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The multifactorial burden of Type 2 Diabetes mellitus: A study from clinical settings of University Hospital, Karachi-Pakistan.

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Abstract

Background: Diabetes is a multifactorial disease posing a socioeconomic threat to the worldwide community. The prevalence of Type 2 Diabetes Mellitus (T2DM) is continuously increasing in Pakistan and becoming a serious concern for the general public as well as concerned clinicians. This case-control study aimed to analyze the modifiable and non-modifiable risk factors associated with T2DM in the Pakistani population.

Methodology: A structured questionnaire was filled by the T2DM patients attending the diabetic clinic at Dow University Hospital. Non-diabetic subjects were recruited from the general population. Participants were questioned regarding their age, body mass index (BMI), educational status, diabetes management practices and comorbidities associated with T2DM.

Results: Our results suggest that BMI, gender, increasing age, educational status are significantly associated with T2DM. Our data also suggested that approximately 80% of T2DM patients had at least one comorbidity, whereas 59 % had two or more comorbidities. The most prevalent comorbidities found in our study group were in the order of Chronic Kidney disease (CKD) (15.8 %), Generalized Anxiety Disorder (GAD) (14.4 %), Bone disease (14 %) and Cardiovascular Disease (CVD) (12.6 %) respectively.

Conclusion: Compared to worldwide data, our results are in accordance with the global prevalence with respect to age, gender and BMI, with CKD being the most prevalent comorbidity in contrast to CVD found worldwide.

Keywords

Type 2 Diabetes Mellitus, Comorbidities, Modifiable Risk Factors, Non-Modifiable Risk Factors, Disease Management.

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Introduction

Type 2 diabetes mellitus is a chronic, non-communicable disease generally characterized by insulin resistance, impaired hepatic glucose production, and decreasing β-cell functioning or total failure[1]. Conferring to the International Diabetes Federation (IDF) estimates, around 463 million adults over the globe were living with diabetes till 2019 that is expected to be raised to 700 million by 2045[2]. This disorder is exceedingly linked with morbidity, mortality and poses a high health cost to the individual patients, their families, and countries, especially developing economies like Pakistan[3]. Pakistan is among the top ten countries poorly affected by diabetes mellitus[4]. The current prevalence of diabetes in Pakistan is estimated to be around 11.7%[5].

Diabetes-related financial burdens will further upsurge due to chronicity-linked clinical outcomes and comorbidities such as CKD, CVD, eye disease, foot diseases, bone disease, sexual diseases, immune-compromised diseases, GAD and skin diseases, among others, are commonly seen in conjunction with a diagnosis of T2DM[6].

These comorbid conditions may potentially impact treatment options, posing barriers to lifestyle changes and self-care behaviors recommended for diabetes management[7]. A better understanding of the nature, prevalence and patterns of comorbidities in T2DM patients may provide key insights for managing patients with multiple conditions in primary care and facilitate a more patient-centered approach in risk assessment and more appropriate and tailored therapeutic interventions. Understanding and forecasting the prevalence of specific comorbidities can inform policy-makers in planning and structuring health services to meet the population's future demands[8].

Diabetic complications remain enormously burdensome. Numerous studies have been carried out on the patterns of comorbidities in T2DM[9]. Certain risk factors, such as overweight/obesity are reported to increase the likelihood of impaired glycemic control in T2DM[10]. Kidney diseases account for 65% of all deaths in people suffering from diabetes. Kidney diseases establish with normal albuminuria, progressing to micro-albuminuria, macro-albuminuria and eventually to end-stage renal disease[11]. Cardiovascular diseases, including coronary heart disease, stroke and peripheral vascular disease, are another cause of death and morbidity among subjects of T2DM. Around seventy-three percent of the population with more inadequate glycemic control has high blood pressure. It represents a two to a six-fold increase in incidence in T2DM compared to non-diabetic patients[12]. Diabetic retinopathy's global prevalence of about 60 % is the leading cause of vision loss in adults with T2DM[13]. This condition usually progresses from mild non-proliferative abnormalities marked by increased vascular permeability progressing to moderate to chronic diabetic retinopathy[14]. Diabetic foot is another common comorbidity of T2DM associated with increased age and duration of diabetes[15]. One-third of the T2DM population all over the globe develops diabetic foot ulcers. Peripheral neuropathy in feet further increases the likelihood of gangrene co-occurring and foot amputation in T2DM[16]. The global prevalence of psychological disorders, including depression and anxiety, is growing at an alarming rate. Being diabetic raised the risk of depression and anxiety by 30 %[17]. Despite advancements in the field of medicine and availability of enormous therapeutic options, the prevalence of T2DM is continuously increasing in Pakistan. One of the most important reasons for difficulties in control and management of T2DM is the occurrence of comorbidities[18].

