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Prevalence of micro and macro vascular complications and their risk factors in type 2 diabetes in Saudi Arabian population: an analysis from SHIS

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Abstract. – OBJECTIVE: Diabetes mellitus is a non-communicable disease (NCD) with metabolic dysfunction that has attained epidemic proportions worldwide. Vascular complications account for the mortality and morbidity associated with diabetes. Hence, the study aimed to estimate the prevalence and risk factors for vascular complications in patients with type 2 diabetes mellitus (T2DM).

PATIENTS AND METHODS: A cross-sectional national multistage survey, the Saudi Health Interview Survey (SHIS), was used in this study, which surveyed individuals aged 15 years or older. After inclusion and exclusion criteria, 1240 diabetic patients' data were analyzed for sociodemographic data, risk factors, and prevalence of micro and macrovascular complications. Binary logistic regression with stepwise backward elimination was performed to build the optimal model to assess the determinants of macrovascular complications in diabetic patients. The strength of the associations was examined by estimating adjusted odds ratios (aOR) with their 95% CI. *p*-value < 0.05 was considered statistically significant. R Studio Version 1.2.1093 was used for statistical analysis

RESULTS: Prevalence of micro and macrovascular complications in the diabetic patients was 6.05%, in which 3.5% had myocardial infarction, 1.2% had stroke and 1.9% had renal failure. The optimal model showed that for each year increase in age (aOR=1.05, 95%CI 1.02-1.07; *p*-value=0.000), smoking history (aOR=4.02, 95%CI 2.23-7.26; *p*-value=0.000), hypertensive patients (aOR=2.71, 95%CI 1.47-4.99; *p*-value=0.001), patients with low physical activity (aOR=4.32, 95%CI 1.26-14.82; *p*-value=0.001) were more likely to develop macro and microvascular complications in diabetic patients.

CONCLUSIONS: The high prevalence of microvascular and macrovascular complications in diabetic patients poses a serious threat to public health in Saudi Arabia. A multisectoral approach needs to be undertaken to properly control and modify common risk factors at the community level.

Key Words:
Diabetes mellitus, Hypertension, Physical activity, Smoking, Saudi Arabia.

Introduction

Diabetes mellitus (DM) is a systemic and metabolic disease caused by a disruption in the metabolism of carbohydrates due to insufficient production of insulin in the body, which fails to meet the metabolic needs[1]. World Health Organization (WHO) has reported 8.5% diabetes among individuals aged more than 18 years globally in 2014[2]. As of 2019, 463 million people were reported to be diabetic worldwide[3]. The International Diabetes Federation (IDF) said that 3.4 million people in Saudi Arabia had diabetes in 2015, accounting for 17.6% of the adult population. According to the IDF Diabetes Atlas, the seventh-highest prev-

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alence of diabetes was found in Saudi Arabia in adults aged 20-79. The majority of diabetes increased by 86 percent in Saudi Arabia from 2010 to 2017, with an estimated 3.85 million people suffering from diabetes[3,4].

In type 2 diabetes mellitus (T2DM), chronic hyperglycemia may cause microvascular complications like neuropathy, retinopathy, and nephropathy and macrovascular complications like stroke, coronary heart disease [CHD], and peripheral arterial disease, which may affect the quality of life and even lead to death[5]. It was found that the prevalence of various microvascular complications ranged from 19.7% to 36.4% for diabetic retinopathy, 5.6% to 65.3% for diabetic neuropathy, and 10.8% to 73.3% for diabetic nephropathy in different parts of Saudi Arabia[6]. Forbes and Cooper[7] reported that the prevalence of various macrovascular complications in diabetic patients was 13.6% for hypertension, 10.1% for coronary heart disease, and 2.6% for cerebrovascular accident. It has been shown[8] an increased risk of premature death and disability with DM, which causes a reduction in life expectancy at all ages and levels of socioeconomic status, which accounts for almost 12% of global health expenditure. In 2016, the seventh leading cause of death was DM worldwide, and it caused 1.6 million deaths 2015[9].

