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Predictors of macrovascular complications in Al-Madinah Al-Munawara type 2 diabetes mellitus patients, Saudi Arabia: A cross-sectional study

Inas R. El-Alameey^{a,b}, Abeer A. Al-Mutairi^a, Rama D. Alamri^a, Raoum S. Saed^a, Rema A. Alqubali^a, Ghada A. Al-Abdudullatif^a, Shroug R. Al-Harbi^a

^aDepartment of Clinical Nutrition, College of Applied Medical Sciences, Taibah University, Al-Madinah Al Munawara, Saudi Arabia, ^bDepartment of Child Health, Medical Research and Clinical Studies Institute, National Research Centre, Cairo, Egypt

Correspondence to Inas R. El-Alameey, PhD, Department of Clinical Nutrition, College of Applied Medical Sciences, Taibah University, Al-Madinah Al Munawara 12612, Saudi Arabia. Tel: +20 100 185 8378/966 552 411 033; e-mail: ielalameey@taibahu.edu.sa

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Background/aim

Diabetes mellitus is a metabolic disease characterized by chronic hyperglycemia, which causes macrovascular complications that account for most of the morbidity, hospitalizations, and deaths. The goal of this study is to evaluate the relationship between macrovascular complications and associated risk factors in Al-Madinah Al-Munawara patients suffering from type 2 diabetes mellitus.

Patients and methods

This descriptive cross-sectional study involved 275 type 2 diabetes mellitus patients who resided in Al-Madinah Al-Munawara and visited the diabetic clinic at King Fahd Hospital on a regular basis. Participants in the study ranged in age from 20 to 65. Hemoglobin, glycated hemoglobin, serum calcium, fasting blood glucose, and lipid profile were analyzed.

Results

Out of 275 patients with type 2 diabetes mellitus, 113 have had macrovascular complications. A significant association (P<0.05) has been observed between the age of the patients and different forms of macrovascular complications, which impact 62.7% of the elderly (41–65 years old). The prevalence of macrovascular complications was higher among females. Glycated hemoglobin levels positively correlated with the number of hospitalizations, high blood pressure, hemoglobin, and serum cholesterol levels. Macrovascular complications are positively correlated with age, sex, hypertension, and therapy type (P<0.05), while physical activity has a negative significant effect on the appearance of macrovascular complications by multiple regression analysis.

Conclusion

In this study, diabetic macrovascular complications were prevalent. The age, sex of participants, and type of treatment were independent predictors of macrovascular complications. Hypertension has a significant positive effect on the appearance of macrovascular complications. Physically inactive patients have a higher risk of macrovascular complications.

Keywords:

Al-Madinah Al-Munawara, macrovascular complications, type 2 diabetes mellitus

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Introduction

Diabetes mellitus is not merely a disorder of carbohydrate metabolism but a cause of vascular disease affecting nearly all blood vessel types and sizes. Chronic hyperglycemia occurs because of relative or absolute insulin deficiency in adults and is associated with an unhealthy diet, lifestyle, physical inactivity, and obesity, which lead to macrovascular complications. Indeed, vascular complications are responsible for the morbidity, hospitalizations, and deaths that occur in diabetic patients [1].

Type 2 diabetes mellitus usually develops when the body's cells become resistant to the action of the hormone insulin. The pancreas will produce more

insulin to overcome this resistance and lower blood sugar levels. Over time, the pancreas will lose its ability to produce insulin. As a result, glucose builds up in the bloodstream instead of being transported to cells where it is used for energy, resulting in a rise in blood sugar levels [2].

In 2019, type 2 diabetes was estimated to impact 463 million people worldwide [3]. It is characterized by insulin resistance, decreased insulin production, and

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eventually pancreatic beta cell loss [4]. Insulin resistance increases glucose synthesis in the liver and decreases glucose absorption in muscle, liver, and adipose tissue, leading to decreased blood flow to the liver, muscle cells, and fat cells [5].

The long-term complications of type 2 diabetes can be divided into two types: microvascular and macrovascular. Because individuals with type 2 diabetes can be presymptomatic for years, they are at higher risk of developing both types of complications, which will worsen the disease and affect the patient's well-being, quality of life, daily activities, and socioeconomic status, thereby increasing morbidity and mortality [6].