Several studies have been reported regarding the association of risk factors in different populations, including Pakistan. The present study aims to target the T2DM patients attending the diabetic clinic and analyzing the prevalent factors responsible for the better management of T2DM.

The data collected reflects the population concerned with the management of T2DM. This could potentially identify the population who does not visit diabetic clinics regularly and also identifies a larger group of chronic patients who prefer the self-management of the disease.

Methodology

In brief, for this cross-sectional study, 1000 participants were recruited. Non-diabetic controls (n=421) were enrolled on the basis of personal communication while diabetic (n=500) and pre-diabetic individuals (n=79) were enlisted on the referral of a trained diabetologist from the outpatient department of the National Institute of Diabetes and Endocrinology, Dow University Hospital, Karachi. The study was carried out from March 2019 till December 2019. The Dow University of Health Science Review Committee (Approval Number, Ref: IRB-1249 / DUHS / Approval/2019) and the Shaheed Zulfikar Ali Bhutto Institute of Science and Technology Research Ethics Boards (Approval Number, IERB(4)/SZABIST-KHI (BIO)/1730108/190007) permit clearance for conducting research.

Approval to conduct the study was also obtained from the respective diabetic clinics. Informed consent for study participation was attained from all study participants. Questions for formative assessments, demographic background, health status, dietary habits and participant's lifestyle preferences were extracted from Michigan Diabetes care profile tests[19]. Study subjects were escorted to the diagnostic laboratory for their hemoglobin A1c (HbA1C), and a fasting serum insulin test was performed according to a standard protocol with cut-off values specified by the World Health Organization (WHO)[20]. BMI was recorded for each participant. Inclusion eligibility criteria for patient enrollment were: the history of type 2 diabetes for a period of six months, age 20–60, BMI 24 or higher, HbA1c 6.5 percent or higher. The analysis excluded patients with a previous history of gestational diabetes, type 1 diabetes and other types of diabetes.

The SPSS ver. 16.0 was administered for all data analysis. Data were analyzed using SPSS version 16.0. Frequencies and percentages were reported for all categorical variables (Table 1, Figure 1). Univariate and multivariate logistic regression was performed to estimate the effect of factors (Socio-Demographic characteristic, Health-related behaviors and Essential health service-related practices) on T2DM participants, and an Odds ratio with 95% CI was reported (Table 2). A value of $p<0.05$ was considered significant.

Results

Characteristics of T2DM cases and controls

A total of 1000 subjects were recruited in this study. Participants were categorized into diagnosed diabetic cases (500), pre-diabetic and Non-diabetic individuals (79 and 421 individuals, respectively). Table 1 analyzes the prevalence of demographic characteristics of the studied population and their health status. Over half of the participants (59.6 %) were male. Their average age at the time of diagnosis of diabetes was 46.6±9 years, whereas female subjects were diagnosed comparatively earlier at the age of 43.9±8.1 years. Approximately 63 % of the study participants were from urban areas. Forty-nine percent of the patients were of normal weight, 22.2 % were overweight, whereas 15 % of the study subjects were obese. There was a mixed representation of all major ethnic groups of Pakistan in our data, with most of the Punjabi population (52.3 %). The majority of the population stated no history of T2DM in their family. Out of the thousand study subjects, 46.2 % attained primary education, and 43.3 % reported having graduation or post-graduation degrees.

