other risk factors of retinopathy were lower level of education, and family history of diabetes.

4. Discussion

This multicentre study provided an update regarding the prevalence of diabetes macro- and micro-vascular complications and the factors related to them in Saudi Arabia. Our results showed that

Table 2
Clinical characteristics by type of macro- and micro-vascular complications.

Variables	CAD 17.0% (n = 189)		Diabetic foot 13.1 (n = 145)		Stroke 3.7% (n = 41)		Neuropathy 20.3% (n = 202)		Renal impairment 14.5% (n = 161)		Retinopathy 42.8% (n = 476)	
	%	p-value	%	p-value	%	p-value	%	p-value	%	p-value	%	p-value
DM Duration % (n)												
<10 years	10.7	<0.001	9.5	0.001	2.1	0.033	15.0	0.001	8.6	<0.001	26.4	<0.001
>10 years	20.9		15.1		4.6		23.7		18.0		52.9	
Family history of diabetes % (n)												
No	14.3	0.158	11.4	0.374	2.9	0.391	15.6	0.028	14.6	0.900	38.2	0.068
Yes	18.0		13.5		4.0		22.0		14.3		44.5	
Modality of treatment												
Oral tablet	11.0	<0.001	8.3	<0.001	3.1	0.170	14.0	<0.001	10.1	<0.001	32.6	<0.001
Insulin	25.9		18.8		5.8		26.4		22.8		54.5	
Oral and insulin	23.3		18.9		3.3		29.8		17.4		56.7	
Medication adherence												
Good adherence	18.8	0.119	10.9	0.023	4.0	0.761	18.5	0.258	14.4	0.894	43.6	0.871
Moderate adherence	13.7		15.4		3.4		22.5		14.3		42.2	
Poor adherence	17.9		18.9		2.8		23.3		16.0		41.5	
Hypertension												
No	6.3	<0.001	10.8	0.147	0.9	0.001	17.2	0.097	6.0	<0.001	33.9	<0.001
Yes	21.6		14.0		4.9		21.7		18.1		46.7	
Body mass index % (n)												
Underweight/normal	11.5	0.014	13.3	0.075	0.9	0.244	14.0	0.001	11.5	0.654	43.4	0.402
Pre-obesity	13.3		9.3		4.0		14.5		14.3		39.3	
Obesity (class I – III)	19.6		14.6		4.1		23.9		14.7		43.9	
Waist/hip ratio % (n)												
Normal	15.9	0.412	12.3	0.284	2.7	0.074	20.3	0.924	11.6	0.034	41.1	0.536
High	17.9		14.7		4.8		20.1		16.3		43.0	
Glycaemic control (HbA1c)												
Good Control (<7%)	15.6	0.768	10.3	0.031	3.0	0.820	14.7	<0.001	16.0	0.672	33.1	<0.001
Poor control (7%–8.9%)	17.3		11.7		3.8		17.2		13.6		43.8	
Very poor control (>9%)	17.7		16.6		4.0		27.9		14.3		48.8	
Total cholesterol % (n)												
Normal	23.3	<0.001	13.9	0.604	5.7	0.026	18.6	0.379	18.2	0.025	47.2	0.065
High	14.5		12.7		2.9		21.0		13.0		41.1	
LDL % (n)												
Normal	21.5	<0.001	13.0	0.152	4.9	0.045	14.7	0.205	20.2	0.001	45.3	0.293
High	11.9		9.6		2.3		18.7		11.0		41.2	
HDL % (n)												
Normal	12.8	0.004	10.1	0.007	2.6	0.254	19.9	0.375	11.3	<0.001	41.0	0.459
Low	20.2		16.6		4.1		17.2		20.7		43.7	
Triglycerides % (n)												
Normal	15.0	0.005	12.1	0.174	3.3	0.586	18.7	0.044	12.9	0.019	42.4	0.499
High	22.2		15.2		4.0		24.5		18.5		44.7	

among people with T2DM, 28% had macrovascular complications, and 54.6% had microvascular complications and these complications were associated with a number of modifiable lifestyle factors.

The prevalence of CAD and stroke in this study was within the reported range in high- and middle-income countries [21]. Previous studies from Saudi Arabia, however, reported slightly higher prevalence of these complications [2,3,11]. The lower prevalence in our study could be explained that they were measured from people attending diabetic centres which are secondary level healthcare facilities in the country. In contrast, the previous studies assessed the prevalence of these complications using hospital level data, where the prevalence is likely to be higher as patients in Saudi Arabia are usually referred to hospitals when they needs specialised level treatment.

Compared to the global prevalence of diabetic neuropathy (15%) and diabetic retinopathy (27%), this study showed a higher prevalence of these complications among people with T2DM [1,22,23]. Nevertheless, our results are comparable to the findings of previous studies in Saudi Arabia [4,5,9,24–26]. A slightly higher prevalence of retinopathy and diabetic foot in our study could be explained that the participants were asked directly about their history of retinopathy and lower extremities' ulcers and amputation. However, the previous studies from Saudi Arabia relied on documented diagnosis in the patients' medical records. Information regarding retinopathy and diabetic foot in medical records may not be complete because the patients may had been followed up for retinopathy and diabetic foot at primary health care or other health care centres.

This study showed that 5.7% of the participants were smokers and 8.5% smoked in the past, while 14% were passive smokers. Moreover, current smoking was independently associated with 2.7-fold increase in the odds of both diabetic foot and neuropathy. Further, ex-smokers and passive smokers were at 2 and 1.9-fold increased odds of diabetic foot respectively. These findings are supported by the results of a previous systematic review [27]. The nicotine in tobacco has an adrenergic-vasoconstrictive effect on blood vessels [28]. This effect can lead to hypoxia, poor wound healing, ulcers, and gangrene among people with impaired vasodilatation activity such as people with diabetes [29].

Hypertension appeared as an independent predictor of CAD, stroke, renal impairment, and retinopathy in this study, while very poor glycaemic control (HbA1c ≥ 9%) increased the risk of neuropathy. Hypertension is more common among people with diabetes than the general population, and its association with diabetes macro- and microvascular complications is well-established [30]. For people with diabetes with poor glycaemic control (HbA1c ≥ 7%)

Table 3
Adjusted association between each of the macrovascular complications and potential risk factors[a].

Variable	CAD[a]			Diabetic foot**			Stroke***		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Age (ref: <60years)									
61–70 years	1.6	1.1, 2.5	0.030						
>70 years	1.9	1.1, 3.4	0.032						
Gender (ref: female)	1.7	1.1, 2.5	0.018				2.2	1.1, 4.7	0.033
Education level (ref: university/college)									
Intermediate/secondary									
Illiterate/primary							2.6	1.2, 5.8	0.017
Income (ref: 9001 SAR and over)									
6001–9000 SAR									
6000 SAR and less				2.2	1.4, 3.5	0.001			
Region (Ref: Riyadh)									
Jeddah	0.6	0.3, 1.1	0.075						
Hofuf	2.2	1.3, 3.7	0.005	2.8	1.7, 4.7	<0.001			
Smoking (ref: never)									
In the past (>one year)				2.0	1.0, 4.1	0.056			
Currently smoking				2.7	1.2, 6.3	0.017			
Passive smoking (ref: no)				1.9	1.1, 3.2	0.021			
Low level of Physical Activity (ref: >150 min/week)				1.7	1.0, 2.8	0.045			
Number of hours of sitting per day	1.1	1.1, 1.2	0.005				1.1	1.0, 1.2	0.008
BMI (ref: normal)									
Pre-obesity									
Obesity (class I – III)	1.7	1.1, 2.6	0.021						
Duration of diabetes >10 years (ref:<10 years)	1.6	1.0, 2.6	0.039						
Treatment (ref: oral)									
Insulin	2.2	1.2, 3.9	0.008	2.5	1.5, 4.3	0.001			
Insulin + oral	1.9	1.2, 3.0	0.008	2.4	1.4, 3.9	0.001			
Hypertension (ref: no)	3.4	1.9, 6.1	<0.001				4.9	1.5, 16.0	<0.001

[a] List of the variables adjusted for in the multivariable analysis for each of the complications is available in the appendix.

Table 4
Adjusted association between each of the microvascular complications and potential risk factors[a].

Variable	Neuropathy[a]			Renal impairment**			Retinopathy***		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Age (ref: <60years)									
61–70 years				2.3	1.3, 3.9	0.002			
>70 years				3.2	1.6, 6.2	0.001	1.5	1.0, 2.2	0.059
Gender (ref: female)	1.9	1.2, 2.9	0.005						
Education level (ref: university/college)									
Intermediate/secondary									
Illiterate/primary							1.3	1.0, 1.7	0.052
Income (ref: 9001 SAR and over)									
6001–9000 SAR				1.7	1.0, 2.9	0.035			
6000 SAR and less	2.4	1.7, 3.5	<0.001						
Region (Ref: Riyadh)									
Jeddah									
Hofuf				2.4	0.9, 6.2	0.079			
Smoking (ref: never)									
In the past (>one year)									
Currently smoking	2.7	1.3, 5.5	0.005						
Low level of Physical Activity (ref: >150 min/week)	1.4	0.9, 2.2	0.087				1.6	1.2, 2.1	0.002
Number of hours of sitting per day	1.1	1.0, 1.1	<0.001	1.1	1.0, 1.1	0.067			
BMI (ref: normal)									
Pre-obesity									
Obesity (class I – III)	1.5	1.0, 2.2	0.044						
Duration of diabetes >10 years (ref:<10)							2.3	1.7, 3.1	<0.001
Family history of diabetes (ref: no)	1.6	1.1, 2.5	0.023				1.5	1.1, 2.0	0.010
Treatment (ref: oral)									
Insulin	1.8	1.1, 2.7	0.013	1.8	1.0, 3.2	0.043	1.9	1.3, 2.6	<0.001
Insulin + oral	2.1	1.4, 3.2	<0.001				1.9	1.4, 2.7	<0.001
HbA1c (ref: < 7.0%)									
Poor control (7%–8.9%)									
Very poor control (>9%)	1.5	1.0, 2.1	0.029						
HDL (ref: normal)				1.9	1.1, 3.1	0.018			
Triglycerides (ref: normal)				1.8	1.1, 3.0	0.026			
Hypertension (ref: no)				2.2	1.2, 4.3	0.017	1.4	1.0, 1.8	0.033

[a] List of the variables adjusted for in the multivariable analysis for each of the complications is available in the appendix.

and high blood pressure the risk of macro- and micro-vascular complications was found to increase independently and additively [31]. About three-quarters (75.9%) of our participant's had poor control of their blood glucose level and more than one third (35.6%) had high blood pressure. Thus, to reduce the risk of macro- and micro-vascular complications for people with diabetes, an intensive treatment plan is required for both hyperglycaemia and hypertension [31].

Our results showed that with every one hour of sitting per day there was a 10% increase in the risk of CAD, stroke, and neuropathy, while less than 150 min of physical activity per week increase the risk of diabetic foot by 70% and retinopathy by 60%. A Danish study showed that people who sit for 10 h or longer per day and are physically inactive during leisure time were at 80% increased risk of myocardial infarction [13]. About 29.4% of our participants were sitting for six to nine hours per day, while 17.3% spent 10 h or more sitting daily. Moreover, more than two-thirds (70.1%) of the participants were not achieving the recommended physical activity target of 150 min per week [32]. Hence, an awareness program about the role of physical activity for prevention of complications is an urgent need in Saudi Arabia.

Diabetes Mellitus is a progressive disease. With longer duration of the disease the function of the pancreas further deteriorates and the risk of complications increases, especially when there is long standing hyperglycaemia. This study showed that a duration of diabetes of more than 10 years was independent predictor of CAD and renal impairment. Similar findings were reported in a previous study form Saudi Arabia [2]. The progression of the disease is also the probable explanation for the association between using insulin and macro- and micro-vascular complications.

This study supports the well-established association between diabetes complications and advanced age as well as male gender among people with diabetes [2,11,12,33]. We have also found that family history of diabetes increase the risk of both neuropathy and retinopathy. Similar findings in regards to retinopathy was reported in a study from Greece [34]. The latter study, however, have found that people with positive family history of diabetes had earlier onset of diabetes [34]. Our data also shows that participants with family history of diabetes had earlier onset of the disease (42.7 ± 11.5 years) compared to those without family history (46.8 ± 12.4 years) (p-value < 0.001). Early onset of diabetes is known to increase the risk of complications [35]. Other than the earlier onset, genetic and epigenetic have also been suggested to contribute in the association between diabetic retinopathy and family history of diabetes [36].

Obesity was an independent risk factors for CAD and neuropathy among people with T2DM in Saudi Arabia. Obesity is well-known risk factor for diabetes as well as for CAD [33,37], and it substantially increases the risk of CAD among people with diabetes especially if it is accompanied by other metabolic syndrome components including hypertension and dyslipidaemia [37]. Given that 62.6% of our study participants were obese and 27.2% were overweight, a program to reduce weight for people with T2DM is likely to be highly beneficial in reducing their risk of macro- and micro-vascular complications.

Our results are in the keeping with previous reports that showed a strong association of macro- and micro-vascular complications with low level of education as well as low income [38,39]. Higher level of education reduces the risk of cardiovascular disease indirectly by encouraging healthier lifestyle behaviours and positive attitude toward health and disease prevention [40,41], while high income increases the likelihood of adherence to healthy diet, physical activity, treatment regimen and access to health care [38]. The socioeconomic status of our participants varied between regions. A larger proportions of participants from Hofuf region had lower level of education and lower household income. This may explain why people from Hofuf had higher prevalence of obesity, smoking, and longer time sitting as well as increased risk of CAD, diabetic foot, and renal impairment. People with low socioeconomic status should be considered as a high risk group and should be provided with more health education and referred to appropriate social support services available in Saudi Arabia to improve their economic status.

In contrast to previous studies [42,43], total cholesterol and LDL did not appear to have an association with macro- or micro-vascular complications in our study, while high triglycerides and low HDL were associated with renal impairment. Compared to participants without complications, a larger proportion of those with complications were having normal total cholesterol and LDL. This is probably because the management for this group of people was intensified to reduce their risk of progression or acquiring further complications. In order to prevent diabetes complications, however, lipid profile as well as hypertension and blood glucose should be controlled adequately before complications manifest [31].

This study has strengths and limitations. The relatively large sample size from three different regions gives strength to this study. The use of pretested electronic questionnaire that was validated to reduce data errors and the exploration of wide variety of potential risk factors also add strength to this study. The cross-sectional study design, however, lack temporality, and we can only infer association rather than causation. In addition, for participants who did not have ophthalmology examination report in their medical file we have relied on self-reporting of retina problem to assess the prevalence of retinopathy which may reduce objectivity. Nonetheless, this study clearly revealed the burden of diabetes macro- and micro-vascular complications among people with T2DM in Saudi Arabia and their associated risk factors. Given the high prevalence of diabetes in Saudi Arabia and that people with diabetes in the country are at high risk of developing complications, future researchers should establish risk prediction tools for diabetes complications. Such essential tools will help clinicians to validate their clinical risk assessment as well as to raise the awareness of people with diabetes about their risk, which will motivate them to adhere to the management plan and lifestyle modifications.

5. Conclusion

Macro- and micro-vascular diabetes complications of coronary artery disease, diabetic foot, stroke, neuropathy, renal impairment, and retinopathy are common among people with T2DM in Saudi Arabia. These complications can be prevented or their progression can be delayed by prioritizing the following lifestyle modification factors in the management plan: increasing physical activity, decreasing sitting time, smoking cessation, maintaining healthy body mass index, and adequate control of hypertension, blood glucose and lipids. The findings of this study will be useful for developing individualise complication prevention strategies based on the risk factors present on the patient. Future research should aim for developing risk prediction tools to predict diabetes complication, which will be useful in validating clinical assessment of these complication as well as raising prevention awareness among the patients.

Declaration of interest

None.

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Conflicts of interest

All authors declare that they have no competing interests.

Author contributions

All authors were involved in the conception and design of the study. MJA, AJA, SMA, GMA, WAA and NAB contributed to the acquisition of data. MJA, BB, DJM, and HAA contributed to data analysis and interpretation of results. MJA and BB drafted the manuscript. All authors critically reviewed the manuscript and approved the final version.

Availability of data and material

The datasets generated during and analysed during the current study are available from the corresponding author on reasonable request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2018.11.007.

Appendix

Operational definition.

- CAD was defined as documented diagnosis of CAD, taking medication for CAD, or underwent a procedure for CAD. Stroke was defined as documented diagnosis of irreversible cerebrovascular accident.
- Diabetic foot was defined as a history of lower extremity ulcers or amputations. Retinopathy was defined as documented diagnosis of retinopathy, or the participant had been told by an ophthalmologist that he or she had retinopathy.
- Diabetes peripheral neuropathy was defined as a score of seven or more using the Michigan Neuropathy Screening Instrument [19].
- Renal impairment was defined as estimated glomerular filtration rate $\leq$60 ml/min/1.73 m^2 which was calculated from serum creatinine using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [44,45].
- Using the Global Physical Activity Questionnaire (GPAQ) [17], the total number of minutes of physical activity per week was categorised into $\geq$150 min and <150 min [46].
- Using the Morisky Medication Adherence questionnaire [18] medication adherence was categorised into good adherence (a score of 0), moderate adherence (a score of 1–2) and poor adherence (a score of 3–4).
- Based on HbA1c level, glycaemic control was categorised into good control (HbA1c < 7.0%)), poor control (HbA1c 7.0%–8.9%), and very poor control (HbA1c $\geq$ 9.0%).
- Body mass index (BMI) was categorised according to the current World Health Organization guidelines into normal (<25.0 kg/m^2), pre-obesity (25.0–29.9 kg/m^2), and obesity (class I, II and II $\geq$ 30.0 kg/m^2).
- High waist-hip ratio was defined as a ratio >0.96 for men and >0.98 for women [47].
- Hypertension was defined as either a documented diagnosis of hypertension, taking antihypertension medications, or three previous high blood pressure measures (systolic $\geq$ 140 mmHg or diastolic $\geq$ 90 mmHg) [46].
- High cholesterol was defined as cholesterol >4.0 mmol/L, high LDL was defined as LDL >2.0 mmol/L, and high triglycerides was defined as triglycerides >2.0 mmol/L, while low HDL was defined as HDL <1.0 mmol/L [48].

Variables adjusted for in the multivariable logistic analysis.

- The risk of Coronary artery disease as adjusted for age, gender, level of education, region, active smoking, physical activity, number of hours of sitting per day, duration of diabetes, modality of treatment, BMI, hypertension, cholesterol, LDL, HDL, triglycerides (area under the receiver operating characteristic curve: 75.7%, Hosmer-Lemeshow goodness-of-fit test p-value: 0.302).
- The risk of diabetic foot was adjusted for age, gender, income, region, active smoking, passive smoking, physical activity, number of hours of sitting per day, duration of diabetes, modality of treatment, adherence to medications, and HDL (area under the receiver operating characteristic curve: 71.7%, Hosmer-Lemeshow goodness-of-fit test p-value: 0.433).
- The risk of stroke was adjusted for age, gender, level of education, physical activity, number of hours of sitting per day, duration of diabetes, hypertension, cholesterol, LDL (area under the receiver operating characteristic curve: 68.8% and the Hosmer-Lemeshow goodness-of-fit test p-value: 0.413).
- The risk of neuropathy was adjusted for age, gender, level of education, location of residence, income, region, active smoking, passive smoking, physical activity, number of hours of sitting per day, duration of diabetes, family history of diabetes, modality of treatment, hypertension, BMI, HbA1c, and triglycerides (area under the receiver operating characteristic curve: 72.8%, Hosmer-Lemeshow goodness-of-fit test p-value: 0.338).
- The risk of renal impairment was adjusted for age, gender, level of education, income, region, physical activity, number of hours of sitting per day, duration of diabetes, modality of treatment, adherence to medication, hypertension, waist-hip ratio, cholesterol, LDL, HDL, and triglycerides (area under the receiver operating characteristic curve: 73.6%, Hosmer-Lemeshow goodness-of-fit test p-value: 0.638).
- The risk of retinopathy was adjusted for age, gender, level of education, income, physical activity, number of hours of sitting per day, duration of diabetes, family history of diabetes, modality of treatment, hypertension, and HbA1c (area under the receiver operating characteristic curve: 70.5%, Hosmer-Lemeshow goodness-of-fit test p-value: 0.667).

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5.1.3 Conference presentation

Oral presentation at the IDF Diabetes Complications Congress, October 2018, Hyderabad, India.

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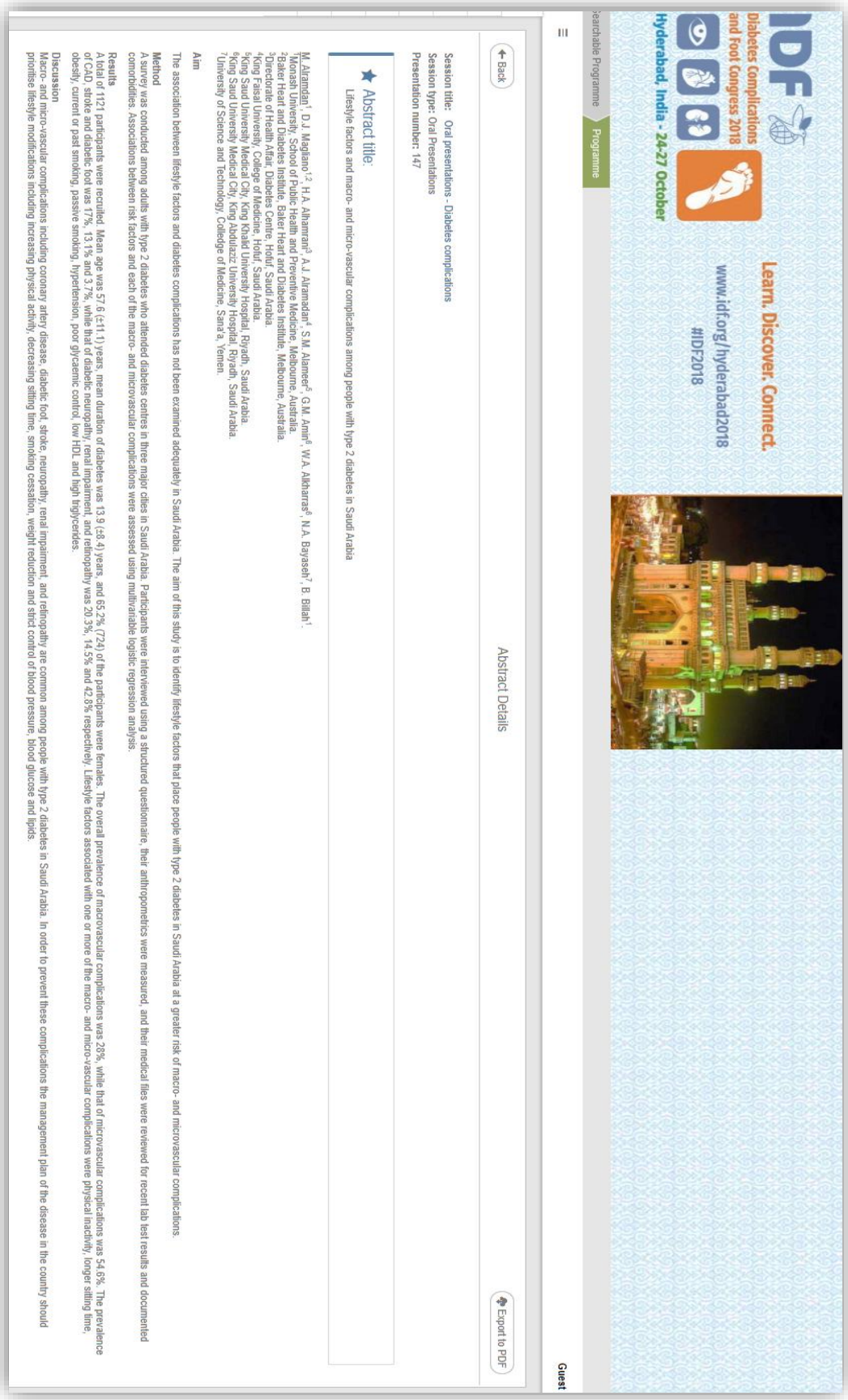

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Lifestyle factors and macro- and micro-vascular complications among people with type 2 diabetes in Saudi Arabia

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Aim

The association between lifestyle factors and diabetes complications has not been examined adequately in Saudi Arabia. The aim of this study is to identify lifestyle factors that place people with type 2 diabetes in Saudi Arabia at a greater risk of macro- and microvascular complications.

Method

A survey was conducted among adults with type 2 diabetes who attended diabetes centres in three major cities in Saudi Arabia. Participants were interviewed using a structured questionnaire, their anthropometrics were measured, and their medical files were reviewed for recent lab test results and documented comorbidities. Associations between risk factors and each of the macro- and microvascular complications were assessed using multivariable logistic regression analysis.

Results

A total of 1121 participants were recruited. Mean age was 57.6 (±11.1) years, mean duration of diabetes was 13.9 (±8.4) years, and 65.2% (724) of the participants were females. The overall prevalence of macrovascular complications was 28%, while that of microvascular complications was 54.6%. The prevalence of CAD, stroke and diabetic foot was 17%, 13.1% and 3.7%, while that of diabetic neuropathy, renal impairment, and retinopathy was 20.3%, 14.5% and 42.8% respectively. Lifestyle factors associated with one or more of the macro- and micro-vascular complications were physical inactivity, longer sitting time, obesity, current or past smoking, passive smoking, hypertension, poor glycaemic control, low HDL and high triglycerides.

Discussion

Macro- and micro-vascular complications including coronary artery disease, diabetic foot, stroke, neuropathy, renal impairment, and retinopathy are common among people with type 2 diabetes in Saudi Arabia. In order to prevent these complications the management plan of the disease in the country should prioritise lifestyle modifications including increasing physical activity, decreasing sitting time, smoking cessation, weight reduction and strict control of blood pressure, blood glucose and lipids.

5.2 Part 2: Risk prediction system for diabetes complications

5.2.1 Introduction

Current diabetes management guidelines recommend the use of diabetes complications risk scoring tools (70, 71). These tools can facilitate counselling and the education of people with diabetes about their risk of diabetes complications, as well as to identify patients at risk.

Currently, a number of hospitals in Saudi Arabia are using the Framingham risk equation (111) for people with diabetes. The Framingham risk equation is for cardiovascular disease only and does not cover other diabetes complications. It also has low sensitivity in people with diabetes who are at increased risk of cardiovascular disease (112). Furthermore, the Framingham tool was developed for the American population, which varies substantially in regards to genetic, environmental, and lifestyle factors compared to the Saudi Arabian population. Thus, the Framingham tool may not predict the risk of complications accurately for the Saudi population with diabetes. This is also applicable to the other available risk prediction tools that have been developed for European and Asian populations (73, 113-122).

This chapter describes the development and validation of risk prediction models for major diabetes macro- and micro-vascular complications for people with T2DM in Saudi Arabia. The developed risk prediction models require easy to obtain information in routine clinical setting and have high accuracy in predicting the risk of major diabetes complications.

5.2.2 Article:

Submitted for publication in the Journal of Diabetes Research and currently under review.

Journal of Diabetes Research

Risk Scoring System for Macro- and Micro-Vascular Complications Related to Type 2 Diabetes in Saudi Arabia

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Abstract

Objective: The aim of this study was to develop a risk scoring system to predict complications related to type 2 diabetes in Saudi Arabia.

Method: Data from a survey conducted among 1121 adults with type 2 diabetes in Saudi Arabia was used. Missing data was imputed and bootstrap-receiver-operation characteristic method was applied for developing models for major diabetes complications of coronary artery disease, diabetic foot, stroke, neuropathy, kidney disease and retinopathy. Models were validated using decile-decile plot and bootstrapping methods.

Results: Age ≥60 years, gender, low education level, body mass index ≥30 kg/m², physical inactivity, longer sitting time, smoking, longer duration of diabetes, insulin use, low adherence to treatment, family history of diabetes, glycated Haemoglobin ≥9%, hypertension and dyslipidaemia appeared as predictors in one or more of the models. The area under receiver operating characteristic curves ranged from 71.2% to 80.5%, and slope calibration ranged from 93.7% to 99.3%.

Conclusion: The developed risk prediction models require readily available information from routine clinical practice and the models have high discrimination and calibration power. Therefore, we recommend the use of the developed risk scoring system in the clinical assessment of major complications for people with type 2 diabetes in Saudi Arabia.

Keywords:

Saudi Arabia, diabetes, complications, prediction model.

Introduction

Diabetes mellitus is a major public-health issue worldwide. The prevalence of diabetes among adults in the Middle East and North Africa was recently reported to be 10.7%, which makes these regions the second most prevalent diabetes regions next to North America and the Caribbean [1]. Some of the countries in the Arabian Peninsula, including Saudi Arabia, United Arab Emirates, Kuwait, Qatar and Bahrain, have a substantially higher prevalence of diabetes compared to other countries in the Middle East [1]. According to a recent estimate, Saudi Arabia has a prevalence of diabetes among adults of 17.7%, which places it among the countries with the highest prevalence of the disease in the region as well as worldwide [1].

