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Abstract

Background: The prevalence of diabetes is steadily increasing everywhere. This study aimed to assess diabetic complications and their risk factors, among type 2 diabetic patients toward reducing the disease burden.

Methodology: A cross-sectional hospital-based study was carried out among 469 patients with T2DM attending medical clinic at King Khalid University Hospital (KKUH) in Riyadh during the period of January to June 2019.

Results: Of 469 DM patients 62.7% females and 37.3% males, the mean age and disease duration were 58.3 ± 10.3 and 10.8 ± 7 years, respectively. Macrovascular complications included coronary arty disease(CAD), stroke, and peripheral vascular disease were found in 9.4%, 1.1%, and 4.7%, respectively; whereas for microvascular complications 31.1%, 69.2%, 45.2%, 2.6%, and 1.3% having diabetic retinopathy, neuropathy, nephropathy, diabetic foot, and lower extremity amputation (LEA), respectively. Among those subjects hypertension, dyslipidemia, overweight/obesity, central obesity, and smoking were found in 76.4%, 76.7%, 71.8%, 33.5% and 13%, respectively. Age, disease duration, and HBA1c were statistically significant risk factors for microvascular complications and diabetic foot while for macrovascular complications was only related to increased age. Occurrence of cardiovascular diseases (CVD), neuropathy, diabetic foot, and LEA was significantly higher among males than females.

Conclusion: This population was at high risk of CVD with high prevalence of hypertension, dyslipidemia, and obesity. Understanding the extent to which DM complications can be reduced from multiple risk factor control can be helpful in providing the evidence-based rationale for composite risk factor control efforts in DM management. In addition, routine screening for detection of new complications need to be emphasized in order to prevent morbidity and mortality.

Keywords: Diabetic Complications; Saudi Arabia; Risk Factors

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Abbreviations

KSA: Kingdom of Saudi Arabia; KKUH: King Khalid University Hospital; T2DM: Type 2 Diabetes Mellitus; CVD: Cardiovascular Disease; CAD: Coronary Artery Disease; LEA: Lower Extremity Amputation; HbA1c: Glycosylated Hemoglobin; BMI: Body Mass Index; PVD: Peripheral Vascular Disease; FBS: Fasting Blood Sugar; PPBS: Postprandial Blood Sugar; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; LDL: Low Density Lipoprotein; HDL: High Density Lipoprotein; TG: Triglyceride

Introduction

Diabetes caused 1.5 million deaths in 2012. Higher-than-optimal blood glucose caused an additional 2.2 million deaths, by increasing the risks of cardiovascular and other diseases. Forty-three percent of these 3.7 million deaths occur before the age of 70 years. Globally, an estimated 422 million adults were living with diabetes in 2014, compared to 108 million in 1980. This reflects an increase in associated risk factors such as being overweight or obese. Over the past decade, diabetes prevalence has risen faster in low- and middle-income countries than in high-income countries [1]. During the last 4 decades, decreased physical activity and consumption of fast food causing amplification of this risk and increasing the incidence of diabetes [2]. Over time diabetes can damage the heart, blood vessels, eyes, kidneys and nerves, and increase the risk of heart disease and stroke. Generally, the injurious effects of hyperglycemia are separated into macrovascular complications (coronary artery disease, peripheral arterial disease, and stroke) and microvascular complications (diabetic nephropathy, neuropathy, and retinopathy). The disease burden of diabetes is mainly attributed to the morbidity and mortality associated with microvascular and macrovascular complications. In Saudi Arabia, 25.5% of the urban population is diabetic in comparison with 19.5% in rural areas. There are also regional differences in the prevalence of T2DM, with the Northern (27.9%) and Eastern (26.4%) provinces experiencing greater rates than the Southern region (18.2%), where a rural lifestyle is more common [3]. The prevalence of diabetes in Saudi Arabia as demonstrated by Al-Nozha, showed a higher ratio in females than in males, with 42%, and 37.2%, respectively [4]. There is a 31% prevalence of diabetic retinopathy in Saudi patients who had T2DM for at least 10 years [5]. Another study from the western part of Saudi Arabia, indicates that the prevalence of neuropathy in diabetic patients is about 82% which is considered one of the highest in the world [6]. Almost one-third of type 2 Saudi diabetic population has diabetic nephropathy [5]. In 2011, it was estimated that 42.5% of end stage renal disease (ESRD) cases in Saudi Arabia were related to diabetes [7]. It is important for physicians to understand the relationship between diabetes and vascular disease because the prevalence of diabetes continues to increase, and the clinical armamentarium for primary and secondary prevention of these complications is also expanding. Even though many studies have been done in different regions in Saudi Arabia, a comprehensive study has not been done recently among the patients attending medical clinic at KKUH in Riyadh.