Previous studies[10,11] have explored the effect of global urbanization and sedentary lifestyle on increased prevalence of diabetes in developing countries. Similar trend was observed in the Kingdom of Saudi Arabia (KSA) over the last 20 years, with an increase in carbohydrates, calories, and fat and a reduction in physical activity. The years lost to disability (YLDs) due to diabetes was 8% in Saudi in 2010, which was high compared to YLDs of ischemic heart disease (0.81 %)[12]. This high prevalence of diabetes has imparted economic constraints on individuals as well as the entire society. According to Institute for Health Metrics and Evaluation (IHME), an amount of 17 billion SR (US$ 4.53 billion) was spent by KSA-MOH (Ministry of Health) on the treatment of diabetes. It was estimated that US$13.6 billion was spent on diabetes care by the Middle East and North Africa (MENA) region, with US$934 spent in Saudi Arabia[13]. Alhowaish et al[14] has reported that the average medical health care cost for each Saudi diabetic patient was ten times higher than the non-diabetic patients. The actual economic burden is expected to be higher in future years if the cost of health care outpaces the overall cost of living or if changes in lifestyle habits increase the prevalence rate of diabetes. Although the cost estimate helps identify and document the national economic burden of diabetes, it does not account for the lost productivity and losses attributable[14,15]. It is essential to estimate the complications due to diabetes concerning the health indicators and the country's economic growth. Hence, the present study intended to estimate the prevalence of micro and macrovascular complications among diabetic patients of KSA.

Patients and Methods

Study design: a Cross-Sectional record-based study that analysed the data from Saudi Health Interview Survey (SHIS)[15].

Study population: all the diabetic patients in KSA who participated in the SHIS.

Inclusion criteria:

- Patients who had diabetes mellitus or pre-diabetes mellitus
- Patients aged 15 years and above.

Exclusion criteria:

- Pregnant women
- Patients who were unable to respond to the questions at the start of the interview were excluded.

Ethical considerations: The approval for the study was obtained from the Institutional Review Board and the Ethics Committee.

Sample Size and Sampling Method

The Saudi Health Interview Survey SHIS recruited the study participants using multistage stratified probability sampling while ensuring probability proportionate to size for each stratum. Stratification was based on the 13 regions of the Kingdom (Al Riyadh; Makkah Al Moukarrama; Eastern Region; Northern Borders; Madinah; Jean; Aseer; Najran; Qaseem; Tabuk; Hail; Al-Jouf; Al-Baha)

The Census Bureau of the KSA has divided it into small clusters with about 140 households in each cluster and labeled them as enumeration units. The primary sampling units (PSU) for the survey were these enumeration units. In each PSU, the number of households was determined based on the population size, density, and geographical spread.

Sample Calculation

From 10821 respondents, cases were removed having missing value, "don't know" and "didn't respond" option on sociodemographic variables and didn't respond on non-communicable diseas-