Macrovascular complications can impact patients with type 2 diabetes in several ways. Coronary heart disease, arrhythmias, cardiomyopathy, sudden cerebrovascular disease, and peripheral artery disease are all results of macrovascular impairment that impacts larger blood vessels. Arrhythmia is a disorder of the heart's rhythm, whereas cardiomyopathy is a heart muscle disease [6,7]. Cardiovascular disease is the leading cause of death among people with diabetics. Finally, cerebrovascular disease affects the brain's blood vessels and blood flow [7]. Early macrovascular complications are associated with atherosclerotic plaque in the vasculature, which supplies blood to the brain, heart, limbs, and other organs [8]. Myocardial infarction, angina pectoris, and stroke are all concerns associated with latestage macrovascular disease, which involves full obstruction of the vessels [9].

The development of macrovascular problems in type 2 diabetes is linked to several risk factors. These factors could be grouped as sociodemographic factors (age, sex, and marital status), behavioral factors (obesity, diet), and clinical factors (durability of diabetes (years), glycated hemoglobin (HbA1c) (mmol/mol), duration of diabetes, and hypertension) [7,9]. According to specific studies, factors such as sex, age, marital status (single or divorced), family history of diabetes mellitus, longer duration of diabetes, hypertension, obesity, poor glycemic control, adherence to diet, mixed medication, and insulin therapy alone were predictors macrovascular complications among type 2 diabetes mellitus patients [10]. The healthcare system in the kingdom has improved more than before, leading to optimal healthcare for diabetic patients. Therefore, there has been a decrease in mortality rates and length of stay in hospitals [11].

This study aims to determine the relationship between macrovascular complications and associated risk factors in patients in Al-Madinah Al-Munawara, Saudi Arabia, who have type 2 diabetes mellitus.

Patients and methods Patients and study design

Between October 2021 and January 2022, an observational, descriptive, cross-sectional survey was created on 275 patients aged from 20 to 65 years old with type 2 diabetes mellitus.

The participants were recruited through an online survey circulated on social media platforms such as WhatsApp and Twitter in Al-Madinah Al-Munawara, Saudi Arabia. The data collected through an online questionnaire consisted of 37 questions that included a detailed personal and medical history of the last 3 months. Next, cases are interviewed at King Fahd Hospital's diabetes clinic. Type 2 diabetes clients visiting the hospitals regularly (every 1 month) as outpatients and available during the data collection period were participants and eligible for this study.

Data related to medical examinations, BMI, and laboratory investigations for the patients with type 2 diabetes were collected from their files and during the personal interview in the diabetes clinic at King Fahd Hospital.

Inclusion criteria included type 2 diabetic patients living in Al-Madinah Al-Munawara aged 20–65 years old. Out of 400 patients with incomplete data, patients suffering from the coronavirus disease of 2019, chest infections, cancer, or pregnant women were excluded.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patients have given their consent for their images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

Ethical consideration

The present study obtained the ethical approval to start this study from the Ethical Committee of the College of Applied Medical Sciences at Taibah University with approval number 2021/107/203 CLN. We clarified that participation is optional and that all participants

are informed they have the right to withdraw from the study at any time before they fill out the questionnaire. The participants' privacy is protected by not mentioning any private information in the study.

Sample size calculation

The targeted sample size for this study was 60 male participants and 60 female participants, as estimated by Epi Info (Epi Info, v. 7.2.4.0; CDC, Atlanta, Georgia, USA) with alpha 0.05, beta 0.10, and a 45% expected difference between males and females, determined based on a two-sided test. The targeted individuals reside in Al-Madinah Al-Munawara. The study population included type 2 diabetic patients aged 20-65 years old.

Methods

The variables under study were sex, age, income, duration of illness, family history of diabetes, physical exercise regimen, BMI, type of treatment, presence of other comorbidities, blood pressure, hemoglobin level, HbA1c level, and serum lipid profile [e.g. low-density lipoprotein (LDL), highdensity lipoprotein (HDL), cholesterol].