People with diabetes are more likely to develop macro- and micro-vascular complications [2]. Coronary artery disease (CAD), diabetic foot and stroke are the major macro-vascular complications, and neuropathy, kidney disease and retinopathy are the major micro-vascular complications. It has been estimated that the prevalence of micro-vascular complications is 10 to 20 times higher among people with diabetes compared to people without diabetes, while it is two to four times higher for macro-vascular complications [2]. The prevalence of these complications among people with diabetes in Saudi Arabia is high, which adds further problems to the burden of diabetes in the country. Studies from Saudi Arabia showed that the prevalence of CAD among people with diabetes was between 23.1% and 24.0%, which is higher than the estimated prevalence in the Middle East and the North African regions (15% and 20%) [3-5]. Similarly, compared to the worldwide prevalence of diabetic neuropathy of 15% [6], studies from Saudi Arabia showed a higher prevalence (17.8% to 65.3%) [7-10]. The majority of the studies from Saudi Arabia also reported a higher prevalence of diabetes retinopathy (31.3% to 36.8%) [11-13] and nephropathy (41.3% to 54.3%) [14, 15] than the global prevalence of these complications (27.2% and 39%, respectively) [16, 17]. This highlights the urgency of the early identification and management of the risk factors of these complications.

Risk prediction tools have an increasingly important role in identifying patients with a high risk of diabetes complications and their use has been recommended in the diabetes management guidelines for preventative intervention [18, 19]. These tools also help in patient counselling through educating patients about their risk of complications. This in turn can motivate people with diabetes to adhere to their management plans. The high prevalence of diabetes complications in Saudi Arabia warrants the use of a risk prediction tool to predict these complications.

Risk prediction tools for diabetes complications have been developed and used not only for Western populations but for many others as well [20-30]. However, studies on risk prediction tools for Saudi Arabia are not available in the literature. Furthermore, due to the variation in lifestyle behaviours, as well as genetic and environmental factors between Saudi Arabian and other populations, the tools developed for other populations may reduce the accuracy of the predicted risk when applied to people with diabetes in Saudi Arabia [22, 31]. Hence, there is an urgent need to develop risk prediction tools specific to Saudi Arabia. Thus, the aim of this study is to develop a risk scoring system to predict major diabetes complications for adults with type 2 diabetes mellitus (T2DM) in Saudi Arabia.

Materials and methods

Study Design and Population

A cross-sectional study was conducted between May 15th and November 30th, 2017. The study methodology has been described in detail in another article [32]. The study population consisted of adults aged 18 years and over with T2DM, who attended diabetes centres in the cities of Hofuf, Riyadh, and Jeddah in Saudi Arabia. Inclusion criteria included documented diagnosis of T2DM, aged 18 years and above, and a duration of diabetes of at least one year. People with other types of diabetes as well as pregnant women were excluded. A systematic random sample of participants were recruited. Informed consent was obtained from all participants, and they were interviewed to fill a structured questionnaire [32]. The questionnaire collected information related to socio-demographics, lifestyle, and medical history. The participants' anthropometrics were measured in a standardised way, and their medical

records were reviewed for lab test results, the prescription of medication and the documented diagnosis of hypertension, coronary artery disease, retinopathy and stroke. A description of the validated tools used in the questionnaire is available in the appendix. Ethical approval was obtained from the Monash University Human Research Ethics Committee in Australia and the Research Ethics Committee of the Ministry of Health in Saudi Arabia. All the study procedures were carried out in accordance with the principles of the Declaration of Helsinki as revised in 2013.

Definitions of Outcomes

CAD was defined as documented diagnosis of CAD, taking medication for CAD, or underwent a procedure for CAD. Stroke was defined as documented diagnosis of irreversible cerebrovascular accident. Diabetic foot was defined as a history of lower extremity ulcers or amputations. Retinopathy was defined as documented diagnosis of retinopathy, or the participant had been told by an ophthalmologist that he or she had retinopathy. Diabetes peripheral neuropathy was defined as a score of seven or more using the Michigan Neuropathy Screening Instrument [33]. Renal impairment was defined as estimated glomerular filtration rate ≤ 60 ml/min/1.73m^2, which was calculated from serum creatinine using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [34, 35].

Data Analysis

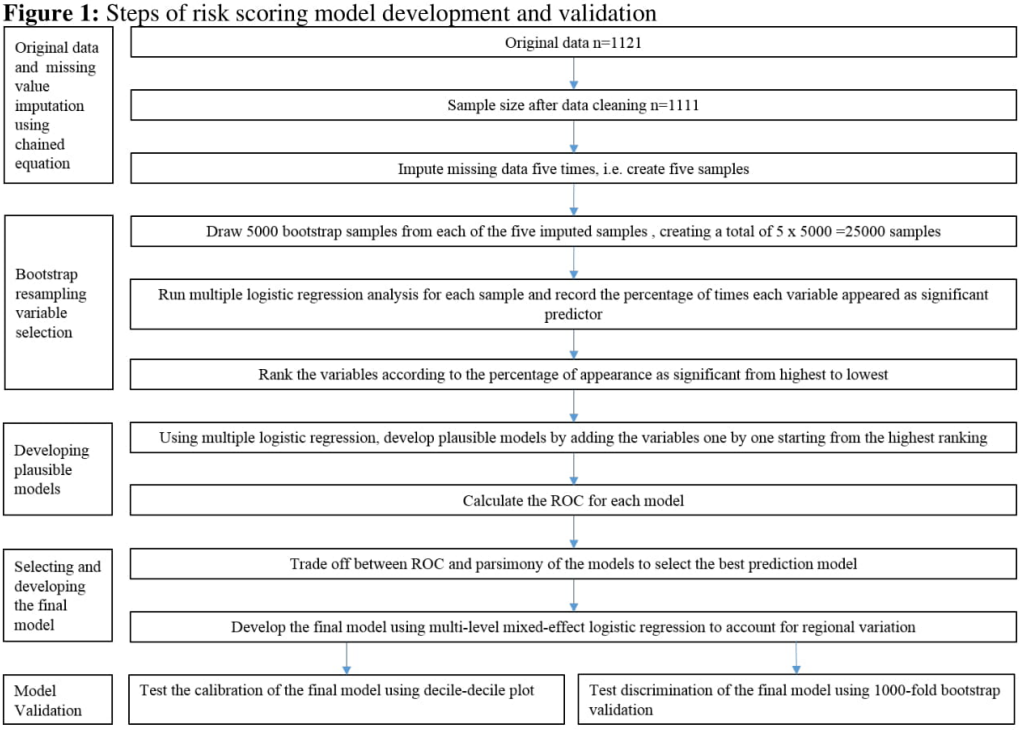
Based on literature review and clinical judgment, the following variables were identified as potential risk factors for macro- and micro-vascular complications: age, gender, education, smoking, physical activity per week, sitting time per day, duration of diabetes, family history of diabetes, treatment modality, adherence to medications, body mass index (BMI), haemoglobin A1c (HbA1c), dyslipidaemia and hypertension. For each outcome complication, the remaining complications were also considered as plausible risk factors. Definitions of these risk factors are available in the appendix. Simple logistic regression analysis was used to examine the univariate association of individual complications with each of the plausible risk factors. Further steps of the analysis were not restricted to the results of the univariate analysis, because univariate analysis does not account for the effect of more than one risk factor.

Each of the following variables had only one (0.09%) observation missing: family history of diabetes, diabetes duration, onset of diabetes and insulin use. Neuropathy had the highest missing value (10.3%), followed by kidney disease (2.6%). The variables BMI, HbA1c, and dyslipidaemia had 0.7%, 0.45% and 1.7% missing values. The overall percentage of missing observations was 14.6%. Missing data was imputed five times (i.e., five imputed samples were created) using the chained equation method [36, 37], and the bootstrap-receiver operating characteristic (BROC) method was used to develop the prediction models [38]. Bootstrap resampling with replacement was used to select 5,000 random samples from each of the imputed samples. This resulted in 25,000 bootstrap samples, each the same size of the original sample. In each sample, a multiple logistic regression was run and the variables that appeared as significant were identified. The percentage of times each variable appeared as significant was calculated and then ranked. Variables were added to the multiple logistic regression model one by one, starting with the most to the least selected in the bootstrap analysis. Thus, the first model (M1) had only one variable, the second model (M2) had two variables, and so on. Variables that had a percentage appearance less than 20% were dropped from model development. The area under the receiver operating characteristic (ROC) for each model was recorded. A trade-off between parsimony of the model and optimisation of ROC was made in order to select the variables for the final prediction model [38]. The selected variables were then entered into multiple mixed-effect logistic regression models in order to account for variations in the locations of diabetic centres (Hofuf, Riyadh, and Jeddah). First order interaction effect and multicollinearity between risk factors were also investigated.

The calibration of the selected model for each complication was tested using the decile-decile plot. A linear regression model was fitted with the deciles of the observed (dependent) and predicted (independent) outcomes to measure the amount of variation in the observed outcome explained by its predicted value (R^2). The model's discrimination was evaluated using 1,000-fold bootstrap validation,

where 1,000 random samples were drawn, each of which were 90% the size of the original sample. The ROC was calculated for each sample and then averaged. The steps undertaken for developing and validating the risk scoring models are illustrated in **Figure 1**. Stata SE version 15.0 was used for data analysis. A p-value of 0.05 or less was considered as significant.

Figure 1: Steps of risk scoring model development and validation



Results

General Characteristics

A total of 1,121 participants were recruited for this study. Out of these 1,121 participants, 10 (0.9%) had substantially incomplete records and were excluded; the data for 1,111 participants was used in the analysis. The participants' demographic and clinical characteristics are presented in **Table 1**. Mean age was 57.6 (±11.1) years and the mean duration of diabetes was 13.9 (±8.4) years. The proportion of female participants was 65.2%. Among the participants, 51.2% achieved primary school education or less, while 17.6% were smokers or had smoked in the past. Among the participants, 55.5% were taking oral medications, 20.2% were taking injectable medications and 24.3% were taking both oral and injectable medications. Mean BMI was 32.9 (±8.1) kg/m² and mean HbA1c was 8.5% (±1.9%). The prevalence of hypertension, CAD, stroke and diabetic foot was 70.0%, 17.0%, 3.7% and 13.0%, while that of neuropathy, renal impairment and retinopathy was 20.3%, 14.5% and 42.8%, respectively [39]. Results of the simple logistic regression analysis are presented in the appendix (**Table E1**).

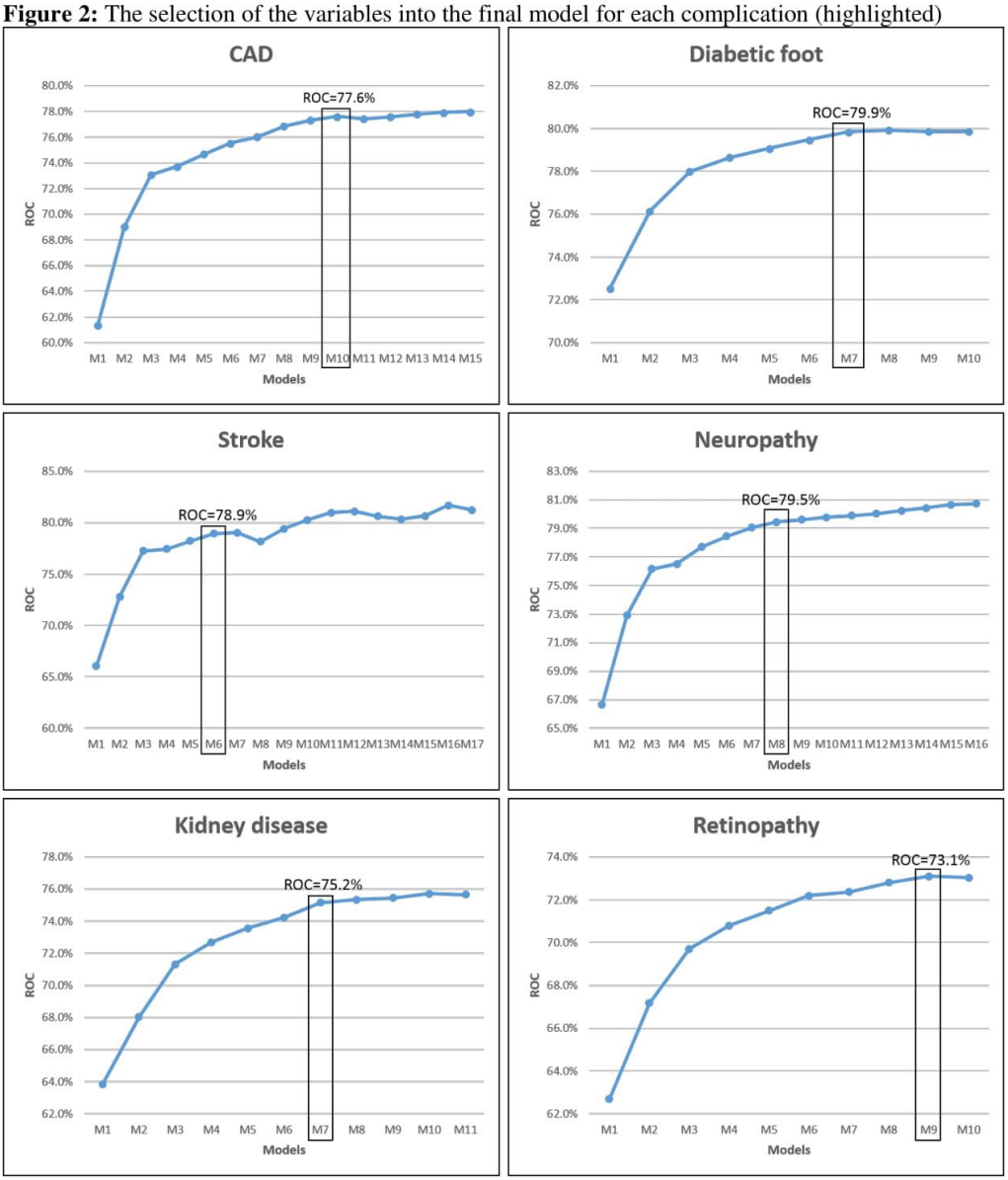
Table 1: demographic and clinical characteristics

Characteristic	Descriptive measure (n= 1111)
Age in years	57.6 ±11.1
Gender (female)	65.2%
Education	
University	17.8%
Intermediate-Tertiary	31.0%
Illiterate-Primary	51.2%
Ever smoked	
No	82.5%
Yes	17.6%
Duration of diabetes in years	13.9 ±8.4
Modality of treatment	
Oral	55.5%
Injectable	20.2%
Oral and injectable	24.3%
BMI Kg/m²	32.9 ±8.1
HbA1c	8.5 ±1.9
Dyslipidaemia	77.2%
Hypertension (yes)	70.0%
CAD (yes)	17.0%
Diabetic foot (yes)	13.0%
Stroke (yes)	3.7%
Neuropathy (yes)	20.3%
Renal impairment (yes)	14.5%
Retinopathy (yes)	42.8%

Risk Models

The percentage of variables appearing as significant in the bootstrap analysis for each complication is presented in the appendix (**Table E2**). The ROC for the plausible models for each complication is presented in **Figure 2** (the selected final model for each complication is highlighted). There was no first order interaction effect or multicollinearity between the risk factors in the selected final models.

Figure 2: The selection of the variables into the final model for each complication (highlighted)



Note: M1: model 1, comprised of one variable; M2: model 2, comprised of two variables; M3: model 3, comprised of three variables; and so on. The variables appearing as significant in bootstrapping were added into the model, starting from the highest to the lowest. A variable upon deletion that does not change the ROC of a model might be useful in the risk stratification of patients. Therefore, importance should be based on a model's parsimony and the clinical importance of the variable in question.

Table 2 shows the beta coefficient and odds ratio (OR) for the predictors after adjustment for regional variation. **Figure 3** shows the 1,000-fold bootstrap validation and **Figure 4** illustrates the slope calibration for the selected models.

Table 2: Beta coefficient and OR (95% CI) for the predictors of complications

CAD*

Variable	Beta coefficient	OR	95%CI
Hypertension	1.0088	2.7	1.7, 4.6
Retinopathy	0.5925	1.8	1.3, 2.6
Male gender	0.5015	1.7	1.1, 2.4
Sitting ≥ 10 hours per day	0.4937	1.6	1.1, 2.5
Insulin use	0.5928	1.8	1.2, 2.6
BMI ≥ 30 kg/m²	0.4538	1.6	1.1, 2.3
Kidney disease	0.5657	1.8	1.1, 2.7
Stroke	0.6319	1.9	0.9, 4.0
Age ≥ 60 years	0.4861	1.6	1.1, 2.3
Constant	-3.9575	0.0	0.0, 0.0

Diabetic foot*

Variable	Beta coefficient	OR	95%CI
Neuropathy	1.8637	6.4	4.3, 9.7
Retinopathy	0.7592	2.1	1.4, 3.2
Ever smoked	0.4888	1.6	1.0, 2.6
Low adherence to treatment	0.4715	1.6	1.1, 2.4
Stroke	0.7651	2.1	0.9, 5.0
Sitting ≥ 10 hours per day	0.5011	1.7	1.0, 2.7
Constant	-3.2202	0.0	0.0, 0.1

Stroke*

Variable	Beta coefficient	OR	95%CI
Neuropathy	1.0925	3.0	1.3, 6.7
Hypertension	1.2967	3.7	1.1, 12.3
CAD	0.6242	1.9	0.9, 12.3
Male gender	0.2380	1.3	0.6, 2.7
dyslipidaemia	0.9446	2.6	0.8, 8.6
Diabetic foot	0.6491	2.0	0.8, 4.5
Constant	-5.9647	0.0	0.0, 0.0

Neuropathy*

Variable	Beta coefficient	OR	95%CI
Diabetic foot	1.9115	6.8	4.4, 10.4
Retinopathy	0.8057	2.2	1.5, 3.2
Female gender	0.7901	2.2	1.4, 3.3
Stroke	1.1660	3.2	1.4, 7.5
Sitting ≥ 10 hours per day	0.6566	1.9	1.2, 3.1
No university education	0.6387	1.9	1.0, 3.4
HbA1c ≥ 9%	0.5345	1.7	1.2, 2.5
Kidney disease	0.3034	1.4	0.8, 2.2
Constant	-3.7037	0.0	0.0, 0.0

Kidney disease*

Variable	Beta coefficient	OR	95%CI
Age ≥ 60 years	0.9332	2.5	1.7, 3.8
Sitting ≥ 10 hours per day	0.6835	2.0	1.2, 3.1
Hypertension	0.9006	2.5	1.4, 4.2
CAD	0.9006	1.6	1.0, 2.4
Diabetes duration > 10 years	0.3265	1.4	0.9, 2.2
Insulin use	0.4817	1.6	1.1, 2.4
Neuropathy	0.3970	1.5	1.0, 2.3
Constant	-3.7069	0.0	0.0, 0.0

Retinopathy*

Variable	Beta coefficient	OR	95%CI
Diabetes duration > 10 years	0.7906	2.2	1.6, 3.0
Neuropathy	0.6883	2.0	1.4, 2.9
Insulin use	0.4727	1.6	1.2, 2.1
Diabetic foot	0.6338	1.9	1.2, 2.9
CAD	0.5531	1.7	1.2, 2.5
Physical activity < 150 minute/week	0.3829	1.5	1.1, 2.0
Family history of diabetes	0.3351	1.4	1.0, 1.9
No university education	0.3550	1.4	1.0, 2.1
Age ≥ 60 years	0.2833	1.3	1.0, 1.8
Constant	-2.2154	0.1	0.1, 0.2

* Accounts for variation in the regions in multiple mixed-effect logistic regression

Figure 3: The discrimination power (1000-fold bootstrap ROC) of the risk scoring models for diabetes complications

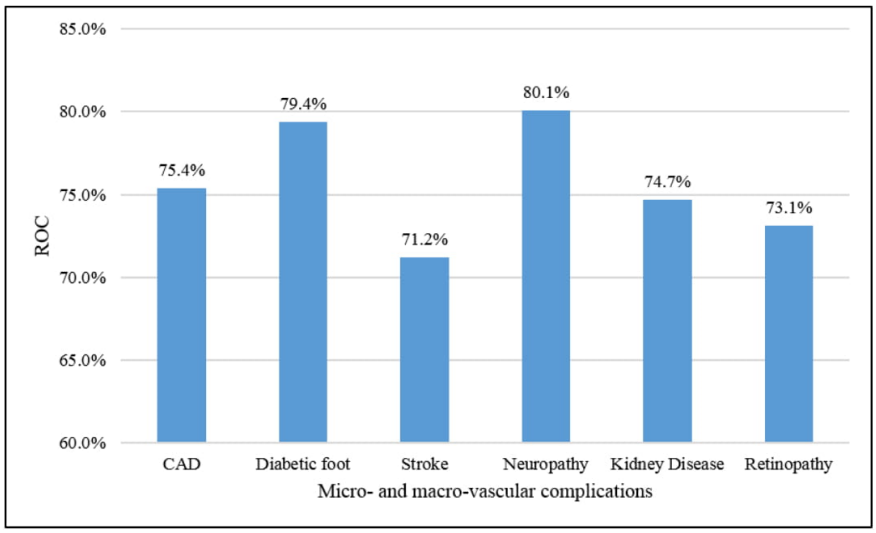
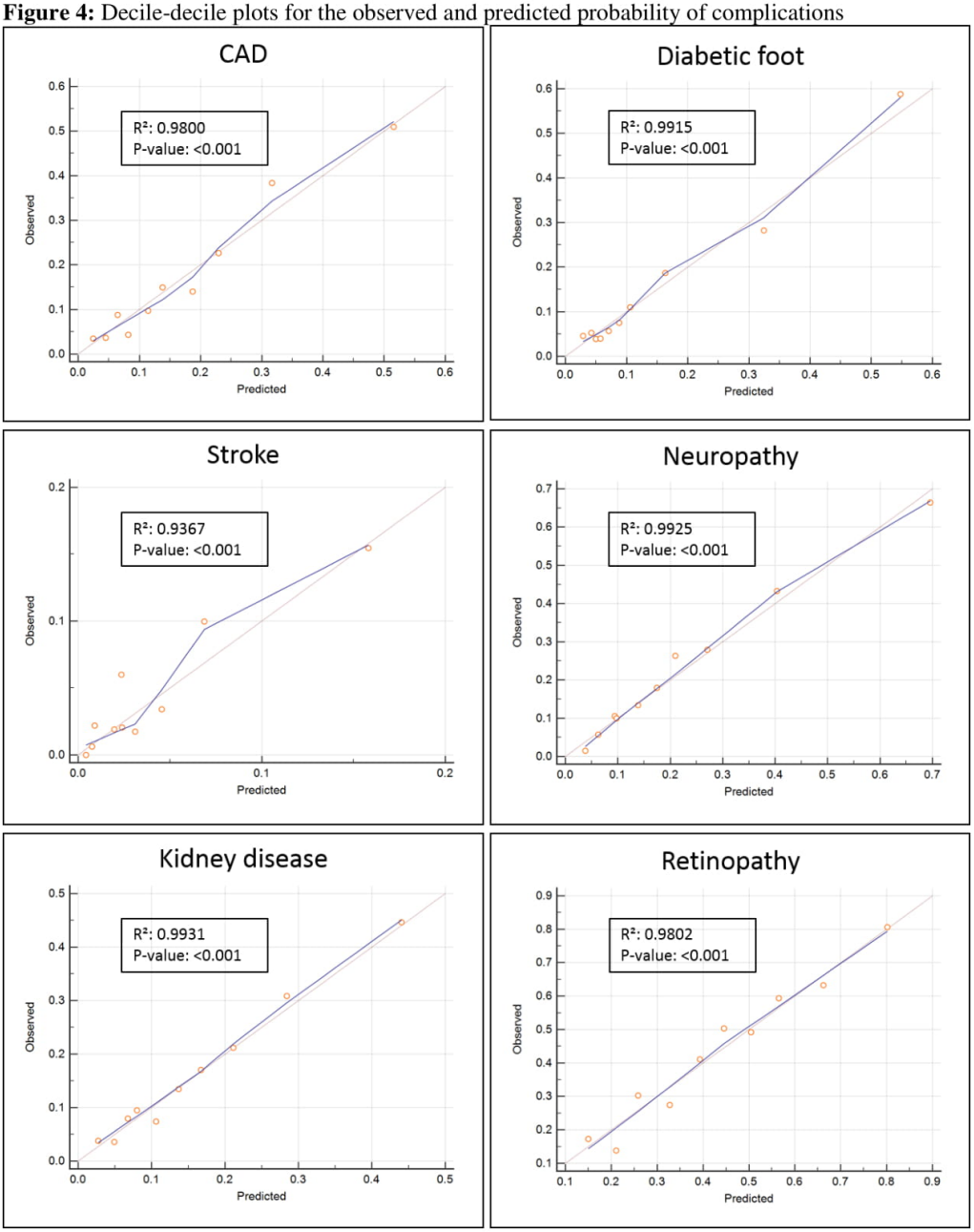


Figure 4: Decile-decile plots for the observed and predicted probability of complications



CAD model: the risk scoring model for CAD included the following nine variables: age ≥ 60 years, male gender, BMI ≥ 30 KG/m², sitting time ≥ 10 hours per day, insulin use, hypertension, retinopathy, kidney disease and stroke (**Table 2**). Males had 70% increased odds of developing CAD. Being hypertensive the odds of CAD increased by 2.7-fold. Furthermore, the odds of CAD increased by 60% among people who were obese, among people who were aged 60 years or above, and people who spent

more than 10 hours sitting per day. History of kidney disease, stroke and retinopathy increased the odds between 80% and 90% and insulin users had 80% higher odds compared to those taking oral tablets. The model has ROC of 75.4% (**Figure 3**) and calibration of 98.0% (p-value < 0.001) (**Figure 4**).

Diabetic foot model: the risk scoring model for diabetic foot has six variables – ever smoked, low adherence to treatment, sitting time ≥ 10 hours per day, neuropathy, retinopathy and stroke. Both 'ever smoked' and 'low adherence to treatment' increased the odds of diabetic foot by 60%, while 'sitting time ≥ 10 hours per day' was associated with 70% increased odds. The odds of diabetic foot increased by 6.4-fold for neuropathy and 2.1-fold for both retinopathy and stroke. The model has high discrimination and calibration powers (ROC of 79.4% and slope calibration of 99.2% with a p-value < 0.001).

Stroke model: the following six variables has been selected for stroke – male gender, dyslipidaemia, neuropathy, hypertension, CAD and diabetic foot. The odds of stroke increased by 3.7-fold for hypertension, 3.0-fold for neuropathy, 2.6-fold for dyslipidaemia, and 2.0-fold for diabetic foot, while CAD and 'the male gender' were associated with 90% and 30% increased odds, respectively. The model has ROC of 71.2% with a calibration of 93.7% (p-value < 0.001).

Neuropathy model: the selected model for neuropathy has eight independent variables – female gender, sitting time ≥ 10 hours per day, education below university degree, HbA1c ≥ 9%, diabetic foot, retinopathy, stroke and kidney disease. 'Female gender' increased the odds of neuropathy by 2.2-fold, while both 'sitting time ≥ 10 hours per day' and 'education below university degree' increased the odds by 90%. Diabetic foot increased the odds of neuropathy by 6.8-fold, stroke by 3.2-fold, retinopathy by 2.2-fold, and kidney disease by 1.4-fold, while HbA1c ≥ 9% was associated with 70% increased odds. The discrimination power was 80.1% and the slope calibration was 99.3% (p-value < 0.001).

Kidney disease model: for kidney disease the final model has the following seven predictors – age ≥ 60 years, sitting time ≥ 10 hours per day, duration of diabetes > 10 years, insulin use, hypertension, CAD and neuropathy. 'Age ≥ 60 years' increased the odds by 2.5-fold, while 'sitting time ≥ 10 hours per day' increased the odds by 100%. 'Insulin use' and 'duration of diabetes > 10 years' increased the odds by 60% and 40% respectively. The odds also increased by 2.5-fold for hypertension, 60% for CAD, and 50% for neuropathy. The model has a 74.7% discrimination power and a slope calibration of 99.3% (p-value < 0.001).

Retinopathy model: the selected risk prediction model for retinopathy has nine variables – age ≥ 60 years, physical activity < 150 minutes per week, education below university degree, insulin use, duration of diabetes > 10 years, family history of diabetes, neuropathy, CAD and diabetic foot. The odds of retinopathy increased between 30% and 50% for 'age ≥ 60 years', 'sitting time ≥ 10 hours per day' and 'education below university degree'. 'Using insulin' and a 'duration of diabetes > 10 years' increased the odds by 60% and 2.2-fold respectively. The odds of retinopathy also increased by 100% for neuropathy, 90% for diabetic foot, and 70% for CAD. The model has a discrimination power of 73.1% and calibration power of 98.0% (p-value 0.001).