Aim of the Study

The study aimed to explore the prevalence of diabetic complications in relation to risk factors among T2DM patients.

Subjects and Methods

Adults (18 years and above) with T2DM for at least six months (confirmed by HbA1c or plasma sugar readings), who were following up in the medical clinic at KKUH, were enrolled in a cross-sectional hospital based study. Data was collected between January and June 2019 by face-to-face interviews using of a standardized questionnaire by which consents were taken from all participants, as well as the hospital scientific and ethical committee. Pregnant patients, patients with gestational diabetes, and patients with type 1 diabetes were excluded. Screening and assessment by expert physicians for diabetic complications, self-assessment risk factors, demographic data, anthropometric measures, and blood testing. Diabetic complications included: cardiovascular conditions, nephropathy, neuropathy, retinopathy, cerebrovascular disease, peripheral vascular disease, and diabetic foot. Demographic data included age, gender, and nationality. Self-assessment risk factors included smoking status, preexisting CVD (CAD, heart attack, transient ischemic attack, stroke, or other peripheral vascular disease). Anthropometric measures included waist circumference, body mass index (BMI), and a single arterial blood

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pressure reading. Blood testing included fasting and postprandial blood sugar (FBS& PPBS), triglyceride (TG) low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol, and glycosylated hemoglobin (HbA1c). Participants with a BMI of 25 to 29.9 were categorized as overweight, and those with a BMI of 30 or greater were categorized as obese [8]. Central obesity was defined according to WHO criteria: Waist Circumference WC \geq 94 cm for men and \geq 80 cm for women or waist-to-height ratio of 0.6 or greater among women and 0.9 or greater among men [9]. Hypertension was defined as a self-reported past history of high blood pressure requiring medication or a single elevated clinical blood pressure reading (systolic blood pressure (SBP) of \geq 140 mmHg or diastolic blood pressure (DBP) of \geq 90 mmHg) [10]. Dyslipidemia was defined as a self-reported history of abnormal cholesterol levels requiring medication or a measured LDL level of 4.1 millimoles per liter or greater or HDL level of 1.0 millimoles per liter or less or triglyceride of 200 mg/dL or more [11]. A current smoker was defined as a person who smokes at least one cigarette per day for the past 3 months or more or had tobacco in any form. Continuous variables were expressed as mean and standard deviation (SD), and categorical variables were expressed as percentages. Differences of means were calculated using independent sample t-test. The χ^2 test was used to measure associations among the different categorical variables. A P value of less than .05 was used as a level of significance. The Results were expressed as odds ratios (OR) and 95% confidence intervals (CI).