Data collection

The tool used for data collection was a questionnaire. A phone number was necessary in the event of follow-up questions. All the questions were translated from English into Arabic and back translated from Arabic into English by two bilingual experts. The questionnaire consisted of 37 questions. The questionnaire was used to collect information on sex, age, duration of illness, family history of diabetes, hospitalization, hospital admission for diabetic ketoacidosis with coma, cardiovascular disease, presence of macrovascular complications, physical activity and patterns of exercise, BMI, presence of other comorbidities, frequency of urination, blood pressure.

The last week's follow-up results related to laboratory investigations for the patients with type 2 diabetes were collected from their files on the computer in the diabetes clinic at King Fahd Hospital. It included HbA1c level, fasting blood glucose, lipid profile (e.g. LDL, HDL, triglycerides, cholesterol), and serum calcium level. The total serum cholesterol level was considered elevated at 200 mg/dl and the triglycerides level was elevated at 150 mg/dl. HDL cholesterol was considered low at 40 mg/dl in males and less than 50 mg/dl in females. LDL cholesterol levels were elevated at 100 mg/dl [12].

Routine analyses

Venous blood samples were withdrawn from all participants after an overnight fast, and the separated sera were stored at -20°C. Fasting serum glucose was measured using standard colorimetric procedures. Serum triglycerides, cholesterol, HDL, and LDL were measured using the colorimetric method using the bio-diagnostic kit. HbA1c was measured using ion exchange chromatography on a D-10 system. The total Bio-Rad concentration was measured using atomic absorption spectrophotometry. The hemoglobin concentration is then determined by the result produced by the photoelectric colorimeter.

Statistical analysis

The statistical analysis of the collected data was carried out using the Statistical Package for the Social Sciences, version 28 (SPSS, Chicago, IL 60606-6307). The variables were categorized according to independent variables, including sociodemographic characteristics such as age, sex, BMI, disease duration, and the HbA1c level, and dependent variables, including macrovascular complications of type 2 diabetes mellitus. The association between disease characteristics (i.e. age, sex, disease duration, glycemic control, BMI, and hypertension) and participants' sociodemographic characteristics was examined using the χ^2 test. Spearman's correlation analysis was conducted between the HbA1c level and continuous variables in the study. The strength of the correlation is described as follows: 0.0-0.19 'very weak,' 0.20-0.39 'weak,' 0.40-0.59 'moderate,' 0.60-0.79 'strong,' and 0.80-1.0 'very strong' [13]. relationship between evaluate the independent and dependent variables, a multiple logistic regression test was used. A P value of 0.05 was used to determine the significance of associations.

Results

Out of 275 patients with type 2 diabetes mellitus, 113 patients have had macrovascular complications. Table 1 shows the results of χ^2 tests for associations between sociodemographic, clinical, and laboratory characteristics of participants with macrovascular complications. Age of the patients is statistically significantly associated with macrovascular problems (*P*=0.002). Macrovascular problems impact 37% of the younger (20-40 years old) and 62.7% of the elderly (41-65 years old). Sex and macrovascular problems are statistically significantly associated (P=0.035).Macrovascular complications affect 61.7% of female patients compared to 47% of male patients.

Macrovascular complications and a family history of diabetes are statistically significantly associated (P=0.042). It impacts 60.4% of individuals with a positive family history of diabetes mellitus. Physical activity and macrovascular complications are statistically significantly associated (P=0.027). Sixty-four percent of people who do not exercise have macrovascular problems. Hypertension and

macrovascular problems are statistically significantly associated (P<0.001), and 78.4% of the patients with hypertension have macrovascular complications (Table 1).