Absolute risk and additive score calculation

Based on the results reported in **Table 2**, the absolute risk of any of the diabetes complications for a patient can be calculated using the following formula: absolute risk = exp(XB)/(1+exp(XB)). 'X' is the risk factor and 'B' is the corresponding beta coefficient and 'XB' is the sum of values of the beta coefficients for the risk factors a patient presented and the constant term. The closer the absolute risk to the value of one (or 100%) the higher the patient's risk of developing diabetes complications.

To further simplify the application of the risk prediction models an additive points-based risk-scoring system was developed [40]. The risk scoring system for each of the complications was calculated as follows. First, the beta coefficients for the variables for each outcome (**Table 2**) was divided by the smallest absolute beta coefficient and multiplied it by a multiplicative factor of 10 (**Table E3** in the appendix), which gave a score corresponding to each variable [41]. It should be noted that the risk

stratification is invariant to the multiplicative factor of beta coefficients. Second, the total additive score for each of the study participants was calculated based on the risk factors they had. Then the calculated scores for all patients were divided into quintiles (five groups) [40], and rounded to the closest whole number for risk stratification. **Table 3** shows the risk quantiles and additive score strata for each of the complications. The higher the additive score the higher the patient's risk of developing diabetes complications.

Table 3: The stratified additive risk score for diabetes complications.

Risk quintiles	Risk groups	Diabetes complications					
		CAD	Diabetic foot	Stroke	Neuropathy	Kidney Disease	Retinopathy
1st (0-20% of patients)	Very low	20 and less	Less than 1	50 and less	39 and less	28 and less	38 and less
2nd (21-40% of patients)	Low	21 - 43	1 - 11	51 – 91	40 – 48	29 – 42	39 – 60
3rd (41-60% of patients)	Moderate	44 - 55	12 – 21	92 – 94	49 – 74	43 – 65	61 – 76
4th (61-80% of patients)	High	56 - 61	22 – 37	95 – 120	74 – 91	66 – 81	77 – 93
5th (81-100% of patients)	Very high	62 and above	38 and above	121 and above	92 and above	82 and above	94 and above

A Case Study for CAD

Consider a male patient of age 65 years who is insulin dependent. The patient spends more than 10 hours per day in a sitting position, his BMI is ≥ 30 kg/m² and he has hypertension, kidney disease, and retinopathy. The absolute risk of having CAD is 0.514 or 51.4%. This means that among a group of 100 patients with exactly the same set of risk factors, 51.4% of them are at risk of having CAD. The additive score for CAD for this patient is 103.5 which falls in the 5th quintile and indicates that the patient has very high risk of CAD.

Discussion

Population specific risk-prediction models are very important to validate the clinical assessment of a disease. However, risk scoring models for T2DM related micro- and macro-vascular complications in Saudi Arabia are not available. Hence, the purpose of this study was to develop a risk scoring system for the major micro- and macro-vascular complications for T2DM in Saudi Arabia. All the models in this study had high discrimination and calibration powers. Among others, modifiable lifestyle factors such as extended sitting hours per day, physical inactivity, obesity, hypertension, smoking, low adherence to treatment, dyslipidaemia and very poor control of HbA1c contributed to an increased risk of diabetes complications. This shows that positive lifestyle changes are urgently required among people with T2DM in Saudi Arabia.

The prevalence of diabetes complications in our study was high and is comparable, in general, to that from previous studies in Saudi Arabia [39]. The risk factors examined and incorporated into our models are supported by the known risk factors of macro- and microvascular complications among people with diabetes. Traditionally, there have been a number of elements used in risk prediction models: patient demographics, clinical factors and comorbidities such as advanced age, gender, low education level, smoking, high BMI, longer duration of diabetes, insulin use, high HbA1c, hypertension, and dyslipidaemia [20-22, 24-26, 31, 42]. Studies also showed that macro- and microvascular complications (related to diabetes) play a strong role in predicting each other [20, 22, 27, 30, 43, 44]. All of the above variables, as well as the majority of complications, appeared as predictors in our models. Previous studies have further showed that non-traditional biomarkers, including B-type natriuretic peptide, osteopontin, and β-2 macroglobulin, can improve risk prediction [26, 42, 45]. However, our data did not have records of these biomarkers, as they are not routinely measured in clinical practice [42].

A few of the existing risk prediction models used 'low level of physical activity' as a predictor of diabetes complication [25, 42], while 'sitting time per day' was given less attention even though studies showed that a longer sitting time was associated with an increased risk of complications [39, 46]. Studies also found that a family history of diabetes was a strong independent risk factor for microvascular complications [39, 47, 48]. Our study results showed that 'sitting for more than 10 hours

per day' was a predictor for CAD, diabetic foot, neuropathy, and kidney disease, while 'family history of diabetes' and 'physical activity less than 150 minutes per week' were predictors for retinopathy.

In this study, the risk prediction models were developed using BROC method in the entire dataset. Splitting the sample into training and validation subsets can decrease the models' accuracy and prediction power [41, 49]. In addition, compared to the automated and other variable selection methods, the BROC method improves results with respect to parsimony and the prediction performance of the model [38, 41, 49]. This was clearly reflected in the results of this study. The prediction models for each of the complications incorporated a small number of predictors, ranging from six to 10 variables, which confirmed their parsimony. In a clinical setting, a simple and easy-to-use scoring system is preferred over a complex model that requires many variables or variables that are not easy to collect such as non-traditional biomarkers.

Bootstrap method was also used to validate the models. The models' ROC was assessed in 1000 samples randomly selected (using with replacement) from the original sample. This method provides bias-corrected discrimination power [41, 49]. All the models developed in this study showed high discrimination (ranging from 71.2% to 80.5%). The models' validity was evaluated further by assessing the slope calibration which is more accurate than the Hosmer-Lemeshow goodness of fit test [50, 51]. The slope calibration for our models is high, ranging from 93.7% to 99.3%. Thus, we recommend the use of these models and the developed risk scoring system in assessing the risk of major macro- and micro-vascular complications for people with T2DM in Saudi Arabia. Such tools will facilitate educating people with diabetes about their risk of complications, which may motivate them to undertake active preventive measures. It will also help clinicians to identify people at high risk.

This study has strengths and limitations. The strengths of the study originate from the consideration of various demographic, lifestyle and clinical factors as the predictors of complications, as well as robust methodology in developing and validating the prediction models. The entire data set has been used to develop and validate the risk prediction models, which is preferable over a split-sample [41, 52]. The risk prediction models developed in this study are parsimonious and have high discrimination and calibration powers. However, the cross-sectional study design was a limitation of this study. Cross sectional studies lack temporality and causation cannot be inferred. Thus, the developed models might be refined in the future using data from a prospective study. Another limitation was the conversion of numerical continuous variables to categorical variables, which may lead to a loss of some information. This conversion, however, helps clinicians and patients to easily interpret the risk attributed to the variables.

Conclusions

The risk models developed in this study are parsimonious and easy to use. They provide a valid method for assessing the risk for each of the six major macro- and micro-vascular complications for patients with T2DM in Saudi Arabia. Furthermore, these models and the risk scoring system provide an opportunity for ongoing counselling of patients regarding their risk of complications.

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Competing interests

All authors declare that they have no competing interests.

Author contributions

All authors were involved in the conception and design of the study. MJA, BJA, NAAlz, and NAAla, contributed to the acquisition of data. MJA, MNK, and BB contributed to data analysis. MJA, MNK, MAB, THA, DJM and BB contributed to interpretation of results. MA and BB developed the online

risk calculator. MJA, BB, and DJM drafted the manuscript. All authors critically reviewed the manuscript and approved the final version.

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Data availability
The data will be available upon reasonable request.

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5.2.3 Conference presentation

Poster presented at the Alfred Health Week Research Poster Display, June 2019, Melbourne, Australia.

MONASH University

School of Public Health & Preventive Medicine

Risk Scoring System for Macro- and Micro-Vascular Complications Related to Type 2 Diabetes in Saudi Arabia

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Background: Saudi Arabia has high prevalence of diabetes related complications. A risk prediction tool to predict these complications is needed to help in patient counselling and early preventive intervention. Due to the variation in lifestyle, genetic, and environmental factors between Saudi Arabian and other populations, a population specific risk prediction tool is preferred.

Objective: to develop risk prediction models for diabetes related complications for adults with type 2 diabetes in Saudi Arabia.

Method: Data from a survey conducted among 1121 adults with type 2 diabetes in Saudi Arabia in 2017 was used. Missing data was imputed and bootstrap-receiver-operating characteristic method was applied for developing models for major diabetes complications including coronary artery disease (CAD), diabetic foot, stroke, neuropathy, kidney disease and retinopathy (**Figure 1** and **2**). Models were validated using decile-decile plot and bootstrapping.

Results: Age ≥60 years, gender, low education level, body mass index ≥30 kg/m², physical inactivity, longer sitting time, smoking, longer duration of diabetes, insulin use, low adherence to treatment, family history of diabetes, glycated haemoglobin ≥9%, hypertension and dyslipidaemia appeared as predictors in one or more of the models (**Table 1**). The area under receiver operating characteristic curves (ROC) ranged from 71.2% to 80.5% (**Figure 3**), and slope calibration ranged from 93.7% to 99.3% (**Figure 4**).

Figure 1: Steps of risk scoring model development and validation

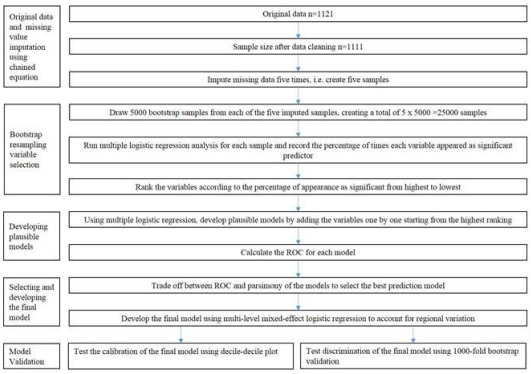


Figure 2: The selection of the best model based on ROC for CAD and diabeteic foot

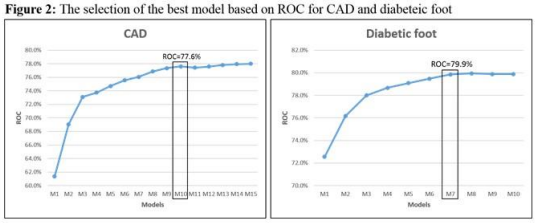


Table 1: Beta coefficient and OR (95% CI) for the predictors of complications

CAD*

Variable	Beta coefficient	OR	95%CI
Hypertension	1.0088	2.7	1.7, 4.6
Retinopathy	0.5925	1.8	1.1, 2.6
Male gender	0.5015	1.7	1.1, 2.4
Sitting ≥ 10 hours per day	0.4937	1.6	1.1, 2.5
Insulin use	0.5928	1.8	1.2, 2.6
BMI ≥ 30 kg/m²	0.4538	1.6	1.1, 2.3
Kidney disease	0.5657	1.8	1.1, 2.7
Stroke	0.6319	1.9	0.9, 4.0
Age ≥ 60 years	0.4861	1.6	1.1, 2.3
Constant	-3.9575	0.0	0.0, 0.0

Diabetic foot*

Variable	Beta coefficient	OR	95%CI
Neuropathy	1.8637	6.4	4.3, 9.7
Retinopathy	0.7592	2.1	1.4, 3.2
Ever smoked	0.4888	1.6	1.0, 2.6
Low adherence to treatment	0.4715	1.6	1.1, 2.4
Stroke	0.7651	2.1	0.9, 5.0
Sitting ≥ 10 hours per day	0.5011	1.7	1.0, 2.7
Constant	-3.2202	0.0	0.0, 0.1

Stroke*

Variable	Beta coefficient	OR	95%CI
Diabetic foot	1.2120	3.4	1.6, 7.1
Hypertension	1.3216	3.7	1.1, 12.6
CAD	0.6220	1.8	0.9, 4.0
Male gender	0.2631	1.3	0.6, 2.7
dyslipidaemia	0.9599	2.6	0.8, 8.7
No university education	0.7965	2.2	0.6, 7.8
Constant	-6.4795	0.0	0.0, 0.0

Neuropathy*

Variable	Beta coefficient	OR	95%CI
Diabetic foot	1.9115	6.8	4.4, 10.4
Retinopathy	0.8057	2.2	1.5, 3.2
Female gender	0.7901	2.2	1.4, 3.3
Stroke	1.1660	3.2	1.4, 7.5
Sitting ≥ 10 hours per day	0.6566	1.9	1.2, 3.1
No university education	0.6387	1.9	1.0, 3.4
HbA1c ≥ 9%	0.5345	1.7	1.2, 2.5
Kidney disease	0.3034	1.4	0.8, 2.2
Constant	-3.7037	0.0	0.0, 0.0

Kidney disease*

Variable	Beta coefficient	OR	95%CI
Age ≥ 60 years	0.9332	2.5	1.7, 3.8
Sitting ≥ 10 hours per day	0.6835	2.0	1.2, 3.1
Hypertension	0.9006	2.5	1.4, 4.2
CAD	0.9006	1.6	1.0, 2.4
Diabetes Duration > 10 years	0.3265	1.4	0.9, 2.2
Insulin use	0.4817	1.6	1.1, 2.4
Neuropathy	0.3970	1.5	1.0, 2.3
Constant	-3.7069	0.0	0.0, 0.0

Retinopathy*

Variable	Beta coefficient	OR	95%CI
Diabetes Duration > 10 years	0.7906	2.2	1.6, 3.0
Neuropathy	0.6883	2.0	1.4, 2.9
Insulin use	0.4727	1.6	1.2, 2.1
Diabetic foot	0.6338	1.9	1.2, 2.9
CAD	0.5531	1.7	1.2, 2.5
Physical activity < 150 minute/week	0.3829	1.5	1.1, 2.0
Family history of diabetes	0.3351	1.4	1.0, 1.9
No university education	0.3550	1.4	1.0, 2.1
Age ≥ 60 years	0.2833	1.3	1.0, 1.8
Constant	-2.2154	0.1	0.1, 0.2

* Accounts for variation in the region in multiple mixed-effect logistic regression

Figure 3: The discrimination power (1000-fold bootstrap) of the risk scoring models for diabetes complications

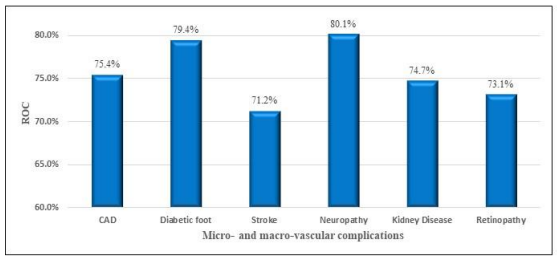
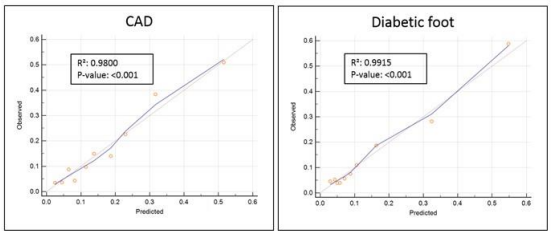


Figure 4: Decile-decile plots for the observed and predicted probability of CAD and diabetic foot



Conclusion: The developed risk prediction models require readily available information from routine clinical practice and the models have high discrimination and calibration power. Therefore, we recommend the use of these models in the clinical assessment of major complications for people with type 2 diabetes in Saudi Arabia.

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Chapter 6:

Obesity, Hypertension, and Dyslipidaemia among People with Type 2 Diabetes in Saudi Arabia

6.1 Introduction

People with diabetes have high risk of diabetes complications when they do not control their blood glucose level and have long-standing hyperglycaemia (13, 14). However, hyperglycaemia is not the only factor that increases the risk. It is well established that obesity, hypertension, and high blood lipids are risk factors for cardiovascular disease in the general population and people with diabetes (20, 45, 123-129). Furthermore, people with diabetes are at increased risk of having these comorbidities at the time of diagnosis of diabetes or acquiring them sooner or later over the course of diabetes (22-24). The current diabetes management guidelines place heavy emphasis on the control of blood glucose level along with body weight, blood pressure, and blood lipid profile (17).

Studies from Saudi Arabia showed that people with diabetes have high prevalence of obesity, hypertension, and dyslipidaemia (45-53). Little attention, however, was given to identify factors that contribute to these comorbidities. To improve the control of these comorbidities and to develop effective preventive strategies, the risk factors of these comorbidities must be identified and managed. This chapter explored the factors that are associated with obesity, hypertension, and dyslipidaemia among people with T2DM in Saudi Arabia and to assess the effect of these comorbidities on the risk of cardiovascular diabetes complications.

6.2 Article:

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Obesity, Hypertension, and Dyslipidaemia among People with Type 2 Diabetes in Saudi Arabia

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Abstract

Objective: To assess the prevalence and factors related to obesity, hypertension, and dyslipidaemia among people with type 2 diabetes mellitus (T2DM) in Saudi Arabia, and to explore how these comorbidities affect cardiovascular disease risk.

Method: A survey was conducted among adults with T2DM who attended diabetes centres in three major regions in 2017. Participants were interviewed and their medical records were reviewed. Bootstrap resampling with logistic regression was used to identify risk factors associated with obesity, hypertension, and dyslipidaemia.

Results: 1,121 participants were recruited. The mean age was 57.6 (±11.1) years. The prevalence of obesity, hypertension, and dyslipidaemia was 62.6%, 70.0%, and 70.7%, respectively. Younger age, female gender, physical inactivity, longer sitting time, and insulin use were associated with obesity. Advanced age, obesity, renal impairment, and lower education were associated with hypertension. Advanced age, low income, insulin use, and lower education were related to dyslipidaemia. Longer diabetes duration was associated with all comorbidities. These comorbidities substantially increased the risk of cardiovascular disease.

Conclusion: Obesity, hypertension, and dyslipidaemia are highly prevalent among people with T2DM in Saudi Arabia and these comorbidities increase the risk of cardiovascular disease. These comorbidities can be prevented by controlling a number of modifiable factors, including lifestyle.

Keywords:

Saudi Arabia, diabetes, obesity, hypertension, dyslipidaemia, metabolic syndrome, cardiovascular complications.

Introduction

The prevalence of diabetes mellitus is growing rapidly worldwide, which makes this disease a pressing global public health issue. It is estimated that in 2017, 451 million people aged 18 years and over were living with diabetes globally, and it is projected that the number will increase to 693 million by 2045 [1]. In addition, diabetes was responsible for 9.9% of the global all-cause mortality among people aged 18 years and older [1]. Diabetes and its related complications present a heavy social and financial burden, and a formidable challenge to healthcare systems across the world.

Compared to a person without diabetes, a person with diabetes has a two to four times higher risk of cardiovascular disease, which is a leading cause of morbidity and mortality for people with diabetes [2]. Furthermore, the risk of cardiovascular disease and its related mortality substantially increases when a person with diabetes has comorbidities such as obesity, hypertension, and dyslipidaemia. A study found that in people with type 2 diabetes mellitus (T2DM) the adjusted relative risks of cardiovascular disease and total mortality for a 5-unit increase in body mass index (BMI) were 13% and 27%, respectively [3]. Another study reported that people with T2DM and hypertension have 4.7-fold higher odds of cardiovascular disease compared to people with T2DM only [4]. People with T2DM and dyslipidaemia were found to have a 1.54-fold higher hazard ratio for coronary artery disease and a 2.13-fold higher hazard ratio for stroke, compared to people with T2DM who have normal a lipid profile [5].

Unfortunately, people with diabetes, type 2 in particular, are predisposed to have or acquire these comorbidities. Compared to a global prevalence of hypertension of 26.4% in the general population [6], the prevalence in people with T2DM can reach over 50% [7]. Similarly, compared to a global prevalence of obesity of 9.8% in the general population [8], the prevalence can reach over 30% in people with T2DM [7]. In regard to dyslipidaemia, studies reported a prevalence between 25.5% and 52.9% in the general population [9-11]. Among people with T2DM, however, the prevalence of dyslipidaemia can reach over 70% [12, 13]. Furthermore, people with T2DM are prone to have a combination of high triglycerides and low high-density lipoprotein, which is known as ‘atherogenic dyslipidaemia’ because of its strong association with cardiovascular disease [5].

Preventing or controlling diabetes comorbidities is key to preventing or delaying diabetes-related complications. It can be achieved by controlling the factors that increase the risk of these comorbidities. Thus, identifying the factors related to obesity, hypertension, and dyslipidaemia as comorbidities of diabetes has great clinical and public health importance. The risk factors related to these comorbidities, however, can vary substantially between populations because of variations in genetic, environmental, and behavioural factors. Therefore, findings from a study conducted in one country may not be generalisable to the population of another country.

Diabetes mellitus is highly prevalent in the Arabian Gulf Cooperation Council Countries, namely, Saudi Arabia, Kuwait, Bahrain, Qatar, United Arab Emirates, and Oman [14]. Saudi Arabia is among the countries with the highest prevalence of diabetes, regionally and globally [14]. Furthermore, the prevalence of diabetes-related complications is also high in Saudi Arabia [15, 16], and according to an estimate in 2014, 13.9% of the country's total healthcare cost was spent on the treatment of people with diabetes and its complications [17, 18]. A number of studies have measured the prevalence of obesity, hypertension and dyslipidaemia among people with diabetes in Saudi Arabia [15, 19-24]. The majority of these studies, however, were single-centred and were underpowered because of their small sample size. Moreover, of these studies only one, which was single centre hospital-based, explored factors associated with hypertension [19], while factors associated with obesity and dyslipidaemia were not explored for the Saudi population with diabetes. There is also a scarcity of evidence about how these comorbidities impact the risk of cardiovascular complications among this high-risk population. Thus, the aim of this study was threefold. Firstly, to measure the prevalence of obesity, hypertension and dyslipidaemia among people with T2DM in Saudi Arabia. Secondly, to identify demographic, behavioural, and clinical risk factors that increased the risk of these comorbidities. Thirdly, to assess the individual and combined effect of these comorbidities on the risk of cardiovascular complications.

Methodology

Study design and population

A cross-sectional survey was conducted to collect data from people with T2DM attending diabetes centres in the Saudi Arabian cities of Hofuf, Riyadh, and Jeddah. The study population consisted of people aged 18 years and over who had a documented diagnosis of T2DM with a duration of diabetes of at least one year. People with other types of diabetes (type 1 diabetes and gestational diabetes), and pregnant women with T2DM, were excluded from the study. The calculated sample size was 1,082 participants based on a sample size calculation with 90% confidence level, 5% significance level, and a 2.5% margin of error for the previously reported prevalence of diabetes complications and comorbidities in Saudi Arabia [25]. Both the Monash University Human Research Ethics Committee in Australia and the Research Ethics Committee of the Ministry of Health in Saudi Arabia approved this research project. All the study procedures were carried out in accordance with the principles of the Declaration of Helsinki as revised in 2013.

Data collection

Consecutive attendees in the diabetic centres were randomly approached between 15 May and 30 November 2017. Upon their agreement to participate, written informed consent was obtained and they were interviewed face-to-face by trained data collectors in order to complete a structured questionnaire [25]. The questionnaire collected data related to socio-demographics, behavioural, and medical history. Socio-demographic data included age, gender, marital status, education, area of residence and household income. Behavioural data included smoking status and level of physical activity (Global Physical Activity Questionnaire (GPAQ) [26]). Medical history data included the duration of diabetes, modality of treatment, and history of diabetes complications and comorbidities. At the end of the interview, participants' blood pressure, height, weight, and waist and hip circumference were measured in a standardised way [25]. Participants' medical records were then reviewed for lab test results, currently prescribed medications, and documented diagnosis of hypertension and diabetes complications.

Operational definitions

BMI was categorised according to the current World Health Organization (WHO) guidelines into normal (< 25.0 kg/m²), pre-obesity (25.0 – 29.9 kg/m²), and obesity (class I, II and II ≥ 30.0 kg/m²). Hypertension was defined as either: documented diagnosis of hypertension; taking antihypertension medications; or three previous high blood pressure measures (systolic ≥ 140 mmHg or diastolic ≥ 90 mmHg) [27]. Dyslipidaemia was defined as taking lipid-lowering drugs or any of the following: cholesterol > 4.0 mmol/L, low density lipoprotein lipase (LDL) > 2.0 mmol/L, triglycerides > 2.0 mmol/L, or high-density lipoprotein lipase (HDL) < 1.0 mmol/L [28]. Using the GPAQ [26], the total number of minutes of physical activity per week was categorised into ≥ 150 minutes and < 150 minutes [27], while the number of hours spent in sitting position per day were categorised into < 10 hours and ≥ 10 hours [29]. Based on haemoglobin A1c (HbA1c) level, glycaemic control was categorised into good control (HbA1c < 7.0%) and poor control (HbA1c ≥ 7.0%). High waist–hip ratio was defined as a ratio of > 0.96 for men and > 0.98 for women [30]. Renal impairment was defined as estimated glomerular filtration rate (eGFR) ≤ 60 ml/min/1.73m², which was calculated from serum creatinine using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [31]. Cardiovascular complications were defined as either documented diagnosis of coronary artery disease, documented diagnosis of irreversible cerebrovascular accident (stroke), or a history of lower extremity ulcers or amputations (diabetic foot).

Data analysis

Stata SE version 15.0 was used for data analysis. Data were summarised and presented as frequency and percentage. Chi-squared test were used to examine univariate associations between demographic, behavioural, and clinical factors with obesity, hypertension and dyslipidaemia. Based on literature review and clinical judgment, age, gender, education, location of residence, household income, smoking, physical activity per week, length of sitting time per day, duration of diabetes, use of insulin, BMI, waist–hip ratio, HbA1c, dyslipidaemia and chronic kidney disease, were all identified as potential risk factors for one or more of the study outcomes. Of these, the variables diabetes duration, insulin use,

BMI, HbA1c, dyslipidaemia, and kidney disease had missing values, ranging between 0.09% for diabetes duration and 10.3% for waist–hip ratio. Missing data was imputed five times using the Chained Equation method [32].

Multiple logistic regression with bootstrap resampling with replacement [33] was used to identify factors associated with each of the outcomes, which included obesity (BMI ≥ 30.0 kg/m²), hypertension, and dyslipidaemia. From each imputed sample, 5,000 samples, each of the same sample size as the original sample, were randomly drawn with replacement, which resulted in 25,000 bootstrap samples. Multiple logistic regression was run for each of the bootstrap samples and the variables that appeared as significantly associated with the comorbidities were recorded. The percentage of times each variable appeared as significant in all the 25,000 samples was calculated. The variables with percentage of appearance as significant predictor of 50% and higher were added to a multilevel mixed-effect logistic regression model that adjusted the variables in the model by regional variation. The adjusted odds ratio, its 95% confidence interval, and p-value for the risk factors were calculated. The discrimination power of the models was evaluated using the area under the receiver operator characteristics (ROC).

In addition, the effect of obesity, hypertension, and high triglycerides combined with low HDL (atherogenic dyslipidaemia) on the risk of cardiovascular complications was examined using multilevel mixed-effect logistic regression adjusted for age, gender, smoking, and duration of diabetes and accounts for regional variation. In all parts of the analysis a p-value of 0.05 or less was considered as significant.

Results

General characteristics

Of the 1,121 participants in the study, ten (0.9%) had substantially incomplete records and were excluded, and the records of 1,111 participants were used in the analysis. The mean age was 57.6 (±11.1) years, and 65.2% (724) of the participants were females. The mean duration of diabetes was 13.9 (±8.4) years. The mean BMI was 32.9 (±8.1) kg/m² and 10.2% of the participants had normal

weight (BMI ≤ 24.9 kg/m²), while 27.2% were overweight (BMI: 25.0 – 29.9 kg/m²) and 62.5% obese (BMI ≥ 30.0 kg/m²). The prevalence of obesity was substantially higher among females (70.7%) compared to males (47.4%). The mean systolic and diastolic blood pressure were 130.5 (±19.2) mmHg and 79.1 (±11.6) mmHg respectively, and 70.0% of the participants had hypertension, with higher prevalence among females (72.6%) compared to males (64.9%). The mean cholesterol, LDL, HDL, and triglycerides was 4.7 (±1.2) mmol/L, 2.7 (±1.1) mmol/L, 1.2 (±0.3) mmol/L, and 1.8 (±0.9) mmol/L, respectively. The prevalence of dyslipidaemia was 70.7%, while the prevalence of high triglyceride combined with low HDL was 40.4%. There was no significant difference in the prevalence of dyslipidaemia between males and females.

Univariate association

Table 1 summarises participants' demographics and behavioural characteristics by different comorbidities. The prevalence of obesity was higher among age group 40–60 years, while the prevalence of hypertension and dyslipidaemia increased with age. Female gender was associated with higher prevalence of obesity and hypertension. Lower education level was associated with increased prevalence of all comorbidities. High household income increased the likelihood of obesity, while low income increased the prevalence of hypertension and dyslipidaemia. Low level of physical activity increased the likelihood of obesity and hypertension. Longer sitting time increased the prevalence of obesity while never having smoked cigarettes increased the prevalence of hypertension.