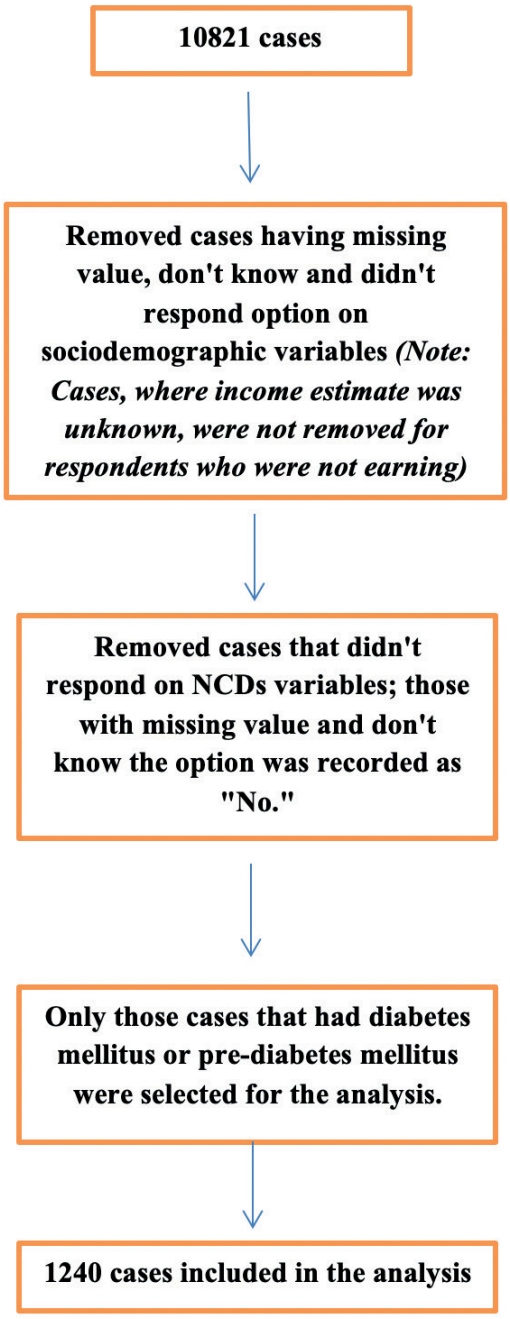

Figure 1. Sample selection.

es (NCDs) (those with missing value and "don't know"). For the final analysis, 1240 diabetic and prediabetic patients were included (Figure 1).

Data Collection

Ethical permission was obtained from the Saudi Ministry of Health and its Institutional Review Board (IRB) for SHIS. Data collection was done by approximately 20 interviewers (10 two-person teams) and a supervisor trained in conducting the interview and clinical examination under SHIS. To ensure that a member of the same sex interviewed the respondents, the households were visited by interviewers in teams of two members of both genders. Blood testing for the participants was done from a local clinic. The blood samples collected from the participants were transported to King Fahd Medical City (KFMC) in Riyadh. To ensure standardization of all measurements, a central lab was used in the survey.

Sociodemographic variables included in the study were age, gender, education, marital status, parents related before marriage, work status, income estimate.

Diabetes Mellitus

Respondents were considered to be diabetic if they met any of the following criteria: (1) measured HbA1c $\geq$ 6.5 % or (2) or if they have been diagnosed and are currently treated for diabetes, but their blood HbA1c level was less than 6.5%. Individuals with their blood HbA1c level 5.7% to less than 6.5% were considered prediabetic. HbA1c was measured using COBAS INTEGRA400 plus.

Hypertension

Individuals were considered hypertensive if they had systolic blood pressure 140 mmHg or more, or diastolic blood pressure 90 mmHg, or if they have been diagnosed or were under treatment for hypertension but their systolic and diastolic blood pressure are below the cited cut-off points.

Physical Activity and Smoking

Moderate to intense exercise fewer than 150 minutes per week was considered a low level of physical activity, 15-300 minutes per week as an intermediate level of physical activity and more than 450 minutes per week as a high level of physical activity. Respondents were questioned about the usage of tobacco products such as cigars or pipes, cigarettes, or Shisha.

Macrovascular and Microvascular Complication

The diagnosed macrovascular and microvascular complications like stroke, myocardial infarction, and renal failure were assessed by asking the respondents the following questions: "Have you ever been told by a doctor, nurse, or another health professional that you had: 1) cerebral infarction, otherwise known as a stroke or brain at-

tack, 2) myocardial infarction, otherwise known as a heart attack 3) chronic renal failure, otherwise known as chronic kidney failure, chronic renal disease, or chronic kidney disease?"; the individuals who diagnosed themselves or by a person other than a doctor were not accepted in the study.

Statistical Analysis

Descriptive analysis was carried out by frequency and proportion for sociodemographic characteristics, macrovascular and microvascular complications among the study population. The association of macrovascular complications with sociodemographic and risk factors was assessed by cross-tabulation and comparison of percentages.