Macrovascular problems affect 79.3% of patients with anemia (hemoglobin>12 g/dl). Hemoglobin and macrovascular complications are statistically

Table 1 Sociodemographic, clinical, and laboratory characteristics of participants with types of macrovascular complications

Variables	Categories	Macrovascular complications (113) [n (%)]		
Age (in years)*	20–40 years 41–65 years	17 (37.0) 96 (62.7)		
Sex*	Male Female	31 (47.0) 82 (61.7)		
Education	No read or write Primary, secondary High school Certificate and above	20 (74.1) 21 (58.3) 19 (61.3) 53 (50.5)		
Income	Low <3000 Moderate 3000–10000 High >10 000	23 (60.5) 54 (56.3) 36 (55.4)		
Family history of diabetes*	Yes No	93 (60.4) 20 (44.4)		
Smoking history	Yes No	14 (66.7) 99 (55.6)		
Physical activity*	Yes No	49 (49.5) 64 (64.0)		
ВМІ	Normal Overweight Obese	20 (43.5) 35 (56.5) 58 (63.7)		
Type of treatment	Oral hypoglycemic therapy Oral hypoglycemic and insulin therapy (mixed therapy)	58 (56.3) 34 (50.0)		
Duration of DM	<5 years	52 (58.4) 61 (55.5)		
Hypertension*	Yes No	69 (78.4) 44 (39.6)		
Serum cholesterol	<200 mg/dl ≥200 mg/dl	31 (66.0) 20 (55.6)		
Serum HbA1c	Accepted control Uncontrolled	56 (57.7) 11 (42.3)		
Serum triglyceride	Less than 150 mg/dl More than 150 mg/dl	23 (56.1) 15 (60.0)		
Serum HDL	Less than 40 mg/dl More than 40 mg/dl	25 (62.5) 11 (55.0)		
Serum LDL	Less than 100 mg/dl More than 100 mg/dl	19 (54.3) 16 (69.6)		
Serum hemoglobin*	Less than 12 g/dl 12–15 g/dl	23 (79.3) 23 (52.3)		
Serum calcium	Less than 9 mg/dl More than 9 mg/dl	18 (69.2) 10 (50.0)		
Hospital follow up	I have not seen a doctor in the last year From 1–2 From 2–5 More than 5 times	24 (60.0) 27 (49.1) 40 (67.8) 22 (48.9)		
Hospital admission in the past 5 years	Yes	35 (59.3)		
Number of hospital admissions in the last year	No No One 2 times and above	78 (55.7) 80 (55.6) 28 (60.9) 5 (55.6)		
Hospitalized due to diabetic coma	Yes No	5 (38.5) 108 (58.1)		

^{*}Significant association with macrovascular complications at (P>0.05) using χ^2 test.

significantly associated (P=0.017). The remaining factors do not appear to be associated with macrovascular complications in any way that is statistically significant (P>0.05). These factors include education level, income, history of smoking, treatment type, duration of diabetes, BMI, dyslipidemia, HbA1c, serum calcium, number of hospital admissions in the past year, hospitalization due to diabetic coma, as shown in Table 1.

Table 2 displays the results of Spearman's correlation analysis between the HbA1c level and continuous

Table 2 Spearman's correlations between continuous variables and glycated hemoglobin level of participants

Variables	Correlation coefficient	P value	
Age	0.057	0.344	
Duration of DM	-0.058	0.337	
BMI	-0.014	0.816	
Serum cholesterol	0.343	<0.001**	
Hemoglobin	0.281	<0.001**	
High blood pressure	0.156	0.010*	
Number of hospitalizations	0.119	0.049*	

DM, diabetes mellitus; HDL, high-density lipoprotein; LDL, lowdensity lipoprotein. *Significant difference at P value less than 0.05. **Highly significant difference at P less than or equal to 0.01. variables in the study. The strongest association was observed between the serum cholesterol level and the HbA1c level (r=0.343, P<0.001), then hemoglobin (r=0.281, P<0.001), then blood pressure (r=0.156,P=0.010). The least significant relationship was the number of hospitalizations (r=0.119, P=0.049). The findings suggest that an elevated level of blood pressure, cholesterol, and hemoglobin corresponds to an elevated HbA1c level (>10). Otherwise, the association between the HbA1c level and other variables such as age, duration of illness, and BMI is not statistically significant (P>0.05).

Table 3 displays the findings of χ^2 tests for an and macrovascular between sex association complications. A statistically significant correlation (P<0.05) has been shown between sex and macrovascular complications. Females experienced macrovascular complications at a higher rate than males (P=0.049). Other than that, peripheral artery disease (diabetic foot), cerebrovascular disease, or cardiovascular disease do not differ statistically significantly (P>0.05) between males and females.