In regard to the clinical factors (**Table 2**), longer duration of diabetes was associated with higher prevalence of hypertension and dyslipidaemia. Insulin use was associated with increased prevalence of obesity and hypertension, and lower prevalence of dyslipidaemia. The prevalence of hypertension and dyslipidaemia increased with overweight and obesity. High waist–hip ratio, dyslipidaemia, and renal impairment were associated with higher prevalence of hypertension.

Adjusted association

Table 3 summarises the results of bootstrap variable selection for each of the diabetes comorbidities. The variables that appeared significantly related to obesity in at least 50% of the bootstrap samples were

age ≥ 60 years, female gender, duration of diabetes > 10 years, physical activity < 150 minutes per week, sitting time ≥ 10 hours per day, and insulin use. The variables age ≥ 60 years, BMI ≥ 30 kg/m², renal impairment, up to secondary level education, duration of diabetes > 10 years, and urban/rural area of residence were significant related to hypertension in bootstrap samples. Duration of diabetes > 10 years, insulin use, household income < 6001 SAR, and up to secondary level education were significant associated with dyslipidaemia in at least 60% of the bootstrap samples.

Age, gender and variables with percentage of appearance of 50% and higher in bootstrap analysis were introduced into multilevel mixed-effect logistic regression models as a predictor for each of the comorbidities (**Table 4**). Female gender was associated with 2.5-fold increased odds of obesity (95% CI: 2.0, 3.3). The odds of obesity increased by 60% for sitting time ≥ 10 hours per day (OR: 1.6, 95% CI: 1.1, 2.3) and duration of diabetes > 10 years (OR: 1.6, 95% CI: 1.2, 2.2). Physical activity < 150 minutes per week (OR: 1.5, 95% CI: 1.1, 2.0), age 46–60 years (OR: 1.5, 95% CI: 1.1, 1.9), and insulin use (OR: 1.5, 95% CI: 1.1, 1.9) increased the odds of obesity by 50%. The model for obesity has an ROC of 66.7%.

Age 46–60 years and above 60 years increased the odds of hypertension by 2.0-folds (95% CI: 1.3, 3.0) and 5.3-folds (95% CI: 3.2, 8.5), respectively. The odds of hypertension increased by 2.7-folds (95%CI: 1.7, 4.2) for BMI ≥ 30 kg/m² and by 2.6-folds (95% CI: 1.5, 4.4) for renal impairment. Duration of diabetes > 10 years (OR: 1.4, 95% CI: 1.0, 1.9), education level up to secondary school (OR: 1.7, 95% CI: 1.2, 2.4), and urban/rural area of residence (OR: 1.8, 95% CI: 1.0, 3.2) increased the odds of hypertension by between 40% to 80%. The regression model for hypertension has an ROC of 72.6%.

Age 46–60 years and above 60 years were associated, respectively, with 2.0-fold (95% CI: 1.3, 3.1) and 2.3-fold (95% CI: 1.5, 3.7) increase in the odds of dyslipidaemia. Duration of diabetes > 10 years (OR: 1.6, 95% CI: 1.2, 2.2) and insulin use (OR: 1.6, 95% CI: 1.2, 2.1) increased the odds of dyslipidaemia by 60%. The odds of dyslipidaemia also increased by 50% for household income < 6001 SAR (OR: 1.5, 95% CI: 1.1, 2.1) and education level up to secondary school (OR: 1.5, 95% CI: 1.0, 2.2). The model for dyslipidaemia has an ROC of 63.9%.

The association between comorbidities and cardiovascular disease

Figure 1 illustrates the adjusted association between diabetes comorbidities and cardiovascular disease. The prevalence of cardiovascular complications among the study participants was 27.9%. The odds of cardiovascular complications were 3.2-fold (95% CI: 1.3, 7.7) and 3.3-fold (95% CI: 1.3, 8.7) higher for patients with hypertension and obesity respectively, while high triglycerides combined with low HDL was associated with 4.1-fold (95% CI: 1.4, 11.6) increased odds. The odds of cardiovascular complications increased further when two or more of these comorbidities coexisted. The odds were 5.5-fold (95% CI: 2.2, 14.3) higher for obesity combined with high triglycerides and low HDL, 6.2-fold (95% CI: 2.6, 15.2) higher for hypertension coexisting with high triglycerides and low HDL, and 7.3-fold (95% CI: 3.2, 16.7) higher for obesity coexisting with hypertension. The odds of cardiovascular complications were 7.5-fold (95% CI: 3.3, 17.4) higher when all the comorbidities coexisted.

Discussion

The aim of this study was to measure the prevalence of obesity, hypertension, and dyslipidaemia, and to explore their risk factors among people with T2DM in Saudi Arabia. The impact of these comorbidities on the risk of cardiovascular disease was also explored. This study showed that the prevalence of obesity, hypertension, and dyslipidaemia was very high, and these comorbidities substantially increased the risk of cardiovascular complications especially when they co-existed. Furthermore, a number of modifiable factors, including physical inactivity, longer sitting time, and high BMI, were associated with these comorbidities.

The prevalence of obesity, hypertension, and dyslipidaemia in this study was high, but comparable with recent local and international studies. Previous studies from Saudi Arabia reported that the prevalence of obesity and hypertension among people with diabetes was respectively 46.5% to 57.9% and 54.2% to 78.1% [15, 19-24]. A systematic review of international studies reported a prevalence of obesity and hypertension among people with T2DM higher than 50.0% [7]. As for dyslipidaemia, studies from

Saudi Arabia showed a prevalence between 53.1% and 77% among people with diabetes [20, 21, 24], while studies from India and Tanzania respectively reported a prevalence among people with diabetes of 70% and 95% [12, 13].

In line with other studies, the current study found that younger people with diabetes were at higher risk of obesity [3, 34]. The loss of body mass with age can partially explain this finding. Another explanation is that older people might be more adherent to healthy diet than younger people because they are more concerned about their health. On the other hand, the current results showed that advanced age substantially increased the risk of hypertension and dyslipidaemia, and these findings are in agreement with the previous literature [19]. As for the duration of diabetes, this study found that longer duration of diabetes was related to all comorbidities. A previous study reported similar findings for hypertension and dyslipidaemia [35]. For obesity, however, a Swedish study showed that longer duration of diabetes was associated with lower BMI [34]. The difference between the two populations might explain the variation in the results between the current and the Swedish studies.

Physical inactivity and long sitting times are well-known risk factors of obesity among the general population as well as among people with diabetes [36]. As was reported previously, more than two-thirds of our participants (70.5%) did not achieve the recommended physical activity per week (≥ 150 min/week), and 46.7% of the participants were spending over six hours in a sitting position daily [16, 37]. The harsh weather, the availability of private automobiles, and the shift to more office-based occupations over the last few decades played an important role in decreasing daily physical activity. Moreover, the reduction in physical activity was accompanied by a change in eating habits, increasing the consumption of unhealthy energy-dense food. As a result, the prevalence of obesity in Saudi Arabia has been rising rapidly over the last few decades [38].

Women in Saudi Arabia are more prone to be physically inactive [39]. Until recently, gymnasiums for women were not available in the country, and for cultural reasons women were not encouraged to undertake physical exercise, particularly outdoors. This might explain the higher prevalence in this study of obesity among women compared to men, which is in agreement with a previous study [40]. In order to reduce the prevalence of obesity among people with diabetes, clinicians and diabetes educators

should emphasise the role of physical activity, healthy eating, and maintaining healthy body weight in the management of diabetes.

We found that insulin use was associated with obesity. Intensifying pharmacological treatment for diabetes can improve glycaemic control and lower the risk of diabetes complications [41]. In addition, insulin use can improve lipid profile, as our results showed, which is in agreement with a previous study [42]. Intensifying pharmacological treatment, however, may result in weight gain, which may adversely affect the prognosis of the disease, as weight gain increases the risk of cardiovascular complications [43]. The promotion of lipogenesis and the increase in carbohydrate intake by patients to avoid hypoglycaemia are two of the main mechanisms through which insulin may increase weight [44]. Insulin-sensitising drugs such as metformin can improve the body's sensitivity to insulin and lower the required insulin dose, reducing its effect on weight. Healthy diet and regular exercise have a similar effect [44]; thus, people with diabetes should always be encouraged to follow a healthy lifestyle.

Our study showed that obesity was related to hypertension. It is estimated that more than two-thirds of hypertension cases can be attributed to obesity [45]. A number of mechanisms to link obesity with hypertension have been suggested, and these include activation of the renin–angiotensin–aldosterone system, increasing sympathetic activity, promoting insulin and leptin resistance, increasing pro-coagulatory activity, endothelial dysfunction, and increasing renal sodium reabsorption [46]. Obesity is also linked to the development and progression of kidney disease, which is strongly associated with hypertension, as our results and previous studies showed [47]. Maintaining a healthy weight should be an essential part of the management of diabetes because of its health benefits on controlling blood sugar, blood pressure, and blood lipids, and on reducing the risk of diabetes complications [48]

Socioeconomic status plays an important role in the development of diabetes comorbidities. This study showed that low education level was associated with a higher risk of hypertension and dyslipidaemia, while low household income increased the risk of dyslipidaemia. Higher education levels and incomes increase the likelihood of adherence to healthier lifestyle behaviours and the positive attitudes toward health and disease prevention which lower the risk of chronic diseases [49].

Metabolic syndrome occurs when multiple comorbidities including obesity, abnormal glucose metabolism, dyslipidaemia, and hypertensions coexist [50]. Patients with metabolic syndrome are at increased risk of cardiovascular disease [51], and our results were in keeping with this finding. We found that among people with T2DM, having one of these comorbidities was associated with substantially increased risk of cardiovascular complications, and that this risk further increased when these comorbidities coexisted. Moreover, the coexistence of these comorbidities (i.e. metabolic syndrome) is common among people with T2DM in Saudi Arabia. About 63.4% of the study participants had two or more other comorbidities, and 19.5% of them had all comorbidities including obesity, dyslipidaemia, and hypertension. People with diabetes comorbidities should be considered a very high-risk group and the measures needed to control these comorbidities should be intensified.

This study has strengths and limitations. The relatively large sample size, drawn from multiple centres in three different regions of Saudi Arabia, adds strength to the study and makes the results more generalisable. The exploration of various demographic, behavioural, and clinical risk factors, using robust methods of analysis, lend it further weight. A limitation of this study, on the other hand, is the cross-sectional design, which allows only the inference of association rather than the assumption of causation. Nevertheless, this study clearly shows that obesity, hypertension, and dyslipidaemia were prevalent among people with T2DM in Saudi Arabia and how these comorbidities substantially increased the risk of cardiovascular disease. This study also shows the importance of lifestyle modification in the management of diabetes and the prevention of its comorbidities.

To conclude, obesity, hypertension, and dyslipidaemia are prevalent among people with T2DM in Saudi Arabia, and these comorbidities substantially increase the risk of cardiovascular complications. The risk of these comorbidities can, however, be reduced by following a healthy lifestyle, which includes practising regular physical activity, reducing sitting time, and maintaining a healthy body weight.

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Competing interests

All authors declare that they have no competing interests.

Author contributions

All authors were involved in the conception and design of the study. MJA, HHA, ASA, NFA, and WFM contributed to the acquisition of data. MJA, BB, AA and HAA contributed to data analysis and interpretation of results. MJA and BB drafted the manuscript. All authors critically reviewed the manuscript and approved the final version.

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Availability of data and material

The datasets generated during and analysed during the current study are available from the

corresponding author on reasonable request.

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Table 1: Demographic and behavioural characteristic by obesity, hypertension, and dyslipidaemia status

Variable	BMI				Hypertension			Dyslipidaemia		
	Normal (BMI ≤ 24.9 kg/m²) 10.2% (n= 113)	Over weight (BMI 25.0-29.9 kg/m²) 27.2% (n= 300)	Obese (BMI ≥ 30 kg/m²) 62.5% (n= 690)	P-value	No 30.0% (n= 333)	Yes 70.0% (n= 778)	P-value	No 29.3% (n= 294)	Yes 70.7% (n= 709)	P-value
Age % (n)										
<46 years	14.6 (20)	26.3 (36)	59.1 (81)	0.036	57.7 (79)	42.3 (58)	<0.001	48.8 (61)	51.2 (64)	<0.001
46 – 60 years	7.9 (46)	26.0 (151)	66.0 (383)		33.6 (196)	66.4 (387)		27.8 (147)	72.2 (382)	
>60 years	12.2 (47)	29.3 (113)	58.6 (226)		14.8 (58)	85.2 (333)		24.6 (86)	75.4 (263)	
Gender: % (n)										
Female	7.8 (56)	21.6 (155)	70.7 (508)	<0.001	27.2 (197)	72.6 (527)	0.006	29.4 (192)	70.6 (461)	0.931
Male	14.8 (57)	37.8 (145)	47.4 (182)		35.1 (136)	64.9 (251)		29.4 (1.2)	70.9 (248)	
Education % (n)										
University/college	11.6 (23)	36.4 (72)	52.0 (1.3)	0.002	45.5 (90)	54.6 (108)	<0.001	35.4 (63)	64.6 (115)	0.049
Up to secondary level	9.9 (90)	25.2 (228)	64.9 (587)		26.6 (243)	73.4 (670)		28.0 (231)	72.0 (594)	
Location of residence										
Urban	10.5 (99)	27.9 (264)	61.7 (584)	0.568	29.5 (281)	70.6 (673)	0.183	28.3 (244)	71.7 (617)	0.231
Rural	10.5 (10)	23.2 (22)	66.3 (63)		28.4 (27)	71.6 (68)		36.4 (32)	63.6 (56)	
Remote	6.7 (4)	23.0 (14)	70.5 (43)		40.3 (25)	59.7 (37)		33.3 (18)	66.7 (36)	
Household income % (n)										
<6001 SAR	10.4 (62)	31.5 (188)	58.1 (346)	0.001	25.5 (131)	74.5 (383)	0.002	33.3 (151)	66.7 (302)	0.011
≥6001 SAR	10.1 (51)	22.1 (112)	67.9 (344)		33.8 (202)	66.2 (395)		26.0 (143)	74.0 (4.7)	
Ever Smoked % (n)										
No	9.8 (89)	27.6 (252)	62.6 (571)	0.454	28.5 (261)	71.5 (655)	0.020	29.0 (239)	71.0 (585)	0.647
Yes	12.6 (24)	25.1 (48)	119 (62.3)		36.9 (72)	63.1 (123)		30.7 (55)	69.3 (124)	
Physical activity % (n)										
≥150 min/week	12.3 (40)	33.1 (108)	54.6 (174)	0.002	35.4 (116)	64.6 (212)	0.011	31.3 (91)	68.7 (200)	0.383
<150 min/week	9.4 (73)	24.7 (192)	65.9 (512)		25.7 (217)	72.3 (566)		28.5 (203)	71.5 (509)	
Sitting time										
<10 hours per day	11.3 (103)	28.3 (259)	60.4 (552)	0.002	30.9 (283)	69.1 (635)	0.139	29.4 (246)	70.6 (590)	0.859
≥10 hours per day	5.3 (10)	21.7 (41)	73.0 (138)		25.5 (49)	74.5 (143)		28.7 (48)	71.3 (119)	

Table 2: Clinical characteristic by obesity, hypertension, and dyslipidaemia status

Variable	BMI				Hypertension			Dyslipidaemia		
	Normal (BMI ≤ 24.9 kg/m²) 10.2% (n= 113)	Over weight (BMI 25.0-29.9 kg/m²) 27.2% (n= 300)	Obesity (BMI ≥ 30 kg/m²) 62.5% (n= 690)	P-value	No 30.0% (n= 333)	Yes 70.0% (n= 778)	P-value	No 29.3% (n= 294)	Yes 70.7% (n= 709)	P-value
DM Duration % (n)										
≤10 years	8.9 (37)	25.2 (105)	66.0 (275)	0.171	37.9 (159)	62.1 (261)	<0.001	36.8 (155)	63.2 (266)	<0.001
>10 years	11.1 (76)	28.5 (195)	60.4 (414)		25.2 (174)	74.8 (516)		25.5 (176)	74.5 (514)	
Insulin use										
No	10.1 (62)	30.7 (188)	59.2 (363)	0.015	33.8 (208)	66.2 (408)	0.002	27.1 (167)	72.9 (450)	0.026
Yes	10.4 (51)	22.9 (112)	66.7 (326)		25.3 (125)	74.7 (369)		33.2 (164)	66.8 (330)	
Body mass index % (n)										
Underweight/normal	-	-	-	-	44.3 (50)	55.8 (63)	<0.001	38.9 (44)	61.1 (69)	0.044
Pre-obesity	-	-	-		37.0 (111)	63.0 (189)		26.3 (79)	73.7 (221)	
Obesity (class I – III)	-	-	-		24.5 (169)	75.5 (521)		29.7 (205)	70.3 (29)	
Waist/hip ratio % (n)										
Normal	-	-	-	-	33.6 (188)	66.4 (372)	0.026	36.1 (65)	63.9 (115)	0.109
High	-	-	-		27.0 (118)	73.0 (319)		30.0 (247)	70.0 (576)	
Glycaemic control										
Good Control (HbA1c <7%)	9.6 (25)	29.9 (78)	60.5 (158)	0.534	28.1 (74)	189 (71.9)	0.508	32.3 (85)	67.7 (178)	0.264
Poor control (HbA1c ≥7%)	10.3 (85)	26.4 (217)	63.3 (531)		30.3 (251)	69.7 (578)		28.7 (238)	71.3 (591)	
Dyslipidaemia % (n)										
N0	-	-	-	-	35.0 (103)	65.0 (191)	0.045	-	-	-
Yes	-	-	-		28.6 (203)	71.4 (506)		-	-	
Renal impairment										
No (eGFR >60 ml/min/1.73m²)	-	-	-	-	33.3 (307)	66.7 (614)	<0.001	-	-	-
Yes(eGFR ≤60 ml/min/1.73m²)	-	-	-		12.4 (20)	87.6 (141)		-	-	

Table 3: Bootstrap resampling variable selection for obesity, hypertension, and dyslipidaemia

Obesity (BMI ≥ 30 kg/m²)		**Hypertension**		**Dyslipidaemia**	
Variable	**% of appearance as significant**	**Variable**	**% of appearance as significant**	**Variable**	**% of appearance as significant**
Female gender	100.0%	Age ≥60 years	100.0%	Duration of Diabetes >10 years	97.1%
Age ≥60 years	90.6%	BMI ≥30 kg/m²	100.0%	Using insulin	82.3%
Duration of Diabetes >10 years	85.0%	Renal impairment	98.5%	Household income <6001 SAR	81.6%
Sitting time ≥10 hours per day	76.3%	Education up to secondary level	75.5%	Education up to secondary level	60.3%
Physical activity <150 min/week	75.6%	Duration of Diabetes >10 years	66.8%	Age ≥60 years	40.2%
Using insulin	72.1%	Urban/rural area of residence	59.6%	Urban/rural area of residence	8.9%
Education up to secondary level	29.9%	hba1c ≥7%	44.4%	Sitting time ≥10 hours per day	7.6%
Urban/rural area of residence	6.4%	Dyslipidaemia	36.1%	hba1c ≥7%	7.1%
Ever smoked	5.7%	High waist-hip ratio	34.8%	Ever smoked	6.7%
Household income <6001 SAR	5.5%	Using insulin	28.5%	Female gender	6.4%
		Ever smoked	28.3%	BMI ≥30 kg/m²	6.3%
		Female gender	20.7%	High waist-hip ratio	5.8%
		Household income <6001 SAR	12.7%	Physical activity <150 min/week	5.5%
		Physical activity <150 min/week	10.4%		
		Sitting time ≥10 hours per day	7.1%		

Table 4: Multivariate analysis of the association between various risk factors and both hypertension and dyslipidaemia

Obesity (BMI ≥30 kg/m²)

Variable	Odds ratio	95% CI	P-value
Age (ref: >60 years)			
46 – 60 years	1.5	1.1, 1.9	0.008
<46 years	1.2	0.7, 1.8	0.535
Female gender (ref: Male)	2.5	2.0, 3.3	<0.001
Physical activity <150 min/week (Ref: ≥150 min/week)	1.5	1.1, 2.0	0.010
Sitting time ≥10 hours per day (ref: <10 hours/day)	1.6	1.1, 2.3	0.015
DM Duration >10 years (ref: ≤10 years)	1.6	1.2, 2.2	0.001
Using insulin (ref: no)	1.5	1.1, 1.9	0.006

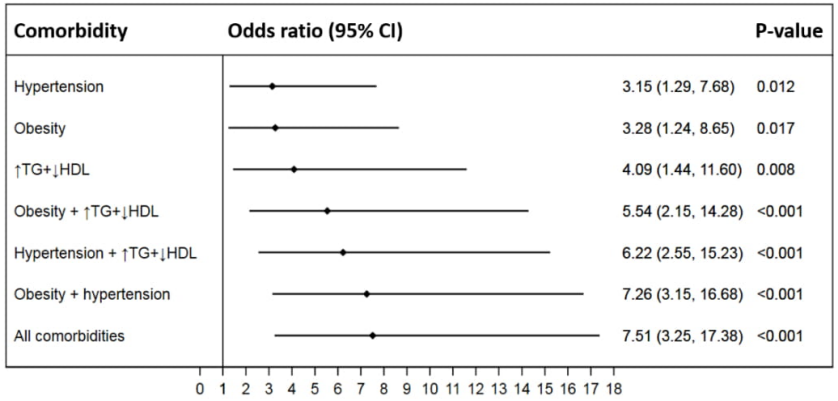
Hypertension

Variable	Odds ratio	95% CI	P-value
Age (ref: <46 years)			
46 – 60 years	2.0	1.3, 3.0	0.001
>60 years	5.3	3.2, 8.5	<0.001
Female gender (ref: Male)	1.2	0.9, 1.6	0.292
BMI (ref <25.0 kg/m²)			
25.0-29.9 kg/m²	1.2	0.8, 2.1	0.275
≥30.0 kg/m²	2.7	1.7, 4.2	<0.001
Renal impairment (ref: no)	2.6	1.5, 4.4	<0.001
Education up to secondary level (ref: university)	1.7	1.2, 2.4	0.006
Duration of diabetes >10 years (ref: ≤10 years)	1.4	1.0, 1.9	0.036
Urban/rural location of residence (ref: remote)	1.8	1.0, 3.2	0.060

Dyslipidaemia

Variable	Odds ratio	95% CI	P-value
Age (ref: <46 years)			
46 – 60 years	2.0	1.3, 3.1	0.001
>60 years	2.3	1.5, 3.7	<0.001
Female gender (ref: Male)	1.0	0.7, 1.4	0.976
Household income <6001 SAR (ref: ≥6001)	1.5	1.1, 2.1	0.007
Duration of diabetes >10 years (ref: ≤10 years)	1.6	1.2, 2.2	0.003
Using insulin (ref: no)	1.6	1.2,2.1	0.003
Education up to secondary level (ref: university)	1.5	1.0, 2.2	0.043

Figure 1: The adjusted* association between cardiovascular diabetes complications and comorbidities (obesity, hypertension and high triglycerides + low HDL)



↑TG: high triglycerides, ↓HDL: low HDL, * Adjusted for age, gender, duration of diabetes, and smoking and accounting for regional variation using multilevel mixed-effect logistic regression

Chapter 7:

Health Related Quality of Life for People with Type 2 Diabetes in Saudi Arabia

7.1 Introduction

Health-related quality of life (HRQoL) is an important tool in evaluating the effect of chronic diseases on the quality of life (130). The HRQoL measures the person's perception of wellbeing, physically and mentally (131). This tool can help clinicians and policy makers to understand the burden of chronic diseases and the cost-effectiveness of health programs and interventions (132).

Diabetes can have a substantial impact on the quality of life of the affected people. The mere awareness of having diabetes was associated with lower HRQoL compared to people without diabetes (133). The HRQoL deteriorates further over the long term of the disease, especially when people with diabetes develop diabetes comorbidities and complications such as hypertension and micro- and macro-vascular complications (25, 28, 29). The main aim of the management of diabetes is to control the disease and prevent diabetes complications so that people with diabetes can live a normal life similar to those without diabetes.

The few studies from Saudi Arabia that explored HRQoL showed that people with diabetes in the country have low HRQoL (27, 64, 134, 135). These studies, however, had a small sample size and covered a small geographical location. In addition, it is difficult to compare these study results as they used different tools to assess HRQoL. Furthermore, not all potential factors that affect HRQoL were explored. To maintain or improve the HRQoL of people with T2DM in Saudi Arabia, all important factors that affect the HRQoL must be investigated. The aim of this chapter was to assess the HRQoL among people with T2DM in Saudi Arabia and to explore the effect of various demographic, behavioural, and clinical factors on the quality of life and its dimensions.

7.2 Article:

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Quality of Life Research

Health Related Quality of Life for People with Type 2 Diabetes in Saudi Arabia

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Abstract

Objectives: To assess the health-related quality of life (HRQoL) and factors that affect it for people with type 2 diabetes in Saudi Arabia.

Methods: A survey was conducted among adults with type 2 diabetes who attended diabetes centres in three major cities in Saudi Arabia in 2017. Participants were interviewed and their medical records were reviewed. The EuroQol 5-Dimension 5-Level was used to assess HRQoL. Bootstrap resampling with multiple regression analysis was used to identify factors associated with the EQ-5D-5L dimensions, utility index and visual analogue scale.

Results: A total of 1121 participants were recruited. The mean age was 57.6 (±11.1) years. The mean utility index was 0.739 ±0.261, and 51.0% of the participants had problems with mobility, 12.3% had problems with self-care, 30.5% had problems with usual activity, 51.6% had problems with pain-discomfort, and 45.8% had problems with anxiety-depression. Factors associated with lower utility index were lower education level, physical inactivity, long sitting time, anxiety, depression, and diabetes complications.

Conclusion: HRQoL is low among people with type 2 diabetes in Saudi Arabia, particularly among women and those who have complications. In order to improve the quality of life, people with diabetes should follow a healthy lifestyle and diabetes complications, anxiety, and depression should be prevented.

Kew words:

Type 2 diabetes, health related quality of life, HRQoL, associated factors, Saudi Arabia

Introduction

Diabetes is a major and continuously growing health issue globally. This chronic disease is the most common endocrine disorder, affecting 8.8% of the adult population worldwide, and it is projected that the global prevalence of the disease will reach 9.9% by 2045 [1]. Diabetes occurs when there is a defect in insulin secretion, insulin action or both which results in chronically elevated blood glucose level [2]. The high blood glucose level can damage large and small blood vessels leading to multiple diabetes complications, disability and reduced life expectancy. There are three major types of diabetes: type 1, type 2 and gestational. Type 2 diabetes mellitus (T2DM), which mainly affect adults, is the most common type, accounting for 90% of cases of diabetes [2]. Unhealthy eating habit, physical inactivity, and obesity are main risk factors for T2DM [2].

T2DM is managed by lifestyle modification and medications to control blood glucose level. The main aim of the management is to maintain the health and quality of life of the affected people so that they live a normal life similar to those without diabetes. The term health related quality of life (HRQoL) was introduced about three decades ago. HRQoL focuses on the person's perception of wellbeing including physical and mental health [3], and is considered a multidimensional concept that involves the evaluation of the positive and negative aspects of a person's life [4]. Currently, HRQoL is recognised an important tool in the assessment of the effect of chronic diseases and their treatments on the quality of life in addition to the traditional measures of clinical outcomes such as morbidity and mortality [5]. HRQoL also allows policy makers to understand the burden of chronic diseases and can be useful for evaluating the cost effectiveness of health programs and interventions [6]. Various generic and diseases-specific tools that assess HRQoL have been used for people with diabetes [7]. Among these tools the EuroQol 5-Dimension (EQ-5D) is the most widely used tool because of its simplicity, reliability and its ability to be used in cost-effectiveness analyses [5, 8].

Maintaining good HRQoL for people with diabetes is challenging for both the affected persons and the healthcare systems. Over the long term, diabetes can lead to complications which can have an adverse effect on health and HRQoL. Many studies showed that people with diabetes have lower HRQoL compared to people without diabetes [9-11], especially when they have diabetes complications [9, 12, 13]. Studies also showed that age, female gender, socioeconomic status, obesity, duration of diabetes, hyperglycaemia, hypoglycaemia, insulin use, and the use of multiple medications were associated with lower HRQoL [12-16]. Furthermore, the mere awareness of having diabetes was found to impact the HRQoL [17]. The person's beliefs, experiences, and expectations can also affect the HRQoL and influence how other factors can affect it. Therefore, factors found to affect HRQoL and their effect may vary between different populations. Thus, identifying factors that affect HRQoL is an essential step to control them to maintain the quality of life for people with diabetes in a population.

The Gulf Cooperation Council Countries including Saudi Arabia, Kuwait, Bahrain, Qatar, United Arab Emirates and Oman have witnessed vast economic and lifestyle changes over the past few decades. Along with these changes there was a rapid increase in the prevalence of diabetes mellitus in these countries. Currently, Saudi Arabia and the other Gulf Cooperation Council countries are among the countries with the highest prevalence of the disease regionally and globally [2]. Compared to the global (8.8%) and the regional (10.7%) prevalence of diabetes among adults, Saudi Arabia has an estimated prevalence of 17.7% [2]. Previous studies also showed that the prevalence of diabetes complications is high among the Saudi population with diabetes [18, 19], and their HRQoL is low [11, 20].