Binary logistic regression with stepwise backward elimination was performed to build the optimal model to assess the determinants of macrovascular complications in diabetic patients. Unknown income estimate was not compared with the reference category in the logistic regression. The model with the lowest AIC was considered the optimal model. [Note: AIC (Akaike Information Criterion) is a single number score that can be used to determine which of the multiple models is most likely to be the best model for a given dataset. Lower the AIC, better the model)]. At the start, a total of 10 predictors were entered, making it a complete model, and at each step, one predictor was removed that lowered the AIC value the most. This procedure stopped when the AIC value could not be lowered with the removal of any predictor. To examine the strength of the associations, estimation of adjusted odds ratios (aOR) with their 95% CI was done. p-value < 0.05 was considered statistically significant. RStudio Version 1.2.1093 was used for statistical analysis. (RStudio Team (2020). RStudio: Integrated Development for R. RStudio, PBC, Boston, MA, USA, URL http://www.rstudio.com/.)

Results

A total of 1240 diabetic respondents aged 15 to 100 were included in the study. The mean age of the study population was 55.97 (SD ±14.18) years, of which majority were males (54.4%), those who can't read and write (33.8%), currently married (75.8%), whose parents were not related before marriage (51.7%), retired (25.1%) and less than 3,000 Riyals income-earning respondents (Table I).

Among 1240 diabetic patients, 43 (3.5%) had a myocardial infarction, and 15 (1.2%) had a stroke. Meanwhile, 24 (1.9%) diabetic patients had renal failure. Three diabetic patients had both stroke and myocardial infarction. Three patients had both stroke and renal failure. One patient had both myocardial infarction and renal failure. The prevalence of micro and macrovascular complications in the study population was found to be 6.05% (Table II).

Table III depicts the prevalence of microvascular complications was found higher in the age group > 60 years, males, those who can read and write only, married, unemployed, whose parents were not related before marriage, less than 3,000 Riyals income-earning respondents, smokers, hypertensive and low physical activity among the diabetic study population.

In the complete model, the AIC value was 408.4. The significant predictors of macrovascular complications in this model were age (aOR=1.04, 95%CI 1.01-1.07; p-value=0.005), education high school completed (aOR=4.43, 95%CI 1.39-14.06; p-value=0.005) as compared to those who can't read and write, smoking history (aOR=3.35, 95%CI 1.67-6.68; p-value=0.001), hypertension (aOR=2.85, 95%CI 1.52-5.36; p-value=0.001) and low physical activity (aOR=4.77, 95% CI 1.32-17.21; p-value=0.017) (Table IV).

The optimal model was formed with four predictors (Age, Smoking history, Hypertension, and Physical activity). In the optimal model, the AIC value was 389.16. The optimal model showed that for each year increase in age, the probability of developing macrovascular complications in diabetic patients increased by 1.05 times (aOR=1.05, 95%CI 1.02-1.07; p-value=0.000). Diabetic patients with smoking history were 4.02 times (aOR=4.02, 95%CI 2.23-7.26; p-value=0.000) more likely to develop microvascular complications than diabetic patients without a smoking history. Diabetic patients with Hypertension were 2.71 times (aOR=2.71, 95%CI 1.47-4.99; p-value=0.001) more likely to develop microvascular complications than diabetic patients without Hypertension. Diabetic patients with low physical activity were 4.32 times (aOR=4.32, 95%CI 1.26-14.82; p-value=0.020) more likely to develop microvascular complications than patients with medium and low physical activity (Table IV).

Discussion

The prevalence of micro and macrovascular complications in diabetic patients was 6.05%, 3.5% had a myocardial infarction, 1.2% had a

Table I. Sociodemographic characteristics of the diabetic study population (N=1240). .