Table 4 presents the results of multiple logistic regression tests performed to detect the relationships

Table 3 Prevalence and association between sex and different types of macrovascular complications in the studied sample

Variables	All diabetic patients [n (%)]	Macrovascular complications [n (%)]	Cardiovascular disease (coronary artery diseases, arrhythmia) [n (%)]	Cerebrovascular disease (stroke) [n (%)]	Peripheral artery disease [n (%)] 27 (100)	
All patients	275 (100)	113 (100)	78 (100)	8 (100)		
Male	90 (32.7)	31 (47)	26 (33.3)	1 (12.5)	10 (27)	
Female	185 (67.3)	82 (61.7)	52 (66.7)	7 (87.5)	17 (63)	
P value	0.888	0.049*	0.893	0.216	0.615	

HbA1c, glycated hemoglobin. *Significant association with macrovascular complications at P value more than 0.05 using χ^2 test.

Table 4 Multiple logistic regressions for factors associated with the occurrence of macrovascular complications

Variables		В	SE	E Wald	DF	Significance	Exp(B)	95% confidence interval for Exp(<i>B</i>)	
								Lower bound	Upper bound
	Intercept	-1.482	1.741	0.725	1	0.395			
	Age	-0.942	0.444	4.491	1	0.034*	0.390	0.163	0.932
	Sex	-0.930	0.370	6.337	1	0.012*	0.394	0.019	0.814
	BMI	-0.008	0.021	0.130	1	0.719	0.992	0.952	1.034
	Duration of DM	0.472	0.370	1.634	1	0.201	1.604	0.777	3.310
	Serum HbA1c (past 3 month)	0.448	0.272	2.715	1	0.099	1.565	0.919	2.665
	Hypertension	2.092	0.386	29.398	3 1	<0.001**	8.105	3.804	17.267
	Dyslipidemia	0.148	0.458	0.105	1	0.746	1.160	0.473	2.846
	Education	0.141	0.170	0.686	1	0.407	1.152	0.825	1.608
	Type of treatment	0.690	0.275	6.297	1	0.012*	1.993	1.163	3.415
	Physical activity	-0.720	0.352	4.191	1	0.041*	0.487	0.024	0.970

DM, diabetes mellitus; HbA1c, glycated hemoglobin. *Significant difference at P value less than 0.05. **Highly significant difference at P value less than or equal to 0.01.

between risk factors associated with the occurrence of macrovascular complications. The results found that macrovascular complications are positively correlated with age, sex, hypertension, and therapy type (P<0.05), while physical activity has a significant negative effect complications macrovascular (P=0.041).Macrovascular diabetes complications are more common among females. Age (B=-0.942, P=0.034) indicates that the higher the age, the higher the macrovascular complications are. Macrovascular complications are more common in diabetics who additionally use insulin therapy, oral hypoglycemic medications (B=2.092, P=0.001), and suffer from hypertension (B=0.69, P=0.012). Finally, physical activity has indicated that the greater the activity, the fewer macrovascular complications occur.

Discussion

The prevalence of type 2 diabetes mellitus has increased rapidly around the world. Chronic diabetes is associated with a high rate of morbidity and mortality, with more than four million people aged 20-79 dying from diabetes-related disorders. Saudi Arabia is one of the top 10 nations where diabetes is most prevalent [14]. According to the International Diabetes Federation, the prevalence of type 2 diabetes mellitus in adults has increased from 366 million in 2011 to 536 million in 2021. By 2030, researchers expect that 643 million people will have this condition. In the Middle East, there are 73 million individuals with type 2 diabetes mellitus, and this number is expected to rise to 95 million by 2030. In Saudi Arabia, type 2 diabetes mellitus affects four million people, with an expected five million by 2030 [6].

In Saudi Arabia, diabetes mellitus is increasing faster and becoming a dangerous medical problem associated with higher morbidity and mortality [14]. Our study included 275 patients with type 2 diabetes mellitus. More than half of the patients (71.3%) were between 41 and 65. Females represented 67.3% of the study sample. Compared to 37% of the younger age group, between 20 and 40 years old, 62.7% of the older age group (41–65 years) experienced macrovascular complications.