A few studies, however, have assessed HRQoL among people with T2DM in Saudi Arabia [11, 20-22]. These studies were limited to small samples and small geographical locations. In addition, it is difficult to compare these studies' results due to the use of different tools to assess the HRQoL. Furthermore, factors associated with low HRQoL and each of its dimensions were not explored adequately. Due to cultural, environmental, and healthcare system differences between Saudi Arabia and other countries, the factors that affect HRQoL and their effect may vary substantially. To maintain HRQoL or improve it for people with T2DM in Saudi Arabia, these factors must be identified and controlled. The aim of

this study was to assess the HRQoL among people with T2DM in Saudi Arabia and to explore the effect of various demographic, behavioural, and clinical factors on the quality of life and its dimensions.

Methods

Study Design and Population

The study was conducted as a cross-sectional survey. The study population consist of attendees of diabetes centres in Hofuf, Riyadh, and Jeddah cities who were 18-year-old and older and had documented diagnosis of T2DM with a duration of diabetes of at least one year. People with other types of diabetes including type 1, gestational, and pregnant women were excluded from the study. The plan was to recruit 1082 participants, which was based on a sample size calculation with 90% confidence level, 5% significance level, 2.5% margin of error, and the previously reported prevalence of diabetes complications and comorbidities in Saudi Arabia [23]. Ethical approval was obtained from the Monash University Human Research Ethics Committee in Australia and the Research Ethics Committee of the Ministry of Health in Saudi Arabia. All the study procedures were carried out in accordance with the principles of the Declaration of Helsinki as revised in 2013 [24].

Data collection

Data collection took place between 15 May and 30 November, 2017. Trained data collectors randomly approached consecutive attendees of the diabetic centres and explained the study to them. Written informed consent was obtained upon their approval to participate. Then they were interviewed face-to-face to fill a structured questionnaire [23]. The collected data include socio-demographics, behavioural, and disease related. Socio-demographic data included gender, age, level of education achieved, area of residence, and household income. Behavioural data include smoking status, and physical activity [25]. Disease related data include duration of diabetes, modality of treatment, hypoglycaemia symptoms last month, anxiety [26], depression [27], cognitive impairment [28], neuropathy [29] and history of diabetes complications and comorbidities.

The HRQoL was assessed using the EuroQol 5-Dimension 5-Level (EQ-5D-5L). The EQ-5D-5L is generic preference-based health status measuring tool [8]. It provides information on health status on five dimensions including mobility, self-care, usual activities, pain-discomfort and anxiety-depression. Each dimension has five possible responses: no problems, slight problems, moderate problems, serious problems, and inability or extreme problems. Using a scoring algorithm the scores in the dimensions can be converted to a single index-based utility score (utility index) [8]. The United Kingdom scoring algorithm is often used when country-specific weights are not available, and has been used for the Saudi population before [20]. The health utility score usually lies between zero and one, where zero indicates very poor health status (death) and one indicates a perfect health status. A score below zero indicates a health status worse than death. Visual analogue scale (VAS) is another part of the EQ-5D instrument in which the respondent can use a 20 centimetre visual analogue scale (VAS) to subjectively rate his/her health status at that day between zero (worst imaginable health status) and 100 (best imaginable health state). The establishers' permissions to use the EQ-5D-5L and the other tools were obtained.

At the end of the interview, the participants' blood pressure, height, and weight were measured in a standardised way [23]. Then, the participants' medical records were reviewed for recent lab test results, currently prescribed medications, and documented diagnosis of hypertension, coronary artery disease, stroke, and retinopathy.

Operational definitions

Body mass index (BMI) was categorised according to the current World Health Organization guidelines into normal (< 25.0 kg/m²), pre-obesity (25.0 – 29.9 kg/m²), and obesity (≥ 30.0 kg/m²). Using the Global Physical Activity Questionnaire [25], the total number of minutes of physical activity per week was categorised into ≥ 150 minutes and < 150 minutes [30]. The number of hours spent in sitting position per day were categorized into < 10 hours and ≥ 10 hours [31]. Based on haemoglobin A1c (HbA1c) level, glycaemic control was categorised into good control (HbA1c < 7.0%) and poor control (HbA1c ≥ 7.0%) [30]. Hypoglycaemia symptoms last month was defined as any symptoms of mild or severe hypoglycaemia including feeling hungry, trembling or shakiness, sweating, confusion, difficulty concentrating, and loss of consciousness. Hypertension was defined as either: documented diagnosis of hypertension, taking antihypertension medications, or three previous high blood pressure measures (systolic ≥ 140 mmHg or diastolic ≥ 90 mmHg) [30]. Coronary artery disease was defined as documented diagnosis of coronary artery disease, taking medication for coronary artery disease, or underwent a procedure for coronary artery disease. Stroke was defined as documented diagnosis of irreversible cerebrovascular accident. Diabetic foot was defined as a history of lower extremity ulcers or amputations. Retinopathy was defined as documented diagnosis of retinopathy, or the participant had been told by an ophthalmologist that he or she had retinopathy. Diabetes peripheral neuropathy was defined as a score of seven or more using the Michigan Neuropathy Screening Instrument [29]. Renal impairment was defined as estimated glomerular filtration rate (eGFR) ≤ 60 ml/min/1.73m² which was calculated from serum creatinine using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [32]. Depression was defined as a score of three and more in the Patient Health Questionnaire-2 (PHQ-2) [27]. Anxiety was defined as a score of three and more in the Generalized Anxiety Disorder Scale (GAD-2) [26]. Impaired cognitive function was defined as a score of ≤ 22 in the Rowland Universal Dementia Assessment Scale (RUDAS) [28].

Data Analysis

Stata SE version 15.0 was used for data analysis. The United Kingdom scoring algorithm was used to convert the scores in the dimensions to a single index-based utility score. The original five response to the EQ-5D dimensions were dichotomized to 'no problems' and 'any problems. Mean and standard deviation or frequency and percentages were used to summarise data, and the univariate association between potential risk factors and the EQ-5D dimensions, utility index, and VAS, was assessed using Chia square, T-test, or ANOVA. Based on literature review and clinical judgment age, gender, education, household income, location of residence, smoking, physical activity per week, length of sitting time per day, duration of diabetes, number of medications, hypoglycaemia events, insulin use, BMI, HbA1c, hypertension, diabetes complications, anxiety, depression, and cognitive impairment were identified as potential risk factors for poor HRQoL. Of these variables, diabetes duration, insulin use, BMI, HbA1c, neuropathy, kidney disease, and cognitive impairment had missing values which ranged between 0.09% for diabetes duration and 11.8% for cognitive impairment. Missing data was imputed five times using the Ice Chained Equation method [33].

To identify factors associated with the EQ-5D dimensions, utility index, and VAS, multiple (logistic or linear) regression with bootstrap resampling with replacement [34, 35] was used. From each of the imputed samples 5000 samples each of the same size as the original sample were randomly drawn with replacement (total of 25,000 bootstrap samples). Multiple regression was run for each of the bootstrap samples and variables that appeared as significantly associated with each of the outcomes were recorded. The percentage of times each variable appeared as significant (p-value ≤ 0.05) in all the 25,000 samples was calculated. The variables with percentage of appearance as significant of 50% and higher were added to a multiple (logistic or linear) regression model adjusted for age and gender. The

adjusted odds ratio or beta coefficient, their 95% confidence interval, and p-value for the risk factors associated with the study outcomes were reported.

Results

General characteristics

A total of 1,121 persons participated in the study. The records of ten participants (0.9%) were excluded, however, because they were substantially incomplete (n = 1,111). The mean age was 57.6 (±11.1) years, and 65.2% (724) of the participants were females. Of the study participants: 51.2% (569) achieved primary education or were illiterate, 31.0% (344) achieved intermediate or tertiary education, and 17.8% (198) achieved university education. The mean duration of diabetes was 13.9 (±8.4) years. The mean utility index was 0.739 ±0.261, while the mean VAS was 69.8 ±18.4. Of the participants, 51.0% had problems with mobility, 12.3% had problems with self-care, 30.5% had problems with usual activity, 51.6% had problems with pain-discomfort, and 45.8% had problems with anxiety-depression.

Unadjusted association

Table 1 summarises participants' demographic and behavioural characteristics by the EQ-5D dimensions, utility index, and VAS. Advanced age was associated with lower utility index and VAS and problems with all the EQ-5D dimensions except anxiety-depression. Females were more likely to have lower utility index and VAS and problems with mobility, usual activities, and pain-discomfort. Up to secondary level education, physical activity less than 150 minutes per week, and sitting for more than ten hours per day were associated with lower utility index and VAS and higher prevalence of problems with all the EQ-5D dimensions. Household income less than 6001 Saudi Arabian Riyals (SAR) was associated with higher prevalence of problems with usual activities, pain-discomfort, and anxiety-depression and lower utility index and VAS. Remote location of residence was associated with higher likelihood of problems with self-care and lower utility index, while smoking was associated with higher likelihood of problems with anxiety-depression.

Table 2 shows disease related and clinical characteristics by the EQ-5D dimensions, utility index, and VAS. Longer duration of diabetes, insulin use, hypoglycaemia events last months, and hypertension were associated with higher prevalence of problems with all the EQ-5D dimensions and lower utility index and VAS. Higher BMI has a similar effect except for no association with problems with self-care, while the number of medications was associated with problems with mobility, pain-discomfort and lower utility index and VAS. Poor glycaemic control (HbA1c $\geq$ 7%) was associated with lower utility index and VAS and higher prevalence of problems with mobility, usual activity, and pain-discomfort. In regards to diabetes complications diabetic foot, neuropathy and retinopathy were associated with lower utility index and VAS and higher prevalence of problems with all the EQ-5D dimensions. Coronary artery disease has similar association except for no association with VAS, while stroke was not associated with VAS or problems with pain-discomfort. Renal disease was associated with lower utility index and VAS and higher prevalence of problems with all the EQ-5D dimensions except anxiety-depression. Depression was associated with higher likelihood of any problems with mobility, self-care, usual activities, and pain-discomfort and lower utility index and VAS. Anxiety was associated with lower utility index and VAS and problems with pain-discomfort. Cognitive impairment was also associated with lower utility index and VAS and higher prevalence of problems in mobility, self-care, and usual activities.

Adjusted association

Results of bootstrap analysis to identify factors that were significantly associated with EQ-5D dimensions, utility index, and VAS are presented in **Table 3**. Along with age and gender, factors that appeared significantly associated in at least 50% of the bootstrap samples were used to develop multiple

logistic regression model for each of the EQ-5D dimensions (**Table 4**), and multiple linear regression model for utility index, and VAS (**Table 5**).

The odds of problems with mobility increased by 60% for education up to secondary level, while long sitting time and physical inactivity increased the odds by 2-folds and 3-folds respectively (**Table 4**). Hypertension increased the odds by 50%. Stroke, neuropathy, and renal impairment were associated with respectively 4.4-fold, 2.8-fold, and 2.1-fold increased odds of problems with mobility.

Regarding problems with self-care, the odds is lower by 50% for female gender, while remote area of residence was associated with 3.2-fold increase in the odds. Long sitting time and physical inactivity increased the odds by 1.8-folds and 3.2-folds respectively. Diabetic foot, neuropathy, and renal impairment were associated with respectively 2.2-fold, 3.4-folds, and 2.4-fold higher odds, while impaired cognitive function increased the odds by 2.3-folds.

The odds of problems with usual activity increased by 2.8-folds for age over 60 years and by 50% for female gender. Long sitting time and physical inactivity were associated with respectively 2.2-fold and 2.7-fold higher odds. The odds of problems with usual activity also increased by: 1.7-folds for coronary artery disease, 2.7-folds for stroke, 3.2-folds for neuropathy, 2.8-folds for renal impairment, and by 1.6-folds for depression.

In regards to problems with pain-discomfort, the odds increased by 2.2-folds for age between 46 and 60 years, and by 3.2-folds for age over 60 years. Physical inactivity and long sitting time increased the odds by 1.8-folds and 2.0-folds respectively, while BMI ≥30.0 kg/m² increased the odds by 60%. Neuropathy and renal impairment were associated with respectively 3.3-fold and 1.8-fold higher odds. There was also an increase in the odds by 90% for anxiety, while impaired cognitive function was associated with 30% lower odds.

The odds of problems with anxiety-depression was higher by 2.1-folds for current or past smoking and by 1.6-folds for physical inactivity. Hypoglycaemia events last month was associated with 1.3-fold higher odds, while Neuropathy increased the odds of problems with anxiety-depression by 2.7-folds.

Results of the multiple linear regression analysis for utility index and VAS are presented in **Table 5**. Factors that were significantly associated with lower utility index were low education level, physical inactivity, long sitting time, coronary artery disease, diabetic foot, stroke, neuropathy, renal impairment, depression, and anxiety. The model has a coefficient of determination (R^2) of 37.5%. Lower VAS score was associated with female gender, long sitting time, using insulin, hypertension, neuropathy, depression, anxiety, and cognitive impairment. The model's R^2 was 21.4%.

Discussion

T2DM and its related complications are highly prevalent in Saudi Arabia, and the affected people had low HRQoL. However, HRQoL and factors that affect it were not studied adequately among people with T2DM in the country. The aim of this study was to assess the HRQoL among this population and to identify demographic, behavioural, and clinical factors that affect the HRQoL and its dimensions. This study shows that the HRQoL for people with T2DM in Saudi Arabia was low especially among females and those who had diabetes complications. This study has also identified a number of lifestyle and other modifiable factors that were associated with lower HRQoL.

The mean utility index (0.74 ±0.26) and VAS (69.8 ±18.4) in this study were comparable to a previous study from Saudi Arabia that used the same tool and reported a mean utility index of 0.71 ± 0.22 and VAS of 68.5 ± 16.8 [20]. A study from Iran also reported a mean utility index of 0.70, however, the VAS score (56.8) was lower [36]. Studies from Norway, Japan, Korea, on the other hand, reported a higher utility index ranging between 0.83 and 0.94 [37-39]. Differences in the populations and

healthcare systems might explain the variation in the utility index between these studies and the current one. The highest prevalence of any problems among this study participants was with pain-discomfort (51.6%) fold by mobility (51.0%), and anxiety-depression (45.8%). Similar findings were reported by studies from Iran, Japan, and Norway [36-38].

Advanced age appeared to be associated with problems with usual activities and pain-discomfort, but not with utility index. Similar findings regarding the utility index were reported in previous studies from Saudi Arabia and Canada [11, 20, 40]. In contrast, other studies Showed that advanced age was associated with lower utility index [6, 10, 41]. With advance age there might be a reduction in the body strength and physical function which may affect the quality of life.

Female participants had lower mean utility index compared to male participants. Many previous studies have reported similar finding [10, 11, 20, 22, 36, 42, 43], and some of them have linked this association to higher rate of physical inactivity and obesity among women [20, 36, 43]. In this study, higher proportions of females were physically inactive (75.1%) compared to males (61.8%), and higher proportion of females were spending more than ten hours per day in a sitting position (19.1% compared to 14.0% among males). The prevalence of obesity among females (70.7%) was, also, substantially higher than males (47.4%). This study also shows that physical inactivity was associated with problems in all the EQ-5D dimensions, while long sitting time had a similar association except for no association with anxiety-depression. Moreover, both physical inactivity and longer sitting time were associated with lower utility index.

Findings regarding physical inactivity and lower HRQoL is in agreement with the finding of previous studies [15, 44, 45]. The association between longer sitting time and lower HRQoL, however, was not explored before. Longer sitting time have been associated with higher risk of diabetes complications, and diabetes complication are strongly linked to lower HRQoL [6, 11, 15, 22, 40, 41, 46]. A study from Saudi Arabia showed that among people with T2DM every one hour of sitting per day was associated with 10% increase in the risk of CAD, stroke, and neuropathy [19]. The role of physical activity and reduced sitting time in lowering the risk of diabetes complications and maintain or improve HRQoL should be emphasis in the management of diabetes.

Obesity can affect the HRQoL mainly through its impact on physical function and mental health. There are, however, conflicting reports regarding the association between obesity and the HRQoL. This study showed that obesity was associated with higher risk of problems with pain-discomfort, however, obesity did not appear to be associated with lower utility index. Similar findings were reported in another study [37]. In contract, some studies have reported a significant association [6, 11]. In this current study obesity was more prevalent in young compared to old people, and young people were less likely to have diabetes complications, which may explain why obesity was not associated with lower utility index. Nevertheless, obesity have been linked to higher risk of diabetes complications among people with T2DM in Saudi Arabia [19]. Therefore, controlling the body weight is an important measure to lower the risk of diabetes complications and maintain HRQoL.

Similar to other studies [10, 36], this study shows that lower level of education was related to problems with mobility and lower HRQoL. Higher level of education increases the likelihood of adherence to disease management plans, healthier lifestyle behaviours, and positive attitude toward health and disease prevention, which lower the risk of diabetes complications and maintain HRQoL [47]. Previous studies also reported an association between poor HRQoL and lower income and rural or remote location of residence [10, 48]. The results of this study showed that while remote area of residence was associated with problems with self-care, both household income and the area of residence were not associated with lower utility index. Similar finding regarding the income was reported in another study from Saudi Arabia [11].

The duration of diabetes did not appear to affect the HRQoL in this study. Previous studies from Saudi Arabia and Iran reported similar findings [11, 20, 36]. The modality of treatment and the number of medications were also not associated with the utility index; however, insulin use was associated with lower VAS score. The results of the previous studies regarding the effect of the modality of treatment and the number of medications were conflicting as some studies found an association [16, 41], while others did not [20, 36].

Fear of hypoglycaemia may not affect the HRQoL directly, but it may have an impact on the general quality of life through its negative effect on independence, spontaneity, and leisure activities enjoyment [37], as well as mental health as this current study showed. Hypoglycaemia was associated with higher risk of problems with anxiety-depression, and anxiety and depression were independently related to lower utility index and VAS score. Previous studies have also reported an association between HRQoL and both anxiety and depression [49, 50]. Ever smoked was also associated with problems with anxiety-depression which was likely because the participants who smoked were aware that smoking increase their risk of diabetes complication. People with diabetes are at increased risk of anxiety and depression and these mental illnesses can negatively affect the control of the disease and increase the risk of diabetes complications [51]. To optimise HRQoL among people with T2DM in Saudi Arabia screening and management of anxiety and depression should be prioritised among this high-risk population.

The mean utility index for people without diabetes complications in this study was 0.84 (±0.17). The utility index dropped to less than 0.70 for those who have coronary artery disease and retinopathy, while for those who have diabetic foot, neuropathy, stroke, and renal disease the utility index dropped less than 0.60. Further analysis showed that people with macrovascular complications only had a mean utility index of 0.76 (±0.17), while the mean for those with microvascular complications only was 0.73 (±0.25). For people who have both types of complications the mean dropped to 0.57 (±0.33). Similar decrement in the mean utility index with diabetes complications has been reported by other studies [40, 46]. After adjustment for other confounders diabetes complications remained strongly associated with lower utility index which is in agreement with the literature that showed the substantial effect of diabetes complications on the HRQoL [6, 11, 15, 22, 40, 41, 46]. Preventing diabetes complications is a key measure in improving the quality of life for people with diabetes.

The study results also showed that diabetes complications can affect a number of the HRQoL dimensions. Neuropathy in particular has an impact on all the HRQoL dimensions and was also associated with lower VAS score. The strong association between neuropathy and diabetic foot and the HRQoL was reported before [5, 10]. This indicates that neuropathy is a serious condition that should be prevented or controlled through adequate screening, treatment, and patient education.

The strengths of this study were the relatively large sample size that were drawn from three different regions as well as the examinations of the effect of various demographic, behavioural, and clinical factors on the HRQoL using a robust analysis method. The use of the EQ-5D-5L tool to assess HRQoL also add strength to this study as it makes it easier to compare the results with other national and international studies. The results of this study, however, need to be interpreted in the light of being a cross-sectional, where only association can be inferred rather than causation. Nevertheless, this study has identified the factors that have strong association with lower HRQoL among people with T2DM in Saudi Arabia. Future research should farther examine the identified association using prospective studies. Healthcare providers and health policy makers should use the finding of this study to develop patient-level interventions and public health strategies to improve the quality of life of people with diabetes in Saudi Arabia.

To conclude People with T2DM in Saudi Arabia had low HRQoL specially among females and those who have diabetes complications. Other risk factors that lower the HRQoL were low level of education, physical inactivity, long sitting time, anxiety, and depression. In order to improve the quality of life for

this high-risk group active lifestyle should be encouraged and anxiety, depression, and diabetes complications should be prevented or controlled. These factors should be the main targets of the patient-level interventions and the public health strategies to manage people with diabetes in the country.

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Competing interests
All authors declare that they have no competing interests.

Author contributions
All authors were involved in the conception and design of the study. MJA, BJA, NAAlz, and NAAla, contributed to the acquisition of data. MJA, MNK, and BB contributed to data analysis. MJA, MNK, MAB, THA, DJM and BB contributed to interpretation of results. MA and BB developed the online risk calculator. MJA, BB, and DJM drafted the manuscript. All authors critically reviewed the manuscript and approved the final version.

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Data availability
The data will be available upon reasonable request.

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Table 1: Demographic and behavioural characteristics by EQ-5D dimensions, utility index, and VAS

Variable	EQ-5D Domains										Utility index 0.739 ±0.261		VAS 69.8 ±18.4	
	Any problems with mobility 51.0% (n=566)		Any problems with self-care 12.3% (n=137)		Any problems with usual activities 30.5% (n=339)		Any problems with pain-discomfort 51.6% (n=573)		Any problems with anxiety-depression 45.8% (n=509)					
	%	P-value	%	P-value	%	P-value	%	P-value	%	P-value	Mean ±SD	P-value	Mean ±SD	P-value
Age														
<46 years	27.7	<0.001	8.0	<0.001	13.1	<0.001	27.7	<0.001	43.8	0.629	0.842 ±0.197	<0.001	76.1 ±16.3	<0.001
46 – 60 years	49.7		9.4		26.8		51.8		47.2		0.745 ±0.259		69.3 ±18.5	
>60 years	39.1		18.2		42.2		59.6		44.5		0.694 ±0.273		68.2 ±18.4	
Gender:														
Female	54.3	0.011	11.1	0.076	34.4	<0.001	56.2	<0.001	47.7	0.093	0.709 ±0.285	<0.001	66.3 ±18.4	<0.001
Male	46.3		14.7		23.3		42.9		42.4		0.795 ±0.197		76.2 ±16.3	
Education														
University /college	33.8	<0.001	6.6	0.006	16.2	<0.001	36.9	<0.001	34.3	<0.001	0.851 ±0.115	<0.001	75.7 ±16.2	<0.001
Up to secondary level	54.7		13.6		33.6		54.8		48.3		0.715 ±0.273		68.5 ±18.6	
Location of residence														
Urban	50.7	0.934	11.1	<0.001	29.8	0.299	50.2	0.052	44.6	0.109	0.747 ±0.252	0.003	70.2 ±18.0	0.072
Rural	52.6		13.7		32.6		56.8		52.6		0.724 ±0.268		66.0 ±19.3	
Remote	51.6		29.0		38.7		64.5		54.8		0.631 ±0.355		68.0 ±22.1	
Household income														
<6001 SAR	54.5	0.029	14.0	0.115	36.2	<0.001	57.6	<0.001	51.8	<0.001	0.685 ±0.303	<0.001	67.0 ±18.6	<0.001
≥6001 SAR	47.9		10.9		25.6		46.4		40.7		0.786 ±0.208		72.1 ±17.9	
Ever smoked														
No	50.4	0.463	12.3	0.991	30.6	0.932	51.8	0.804	42.7	<0.001	0.743 ±0.266	0.312	69.9 ±18.8	0.469
Yes	53.3		12.3		30.3		50.8		60.5		0.722 ±0.234		68.9 ±16.5	
Physical activity														
≥150 min/week	27.4	<0.001	4.0	<0.001	12.8	<0.001	33.8	<0.001	35.7	<0.001	0.855 ±0.167	<0.001	74.0 ±16.4	<0.001
<150 min/week	60.8		15.8		37.9		59.0		50.1		0.690 ±0.278		68.0 ±18.9	
Sitting time														
<10 hours per day	46.0	<0.001	9.4	<0.001	25.5	<0.001	47.1	<0.001	42.8	<0.001	0.778 ±0.220	<0.001	71.5± 17.5	<0.001
≥10 hours per day	74.5		26.6		54.7		72.9		60.4		0.554 ±0.351		61.6± 20.3	

Table 2: Disease related and clinical characteristics by EQ-5D dimensions, utility index, and VAS

Variable	EQ-5D Domains										Utility index 0.739 ±0.261		VAS 69.8 ±18.4	
	Any problems with mobility 51.0% (n=566)		Any problems with self-care 12.3% (n=137)		Any problems with usual activities 30.5% (n=339)		Any problems with pain-discomfort 51.6% (n=573)		Any problems with anxiety-depression 45.8% (n=509)					
	%	P-value	%	P-value	%	P-value	%	P-value	%	P-value	Mean ±SD	P-value	Mean ±SD	P-value
Diabetes duration														
≤10 years	42.6	<0.001	8.6	0.004	22.6	<0.001	41.2	<0.001	41.0	0.011	0.789 ±0.222	<0.001	71.4 ±17.4	0.025
>10 years	55.9		14.5		35.2		57.8		48.8		0.709 ±0.278		68.8 ±18.9	
Insulin use														
No	45.5	<0.001	7.5	<0.001	23.7	<0.001	44.5	<0.001	42.4	0.009	0.784 ±0.219	<0.001	72.7± 17.2	<0.001
Yes	57.7		18.2		38.9		60.3		50.2		0.682 ±0.296		66.1 ±19.1	
Number of medications														
0-2 medications	41.4	0.014	8.1	0.247	24.7	0.134	39.1	0.001	39.1	0.154	0.800 ±0.235	0.004	72.7 ±18.0	0.027
3-4 medications	51.3		12.7		29.5		52.1		47.7		0.738 ±0.254		70.2 ±17.6	
5 and more	54.3		12.4		32.7		54.9		46.3		0.726 ±0.260		68.5 ±18.7	
Hypoglycaemia event during last month														
No	47.4	0.005	9.7	0.002	26.2	<0.001	45.3	<0.001	39.7	<0.001	0.773 ±0.244	<0.001	71.3 ±17.7	0.001
Yes	55.9		16.0		36.5		60.1		54.2		0.692 ±0.667		67.6 ±19.1	
Body mass index														
Underweight/normal	38.9	<0.001	11.5	0.106	25.7	<0.001	42.5	<0.001	43.4	<0.001	0.796 ±0.192	<0.001	74.3 ±17.0	<0.001
Pre-obesity	40.3		9.0		21.3		41.7		36.3		0.812 ±0.195		73.1 ±17.3	
Obesity	57.4		13.8		35.2		57.4		50.3		0.698 ±0.286		67.6 ±18.4	
Glycaemic control														
HbA1c <7%	45.3	0.029	9.9	0.161	24.7	0.023	44.5	0.008	43.7	0.402	0.773 ±0.235	0.017	71.8 ±16.5	0.029
HbA1c ≥7%	53.0		13.2		32.1		53.9		46.7		0.729 ±0.265		69.0 ±18.9	
Hypertension														
No	38.7	<0.001	6.9	<0.001	21.9	<0.001	42.0	<0.001	40.8	0.029	0.796 ±0.226	<0.001	74.1 ±17.1	<0.001
Yes	56.2		14.7		34.2		55.7		47.9		0.715 ±0.271		67.9 ±18.6	
Coronary artery disease														
No	47.9	<0.001	10.2	<0.001	27.0	<0.001	48.3	<0.001	43.6	0.001	0.761 ±0.245	<0.001	70.2 ±17.9	0.056
Yes	65.6		22.8		47.6		67.7		56.6		0.632 ±0.309		67.4 ±20.4	
Diabetic foot														
No	45.5	<0.001	9.3	<0.001	26.9	<0.001	46.4	<0.001	42.8	<0.001	0.776 ±0.233	<0.001	71.5 ±18.1	<0.001
Yes	70.6		32.2		50.4		73.4		61.5		0.552 ±0.340		63.8 ±19.5	
Stroke														
No	49.5	<0.001	11.5	<0.001	29.3	<0.001	51.0	0.062	44.8	<0.001	0.747 ±0.254	<0.001	69.8 ±18.2	0.477
Yes	87.8		35.2		63.4		65.9		73.2		0.532 ±0.351		67.8 ±21.6	
Retinopathy														
No	45.4	<0.001	8.4	<0.001	23.9	<0.001	43.6	<0.001	40.9	<0.001	0.785 ±0.223	<0.001	72.1 ±17.0	<0.001
Yes	58.4		17.7		39.3		62.2		52.3		0.677 ±0.293		66.7 ±19.7	
Neuropathy														
No	52.9	<0.001	8.2	<0.001	23.5	<0.001	43.1	<0.001	39.9	<0.001	0.796 ±0.218	<0.001	72.5 ±18.0	<0.001
Yes	73.8		29.7		56.9		78.2		67.8		0.536 ±0.320		62.1 ±18.1	
Renal disease														
No	47.3	<0.001	9.2	<0.001	26.2	<0.001	48.4	<0.001	45.5	0.258	0.764 ±0.229	<0.001	70.8 ±17.9	<0.001
Yes	72.1		28.0		55.9		70.2		50.3		0.593 ±0.359		63.9 ±19.8	
Depression														
No	49.2	0.011	11.1	0.006	27.4	<0.001	48.3	<0.001	-	-	0.772 ±0.239	<0.001	72.3 ±17.1	<0.001
Yes	59.5		18.4		46.0		68.1				0.573 ±0.301		56.8 ±19.2	
Anxiety														
No	50.5	0.518	11.6	0.080	29.5	0.076	48.5	<0.001	-	-	0.765 ±0.243	<0.001	71.6 ±17.5	<0.001
Yes	53.2		16.4		36.3		68.4				0.596 ±0.307		59.3 ±19.5	
Cognitive impairment														
No	46.2	0.016	8.6	<0.001	26.4	<0.001	48.7	0.199	44.5	0.352	0.771 ±0.231	<0.001	72.4 ±18.3	<0.001
Yes	54.8		22.8		39.3		53.3		47.8		0.679 ±0.329		66.0 ±18.0	