Characteristics		Frequency	Percentage
Age group	15 to 30	50	4.0%
	31 to 45	237	19.1%
	46 to 60	504	40.6%
	>60	449	36.2%
Sex	Female	565	45.6%
	Male	675	54.4%
Education	I can't read or write	419	33.8%
	Can read and write only	145	11.7%
	Primary school completed	175	14.1%
	High school completed	177	14.3%
	The intermediate school completed/Technical training	172	13.9%
	College / University/Postgraduate completed	152	12.3%
Marital status	Currently married	940	75.8%
	Single (Never married/Divorced/Separated/ Widowed)	300	24.2%
Parents related before marriage	Not related	641	51.7%
	Related	599	48.3%
Work status	Government employee	282	22.7%
	Non-government employee/Self-employed	81	6.5%
	Retired	311	25.1%
	Unemployed	235	19.0%
	Others (Homemakers/ Students)	331	26.7%
Income estimate	Less than 3,000 Riyals	252	20.3%
	3,000 Riyals to less than 5,000 Riyals	216	17.4%
	5,000 Riyals to less than 7,000 Riyals	160	12.9%
	7,000 Riyals to less than 10,000 Riyals	158	12.7%
	10,000 Riyals to less than 15,000 Riyals	153	12.3%
	15,000 Riyals to less than 20,000 Riyals	75	6.0%
	20,000 Riyals or more	55	4.4%
	Unknown	171	13.8%

stroke, and 1.9% had renal failure. The optimal model showed that for each year increase in age, the probability of developing macrovascular complications in diabetic patients increased by 1.05 times, 4.02 times in those with smoking history, 2.71 times in those with Hypertension, and 4.32 times in those with low physical activity.

The present study's findings revealed a prevalence of 3.5% for MI, which was lower than that reported in the United Kingdom Prospective Diabetes Study (UKPDS) (15.3%)[16]. However, Avogaro et al[7] have reported a prevalence of 2.2% for MI in diabetic patients. More than 40 years ago, the Association between diabetes mellitus and macrovascular disease was reported, and myocardial infarction (MI) and cardiovascular death were found to have a higher risk in the diabetic population[18,19]. In a case-control study, the INTERHEART global study, it was found that there was an increased risk of MI in diabetic women compared to other risk factors. Some studies reported a twofold increase in RR of death and myocardial infarction in smokers than non-smokers who had diabetes, and cessation of the smoking habit significantly reduced this risk[20,21].

The prevalence of stroke was 1.2% in this study. The UKPDS and Alaboud et al[22] reported a prevalence of 3.7% for cerebrovascular accidents in their studies[16]. In patients who are diabetic the risk of stroke was higher than those with controlled blood glucose levels[23]. The presence of the metabolic syndrome doubles the risk of the first stroke, but recurrent stroke is not affected. The outcome from stroke was found to be worsened by diabetes

Table II. Vascular complications among the diabetic population (n = 1240).

Complications	Frequency	Percentage
Macrovascular complications		
Stroke	15	1.2%
Myocardial infarction	43	3.5%
Microvascular complications		
Renal failure	24	1.9%

Table III. Prevalence of macrovascular complication in diabetic study population according to socio-demographic and risk factors (n =1240).