Results

Subject sampled between 1 January and 31 June 2019 were type 2 diabetic patients of either gender aged 18 years or above. Out of 469 sampled patients, 294 were females (62.6%) and 175 were males (37.2%). The mean age (± SD) was 50.62 (± 11.2) years with 66.5% of them falling within age group of 45 - 70, whereas only 5% of them were below the age of 40. The mean duration of diabetes (\pm SD) was 6.2 (± 4.2) years with more than half of patients having disease duration of 5 years or more. Regarding cardiovascular risk factors illustrated in figure 1 showed the prevalence of hypertension was 76.4% with no significant difference between the genders despite, the treatment. Among the males, 13% were current smokers while almost all the females (99.5%) said they have never smoked. The mean BMI was significantly high (26.3 ± 4.6), where 71.8% of study population either overweight or obese with a BMI of > 25. Higher BMI found in females compared to males (26.1 vs 24.2). However, males are found to be higher in central obesity than females (38.7% vs 30.3%). In table 1, the metabolic parameters included FBS and PPBS, blood pressure, and lipid profile where higher among females than males, but the only noticed difference was for HbA1c (p = 0.04), FBS (p = 0.005), and SBP (p < 0.001). According to the lipid profile, low HDL levels presents in 68.5% of the females and 40.1% of the males. In contrast, high LDL levels found in 49.7% of the females and 30.3% of the males. Prevalence of vascular complications are summarized in table 2 showed 9.4% of the population with CAD in which 2% undergo grafting. Neuropathy was the highest among other vascular complications (69.2%) followed by nephropathy (45.2%), retinopathy (31.1%) and diabetic foot (2.6%). However, statistically significant difference was observed with CAD (P = 0.007), neuropathy (P = 0.001), diabetic foot (P=0.001), and LEA (P = 0.001) only. Among the study population at least one macrovascular complication were seen in 14.6%, while 79.1% had at least one microvascular complication. The males were more exposed to all vascular complications than the females, except for peripheral vascular disease, retinopathy and nephropathy were more prevalent among the females. The relation of diabetic complications with age and disease duration is illustrated in figure 2 and 3, respectively. In these graphs, it is obvious that all the complications were increased with age and disease duration. Patients who had T2DM for more than 10 years, 70.8% were having neuropathy whereas nephropathy and retinopathy were noticed in 54.9% and 48.2% of them, respectively. Microvascular complications were significantly associated with age > 60 years (P < 0.001), duration of diabetes > 10 years (P < 0.001) and HBA1c > 7% (P < 0.04) while macrovascular complications were associated with age > 60 years (P < 0.001) only, as shown in table 3.

Discussion

With the increase of prevalence of DM, we are facing an increase in the long-term complications of DM, that considered a major public health problem. The link between high glycemic control and the high prevalence of DM complications in patients with T2DM is well established elsewhere [12-14]. Our findings reinforce the well-known phenomenon that T2DM complications are strongly related to duration of diabetes. The present study revealed that overall, 371 (79.1%) participants with T2DM had at least one microvascular complication,

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Variable	Females (n = 294) Mean ± (SD)	Males (n = 175) Mean ± (SD)	Total (n = 469) Mean ± (SD)	T value	P value
Basal metabolic index (BMI)	26.1 ± (4.5)	24.2 ± (4.5)	26.3 ± (4.6)	1.06	0.289
Waist circumference (WC) (cm)	80.2 ± (2.0)	96 ± (1.8)	88.5 ± (2.0)	1.02	0.10
HBA1c (%)	8.46 ± (1.8)	8.0 ± (3.7)	8.3 ± (2.5)	2.85	0.04
Fasting blood sugar (mg/dl)	159.6 ± (35.5)	127.9 ± (35.5)	137 ± (40.1)	2.80	0.005
Postprandial blood sugar (mg/dl)	162.6 ± (30.1)	156.0 ± (29.2)	161.1 ± (32.5)	0.92	0.35
Systolic blood pressure (mmHg)	131.5 ± (20.1)	128 ± (10.1)	130 ± (19.9)	3.92	0.001
Diastolic blood pressure (mmHg)	79.4 ± (10.2)	79.1 ± (11.8)	79.4 ± (10.7)	0.29	0.77
Low-density lipoprotein (mg/dl)	99.7 ± (9.1)	98.8 ± (18.7)	99.78 ± (14.1)	1.83	0.06
High-density lipoprotein (mg/dl)	47.8 ± (10.8)	45.8 ± (10.5)	46.93 ± (10.5)	1.35	0.17
Triglyceride (mg/dl)	127.8 ± (35.3)	118.1 ± (29.5)	127.92 ± (35)	1.61	0.10

Table 1: Metabolic profile and its significance to the study population by gender.