Table 3: Percentage of appearance of variables as significantly associated with the EQ-5D dimensions, utility index, and VAS

Variable	EQ-5D Domain					Utility index	VAS
	Any problems with mobility	Any problems with self-care	Any problems with usual activities	Any problems with pain -discomfort	Any problems with anxiety-depression		
Age ≥ 61 years	66.0%*	14.8%	93.4%*	86.3%*	41.6%	36.2%	18.3%
Female gender	10.5%	97.4%*	14.6%	11.8%	7.2%	3.8%	100.0%*
Education up to secondary level	78.3%*	43.3%	46.0%	32.0%	41.7%	89.6%*	16.2%
Remote location of residence	8.0%	91.3%*	7.1%	20.1%	6.3%	46.7%	19.8%
Household income <6001 SAR	36.9%	61.8%*	9.5%	5.8%	6.2%	6.4%	28.9%
Ever smoked	11.7%	9.0%	5.9%	11.7%	77.3%*	5.1%	11.8%
Physical activity <150 min/week	100.0%*	97.2%*	99.5%*	96.1%*	56.4%*	100.0%*	18.6%
Sitting time ≥10 hours per day	96.8%*	60.3%*	90.6%*	86.7%*	47.5%	100.0%*	96.6%*
Diabetes Duration >10 years	19.6%	8.0%	5.9%	26.3%	31.2%	9.7%	43.4%
Insulin use	5.7%	52.9%*	19.9%	6.4%	7.0%	14.8%	91.6%*
Number of medications ≥ 4 types	10.4%	32.8%	17.5%	8.3%	19.6%	10.0%	30.6%
Hypoglycaemia symptoms last month	12.1%	19.4%	16.8%	57.1%*	59.8%*	20.3%	5.1%
Body mass index ≥ 30.0 kg/m²	96.3%*	13.7%	59.8%*	81.6%*	48.5%	99.0%*	26.7%
Poor glycaemic control (HbA1c ≥7%)	19.8%	4.8%	25.1%	21.6%	6.6%	8.6%	7.6%
Hypertension	60.5%*	46.6%	8.7%	22.9%	24.5%	22.7%	89.2%*
Coronary artery disease	17.7%	20.5%	50.3%*	48.2%	29.5%	64.2%*	11.4%
Diabetic foot	44.6%	80.2%*	15.8%	40.3%	13.5%	84.9%*	24.8%
Stroke	86.4%*	28.6%	69.8%*	6.5%	41.9%	69.0%*	19.0%
Retinopathy	4.9%	6.8%	9.5%	21.9%	14.8%	13.7%	15.2%
Neuropathy	99.6%*	98.3%*	99.9%*	99.9%*	79.0%*	100.0%*	64.8%*
Renal disease	86.8%*	85.6%*	98.5%*	58.0%*	8.0%	98.1%*	42.8%
Depression	23.7%	23.2%	83.8%*	24.1%	-	99.2%*	100.0%*
Anxiety	38.4%	10.3%	45.5%	55.9%*	-	60.6%*	79.1%*
Impaired cognitive function	41.1%	84.2%*	8.1%	84.5%*	14.6%	9.5%	69.2%*

* Variable used in model development (appeared as significantly associated in 50% or more of the bootstrap samples)

Table 4: Adjusted association between various risk factors and each of the EQ-5D dimensions

Variable	Any problems with mobility			Any problems with self-care			Any problems with usual activities			Any problems with pain-discomfort			Any problems with anxiety-depression		
	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value
Age (ref: <46 years)															
46 – 60 years	1.5	0.9, 2.4	0.088	0.7	0.3, 1.6	0.399	1.7	0.9, 3.1	0.108	2.2	1.4, 3.6	0.001	1.1	0.7, 1.6	0.774
>60 years	1.6	1.0, 2.8	0.051	1.0	0.4, 2.3	0.986	2.8	1.5, 5.4	0.001	3.2	1.9, 5.3	<0.001	0.9	0.6, 1.4	0.572
Female gender (ref: Male)	0.8	0.6, 1.1	0.140	0.5	0.3, 0.8	0.009	1.5	1.1, 2.2	0.024	1.2	0.9, 1.7	0.172	1.1	0.8, 1.4	0.658
Education up to secondary level (ref: university)	1.6	1.1, 2.4	0.023	-	-	-	-	-	-	-	-	-	-	-	-
Household income <6001 SAR (ref: ≥6001)	-	-	-	0.7	0.4, 1.2	0.224	-	-	-	-	-	-	-	-	-
Remote area of residence (ref: urban / rural)	-	-	-	3.2	1.5, 7.1	0.003	-	-	-	-	-	-	-	-	-
Ever smoked (ref: no)	-	-	-	-	-	-	-	-	-	-	-	-	2.1	1.5, 2.9	<0.001
Physical activity <150 min/week (Ref: ≥150 min/week)	3.0	2.1, 4.1	<0.001	3.2	1.6, 6.3	0.001	2.7	1.8, 4.1	<0.001	1.8	1.3, 2.5	<0.001	1.6	1.2, 2.2	0.001
Sitting time ≥10 hours per day (ref: <10 hours/day)	2.0	1.3, 3.2	0.002	1.8	1.0, 3.0	0.039	2.2	1.4, 3.4	<0.001	2.0	1.3, 3.1	0.003	-	-	-
Using insulin	-	-	-	1.4	0.9, 2.3	0.132	-	-	-	-	-	-	-	-	-
Hypoglycaemia events last month (ref: no)	-	-	-	-	-	-	-	-	-	1.3	1.0, 1.8	0.062	1.3	1.0, 1.7	0.045
BMI (ref <25.0 kg/m²)															
25.0-29.9 kg/m²	0.9	0.5, 1.4	0.580	-	-	-	0.7	0.4, 1.3	0.272	1.0	0.6, 1.7	0.961	-	-	-
≥30.0 kg/m²	1.5	0.9, 2.4	0.113	-	-	-	1.1	0.6, 1.9	0.708	1.6	1.0, 2.6	0.048	-	-	-
Hypertension (ref: no)	1.5	1.1, 2.0	0.022	-	-	-	-	-	-	-	-	-	-	-	-
Coronary artery disease (ref: no)	-	-	-	-	-	-	1.7	1.1, 2.5	0.015	-	-	-	-	-	-
Diabetic foot (ref: no)	-	-	-	2.2	1.3, 3.8	0.004	-	-	-	-	-	-	-	-	-
Stroke (ref: no)	4.4	1.5, 13.3	0.008	-	-	-	2.7	1.2, 6.2	0.017	-	-	-	-	-	-
Neuropathy (ref: no)	2.8	1.9, 4.2	<0.001	3.4	2.0, 5.6	<0.001	3.2	2.2, 4.6	<0.001	3.3	2.2, 5.0	<0.001	2.7	1.9, 3.8	<0.001
Renal impairment (ref: no)	2.1	1.4, 3.3	0.001	2.4	1.4, 3.9	0.001	2.8	1.8, 4.3	<0.001	1.8	1.2, 2.8	0.008	-	-	-
Depression (ref: no)	-	-	-	-	-	-	1.6	1.0, 2.4	0.033	-	-	-	-	-	-
Anxiety (ref: no)	-	-	-	-	-	-	-	-	-	1.9	1.3, 3.0	0.002	-	-	-
Impaired cognitive function (ref: no)	-	-	-	2.3	1.4, 3.7	0.001	-	-	-	0.7	0.5, 1.0	0.046	-	-	-

Note: The area under the receiver operational characteristics curve for the models predicting problems with mobility, self-care, usual activities, pain-discomfort, and anxiety-depression were respectively 75.6%, 81.7%, 79.1%, 74.5%, 66.5%.

Table 5: Adjusted association between various risk factors and utility index and VAS

Variable	Utility index			VAS		
	Beta coefficient	95% CI	P-value	Beta coefficient	95% CI	P-value
Age (ref: <46 years)						
46 – 60 years	-0.012	-0.054, 0.030	0.566	-2.236	-5.471, 0.999	0.175
>60 years	-0.031	-0.077, 0.015	0.185	-2.688	-6.242, 0.867	0.138
Female gender (ref: Male)	-0.021	-0.050, 0.008	0.163	-6.176	-8.335, -4.016	<0.001
Education up to secondary level (ref: university)	-0.056	0.092, -0.020	0.003	-	-	-
Physical activity <150 min/week (Ref: ≥150 min/week)	-0.074	-0.104, -0.043	<0.001	-	-	-
Sitting time ≥10 hours per day (ref: <10 hours/day)	-0.133	-0.173, -0.094	<0.001	-4.875	-7.941, -1.808	0.002
Using insulin	-	-	-	-3.589	-5.715, -1.462	0.001
BMI (ref <25.0 kg/m²)						
25.0-29.9 kg/m²	0.015	-0.032, 0.063	0.520	-	-	-
≥30.0 kg/m²	-0.043	-0.087, 0.001	0.056	-	-	-
Hypertension (ref: no)	-	-	-	-4.279	-6.607, -1.952	<0.001
Coronary artery disease (ref: no)	-0.068	-0.104, -0.032	<0.001	-	-	-
Neuropathy (ref: no)	-0.138	-0.175, -0.101	<0.001	-4.788	-7.520, -2.056	0.001
Renal impairment (ref: no)	-0.101	-0.140, -0.063	<0.001	-	-	-
Stroke (ref: no)	-0.146	-0.220, -0.071	<0.001	-	-	-
Diabetic foot (ref: no)	-0.074	-0.115, -0.032	0.001	-	-	-
Depression (ref: no)	-0.095	-0.136, -0.053	<0.001	-10.910	-14.187, -8.634	<0.001
Anxiety (ref: no)	-0.062	-0.104, -0.019	0.004	-4.077	-7.437, -0.716	0.017
Impaired cognitive function (ref: no)	-	-	-	-3.226	-5.641, -0.810	0.009

Note: the utility index model adjusted R^2 was 37.5%. The VAS model adjusted R^2 was 21.4%.

Chapter 8:

Discussion, Implications, and Conclusion

8.1 Overview of the main findings

This thesis has five main objectives: to measure the prevalence of poor glycaemic control and its determinants among people with T2DM in Saudi Arabia (chapter 4); to determine the prevalence of major micro- and macro-vascular complications and their correlates (chapter 5); to develop a risk- scoring system to predict major diabetes complications (chapter 5); to measure the prevalence of obesity, hypertension, and dyslipidaemia and explore their risk factors (chapter 6); and to assess HRQoL and factors that affect it among people with T2DM in Saudi Arabia (chapter 7). The key findings of each chapter are summarised below.

8.1.1 Chapter 4: Factors Associated with poor glycaemic control among people with type 2 diabetes in Saudi Arabia

The main objective of the management of diabetes is to maintain blood glucose levels within or close to normal ranges. Good control of blood glucose prevents the harmful effect of hyperglycaemia and reduces the risk of diabetes complications (13-16, 82). The results in this chapter showed that only 24.1% of the study participants had good glycaemic control (HbA1c < 7%), while the majority (75.9%) had inadequate control (HbA1c ≥ 7%). Furthermore, 34.1% of the participants had very poor glycaemic control (HbA1c > 9%). Similar findings were reported in previous studies from Saudi Arabia (43, 44, 79, 105, 136), and this indicates that inadequate glycaemic control is a common problem among people with T2DM in the country.

In this chapter, we have also identified a number of modifiable lifestyle and other factors that increase the risk of inadequate glycaemic control. A large proportion of the study participants did not follow the current guidelines on consuming fruit and vegetables on a daily basis and did not achieve the recommended length of time of physical activity per week, which increased their risk of inadequate glycaemic control (82). High waist-hip ratio, which is a factor related to an unhealthy lifestyle, was also independently associated with inadequate glycaemic control. High waist-hip ratio is strongly linked to T2DM, poor glycaemic control, and cardiovascular disease (137).

Only 31.9% of the study participants were aware of HbA1c and knew the recommended target (< 7%). Similar to previous studies (138, 139), we found that lack of knowledge of HbA1c or lack of awareness of the recommended HbA1c target was associated with inadequate glycaemic control. Other risk factors that were associated with inadequate glycaemic control were young age, longer duration of diabetes, living in a remote location, low household income, low adherence to medication, and use of injectable medications. To improve glycaemic control, diabetes management plans should consider these factors.

8.1.2 Chapter 5 Part 1: Prevalence and factors related to macro- and micro-vascular diabetes complications

The aim of this study was to measure the prevalence of diabetes macro- and micro-vascular complications and to explore the factors related to them in Saudi Arabia. The prevalence of CAD, diabetic foot, and stroke was 17.0%, 13.1% and 3.7%, respectively, and that of neuropathy, renal impairment, and retinopathy was 20.3%, 14.5%, and 42.8%, respectively (140). The prevalence of CAD and stroke in this study was within the reported range in high- and middle-income countries (141). Previous studies from Saudi Arabia, which were hospital-based, reported slightly higher prevalence of these complications (50, 54, 142). Results regarding the prevalence of diabetic neuropathy and retinopathy were similar to the findings of previous studies from Saudi Arabia (57, 58, 61, 63, 143).

This current study also showed that every hour of sitting per day increased the risk of CAD, stroke, and neuropathy by 10%, while less than 150 minutes of physical activity per week increased the risk of diabetic foot and retinopathy by 70% and 60% respectively. It is well known that a sedentary lifestyle increases the risk of

cardiovascular disease and mortality (67). Smoking was also associated with increased risk of diabetic foot and neuropathy, while ex-smokers and passive smokers had higher risk of diabetic foot. Similar associations were reported previously (144). Hypertension increased the risk of CAD, stroke, renal impairment, and retinopathy, while very poor glycaemic control (HbA1c ≥ 9%) increased the risk of neuropathy, which is in agreement with a previous study (123).

Similar to previous studies (145, 146), we found that obesity was an independent risk factor for CAD and neuropathy. Other risk factors that were associated with diabetes complications were longer duration of diabetes, advanced age, male gender, family history of diabetes, level of education, low income, and dyslipidaemia. Increasing physical activity, reducing sitting time, smoking cessation, maintaining a healthy body weight, and adequate control of hypertension, blood glucose and lipids are recommended to lower the risk of diabetes complications in Saudi Arabia.

8.1.3 Chapter 5 Part 2: Risk prediction system for diabetes complications

The aim of this study was to develop a risk-scoring system to predict major diabetes complications for adults with T2DM in Saudi Arabia. The diabetes complications considered in this study were CAD, diabetic foot, stroke, neuropathy, kidney disease, and retinopathy. The risk prediction models were developed using the bootstrap-receiver-operation characteristic method, which showed improved model parsimony and prediction performance compared to other methods (84, 90, 92). Each of the developed models incorporated six to ten of the following factors: age ≥ 60 years, gender, low level of education, body mass index ≥ 30 kg/m², physical inactivity, longer sitting time, smoking, longer duration of diabetes, insulin use, low adherence to treatment, family history of diabetes, HbA1c ≥ 9%, hypertension, and dyslipidaemia. All these factors have been associated with diabetes complications and the majority of them have been used previously in risk prediction models (67, 73, 74, 95, 113, 114, 116-119, 122, 140, 147-150). The developed models were validated using bootstrap method and slope calibration and showed high discrimination (ranging from 71.2% to 80.5%) and high calibration (ranging from 93.7% to 99.3%) powers.

The developed risk prediction models are simple and require readily available information, and they showed good performance in predicting the risk. An additive points-based risk-scoring system was developed to make it easier for clinicians to use the risk prediction models. We recommend the use of this tool in the routine clinical assessment of people with T2DM in Saudi Arabia. These tools should help in educating patients about the risk of diabetes complications as well as help clinicians to identify people who are at high risk.

8.1.4 Chapter 6: Obesity, hypertension, and dyslipidaemia among people with type 2 diabetes in Saudi Arabia

The comorbidities of obesity, hypertension, and dyslipidaemia were not explored adequately among people with T2DM in Saudi Arabia in the previous studies. Results of this current study showed that the prevalence of obesity (62.6%), hypertension (70.0%), and dyslipidaemia (70.7%) was very high among the study participants. In addition, 63.4% of the participants had two or more of these comorbidities, and these comorbidities significantly increased the risk of cardiovascular disease.

One of our key findings is that an unhealthy lifestyle increased the risk of these comorbidities. Similar to a previous study, we found that physical inactivity and long sitting time were associated with higher risk of obesity (151). Insulin use also increased the risk of obesity, which is in agreement with the previous studies (152). Furthermore, obesity was strongly associated with increased risk of hypertension, as reported previously (153). Longer duration of diabetes increased the risk of obesity, hypertension and dyslipidaemia. Other risk factors associated with obesity include younger age and female gender, while advanced age and lower education level increased the risk of hypertension and dyslipidaemia. Renal impairment was also associated with hypertension,

while household income and insulin use were related to dyslipidaemia. A healthy lifestyle is a key in the prevention or control of obesity, hypertension, and dyslipidaemia among people with T2DM in Saudi Arabia.

8.1.5 Chapter 7: Health-related quality of life of people with type 2 diabetes in Saudi Arabia

In this chapter, we assessed the HRQoL and its related factors. HRQoL is an important tool in the assessment of the burden of chronic diseases and the effect of treatments on the quality of life, and it has clinical and economic implications. The EQ-5D-5L was used to assess the HRQoL. The mean utility index of the quality of life was 0.739 ±0.261, which was comparable to findings of studies conducted in Saudi Arabia and Iran (64, 154). Studies from developed countries, however, reported a higher utility index (155-157). In this current study, the highest prevalence of any problems among this study's participants was for pain-discomfort (51.6%), followed by mobility (51.0%), and anxiety-depression (45.8%), which agree with previous studies (154-156).

The mean utility index among female participants (0.709 ±0.285) was markedly lower than among males (0.795 ±0.197). The higher prevalence of physical inactivity and obesity among females is a possible explanation for this finding. Physical inactivity and longer sitting time were also associated with problems in the EQ-5D-5L dimensions and a lower utility index. Similar findings regarding gender and physical inactivity were reported in the previous studies (27, 31, 64, 154, 158-160). However, the association between longer sitting time and low quality of life was not explored previously. Longer sitting time increases the risk of diabetes complications (140), which are known to lower HRQoL (31, 135, 161, 162).

Though hypoglycaemia and smoking were not related to a lower utility index, both were associated with problems with anxiety-depression. Anxiety and depression were strongly associated with a lower utility index, which aligns with previous studies (163, 164). Diabetes complications were also strongly related to lower utility index. Compared to the overall mean utility index among our participants, those who have multiple diabetes complications had a mean of 0.57 ±0.33. A similar decrement due to diabetes complications was reported earlier (162, 165). To improve the quality of life of people with diabetes, they should follow a healthy lifestyle, and control anxiety, depression, and diabetes complications.

8.2 Strengths and limitations

The strengths and limitations specific to each of the studies in chapters 4 to 7 were outlined in the respective sections. In this section, we provide a summary of the strengths and limitations of these studies in general as they were based on one dataset.

8.2.1 Strengths

The main strengths of this research project are as follows:

- **Large sample drawn from multiple centres**
  The original studies of this thesis were based on a relatively large sample size. The sample was randomly drawn from multiple centres from three different regions of Saudi Arabia. These centres receive visitors residing in remote, rural and urban locations and from various professional backgrounds. All these aspects increase the reliability and generalisability of the findings of these studies.
- **The consideration of various potential risk factors**
  Each of the studies examined the association of the outcomes with several potential risk factors, including demographic, behavioural, and clinical factors. The associations were also examined after adjusting these factors for each other, which removed any confounding effect or modifying effect.
- **The strong methodology**
  The data was collected using known reliable and validated tools. The questionnaire was completed online by trained data collectors using a web-based application. The application allows the automatic

and error-free exportation of the data to statistical software. Furthermore, a robust methodology of data analysis was used in the majority of the studies. All these aspects increase the strength of these studies.

8.2.2 Limitations

- **The cross-sectional design**
  The data was collected using a cross-sectional study design. Cross-sectional studies lack temporality as they assess outcomes and risk factors at the same point in time. Therefore, only association can be inferred, while to infer a causal relation, a prospective study is needed.
- **Loss of information due to categorizing continuous variables**
  The conversion of numerical continuous variables to categorical variables can simplify the interpretation of the results of the statistical analysis; however, it may lead to a loss of some information.
- **Some potential associated factors might not have been considered**
  In all the studies in this thesis, we might have missed to examine and adjust the association for potentially important risk factors due to a lack of data regarding these factors.
- **The results might not be generalisable to all people with diabetes in Saudi Arabia**
  The study population was limited to attendees of diabetes centres with T2DM and aged 18 years and older. Therefore, people younger than 18 and those with other types of diabetes (type 1 and gestational) were not included. In addition, some people with T2DM with very poor health condition due to diabetes complications may have their follow-ups in hospitals rather than diabetes centres. As such, the results of the studies might not be generalisable to all people with diabetes in Saudi Arabia.

8.3 Implications and Future Research Directions

Several clinical and public health policy implications as well as suggestions for future research arise from the studies included in this thesis. These implications and suggestions for future research are summarised below.

8.3.1 Clinical implications

- Lifestyle modifications play a vital role in improving glycaemic control, preventing diabetes comorbidities and complications, and maintaining quality of life (chapters 4 to 7). Therefore, clinicians should prioritise the role of healthy eating, physical activity, and reduced sitting time in the management of diabetes. A healthy lifestyle will ensure the maintaining of a healthy body weight, which should also be an essential part of the management because of its health benefits in controlling blood sugar, blood pressure, and in reducing the risk of diabetes complications (chapters 4 to 6). People with diabetes should be educated about the need to follow a healthy lifestyle, and this should be emphasised in every follow up visit. Healthcare providers should encourage people with diabetes to consume 8-10 servings of fruits and vegetables every day and reduce the intake of calorie-dense processed food such as white rice, white bread, and foods rich in oil, fat, and sugar (17). They should also be motivated to perform at least 150 minutes of moderate to vigorous intensity physical activity per week and reduce sitting time (17).

- Healthcare providers should educate people with diabetes about all the aspects of the disease and its management. To improve glycaemic control, people with diabetes should be fully aware of their actual HbA1c level as well as the target that they should achieve (chapter 4). More importantly, healthcare professionals should help patients to understand the implications of their HbA1c results. Studies shows that a good understanding of HbA1c improves self-management behaviour and lower HbA1c values (166). For patients with low education level, graphical representation of HbA1c in the form of a face whose emotion reflects HbA1c level can be effective in improving understanding (167).

- People with diabetes should also be educated about the factors that may increase their risk of diabetes comorbidities and complications so that they take active measures to reduce their risk (chapters 5 and 6). The developed risk-scoring system in chapter 5 should be an effective and easy-to-use tool in educating people about the risk of complications.

- Our studies showed that people with no diabetes complications had poor control of their blood glucose, blood lipids, blood pressure and body weight, while those who have complications had better control (chapters 4 and 6). This is probably due to the fact that the management for those who had diabetes complications was intensified to reduce their risk of progression. The aim of clinicians should be to prevent diabetes complications by early detection and management of these risk factors.

- Diabetes and its comorbidities and complications can increase the risk of anxiety and depression. These mental illnesses can substantially lower the quality of life of the affected people (chapters 7). Healthcare providers should frequently screen people with diabetes for these mental disorders and manage them or refer them. If the consultation time is limited, the screening can be done using the two-question Patient Health Questionnaire-2 (PHQ-2)) for depression (98) and the two-question Generalized Anxiety Disorder Scale (GAD-2)) for anxiety (99). Based on the patient responses, a more diagnostic tools can be used.

8.3.2 Public health implication

- An important finding in our study was that people in Saudi Arabia acquired diabetes early in their life (chapter 4). Early onset T2DM is associated with poor diabetes outcomes, including higher risk of comorbidities and complications (168). Public health in Saudi Arabia should develop and implement effective national diabetes prevention strategies. Key actions of these strategies should include promotion of fruit and vegetable consumption, reduction of intake of processed foods, promotion of physical activity at school, work, and leisure time, and urban planning that encourages walking and biking. The diabetes prevention strategies should also embrace systematic risk assessment, active screening programs, and intensive management protocols to identify and treat people at risk of diabetes.

- Health policy makers should use the findings of this thesis to develop public health strategies that can be tailored at the patient level to improve the control of the disease, prevent diabetes comorbidities and complications, and maintain quality of life. Public health policy should give special attention to the issues of poor glycaemic control, obesity, hypertension, and dyslipidaemia. Our findings showed that these comorbidities were highly prevalent among people with T2DM in Saudi Arabia, and they were associated with poor outcomes (chapters 4 to 6). Promotion of healthy lifestyle is a key in preventing and managing these diabetes comorbidities.

- Education is an economical and effective way to improve diabetes outcomes, and public awareness campaigns using mass media is a cost-effective method (169). The health system in Saudi Arabia should establish long-term continuous public awareness campaigns using mass media such as television, radio, mobile massages, and other channels. The focus of these campaigns should be to raise the awareness of healthy lifestyle choices and their role in preventing and managing diabetes and other chronic diseases. Improving self-management is another area that need special attention from the educational campaigns because of its role in improving health outcomes and quality of life. People with diabetes should have the knowledge and skills to successfully self-manage the disease and its related conditions.

- Health policy makers should tackle the issue of poor control of diabetes among some disadvantaged groups including those who live in remote locations. The healthcare system could provide special diabetes education programs for healthcare providers working in remote locations and provide them

with direct access to endocrinologists, ophthalmologists and podiatrists for consultation. Allied health professionals could also contact patients by phone and provide them with ongoing education if they are not assigned to the remote location where patients live.

8.3.3 Future research directions

Lifestyle modifications play a key role in the management of diabetes and the prevention of diabetes comorbidities and complications. Our findings showed, however, that a large proportion of people with T2DM were not following the current guidelines with regard to healthy eating and regular physical activity. Identifying the barriers to adhering to lifestyle modifications can help to develop effective strategies to improve the adherence. Therefore, future research should investigate barriers to adhering to a healthy lifestyle.

The risk prediction models for diabetes complications developed in chapter 5 were validated using the same dataset. Future research should validate these models using another dataset from Saudi Arabia. The effectiveness of the risk-scoring system in educating people and preventing diabetes complications should also be investigated. In addition, the risk-scoring system was developed based on data generated from a cross-sectional study. Therefore, future research might improve the risk-scoring system using data from a prospective study.

8.4 Conclusion

T2DM is highly prevalent in Saudi Arabia, and people with the disease have uncontrolled blood glucose level, high blood pressure, dyslipidaemia, and obesity. Furthermore, the prevalence of major diabetes related complications is high among them and the quality of life is low, especially among females and those who have complications. This body of work showed that all these poor diabetes outcomes can be prevented or controlled by targeting a number of modifiable factors, including lifestyle factors such as healthy eating, increasing physical activity, and reducing sitting time. Raising awareness of the disease and the importance of lifestyle modifications in its management should be the main aim of continuous education programs. The risk-scoring system that we have developed should help in educating people with diabetes about their risk of complications. This tool should also help clinicians to identify people at risk of diabetes related complications. Health policy makers can use the findings of our studies to develop prevention strategies to lower the risk of diabetes comorbidities and complications and to improve the quality of life of people with T2DM. Future research should investigate the effectiveness of education programs targeting people with diabetes and barriers to adhering to lifestyle modifications. Researchers could also improve the risk-scoring tools using data from a longitudinal study.

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Appendixes

Appendix 1: Research Ethics Approval

Appendix 2: Informed consent form

Appendix 3: Research questionnaire in English

Appendix 4: Research questionnaire in Arabic

Appendix 1: Research Ethics Approval

Monash University Human Research Ethics Committee approval

MONASH University

Monash University Human Research Ethics Committee

Approval Certificate

This is to certify that the project below was considered by the Monash University Human Research Ethics Committee. The Committee was satisfied that the proposal meets the requirements of the *National Statement on Ethical Conduct in Human Research* and has granted approval.