Characteristics	Any one of vascular complications (n=55)	No vascular complication (n=1185)	
Age group	15 to 30 (n=50)	0 (0.0%)	50 (100.0%)
	31 to 45 (n=237)	5 (2.1%)	232 (97.9%)
	46 to 60 (n=504)	11 (2.2%)	493 (97.8%)
	>60 (n=449)	39 (8.7%)	410 (91.3%)
Sex	Female (n=565)	16 (2.8%)	549 (97.2%)
	Male (n=675)	39 (5.8%)	636 (94.2%)
Education	Can't read or write (n=419)	21 (5.0%)	398 (95.0%)
	Can read and write (n=145)	10 (6.9%)	135 (93.1%)
	Primary school completed (n=175)	6 (3.4%)	169 (96.6%)
	High school completed (n=177)	8 (4.5%)	169 (95.5%)
	Intermediate school completed/Technical training (n=172)	8 (4.7%)	164 (95.3%)
	College / University/Postgraduate completed (n=152)	2 (1.3%)	150 (98.7%)
Marital status	Currently married (n=940)	43 (4.6%)	897 (95.4%)
	Single (n=300)	12(4.0%)	288 (96.0%)
Parents related before marriage	Not related (n=641)	34 (5.3%)	607 (94.7%)
	Related (n=599)	21 (3.5%)	578 (96.5%)
Work status	Government employee (n=282)	3 (1.1%)	279 (98.9%)
	Non-government employee/Self-employed (n=81)	4 (4.9%)	77 (95.1%)
	Retired (n=311)	23 (7.4%)	288 (92.6%)
	Unemployed (n=235)	19 (8.1%)	216 (91.9%)
	Others (n=331)	6 (1.8%)	325 (98.2%)
Income estimate	Less than 3,000 Riyals (n=252)	16 (6.3%)	236 (93.7%)
	3,000 Riyals to less than 5,000 Riyals (n=216)	12 (5.6%)	204 (94.4%)
	5,000 Riyals to less than 7,000 Riyals (n=160)	5 (3.1%)	155 (96.9%)
	7,000 Riyals to less than 10,000 Riyals (n=158)	8 (5.1%)	150 (94.9%)
	10,000 Riyals to less than 15,000 Riyals (n=153)	2 (1.3%)	151 (98.7%)
	15,000 Riyals to less than 20,000 Riyals (n=75)	2 (2.7%)	73 (97.3%)
	20,000 Riyals or more (n=55)	2 (3.6%)	53 (96.4%)
	Unknown (n=171)	8 (4.7%)	163 (95.3%)
Smoking history	Yes (n=256)	23 (9.0%)	233 (91.0%)
	No (n=984)	32 (3.3%)	952 (96.7%)
Hypertension	Yes (n=256)	38 (8.2%)	423 (91.8%)
	No (n=779)	17 (2.2%)	762 (97.8%)
Physical activity	High (n=319)	3 (0.9%)	316 (99.1%)
	Medium (n=365)	11 (3.0%)	354 (97.0%)
	Low (n=556)	41 (7.4%)	515 (92.6%)

mellitus, similar to the course seen in people with diabetes with coronary artery diseases[24,25]. Yeap et al[26] found that diabetes mellitus significantly increased the risk of death in patients with stroke. In the Nurses' Health Study, an increased risk of both hemorrhagic and ischemic strokes was seen in association with type 1 diabetes mellitus. In contrast, type 2 diabetes mellitus was associated with an increased risk of ischemic stroke only[27].

Al-Wakeel et al[28] reported that the Saudi population had a progressive and aggressive diabetic nephropathy (DN) course with a peak incidence between 50 to 70 years, anticipating a future burden on dialysis units. Alwakeel et al[29] concluded that there is a high prevalence of both micro and macrovascular complications in diabetic patients, with 32.1% developing nephropathy in at least ten years of diabetes. A general increase in macrovascular complications and mortality was observed in patients with type 1 diabetes who were cigarette smokers. Gay et al[30] found that smokers were three times more likely to be hospitalized than non-smokers who had type 1 diabetes. Several studies have confirmed that smoking increases the risk of stroke in patients with diabetes, especially T2DM[21,31]. In the Multinational Study of Vascular Disease in Diabetics, a study by WHO, it was evident that smoking has an adverse effect on diabetic patients who have CHD[32]. RR of 1.55 for total mortality and 1.49 for cardiovascular mortality,

1.54 for stroke, 2.15 for peripheral arterial disease, and 1.43 for heart failure was reported in diabetic patients who were active smokers in a systematic review and meta-analysis[33].

It is recommended to keep blood pressure below 130/80 mmHg for diabetics by the American Diabetes Association and the National Heart, Lung, and Blood Institute. A considerable influence of blood pressure on coronary artery disease was reported by the Diabetes drafting group and other studies[34,35]. High BP was found to be a modifiable cardiovascular risk factor in diabetic patients. The odds of developing microvascular complications increased by 4% and macrovascular complications by 2%, with each increment in age by one year[22].