Disease complication	Overall prevalence n = 469	Females n = 294	Males n = 175	X ² value	Significanc e
Cardiovascular disease	45 (9.4%)	26 (9%)	19 (11%)	7.15	0.007
Stroke	10 (2.1%)	5 (1.8%)	5 (2.9%)	3.81	0.05
PVD	17 (3.7%)	11 (3.8%)	6 (3.4%)	0.81	0.36
Retinopathy	145 (31.1%)	94 (32%)	51 (29%)	2.62	0.10
Neuropathy	324 (69.2%)	198(67.3%)	126 (72%)	20.3	0.001
Nephropathy	212 (45.2%)	135 (46%)	77 (44%)	2.77	0.96
Diabetic foot	11 (2.4%)	3 (1.3%)	8 (4.7%)	19.45	0.001
Lower extremity amputation	8 (1.7%)	3 (1.2%)	5 (3.3%)	15.09	0.001

Table 2: Vascular complication by gender.

Complication	Risk factor	Odd ratio (95% confidence interval)	P value
Microvascular disease	Age (< 60 yrs vs > 60)	1.9 (1.4 - 2.7)	0.001
	Duration of diabetes (< 10 yrs vs > 10)	2.1 (1.6 - 2.9)	0.001
	HbA1c (< 7% vs > 7%)	1.4 (1.0 - 1.9)	0.04
Macrovascular disease	Age (< 60 yrs vs > 60)	1.8 (1.4 - 2.4)	0.001
Diabetic foot	Age (< 60 yrs vs > 60)	2.1 (1.1 - 3.8)	0.01
	Duration of diabetes (< 10 yrs vs > 10)	2 (1.1 - 3.7)	0.03
	HbA1c (< 7% vs > 7%)	2.2 (1.0 - 4.8)	0.04

Table 3: Logistic regression analysis showing risk factors which were significantly associated with chronic complications.

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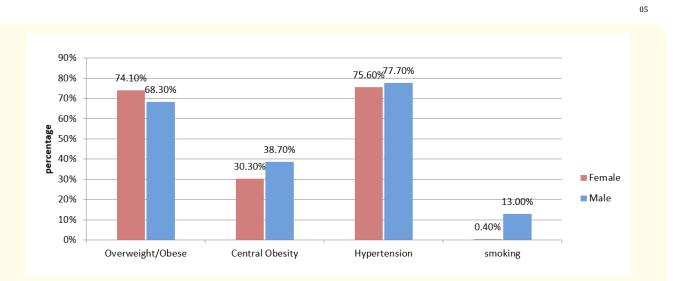


Figure 1: Prevalence of cardiovascular risk factors in the study population by gender (females n = 294, males n = 175).

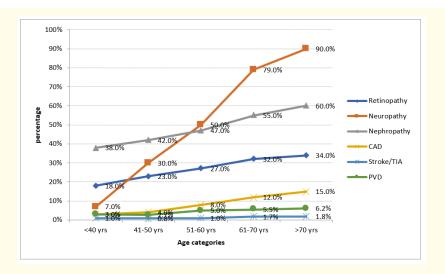


Figure 2: Variation of chronic complications with age among 469 patients with type 2 diabetes.

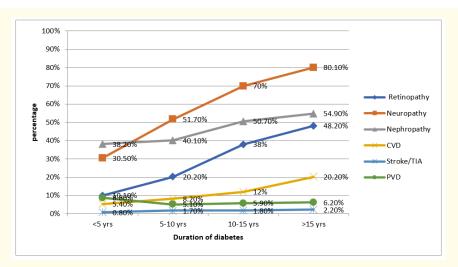


Figure 3: Variation of chronic complications with disease duration among 469 patients with type 2 diabetes.