Project Number:	1188
Project Title:	Determinants of Glycaemic Control, Complications and Health Related Quality of Life for People with Type 2 Diabetes in Saudi Arabia
Chief Investigator:	Mr Md Billah
Expiry Date:	21/11/2021

Terms of approval - failure to comply with the terms below is in breach of your approval and the *Australian Code for the Responsible Conduct of Research*.

1. The Chief Investigator is responsible for ensuring that permission letters are obtained, if relevant, before any data collection can occur at the specified organisation.
2. Approval is only valid whilst your hold a position at Monash University.
3. It is responsibility of the Chief Investigator to ensure that all investigators are aware of the terms of approval and to ensure the project is conducted as approved by MUHREC.
4. You should notify MUHREC immediately of any serious or unexpected adverse effects on participants or unforeseen events affecting the ethical acceptability of the project.
5. The Explanatory Statement must be on Monash letterhead and the Monash University complaints clause must include your project number.
6. Amendments to approved projects including changes to personnel must not commence without written approval from MHUREC.
7. Annual Report - continued approval of this project is dependent on the submission of an Annual Report.
8. Final Report - should be provided at the conclusion of the project. MUHREC should be notified if the project is discontinued before the expected completion date.
9. Monitoring - project may be subject to an audit or any other form of monitoring by MUHREC at any time.
10. Retention and storage of data - The Chief Investigator is responsible fo the storage and retention of the original data pertaining to the project for a minimum period of five years.

Thank you for your assistance.

Professor Nip Thomson

Chair, MUHREC

CC: Assoc Professor Dianna Magliano, Mr Mohammed Alramadan

Page 1 of 1

Saudi Ministry of Health-King Fahad Medical City Institutional Review Board approval

Kingdom of Saudi Arabia
Ministry of Health
King Fahad Medical City
(162)

المملكة العربية السعودية
وزارة الصحة
مدينة الملك فهد الطبية
(١٦٢)

وزارة الصحة
مدينة الملك فهد الطبية
King Fahad Medical City

IRB Registration Number with KACST, KSA: H-01-R-012
IRB Registration Number with OHRP/NIH, USA: IRB00010471
Approval Number Federal Wide Assurance NIH, USA: FWA00018774

December 8, 2016
IRB Log Number: 16-429E
Department: External
Category of Approval: EXEMPT

Dear Mohammed Alramadan,

I am pleased to inform you that your submission dated November 29, 2016 for the study titled '**Determinants of Glycaemic Control, Complications and Health Related Quality of Life for People with Type 2 Diabetes in Saudi Arabia**' was reviewed and was approved. Please note that this approval is from the research ethics perspective only. You will still need to get permission from the head of department or unit in KFMC or an external institution to commence data collection.

We wish you well as you proceed with the study and request you to keep the IRB informed of the progress on a regular basis, using the IRB log number shown above.

Please be advised that regulations require that you submit a progress report on your research every 6 months. You are also required to submit any manuscript resulting from this research for approval by IRB before submission to journals for publication.

As a researcher you are required to have current and valid certification on protection human research subjects that can be obtained by taking a short online course at the US NIH site or the Saudi NCBE site followed by a multiple choice test. Please submit your current and valid certificate for our records. Failure to submit this certificate shall a reason for suspension of your research project.

If you have any further questions feel free to contact me.

Sincerely yours,

F M
Approved
06 DEC 2016
I R B

Prof. Omar H. Kasule
Chairman, Institutional Review Board (IRB)
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King Saud University Institutional Review Board approval

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جامعة الملك سعود
King Saud University
المدينة الطبية الجامعية

29.01.2017 (01.05.1438)
Ref. No. 17/0040/IRB

To: **Dr. Mohammed Alramadan**
Principal Investigator
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Subject: **Research Project No. E-17-2238**

Project Title: "Determinants of Glycaemic Control, Complications and Health Related Quality of Life for People with Type 2 Diabetes in Saudi Arabia"

CC: Dr. Baki Billah
Dr. Turky H. Almigbal
Dr. Mohammed Ali Batias
Co-Investigators

Type of Review: Expedite
Date of Approval: 22 January 2017
Date of Expiry: 29 January 2018

Dear Dr. Mohammed Alramadan,

I am pleased to inform you that your above-mentioned research project was reviewed and approved on 22 January 2017 (24 Rabi-II 1438). You are now granted permission to conduct study given that your study does not disclose patient identity and poses no risk to the patients.

As principal investigator, you are required to abide by the rules and regulations of the kingdom of Saudi Arabia and the research policies and procedures of the KSU IRB. If you make any changes to the protocol during the period of this approval, you must submit a revised protocol to the IRB for approval prior to implementing the changes. Please quote the project number shown above in any future correspondence or follow-ups related to this study.

We wish you success in your research and request you to keep the IRB informed about the progress and final outcome of the study in a regular basis. If you have any question, please feel free to contact me.

Thank you!

Sincerely yours,

Dr. Ayman Al-Eyadhy
Chairman, Institutional Review Board
King Saud University College of Medicine
King Saud University Medical City
P.O. Box 7805 Riyadh 11472 K.S.A.
E-mail: aleyadhy@ksu.edu.sa

لجنة أخلاقيات البحوث الطبية
كلية الطب
College Medicine
Institutional Review Board (IRB)

/braezell

Appendix 2: Informed consent form

Minimal Risk Informed Consent Template

إقرار بالموافقة المستنيرة علي المشاركة في بحث علمي يشتمل علي الحد الأدنى من المخاطر

Protocol Number: _____

رقم البحث العلمي: _____

Name of Subject: _____

اسم المشارك: _____

Medical Record Number: _____

رقم السجل الطبي: _____

Study Title:
Determinants of Glycaemic Control, Complications and Health Related Quality of Life for People with Type 2 Diabetes in Saudi Arabia

عنوان البحث العلمي
العوامل المؤثرة على السيطرة على مستوى السكر بالدم و العوامل المؤثرة على حدوث مضاعفات و العوامل المؤثر على نوعية الحياة لدى الأشخاص المصابين بمرض السكر من النوع الثاني بالمملكة العربية السعودية

Principal Investigator:
Dr Mohammed Jassim Alramadan

الباحث الرئيس
د. محمد جاسم أحمد الرمضان

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Why Is This Study Being Done?
To evaluate the effect of sociodemographic factors, lifestyle, adherence to treatment, anxiety, depression, cognitive function on the glycaemic control, diabetes complications and health related quality of life in patients with type 2 diabetes mellitus in Saudi Arabia.

ما سبب القيام بهذا البحث العلمي ؟
الهدف من هذا البحث هو دراسة تأثير العوامل الاجتماعية والديموغرافية وأسلوب الحياة والالتزام بالعلاج، والقلق، والاكتئاب، والادراك على التحكم في نسبة السكر في الدم، ومضاعفات مرض السكري و نوعية الحياة لدى المرضى الذين يعانون من النوع الثاني من داء السكري في المملكة العربية السعودية.

How Many People Will Take Part in This Study?
The study will include a total of 1082 persons who have type 2 diabetes

كم عدد الأشخاص المفترض مشاركتهم في هذا البحث العلمي؟
ستتم دعوة 1082 شخص مصاب بمرض السكري من النوع الثاني للمشاركة في هذه الدراسة

What is involved in the Study?
Patients with type 2 diabetes who visit diabetes centres in Hofuf, Riyadh, and Jeddah will be invited to participate in this study. A total of 1082 participants will be interviewed and their medical records will be reviewed to complete a questionnaire. The association between the aforementioned factors and the

ماذا يتضمن هذا البحث العلمي؟
سيتم دعوة المرضى الذين يعانون من داء السكري من النوع الثاني الذين يزورون مراكز السكري في الهفوف والرياض وجدة للمشاركة في هذه الدراسة. سيتم مقابلة المشاركين وستتم مراجعة سجلاتهم الطبية لاستكمال الاستبيان. و من ثم ستتم دراسة العلاقة بين العوامل الاجتماعية و الديموغرافية وأسلوب الحياة والالتزام بالعلاج، والقلق، والاكتئاب، والادراك ومستوى التحكم بالسكر في الدم، ومضاعفات السكري و

level of glycaemic control, diabetes complications and health related quality of life will be evaluated using multi-level mixed effect logistic regression.

نوعية الحياة باستخدام الوسائل الاحصائية المناسبة .

Study location:

Diabetes Centres at Hofuf, Riyadh and Jeddah

موقع إجراء هذا البحث العلمي:

مراكز السكر في كل من الأحساء و الرياض و جدة

What is Expected of Me During the Study?

Upon your agreement to participate the interviewer will do the following:

1- Request you to read and sign the consent form.
2- Ask you some questions to fill a questionnaire. The questions will cover name, contact information, age, gender, marital status, education, medical history, diet, physical activity, psychological status, cognitive function and quality of life status.
3- Take your weight, height, waist/hip/neck circumferences and blood pressure. Participant is free to leave after taking these measures.
4- Review your medical records to get information about your recent blood investigations, medical history and medications.

The interview will take around 40 minutes

ما المطلوب مني خلال هذا البحث العلمي؟

بناء على موافقتك على المشاركة في الدراسة سوف يتم عمل التالي:

1- سيطلب منك أن تقرأ والتوقع على استمارة الموافقة المستنيرة.
2- سيتم طرح بعض الأسئلة عليك لملء الاستبيان.الأسئلة تشمل الاسم، ومعلومات الاتصال، العمر، الجنس، الحالة الاجتماعية، والتعليم، والتاريخ الطبي، والنظام الغذائي، والنشاط البدني، الحالة النفسية، وظيفة الادراك ونوعية الحياة.
3- سيتم أخذ الوزن، الطول، محيط الخصر / الورك / محيطات العنق وضغط الدم. بعد هذه الخطوة يمكن للمشارك المغادرة.
4- سيتم مراجعة السجل الطبية الخاصة بك للحصول على معلومات حول فحوصات الدم التي تم اجراءها لك، والتاريخ الطبي والأدوية.

سوف تستغرق المقابلة حوالي 40 دقيقة

How Long Will I Be in This Study?

The interview will take around 40 minutes

كم مدة مشاركتي في هذا البحث العلمي؟

تستغرق المقابلة حوالي 40 دقيقة

Can I Stop Being in This Study?

You can decide to stop at any time. Taking part is purely voluntary.

هل يمكنني إنهاء المشاركة في هذا البحث العلمي؟

المشاركة طوعيه محضة ويمكنك أن تنهيها في أي وقت تشاء.

What are the Benefits of This Study?

We cannot guarantee or promise that this survey will directly benefit you but we hope that this work will help people with diabetes, physicians and the government to improve the management of diabetes diseases and reduce its complications.

ما هي فوائد هذا البحث العلمي؟

لا يمكننا أن نضمن أو نعد المشاركين بأن هذه الدراسة سوف تفيدهم بشكل مباشر و لكن نحن نأمل ان تساعد نتائج هذه الدراسة مرضى السكري والأطباء والجهات المسؤولة في تحسين علاج مرض السكري والحد من مضاعفاته.

What are the Risks of This Study?

This research will not involve any intervention with the participants group and it is not expected to have any significant risk on participants.

ما هي المخاطر المتوقعة من المشاركة في هذا البحث العلمي؟

هذا البحث لا يشتمل على أي تدخل جراحي أو علاجي مع المشاركين. لذلك لن يكون لهذه الدراسة أي خطر يذكر على المشاركين.

What are the Costs of This Study?

There are no costs to you if you take part in this study.

وما هي تكاليف المشاركة في هذا البحث العلمي؟

لا توجد تكاليف للمشاركة في هذه هذا البحث العلمي.

Will I Be Paid for Taking Part in This Study?

No, participants will not be paid

هل هنالك اجر مقابل المشاركة في هذا البحث العلمي؟

لا يوجد مقابل مالي للمشاركة في هذه الدراسة.

Will My Information Be Kept Private?

Your personal information will be kept private. It will be given out only if required by law. Your personal information will not be used in any reports.

هل سيتم الحفاظ علي معلوماتي بسرية؟

معلوماتك الشخصية سيتم الحفاظ عليها بسرية تامة. ولن تعطى لأي جهة إلا إذا اقتضى الأمر وذلك في حدود النظم والقوانين المطبقة بهذا الخصوص. معلوماتك الشخصية لن تستخدم في أي تقارير تنتج عن هذه الدراسة.

What are My Rights if I Take Part in This Study?

Taking part in this study is your choice. You may choose to take part or not to take part. If you decide to take part in the study, you can quit at any time. There will be no penalty to you for your decision. Your medical care will not change.

ما هي حقوقي إذا شاركت في هذا البحث العلمي؟

المشاركة في هذا البحث العلمي هي بمحض اختيارك. يمكنك أن تختار المشاركة أو لا. إذا قررت أن تشارك في هذا البحث العلمي، يمكنك التوقف في أي وقت تشاء. وإذا لم تشارك لن تكون هناك أي عقوبة لك, ولا تتأثر الرعاية الطبية المقدمة لك بسبب هذا القرار.

Who Do I Call if I Have Questions or Problems?

If you have questions about the study, you can call phone number +61 408 624 942.
If you have any questions about "rights of human subjects," you may call the Executive Officer, Monash University Human Research Ethics (MUHREC)at +61 3 9905 2052.

بمن يمكنني الاتصال إذا كان لدي أسئلة أو مشاكل؟

إذا كانت لديك أسئلة عن هذا البحث العلمي ، يمكنك الاتصال بالباحث الرئيس على هذا الرقم

+61 408 624 942.

إذا كانت لديك أي شكوى بخصوص هذه الدراسة يمكنك الاتصال برئيس لجنة أخلاقيات البحث العلمي بجامعة موناش على الرقم 2052 9905 3 61+ .

CONSENT:

إقرار بالموافقة

Subject

I will receive a signed copy of this consent form.

المشارك

أقر أنا _____ بأن هذا البحث العلمي وإجراءاته قد تم شرحها لي. لقد سمح لي بأن اسأل كل سؤال لدي الآن. ويمكنني أن اسأل أي أسئلة إضافية في أي وقت لاحق. كما يمكنني إنهاء المشاركة في هذا البحث العلمي في أي وقت دون أن تتأثر الرعاية الصحية المقدمة لي.

Subject Signature _____

توقيع المشارك

Date: / /

التاريخ / /

Person Obtaining Consent:

الشخص الحاصل علي الإقرار بالموافقة

I have explained the nature and purpose of the study and the risks involved. I have answered and will answer questions to the best of my ability. I will give a signed copy of the consent form to the subject.

أقر بأنني قد شرحت بصورة كاملة, طبيعة هذا البحث العلمي والغرض منه وما ينطوي عليه من مخاطر. ولقد أجبت على جميع الأسئلة بقدر الإمكان. سأعطي نسخة موقعة من الإقرار بالموافقة للمشارك المذكور أعلاه.

Signature of Person Obtaining Consent

توقيع الشخص الحاصل علي الإقرار بالموافقة

Date / /

التاريخ: / /

Principal Investigator

الباحث الرئيس

Signature of Principal Investigator

توقيع الباحث الرئيس

Appendix 3: Research questionnaire in English

MONASH University
Medicine, Nursing and Health Sciences

Glycaemic Control and Complications Among people with Type 2 diabetes in Saudi Arabia Questionnaire

(Version 03)

(Only to be used for people known to have type 2 diabetes prior to survey)

Data collection date in Gregorian

Day	Month	year

1. Diabetes Centre information

No.	Question	Response
1	Centre Name	
2	City	

2. Patient's name

No.	Question	Response
1	Patient's name	First: _____ Middle: _____ Surname: _____

3. Patient's demographic characteristics

No.	Question	Response and coding		Skip
1	What is your date of birth?	I was born in _____/_____/_____ DD / MM / Year		
2	What is your gender?	☐ Male ☐ Female	0 1	
3	What is your marital status?	☐ Single (never married) ☐ Married ☐ Divorced (separated) ☐ Widowed	0 1 2 3	
4	What is your highest education level achieved?	☐ None (Illiterate) ☐ Primary school ☐ Intermediate school ☐ Tertiary school ☐ University degree	0 1 2 3 4	

5	Nationality	☐ Saudi ☐ Non-Saudi	0 1	
		Specify: _____		
6	Which of the following best describes your **main work** status over the past 12 months?	☐ working ☐ Not working (able to work) ☐ Not working (unable to work) ☐ Homemaker (house-wife) ☐ Student ☐ Retired	0 1 2 3 4 5	
7	Which of the following best describe your **total household** monthly income?	☐ ≤ 3000 Saudi Riyals ☐ 3001–6000 Riyals ☐ 6001–9000 Riyals ☐ 9001–12000 Riyals ☐ ≥ 12001 Riyals	0 1 2 3 4	
8				

4. Patient's Medical history:

No.	Question	Response and coding		Skip
1	At what year have you been diagnosed to have diabetes?	Year _____		
2	Where do you usually follow up for your diabetes?	☐ Primary health care centre ☐ Diabetic Centre ☐ Public Hospital ☐ Private Centres	0 1 2 3	
3	How frequent are you following up for diabetes?	☐ Monthly ☐ Every 2 months ☐ Every 3 months ☐ Every 6 month ☐ 1 year ☐ Irregular	0 1 2 3 4 5	
4	How are you managing you diabetes currently?	☐ Diet **only** ☐ Oral tablets ☐ Insulin ☐ Oral and insulin	0 1 2 3	
Self-measure of blood glucose				
5	Do you have self-monitoring of blood glucose device at home?	☐ No ☐ Yes	0 → 1	
6	How often do you measure your blood glucose at home over the last month?	☐ Daily (once or more) ☐ 2 – 6 times every week ☐ Once weekly ☐ 1 – 2 times a month ☐ Did not use it	0 1 2 3 4	
Hypoglycaemia events				
7	How many times in the last month have you had a low blood sugar reaction with symptoms such as sweating, weakness, anxiety, trembling, hunger, headache or passing out?	☐ 0 times ☐ 1-5 times ☐ 6-10 times ☐ More than 10 times ☐ Do not know	0 1 2 3 4	

History of other diseases and diabetes complications				
		☐		
		☐		
10	Have you ever been told by a doctor that you have heart disease or coronary artery disease? If yes specify when you were told so.	☐ No ☐ I do not know ☐ Yes	0 1 2	
11	Have you been diagnosed by a doctor to have a stroke before? If yes specify when the first stroke event was.	☐ No ☐ I do not know ☐ Yes	0 1 2	
		☐		
13	Have you ever been told by a doctor that your diabetes have affected your eyes (retina) before? If yes specify when the first time you were told so.	☐ No ☐ I do not know ☐ Yes	0 1 2	
		☐		
		☐		
		☐		
		☐		
		☐		

5. Adherence to medication (Morisky Medication Adherence Questionnaire)

No.	Question	Response and coding		Skip
1	Do you ever forget to take your medicine?	☐ No ☐ Yes	0 1	
2	Are you careless at times about taking your medicine?	☐ No ☐ Yes	0 1	
3	Sometimes if you feel worse when you take the medicine, do you stop taking it?	☐ No ☐ Yes	0 1	
4	When you feel better do you sometimes stop taking your medicine?	☐ No ☐ Yes	0 1	

6. Family support

No.	Question	Response and coding		Skip
Does your family help and support you to do the following?				
1	• Follow a diabetic diet	☐ No ☐ Sometimes ☐ Yes, all the time	0 1 2	
2	• Take your medication	☐ No ☐ Sometimes ☐ Yes, all the time	0 1 2	
3	• Do physical activity	☐ No ☐ Sometimes ☐ Yes, all the time	0 1 2	
4	• Test your blood sugar at home	☐ No ☐ Sometimes ☐ Yes, all the time	0 1 2	
5	• Follow up regularly with your physician(s)	☐ No ☐ Sometimes ☐ Yes, all the time	0 1 2	

7. Utilization of healthcare services

No.	Question	Response and coding		Skip
1	Within the past 12 months have you ever received any diabetes education provided by physician or other health care worker? (Diet, physical activity, foot care)	☐ No ☐ Yes ☐ Cannot recall	0 1 2	
Within the past 12 months have you seen the following health professionals:				
2	• Diabetes educator	☐ No ☐ Yes ☐ Cannot recall	0 1 2	
3	• Dietician	☐ No ☐ Yes ☐ Cannot recall	0 1 2	
4	• Podiatrist	☐ No ☐ Yes ☐ Cannot recall	0 1 2	

8. Smoking

No.	Question	Response and coding		Skip
1	Do you or did you smoke any tobacco products such as	☐ No, never smoked ☐ Yes, in the past (more than 1 month)	0 1	

	cigarettes or Shisha (water pipe)?	☐ Yes, currently smoking	2	
2	Does anyone at your house currently smoke cigarettes or Shisha (water pipe)?	☐ No ☐ Yes, away from you (not exposed to the smoke) ☐ Yes, in front of you (You are exposed to the smoke)	0 1 2	

9. Diet (The UK Diabetes and Diet Questionnaire)

No.	Question	Response and coding		Skip
Think of your diet over the last **month**				
1	How often did you eat a portion of fruit? Include fresh, frozen, tinned and dried fruit. Do not count fruit juices.	☐ Never or very rare ☐ Once a week or less ☐ 2 – 4 times a week ☐ 5 – 6 times a week ☐ 1 – 2 times a day ☐ 3 or more times a day	0 1 2 3 4 5	
2	How often did you eat a portion of vegetables? Include fresh, tinned and frozen vegetables.	☐ Never or very rare ☐ Once a week or less ☐ 2 – 4 times a week ☐ 5 – 6 times a week ☐ 1 – 2 times a day ☐ 3 or more times a day	0 1 2 3 4 5	
3	How often did you eat red meat? Including camel, lamb, beef, and veal.	☐ 3 or more times a day ☐ 1 – 2 times a day ☐ 5 – 6 times a week ☐ 2 – 4 times a week ☐ Once a week or less ☐ Never or very rare	0 1 2 3 4 5	
4	How often did you eat rice?	☐ 3 or more times a day ☐ 1 – 2 times a day ☐ 5 – 6 times a week ☐ 2 – 4 times a week ☐ Once a week or less ☐ Never or very rare	0 1 2 3 4 5 →	
5	What amount of cooked rice did you usually eat in one meal?	☐ 4 or more cups ☐ 3 cups ☐ 2 cups ☐ One cup ☐ Less than a cap	0 1 2 3 4	
6	How often did you eat bread?	☐ 3 or more times a day ☐ 1 – 2 times a day ☐ 5 – 6 times a week ☐ 2 – 4 times a week ☐ Once a week or less ☐ Never or very rare	0 1 2 3 4 5 →	
7	What amount of bread did you usually eat in one meal?	☐ 5 or more slices of bread or more than one large Arabic bread	0	

		☐ 4 slices of bread or one large Arabic bread ☐ 2 slices of bread or ½ large Arabic bread ☐ one slice of bread or ¼ large Arabic bread ☐ Less than one slice of bread or less than ¼ large Arabic bread	1 2 3 4	
8	**How often did you eat** cake, sweet pastry, biscuits, chocolate, halva or other types of sweet pastries or desserts?	☐ 3 or more times a day ☐ 1 – 2 times a day ☐ 5 – 6 times a week ☐ 2 – 4 times a week ☐ Once a week or less ☐ Never or very rare	0 1 2 3 4 5	
9	**How often did you eat** dates?	☐ 3 or more times a day ☐ 1 – 2 times a day ☐ 5 – 6 times a week ☐ 2 – 4 times a week ☐ Once a week or less ☐ Never or very rare	0 1 2 3 4 5	
		☐		
11	**How often did you** drink sugary drinks? Including, non-diet soft drink (soda) and sugar sweetened fruit juice, tea, coffee or milk?	☐ 3 or more times a day ☐ 1 – 2 times a day ☐ 5 – 6 times a week ☐ 2 – 4 times a week ☐ Once a week or less ☐ Never or very rare	0 1 2 3 4 5	
12	How often did you use butter or animal fat in your rice, bread or cooking? (for example for cooking rice, vegetables and pastries)	☐ 3 or more times a day ☐ 1 – 2 times a day ☐ 5 – 6 times a week ☐ 2 – 4 times a week ☐ Once a week or less ☐ Never or very rare	0 1 2 3 4 5	
		☐		
		☐		
		☐		

10. Physical activity (WHO STEPS Instrument)

No.	Question	Response and coding	Skip
I would like to ask you about the usual way you travel to and from places. For example to work, for shopping, to market, to place of worship			
1	Do you walk for at least 10 minutes continuously to get to and from places?	☐ No 0 ☐ Yes 1	→
2	In a typical week, on how many days do you walk at least 10 minutes continuously to get to and from places?	Number of days:_____	

3	How much time do you spend walking for travel on a typical day?	Hours : minutes _____:_____		
The next questions exclude the work and transport activities that you have already mentioned. Now I would like to ask you about sports, fitness and recreational activities (leisure).				
4	Do you do any sports, fitness or recreational *(leisure)* activities that cause increases in breathing or heart rate for at least 10 minutes continuously? like *running, brisk waking, football or swimming*	☐ No ☐ Yes	0 → 1	
5	In a typical week, on how many days do you do this sports, fitness or recreational *(leisure)* activities?	Number of days:_____		
6	How much time do you spend doing this sports, fitness or recreational activities on a typical day?	Hours : minutes _____:_____		

11. Depression (PHQ-2)

No.	Question	Response and coding		Skip
How often during the past 2 weeks were you bothered by the following problems?				
1	Little interest or pleasure in doing things	☐ Not at all ☐ Several days ☐ More than half the days ☐ Nearly every day	0 1 2 3	
2	Feeling down, depressed, or hopeless.	☐ Not at all ☐ Several days ☐ More than half the days ☐ Nearly every day	0 1 2 3	

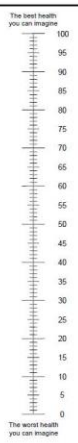
12. Anxiety (GAD-2)

No.	Question	Response and coding		Skip
Over the last 2 weeks, how often have you been bothered by the following problems?				
1	Feeling nervous, anxious or on edge	☐ Not at all ☐ Several days ☐ More than half the days	0 1 2	

		☐ Nearly every day	3	
2	Not being able to stop or control worrying	☐ Not at all ☐ Several days ☐ More than half the days ☐ Nearly every day	0 1 2 3	
		☐		
		☐		
		☐		
		☐		
		☐		

13. Patient's quality of life (EQ-5D-5L)

No.	Question	Response and coding		Skip
Under each heading, please tick the ONE box that best describes your health TODAY.				
1	MOBILITY	☐ I have no problems in walking about ☐ I have slight problems in walking about ☐ I have moderate problems in walking about ☐ I have severe problems in walking about ☐ I am unable to walk about	1 2 3 4 5	
2	SELF-CARE	☐ I have no problems washing or dressing myself ☐ I have slight problems washing or dressing myself ☐ I have moderate problems washing or dressing myself ☐ I have severe problems washing or dressing myself ☐ I am unable to wash or dress myself	1 2 3 4 5	
3	USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*	☐ I have no problems doing my usual activities ☐ I have slight problems doing my usual activities ☐ I have moderate problems doing my usual activities ☐ I have severe problems doing my usual activities ☐ I am unable to do my usual activities	1 2 3 4 5	
4	PAIN / DISCOMFORT	☐ I have no pain or discomfort ☐ I have slight pain or discomfort ☐ I have moderate pain or discomfort ☐ I have severe pain or discomfort ☐ I have extreme pain or discomfort	1 2 3 4 5	
5	ANXIETY / DEPRESSION	☐ I am not anxious or depressed ☐ I am slightly anxious or depressed ☐ I am moderately anxious or depressed ☐ I am severely anxious or depressed ☐ I am extremely anxious or depressed	1 2 3 4 5	

6	We would like to know how good or bad your health is TODAY. This scale is numbered from 0 to 100. 100 means the best health you can imagine. 0 means the worst health you can imagine. Mark an X on the scale to indicate how your health is TODAY.	 Your health today is: ☐	