It has been found that susceptibility to the complications associated with diabetes varies between different ethnic races and among different individuals. The white Americans were less susceptible to diabetic complications than the Pima Indians and black Hispanics[36]. Other races might also show such differences; hence, it is necessary to research different races to obtain future reforms,

Table IV. Logistic regression results of sociodemographic and risk factors associated with macrovascular complication in diabetic patients.

Model	Characteristics		AIC	aOR (95% CI)	*p*-value
Complete model		Age		1.04 (1.01-1.07)	0.005*
	Sex	Female		1	
		Male		1.24 (0.42-3.61)	0.695
	Education	I can't read or write.		1	
		Can read and write		1.54 (0.63-3.81)	0.346
		Primary school completed		1.03 (0.34-3.13)	0.956
		High school completed		4.43 (1.39-14.06)	0.012*
		The intermediate school completed/Technical training.		2.08 (0.71-6.08)	0.179
		College/University/Postgraduate completed		1.38 (0.23-8.13)	0.721
	Marital status	Married		1	
		Single	408.4	1.02 (0.44-2.36)	0.960
	Parents related before marriage	Not related		1	
		Related		0.68 (0.37-1.25)	**0.212**
	Work status	Government employee		1	
		Non-government employee		3.05 (0.6-15.44)	0.177
		Retired		2.24 (0.58-8.72)	0.244
		Unemployed		3.73 (0.81-17.15)	0.091
		Others		1.46 (0.25-8.41)	0.672
	Income estimate	Less than 3,000 Riyals		1	
		3,000 Riyals to less than 5,000 Riyals		1.15 (0.48-2.76)	0.754
		5,000 Riyals to less than 7,000 Riyals		0.59 (0.19-1.86)	0.370
		7,000 Riyals to less than 10,000 Riyals		1.27 (0.45-3.62)	0.654
		10,000 Riyals to less than 15,000 Riyals		0.43 (0.08-2.18)	0.309
		15,000 Riyals to less than 20,000 Riyals		0.71 (0.13-3.91)	0.690
		20,000 Riyals or more		0.70 (0.14-3.62)	0.674
	Smoking history	No		1	
		Yes		3.35 (1.67-6.68)	**0.001***
	Hypertension	No		1	
		Yes		2.85 (1.52-5.36)	**0.001***
	Physical activity	High		1	
		Medium		3.39 (0.89-12.88)	0.073
		Low		4.77 (1.32-17.21)	**0.017***
Optimal model (Lowest AIC value)		Age	389.16	1.05 (1.02-1.07)	**0.000***
	Smoking history	No		1	
		Yes		4.02 (2.23-7.26)	**0.000***
	Hypertension	No		1	
		Yes		2.71 (1.47-4.99)	**0.001***
	Physical activity	High		1	
		Medium		2.90 (0.79-10.66)	0.109
		Low		4.32 (1.26-14.82)	**0.020***

identify high-risk groups, and provide exceptional care. According to the international reports, better accessibility to the preventive healthcare, more widespread diagnosis, and more intensive management of disease could significantly eliminate the health problems caused by diabetes and thereby help in improving the quality of life of people with diabetes and their families[14].

Limitations

Our study has some limitations. First, our results were from a cross-sectional study, causality could not be determined. Second, physical activity and vascular problems are self-reported, which may be influenced by social desirability biases and recall biases. However, our study is based on a large sample and used a standardized methodology for all its measures. The study included prediabetic patients and self-reporting of the complications, which may underestimate the prevalence of the present study.

Conclusions

The vascular complications of diabetes mellitus make a significant impact on the social and economic resources of the country; thus, its necessary to implement diabetes prevention strategies through active screening and intensive management. Health education programs and promotion campaigns should also be promoted to raise the awareness of diabetes, the associated complications, and the importance of lifestyle modification to reduce the impact of disease in the country and improve its patients' health. Special measures must be taken to improve glycemic control in the diabetic population.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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