To our knowledge, this is the first study done in Al-Madinah Al-Munawara to evaluate the relationship between macrovascular complications and associated risk factors in patients with type 2 diabetes mellitus.

In our study, females had a larger prevalence of macrovascular problems than males, with 61.7%

against 47%. In contrast to the Upper Egypt study conducted by Hussein and Menasri [6], they found that 60% of males had a higher cardiovascular disease risk factor than females; this difference was related to smoking, physical activity, and family history.

In our study, those who did not engage in any form of physical exercise (64%) had a higher risk of getting macrovascular complications, whereas those who were physically active (49.5%) had a lower risk. In a study conducted in Upper Egypt, only 98 (12.25%) of 800 individuals were physically inactive. The difference is justifiable since the major economic activity in the villages is farming [15]. In our study, 78.4% of the patients with hypertension had macrovascular complications.

The present study reported that HbA1c and serum total cholesterol showed a strong positive correlation. Consequently, a larger distribution of atherogenic cholesterol is linked to abnormal glycemic control, higher weight, and greater insulin resistance in both men and women with diabetes mellitus [15], which explains the relationship between serum total cholesterol and glycemic control. Furthermore, there exists a substantial correlation between elevated HbA1c levels and elevated blood pressure. Peng et al. [16] supported our results. Individuals with higher HbA1c were found to have high blood pressure and higher lipid profiles as measured by LDL cholesterol and total cholesterol. Results from Blecker et al. [17] corroborate this conclusion.

A possible explanation for the significant correlation between hyperglycemia and hypertension could be the existence of common risk factors, particularly obesity. In addition, the emergence of hyperglycemia and hypertension are both influenced by inflammatory processes [18]. According to our analysis, patients with higher HbA1c values experienced noticeably more hospitalizations. Findings from Blecker *et al.* [17] corroborate this conclusion.

In the present study, out of 275 patients with type 2 diabetes mellitus, 41% had macrovascular complications. Females were more likely than males to have macrovascular problems, with 61.7% compared to 47%. However, our percentage is higher and opposite to the study in Saudi Arabia, where macrovascular complications were more common in males (5.8%) than in females (2.8%) [19].

Multiple logistic regression analyses were used to investigate the factors associated with the appearance

of macrovascular complications. According to our development macrovascular study, the of complications was significantly positively impacted by older age, female sex, hypertension, and kind of treatment (P<0.05). This is in line with a study done in Riyadh by Alaboud et al. [14], which revealed that females had a higher risk of macrovascular complications than males and that complications increased with age.

The macrovascular complications affected 62.7% of the older adults aged 41-65 years; this might be related to a long history of smoking and high cholesterol, hypertension, or obesity [7]. Females have a higher prevalence of macrovascular complications than males due to high cholesterol levels and obesity [20]. Diabetic patients with macrovascular issues are hypertensive because hypertension is linked to an increased risk of heart disease and stroke [21].

According to our study, physical activity has a significant negative effect on macrovascular function (heart and coronary artery health). The macrovascular incidence rate remained higher in less active females. A study done in Egypt by Hussein et al. [15] shows that physically inactive patients have a higher risk of cardiovascular disease, and this agrees with our study. First, it has been suggested that physical activity increases insulin sensitivity. Second, physical activity has also been found to reduce intraabdominal fat, a known risk factor for insulin resistance [22].

Conclusion

This study is the first of its kind in Al-Madinah Al-Munawara and provides insight into the severity of macrovascular complications in type 2 diabetic patients. The findings indicated that macrovascular complications were a major cost to the nation. The chance of developing macrovascular complications is increased when other chronic medical conditions, such dyslipidemia, ischemic heart disease, hypertension, coexist. Our results showed that the age of participants, sex, and type of treatment were independent predictors of macrovascular complications. Hypertension has a significant positive effect on the appearance of macrovascular complications. Physically inactive patients have a higher risk of macrovascular complications.

Recommendation

Increased knowledge and focus on the macrovascular complications that type 2 diabetics may face are needed in our area. Aggressive health education and promotion programs, along with improved public health awareness services, will lower the nation's fatal macrovascular consequences from diabetes mellitus.

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Conflicts of interest

There are no conflicts of interest.

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