14. Cognitive Impairment Test (RUDAS)

No.	Question	Response and coding		Skip
1. I want you to imagine that we are going shopping. Here is a list of grocery items. I would like you to remember the following items which we need to get from the shop. When we get to the shop in about 5 minutes time I will ask you what it is that we have to buy. You must remember the list for me. Tea Cooking Oil Eggs Soap Please repeat this list for me (Ask person to repeat the list 3 times)				
2	I am going to ask you to identify/show me different parts of the body.			
	(1) show me your right foot	☐ Correct ☐ Incorrect	1 0	
	(2) show me your left hand	☐ Correct ☐ Incorrect	1 0	
	(3) with your right hand touch your left shoulder	☐ Correct ☐ Incorrect	1 0	
	(4) with your left hand touch your right ear	☐ Correct ☐ Incorrect	1 0	
	(5) which is (point to/indicate) my left knee	☐ Correct ☐ Incorrect	1 0	
	(6) which is (point to/indicate) my right elbow	☐ Correct ☐ Incorrect	1 0	
	(7) with your right hand point to/indicate my left eye	☐ Correct ☐ Incorrect	1 0	
	(8) with your left hand point to/indicate my left foot	☐ Correct ☐ Incorrect	1 0	
3	I am going to show you an action/exercise with my hands. I want you to watch me and copy what I do. Copy me when I do this . . . (i.e. demonstrate - put one hand in a fist, and the other hand	☐ Normal ☐ Partially Adequate ☐ Failed	2 1 0	

	palm down on the table or your knees and then alternate simultaneously.) Now do it with me. I would like you to keep doing this action at this pace until I tell you to stop - approximately 10 seconds or 5 – 6 sequences. (Demonstrate at moderate walking pace).			
4	Please draw this picture exactly as it looks to you.  1) Has person drawn a picture based on a square? (2) Do all internal lines appear in person's drawing?  (3) Do all external lines appear in person's drawing? 	☐ yes ☐ No ☐ yes ☐ No ☐ Yes ☐ No	1 0 1 0 1 0	
5	You are standing on the side of a busy street. There is no pedestrian crossing and no traffic lights. Tell me what you would do to get across to the other side of the street safely. (If person gives incomplete answer use prompt: "Is there anything else you would do?") Record exactly what patient says and circle all parts of response which were prompted.			
	Did person indicate that they would look for traffic? Did person make any additional safety proposals?	☐ Yes ☐ Yes prompted ☐ No ☐ Yes ☐ Yes prompted ☐ No	2 1 0 2 1 0	
1	We have just arrived at the shop. (Can you remember the list of groceries we need to buy? (Prompt: If person cannot recall any of the list, say "The first one was 'tea'."	☐ Tea ☐ Cooking Oil ☐ Eggs ☐ Soap	2 2 2 2	
6	I am going to time you for one minute. In that one minute, I would like you to tell me the names of as many different animals as you can. We'll see how many different animals you can name in one minute. (Repeat instructions if necessary). Maximum score for this item is 8. If person names 8 new animals in less than one minute there is no need to continue.	Number of animals named (out of 8): _____		

15. Katz Index of Independence in Activities of Daily Living

No.	Question	Response and coding		Skip
1	Bathing	☐ **Independent** Bathes self completely or needs help in bathing only a single part of the body such as the back, genital area or disabled extremity. ☐ **Dependent** Needs help with bathing more than one part of the body, getting in or out of the tub or shower. Requires total bathing.	1 0	
2	Dressing	☐ **Independent** Gets clothes from closets and drawers and puts on clothes and outer garments complete with fasteners. May have help tying shoes. ☐ **Dependent** Needs help with dressing self or needs to be completely dressed.	1 0	
3	Toileting	☐ **Independent** Goes to toilet, gets on and off, arranges clothes, cleans genital area without help. ☐ **Dependent** Needs help transferring to the toilet, cleaning self or uses bedpan or commode.	1 0	
4	Transferring	☐ **Independent** Moves in and out of bed or chair unassisted. Mechanical transferring aides are acceptable. ☐ **Dependent** Needs help in moving from bed to chair or requires a complete transfer.	1 0	
5	Continence	☐ **Independent** Exercises complete self-control over urination and defecation. **Dependent** Is partially or totally incontinent of bowel or bladder.	1 0	
6	Feeding	☐ **Independent** Gets food from plate into mouth without help. Preparation of food may be done by another person. ☐ **Dependent** Needs partial or total help with feeding or requires parenteral feeding.	1 0	

16. Neuropathy screening

(The Michigan Neuropathy Screening Instrument)

No.	Question	Response and coding		Skip
1	Are your legs and/or feet numb?	☐ Yes ☐ No	1 0	

2	Do you ever have any burning pain in your legs and/or feet?	☐ Yes ☐ No	1 0	
3	Are your feet too sensitive to touch?	☐ Yes ☐ No	1 0	
4	Do you get muscle cramps in your legs and/or feet?	☐ Yes ☐ No	1 0	
5	Do you ever have any prickling feelings in your legs or feet?	☐ Yes ☐ No	1 0	
6	Does it hurt when the bed covers touch your skin?	☐ Yes ☐ No	1 0	
7	When you get into the tub or shower, are you able to tell the hot water from the cold water?	☐ Yes ☐ No	1 0	
8	Have you ever had an open sore on your foot?	☐ Yes ☐ No	1 0	
9	Has your doctor ever told you that you have diabetic neuropathy?	☐ Yes ☐ No	1 0	
10	Do you feel weak all over most of the time?	☐ Yes ☐ No	1 0	
11	Are your symptoms worse at night?	☐ Yes ☐ No	1 0	
12	Do your legs hurt when you walk?	☐ Yes ☐ No	1 0	
13	Are you able to sense your feet when you walk?	☐ Yes ☐ No	1 0	
14	Is the skin on your feet so dry that it cracks open?	☐ Yes ☐ No	1 0	
15	Have you ever had an amputation?	☐ Yes ☐ No	1 0	

17. Anthropometrics

No.	Question	Response and coding
1	Blood pressure in mm Hg	Blood pressure Systolic: _____ mm Hg Diastolic: _____ mm Hg
2	Patient's height in centimetre (cm)	Height: _____ cm
3	Patient's weight in kilogram (Kg)	Weight: _____ kg
4	Neck circumference	Neck: _____ cm
4	Waist circumference in cm	Waist : _____ cm
5	Hip circumference in cm	Hip: _____ cm

18. Information from patient medical records

No.	Question	Response and coding			
1	Must recent 3 Blood pressure readings (mm Hg)		systolic	diastolic	
		1st reading			
		2nd reading			
		3rd reading			

2	Most recent fasting blood sugar measurement	1st reading: _____ mg/dl 2nd reading: _____ mg/dl 3rd reading: _____ mg/dl	
3	Most recent Haemoglobin A1c (HbA1c) measurement (%)	HbA1c: _____ %	
4	Most recent serum creatinine reading (mg/dl)	Creatinine: _____	
5	Most recent Albumin/creatinine ratio test results	Albumin/creatinine ratio: _____	
6	Most recent eGFR (ml/min)	eGFR: _____	
7	Most recent lipid profile test (Total cholesterol, LDL, HDL, Triglycerides) in mg/dl	Total chole: _____ mg/dl LDL: _____ mg/dl HDL: _____ mg/dl Triglyc. : _____ mg/dl	
8	Has the patient been diagnosed to have hypertension?	☐ No ☐ Yes	0 1
9	Has the patient been diagnosed to have coronary artery disease?	☐ No ☐ Yes	0 1

19. The patient is on the following medications

	Medication Name	dose	Daily Repeat
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			
11			
12			
13			
14			
15			

---------- End of questionnaire ----------

Appendix 4: Research questionnaire in Arabic

السيطرة على السكر في الدم وانتشار المضاعفات بين الأشخاص الذين لديهم داء السكري نوع 2

دراسة استبيانية — الطبعة 1

(لاستخدام الأشخاص المعروف أن لديهم داء السكري نوع 2 قبل إجراء الإستبيان فقط)

1. معلومات عن المركز الخاص بداء السكري
   1. إسم المركز: _____
   2. المدينة: _____
2. إسم المريض ومعلومات الإتصال
   1. إسم المريض
      الإسم الأول: _____
      إسم الأب: _____
      العائلة: _____
   2. رقم الملف الطبي: _____
3. الخصائص الديموغرافية للمريض
   1. ما هو تاريخ ميلادك؟ ____/____/_____
   2. ماهو جنسك؟
      - □ ذكر
      - □ أنثى
   3. الحالة الاجتماعية
      - □ أعزب (لم تتزوج أبداً)
      - □ متزوج
      - □ مطلق (منفصل)
      - □ أرمل
   4. ما هو أعلى مستوى تعليمي حصلت عليه؟
      - □ لا يوجد (أمي)
      - □ المدرسة الإبتدائية
      - □ المدرسة المتوسطة
      - □ المدرسة الثانوية
      - □ شهادة جامعية
   5. ما هي جنسيتك؟
      - □ سعودي
      - □ غير سعودي: (حدّد): _____
   6. أي من الأوصاف التالية أفضل وصف **لعملك الرئيسي** لفترة 12 شهر الأخيرة؟
      - □ أعمل
      - □ لا أعمل (أستطيع العمل)
      - □ لا أعمل (لا أستطيع العمل)
      - □ عمل منزلي (ربة بيت)
      - □ طالب
      - □ متقاعد
   7. أي من الأوصاف التالية أفضل وصف **لمجموع دخل الأسرة** الشهري؟

1

- □ 3000 ريال سعودي أو أقل
- □ 3001 — 6000 ريال
- □ 6001— 9000 ريال
- □ 9001—12000 ريال
- □ 12001 ريال سعودي أو أكثر

4. **التاريخ الطبي للمريض**

قسم 1: داء السكري

1. في أي سنة تم تشخيص إصابتك بالداء السكري؟
   سنة _____
2. أين تقوم بمتابعة مرضك بداء السكري عادةً ؟
   - □ مركز الرعاية الصحية الأولية
   - □ مركز داء السكري
   - □ المستشفى العام
   - □ مراكز خاصة
3. ماهو تكرار متابعتك لداء السكري؟
   - □ شهرياً
   - □ كل شهرين
   - □ كل 3 أشهر
   - □ كل 6 أشهر
   - □ سنة واحدة
   - □ غير منتظم
4. كيف تقوم حالياً بالتحكم بداء السكري لديك؟
   - □ الحمية الغذائية **فقط**
   - □ أقراص عن طريق الفم
   - □ إنسولين
   - □ أقراص وإنسولين
5. هل لديك بالمنزل جهاز للرصد الذاتي لغلوكوز الدم؟
   - □ لا
   - □ نعم
6. كم مرة قمت بقياس غلوكوز الدم بالمنزل خلال الشهر الماضي؟
   - □ يومياً (مرة أو مرتان)
   - □ 2—6 مرات أسبوعياً
   - □ مرة واحدة أسبوعياً
   - □ 1—2 مرة شهرياً
   - □ لم أستخدمه
7. كم مرة في الشهر الماضي حصل لديك رد فعل بسبب انخفاض السكر في الدم مع أعراض مثل التعرّق أوالضعف أوالقلق أو الرجفة أو الجوع أو الإغماء؟
   - □ صفر
   - □ 1—5 مرات
   - □ 6—10 مرات
   - □ أكثر من 10 مرات
   - □ لا أعرف

قسم 2: التاريخ الطبي للأمراض الأخرى ومضاعفات داء السكري

1. هل سبق أن أخبرك في أي وقت مضى أي طبيب أو ممرض بأن لديك ارتفاع في ضغط الدم؟ لو كانت الإجابة نعم فمتى تم إخبارك بذلك أول مرة؟
   - □ لا
   - □ لا أعرف
   - □ نعم: حدد متى كان ذلك: قبل _____ سنوات
2. هل سبق أن اخبرك في أي وقت مضى أي طبيب بأن لديك ارتفاع في نسبة الدهون أو الكوليسترول؟ لو كانت الإجابة نعم فمتى تم إخبارك بذلك أول مرة؟
   - □ لا
   - □ لا أعرف
   - □ نعم: حدد متى كان ذلك: قبل _____ سنوات
3. هل سبق أن اخبرك في أي وقت مضى أي طبيب بأن لديك مرض القلب أو مرض الشريان التاجي؟ لو كانت الإجابة نعم فمتى تم إخبارك بذلك أول مرة؟
   - □ لا
   - □ لا أعرف
   - □ نعم: حدد متى كان ذلك: قبل _____ سنوات
4. هل قام أي طبيب بتشخيص إصابتك بجلطة دماغية سابقاً؟ لو كانت الإجابة نعم حدد متى حدث ذلك؟
   - □ لا
   - □ لا أعرف
   - □ نعم: حدد متى كان ذلك: قبل _____ سنوات
5. هل سبق أن اخبرك في أي وقت مضى أي طبيب بأن داء السكري قد أثر على كليتيك؟ لو كانت الإجابة نعم فمتى تم إخبارك بذلك أول مرة؟
   - □ لا
   - □ لا أعرف
   - □ نعم: حدد متى كان ذلك: قبل _____ سنوات
6. هل سبق أن اخبرك في أي وقت مضى أي طبيب بأن داء السكري قد أثر على عينيك (الشبكية)؟ لو كانت الإجابة نعم فمتى تم إخبارك بذلك أول مرة؟
   - □ لا
   - □ لا أعرف
   - □ نعم: حدد متى كان ذلك: قبل _____ سنوات
7. هل لديك أي إحساس غير طبيعي بالألم في قدميك؟ لو كانت الإجابة نعم فمتى بدأ ذلك؟
   - □ لا
   - □ لا أعرف
   - □ نعم: حدد متى كان ذلك: قبل _____ سنوات
8. هل يوجد الآن في قدميك أو كان يوجد سابقاً أي جرح أو قرحة غير ملتئمة؟ لو كانت الإجابة نعم حدد متى بدأ ذلك؟
   - □ لا
   - □ لا أعرف
   - □ نعم: حدد متى كان ذلك: قبل _____ سنوات
9. هل أجريت عملية بتر لطرفيك السفليين؟ لو كانت الإجابة نعم حدد متى حصلت عملية البتر الأولى؟
   - □ لا
   - □ لا أعرف
   - □ نعم: حدد متى كان ذلك: قبل _____ سنوات
10. هل تم إدخالك للمستشفى بسبب أي من الحالات المذكورة أعلاه؟ لو كانت الإجابة نعم فمتى كان ذلك؟
    - □ لا
    - □ لا أعرف
    - □ نعم: حدد متى كان ذلك: قبل _____ سنوات

5. الإلتزام بالدواء

1. هل تنسى في بعض الأحيان تناول الدواء ؟
   - □ لا
   - □ نعم
2. هل أنت مهمل احياناً بتناول الدواء؟
   - □ لا
   - □ نعم
3. حين تشعر بأنك أسوأ حالاً هل تتوقف عن تناول الدواء ؟
   - □ لا
   - □ نعم
4. حين تشعر بأنك أحسن حالاً هل تتوقف عن تناول الدواء؟
   - □ لا
   - □ نعم

6. مساندة الأسرة

هل تساعدك أسرتك أو تساندك في القيام بما يلي:

1. اتباع نظام غذائي خاص بمرضى السكري؟
   - □ لا
   - □ أحياناً
   - □ نعم، كل الوقت
2. تناول الدواء؟
   - □ لا
   - □ أحياناً
   - □ نعم، كل الوقت
3. القيام بنشاط بدني؟
   - □ لا
   - □ أحياناً
   - □ نعم، كل الوقت
4. فحص نسبة السكر في الدم بالمنزل؟
   - □ لا
   - □ أحياناً
   - □ نعم، كل الوقت
5. المتابعة المنتظمة مع طبيبك/أطبائك؟
   - □ لا
   - □ أحياناً
   - □ نعم، كل الوقت

7. الإستفادة من خدمات الرعاية الصحية

1. خلال 12 شهر الماضية هل حصلت في أي وقت على تثقيف عن داء السكري زوده أحد من الأطباء أو العاملين في الرعاية الصحية؟ (مثلاً: الحمية الغذائية، النشاط البدني، العناية بالأقدام)
   - □ لا
   - □ نعم
   - □ لا أتذكر

خلال 12 شهر الماضية هل زرت المختصين الصحيين التالين؟

2. مثقف صحي لمرض السكري
   - □ لا

- □ نعم
- □ لا أتذكر

3. أخصائي التغذية
   - □ لا
   - □ نعم
   - □ لا أتذكر
4. أخصائي الأقدام
   - □ لا
   - □ نعم
   - □ لا أتذكر

8. حالك مع التدخين

1. هل تدخن أو دخنت أياً من منتجات التبغ مثل السجائر أو الشيشه (الأركيله)؟
   - □ لا، لم أدخن أبداً
   - □ نعم، في الماضي (أكثر من شهر)
   - □ نعم، أدخن حالياً
2. هل يدخن أي أحد من أفراد أسرتك السجائر أو الشيشه (الأركيله)؟
   - □ لا
   - □ نعم، بعيداً عنك (غير معرض للدخان)
   - □ نعم، أمامك (أنت معرض للدخان)

9. عاداتك الغذائية

فكر في غذائك خلال **الشهر** الماضي

1. كم مرة أكلت مقداراً من الفاكهة؟ إشمل الفاكهة الطازجة والمجمدة والمعلبة والمجففة. لا تأخذ في الإعتبار عصير الفواكه.
   - □ أبداً أو نادراً جداً
   - □ مرة واحدة أسبوعياً أو أقل
   - □ 2—4 مرات أسبوعياً
   - □ 5—6 مرات أسبوعياً
   - □ 1—2 مرة يومياً
   - □ 3 مرات أو أكثر يومياً
2. كم مرة أكلت مقداراً من الخضراوات؟ إشمل الخضراوات الطازجة والمجمدة والمعلبة والمجففة.
   - □ أبداً أو نادراً جداً
   - □ مرة واحدة أسبوعياً أو أقل
   - □ 2—4 مرات أسبوعياً
   - □ 5—6 مرات أسبوعياً
   - □ 1—2 مرة يومياً
   - □ 3 مرات أو أكثر يومياً
3. كم مرة أكلت لحوماً حمراء؟ إشمل لحم الجمل والخروف والبقر والعجل.
   - □ 3 مرات أو أكثر يومياً
   - □ 1—2 مرة يومياً
   - □ 5—6 مرات أسبوعياً
   - □ 2—4 مرات أسبوعياً

- □ مرة واحدة أسبوعياً
- □ أبداً أو نادراً جداً

4. كم مرة أكلت الرز؟

- □ 3 مرات أو أكثر يومياً
- □ 1—2 مرة يومياً
- □ 5—6 مرات أسبوعياً
- □ 2—4 مرات أسبوعياً
- □ مرة واحدة أسبوعياً أو أقل
- □ أبداً أو نادراً جداً

5. ما كمية الرز المطبوخ التي تتناولها عادة في الوجبة الواحدة؟

- □ 4 أكواب أو أكثر
- □ 3 أكواب
- □ كوبان اثنان
- □ كوب واحد
- □ أقل من كوب

6. كم مرة أكلت الخبز؟

- □ 3 مرات أو أكثر يومياً
- □ 1—2 مرة يومياً
- □ 5—6 مرات أسبوعياً
- □ 2—4 مرات أسبوعياً
- □ مرة واحدة أسبوعياً أو أقل
- □ أبداً أو نادراً جداً

7. ما هي كمية الخبز التي تأكلها في الوجبة الواحدة ؟

- □ 5 شرائح من الخبز أو أكثر من قرص واحد من الخبز العربي الكبير
- □ 4 شرائح من الخبز أو قرص واحد من الخبز العربي الكبير
- □ شريحتان اثنتان من الخبز أو نصف قرص من الخبز العربي الكبير
- □ شريحة واحدة من الخبز أو ربع قرص من الخبز العربي الكبير
- □ أقل من شريحة واحدة من الخبز أو ربع قرص من الخبز العربي الكبير

8. كم مرة أكلت الكعك أو المعجنات الحلوة أو الشيكولاته أو الحلاوه أو أنواع أخرى من المعجنات الحلوة أو الحلويات؟

- □ 3 مرات أو أكثر يومياً
- □ 1—2 مرة يومياً
- □ 5—6 مرات أسبوعياً
- □ 2—4 مرات أسبوعياً
- □ مرة واحدة أسبوعياً أو أقل
- □ أبداً أو نادراً جداً

9. كم مرة أكلت التمر؟

- □ 3 مرات أو أكثر يومياً
- □ 1—2 مرة يومياً
- □ 5—6 مرات أسبوعياً
- □ 2—4 مرات أسبوعياً
- □ مرة واحدة أسبوعياً أو أقل

- □ أبداً أو نادراً جداً

10. في جلسة واحدة كم تمرة تأكل عادة؟

- □ 14 تمرة أو أكثر
- □ 10—13 تمرة
- □ 7—9 تمرات
- □ 4—6 تمرات
- □ 1—3 تمرات

11. كم مرة شربت مشروبات سكرية؟ يشمل مشروبات غازية عادية (صودا) و مشروبات محلاة بالسكر - عصير الفاكهة أوالشاي أوالقهوة أو الحليب؟

- □ 3 مرات أو أكثر يومياً
- □ 1—2 مرة يومياً
- □ 5—6 مرات أسبوعياً
- □ 2—4 مرات أسبوعياً
- □ مرة واحدة أسبوعياً أو أقل
- □ أبداً أو نادراً جداً

12. كم مرة استخدمت الزبدة أو الشحم الحيواني مع الرز أو الخبز أو في الطبخ؟

- □ 3 مرات أو أكثر يومياً
- □ 1—2 مرة يومياً
- □ 5—6 مرات أسبوعياً
- □ 2—4 مرات أسبوعياً
- □ مرة واحدة أسبوعياً أو أقل
- □ أبداً أو نادراً جداً

13. ما هو نوع منتجات الحليب/الألبان التي كنت تستخدمها اعتيادياً؟ يشمل الحليب ولبن الزبادي ولبن الشرب.

- □ كامل الدسم
- □ أحياناً كامل الدسم وأحياناً قليل الدسم — صفر (خالي من الدسم)
- □ قليل الدسم
- □ صفر (خالي من الدسم)
- □ الصويا أو اللوز أوحليب غير ناتج من الألبان

14. كم مرة شربت الشاي (الأسود أو الأخضر)؟

- □ 3 مرات أو أكثر يومياً
- □ 1—2 مرة يومياً
- □ 5—6 مرات أسبوعياً
- □ 2—4 مرات أسبوعياً
- □ مرة واحدة أسبوعياً أو أقل
- □ أبداً أو نادراً جداً

15. كم مرة شربت القهوة (العربية أو التركية أو الأمريكية أو أي نوع آخر)؟

- □ 3 مرات أو أكثر يومياً
- □ 1—2 مرة يومياً
- □ 5—6 مرات أسبوعياً
- □ 2—4 مرات أسبوعياً
- □ مرة واحدة أسبوعياً أو أقل

□ أبداً أو نادراً جداً

10. مقياس الإدراك

١- الذاكرة

أريدك أن تتخيل أننا ذاهبون للتسوق وسنصل إلى السبرماركت بعد خمس دقائق. لدينا قائمة باصناف نحتاج إلى شرائها. أود منك أن تحفظ هذه القائمة وسأطلب منك أن تذكرها لي بعد قليل.

شاي, زيت الطهي, بيض, صابون

(أعد القائمة على الشخص من ٣ - ٥ مرات و اطلب منه تكرارها ٣ مرات)

٢- أجزاء الجسم

سوف أطلب منك تحديد أجزاء مختلفة من الجسم

(إذا أجاب الشخص عن ٥ أسئلة بشكل صحيح انتقل للفقرة التالية)

1)) أرني قدمك اليمنى -((1) إذا كانت الإجابة صحيحة)

(2) أرني يدك اليسرى -((1) إذا كانت الإجابة صحيحة)

(3) بيدك اليمنى إلمس كتفك الأيسر -((1) إذا كانت الإجابة صحيحة)

(4) بيدك اليسرى إلمس أذنك اليمنى -((1) إذا كانت الإجابة صحيحة)

(5) أشر إلى ركبتي اليسرى -((1) إذا كانت الإجابة صحيحة)

(6) أشر إلى كوعي (مرفقي) الأيمن -((1) إذا كانت الإجابة صحيحة)

(7) بيدك اليمنى أشر إلى عيني اليسرى -((1) إذا كانت الإجابة صحيحة)

(8) بيدك اليسرى أشر إلى قدمي اليسرى -((1) إذا كانت الإجابة صحيحة)

الدرجة النهائية (من ٥):-

٣- حركة اليدين

سأريك تمرين سأقوم به بيدي و سأطلب منك أن تقوم بأدائه بنفسك بعد قليل.

(ضع يديك على الطاولة أو على ركبتيك بحث تكون واحدة مقبوضة و الأخرى مفتوحة و باطن الكف إلى أسفل. إفتح اليد المقبوضة و اقبض المفتوحة و استمر في تكرار حركة اليدين بالتناوب و بشكل رتيب)

قم بأداء التمرين معي..

الآن استمر في أداء التمرين لوحدك لمدة ١٠ ثواني (أو أكمل ٦ دورات من الحركة)

طبيعي (٢) (عدد قليل جدا من الأخطاء مع تصحيح ذاتي و تحسن تدريجي و نقص طفيف في التزامن).

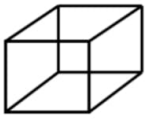
مقبول جزئياً (١) (أخطاء ملحوظة مع بعض محاولات التصحيح الذاتي. ضعف في التزامن).

فاشل (٠) (لا يمكن القيام بهذه المهمة).

٤. رسم المكعب

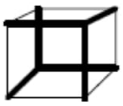
أريد منك ان ترسم هذه الصورة تماما كما تبدو لك

(أعرض رسمة المكعب للمشارك)

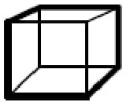


(1)هل رسم شخص صورة على أساس مربع؟

(2)هل تظهر جميع الخطوط الداخلية في الرسم الشخصي؟



(3)هل تظهر جميع الخطوط الخارجية في الرسم الشخصي؟



٥. حسن الحكم

أنت تقف على جانب شارع مزدحم بالسيارات المسرعة و ترغب في قطعه إلى الجانب الآخر ولكن لا يوجد خطوط مشاة ولا إشارات المرور. ما الذي ستفعله لقطع الشارع و الوصول الى الجانب الآخر بأمان.

(إذا أعطى الشخص إجابة غير مكتملة إسأله "هل هناك أي شيء آخر سوف تفعل؟")

هل أشار الشخص إلى أنه سيتأكد من حركة المرور؟

(أمثلة: "سأنظر إلى اليمين و اليسار" أو "سأتأكد من خلو الطريق من السيارات")

نعم

لا

هل قدم الشخص أي اقتراحات إضافية للسلامة

(أمثلة: "سأكون حذراً" أو "سأتأكد مرة أخرى من عدم قدوم سيارات و أنا اعبر" أو "سأنتظر قدوم أشخاص للعبور معهم" أو "سأطلب المساعدة")

نعم

لا

١ـ الذاكرة

وصلنا للتو إلى السبرماركت. أرجو منك ان تذكر لي قائمة الأصناف التي نحتاجها.

(إذا لم يتذكر الشخص أي من الاصناف قم بتذكيره بقول: "الصنف الأول هو الشاي" فقط)

(نقطتين لكل عنصر تم تذكره من دون مساعدة)

الشاي ..... 2.

زيت الطهي ..... 2.

بيض ..... 2.

الصابون ..... 2.

... / 8

٦ـ اللغة

خلال دقيقة واحدة أرجو منك أن تذكر لي أسماء أكبر عدد ممكن من الحيوانات.

(إذا ذكر الشخص اسماء ٨ حيوانات في اقل من دقيقة لا حاجة للأستمرار)

عدد الحيوانات المذكورة خلال دقيقة (من ٨)

13. فحص الإعتلال العصبي

1. هل يوجد خدر في ساقيك و/أو قدميك؟

   □ نعم
   □ لا

2. هل حصل لك في أي وقت مضى ألم حارق في ساقيك و/أو قدميك؟

   □ نعم
   □ لا

3. هل قدماك حساستان للّمس بشكل مفرط؟

   □ نعم
   □ لا

4. هل يحصل لك تشنج عضلي في الساقين و/أو القدمين؟

   □ نعم
   □ لا

5. هل حصل لك في أي وقت مضى شعور بالوخز في ساقيك أو قدميك؟

   □ نعم
   □ لا

6. هل تشعر بالألم عندما يمس بشرتك غطاء السرير؟

   □ نعم
   □ لا

7. حين تكون في حوض الإستحمام أو الدّش هل تستطيع أن تلحظ الفرق بين الماء الحار والماء البارد؟

   □ نعم
   □ لا

8. هل كان لديك في أي وقت مضى تفرح مفتوح على قدمك؟

   □ نعم
   □ لا

9. هل أخبرك طبيبك في أي وقت مضى أنك مصاب بإعتلال أو ضعف في الأعصاب بسبب مرض السكر ؟

   □ نعم
   □ لا

10. هل تشعر بالضعف العام بالجسم في معظم الوقت؟

    □ نعم

□ لا

11. هل الأعراض أسوأ في الليل؟

□ نعم
□ لا

12. هل تؤلمك ساقاك عند المشي؟

□ نعم
□ لا

13. هل تستطيع الإحساس بقدميك عندما تمشي؟

□ نعم
□ لا

14. هل بشرة قدميك جافة بحيث تتشقق؟

□ نعم
□ لا

15. هل أجريت لك في أي وقت مضى عملية بتر؟

□ نعم
□ لا

***** نهاية الإستبيان *****

I, Hussain Alrikabi, accredited NAATI translator, certify that this is a true and accurate translation of the quetionnaire whose title is indicated below. 11-10-2016.

أشهد أنا، حسين الركابي، المترجم المعتمد لدى السلطة الوطنية لاعتماد المترجمين (*NAATI*)، أن النص اعلاه ترجمة صحيحة ودقيقة عن الإستبيان المذكور عنوانه أدناه. *11—10—2016*.

Control of Blood Sugar and prevalence of Complications Among people with Type 2 diabetes Study Questionnaire Version 1