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which indicates that severe complications of T2DM exert a huge burden on the health care system in Saudi Arabia. This estimate is much higher than most studies conducted in the KSA [15] and studies conducted in Arab countries [11,12] and globally [16,17]. This study also found that cardiovascular conditions constituted a predominant chronic condition among T2DM patients over other morbidities similar to other studies carried out in the KSA [15]. Yet the present study revealed a higher prevalence of diabetic neuropathy among other studies conducted in the KSA [18]. Diabetic foot complication have been identified as the single most common cause of morbidity among diabetic patients [19]. According to our findings, age, duration of diabetes, and poor glycemic control were all significantly associated with diabetic foot. Another studies have also shown that hypertension and smoking play a significant role in microangiopathy [20,21]. Comparing to a study done in Jazan southwestern of Saudi Arabia, prevalence of diabetic foot was higher than in our study population [22]. In a study conducted in Egypt, 4357 patients were surveyed, 42% had retinopathy, 22% had peripheral neuropathy, 21% had nephropathy and 1% had foot ulcers [23]. In Oman, prevalence of diabetic retinopathy was 14.4% [24]. In Jordan, 45% of diabetic patients had retinopathy, 33% had nephropathy and 5% had amputations [25]. These differences may be attributed to data collection methods and the study scales. In this study, microvascular complications were significantly associated with age, disease duration and glycemic control while the only factor significantly associated with macrovascular complications was age. High systolic blood pressure was only associated with retinopathy, and none of the chronic complications were associated with smoking. In order to determine the exact effects of these risk factors on vascular complications, there must be an assessment of long-term follow up of randomized clinical trails. Aplenty of evidence shows that diabetes is a risk factor for CAD, However, we were unable to find any significant association between these risk factors and the occurrence of CAD in this population. Obesity seems to be a major problem with almost 71.8% of the patients with diabetes being overweight or obese. Most of these patients are invariably suffering from metabolic syndrome. The prevalence of obesity is increasing at an alarming rate in many parts of the world contributed to the global incidence of cardiovascular disease, type 2 diabetes mellitus, hypertension, stroke, cancer, osteoarthritis, sleep apnea and many others. Obesity has a more pronounced impact on morbidity than on mortality [26]. Mainly, central obesity confers a significant threat on the cardio-metabolic health of individuals, independently of overall obesity. The prevalence of overweight and obese individuals in our study population was critically high reaching 71.8% and 33.5% for central obesity. Horaib research that covered five KSA military regions, finds 40.9% of the respondents are overweight; 42% have central obesity and 29% are obese [27]. Hypertension is an extremely common comorbid condition in diabetes, In previous study conducted among 45,379 Arabian patients revealed that the overall prevalence of hypertension was 29.5%, which indicates a higher prevalence of hypertension among Arabs compared to people from the USA (28%) and sub-Saharan African (27.6%) [28]. Hypertension substantially increases the risk of both macrovascular and microvascular complications, including stroke, coronary artery disease, and peripheral vascular disease, retinopathy, nephropathy, and possibly neuropathy [29]. The prevalence of hypertension was 76.4% among this population which was significantly higher than nieghboring countries [28]. It is worthy to say that blood pressure among this population was uncontrolled in almost half of the patients despite the treatment. Dyslipidemia is one of the cardiovascular risk factors in diabetic patients. In our study population, 76.7% of the subjects had dyslipidemia, as high LDL, high TG, and low HDL seen in 42.5%, 23%, and 58% respectively. Despite the fact that, 80.6% of the patients were on statin therapy. The gender differences was obvious as all lipid parameters were higher among females. This could be due to that most female subjects were menopause. All metabolic parameters were higher in females. Yet, statistically difference was only for FBS, HBA1c, and SBP. On the other hand, most of the vascular complications were more prevalent in males than in females with significant difference in CAD, neuropathy, diabetic foot, and LEA.

Limitations

The study sample attended the clinic were exposed to multiple disease burden. Thus, the reported result might be overestimation of the actual disease burden. Most of the vascular complications were collected from the medical records without respect of patients symptoms.

Conclusions and Recommendations

This population was at high risk of CVD with high prevalence of hypertension, dyslipidemia, and obesity. Understanding the extent to which DM complications can be reduced from multiple risk factor control can be helpful in providing the evidence-based rationale for

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composite risk factor control efforts in DM management. In addition, routine screening for detection of new complications need to be emphasized in order to prevent morbidity and mortality.

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Ethical Approval

Informed consent was obtained from all the participants.

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