Table 1: Distribution of study participants based on health status (n=1000)

Characteristics	Health Status n(%)			
	Non-diabetic	Prediabetic	Diabetic	Generalized variables
	421(42.1)	79(7.9)	500(50)	
Age Groups (Years)				
20-30	69(16.3)	11(13.9)	77(15.4)	157(15.7)
31-40	125(29.6)	21(26.5)	147(29.4)	293(29.3)
41-50	134(31.8)	21(26.5)	182(36.4)	337(33.7)
51 above	93(22)	26(32.9)	94(18.8)	213(21.3)
Gender				
Male	237(56.2)	43(54.4)	316(63.2)	596(59.6)
Female	184(43.7)	36(45.5)	184(36.8)	404(40.4)
Area				
Urban	265(62.9)	54(68.3)	311(62.2)	630(63)
Rural	156(37)	25(31.6)	189(37.8)	370(37)
BMI				
Underweight = <18.5	39(9.2)	2(2.5)	95(19)	136(13.6)
Normal weight = 18.5–23	259(61.5)	35(44.5)	198(39.6)	492(49.2)
Overweight = 23–27.5	78(18.5)	25(31.6)	119(23.8)	222(22.2)
Obesity = > 27.5	45(10.6)	17(21.5)	88(17.6)	150(15)
Family history				
Positive	130(30.8)	20(25.3)	155(31)	305(30.5)
Negative	291(69.1)	59(74.6)	345(69)	695(69.5)
Ethnicity				
Urdu	96(22.8)	18(22.7)	141(28.2)	255(25.5)
Punjabi	219(52)	39(49.3)	265(63)	523(52.3)
Sindhi	42(9.9)	9(11.3)	36(7.2)	87(8.7)
Balochi	27(6.4)	8(10.1)	31(6.2)	66(6.6)
Kashmiri	37(8.7)	5(6.3)	27(5.4)	69(6.9)
Socioeconomic Status				
Low	43(10.2)	11(13.9)	42(8.4)	96(9.6)
Middle	355(84.3)	62(78.4)	415(83)	832(83.2)
High	23(5.4)	6(7.5)	43(8.6)	72(7.2)
Education				
Primary	210(49.8)	40(50.6)	212(42.4)	462(46.2)
Below 12 grade	33(7.8)	8(10.1)	34(6.8)	75(7.5)
Undergraduate	15(3.5)	3(3.7)	12(2.4)	30(3)
Graduate	89(21.1)	14(17.7)	102(20.4)	205(20.5)
Postgraduate	74(17.5)	14(17.7)	140(28)	228(22.8)

BMI-Body Mass Index

Factors associated with having T2DM

Table 2 shows adjusted odds ratios (OR; 95% CI) of socio-demographics, health-related behaviors and essential health service-related practices among diabetic participants of the study. In univariate logistic regression analysis, a significant association between gender, BMI, duration of diabetes, visits to the diabetic center, practicing self-monitoring of blood glucose and T2DM was observed. OR value greater than 1 represents a higher risk of T2DM among the age group of 31-50 years and with higher education level (adjusted OR 1.84, p<0.001) compared with cases attained primary education. Similarly, there was a high risk of T2DM with high socioeconomic status (adjusted OR 1.90, p<0.041) compared with Low status. T2DM was found to be more prevalent among married (adjusted OR 2.62, p<0.001) than with single people. Likewise, there was a significantly high likelihood of T2DM in cases that did not adhere to physical activity (adjusted OR 1.75, p<0.001).

In multivariate logistic regression analysis, a significantly higher association of having T2DM was found among female (adjusted OR 2.414, p<0.003), overweight and obese participants (adjusted OR 16.2, p<0.001; adjusted OR 1.86, p<0.025 respectively), and cases who did not adhere to physical activity (adjusted OR 1.79, p<0.001).

Table 2: Logistic regression analysis of T2DM participants (n=500).

	Univariate OR (95% CI)	P-value	Multivariate OR (95% CI)	P-value
Age (Years)				
20-30	1		1	
31-40	1.06(0.72-1.56)	0.767	1.31(0.81-2.14)	0.267
41-50	1.22(0.83-1.78)	0.304	1.27(0.84-1.91)	0.255
51 above	0.83(0.55-1.26)	0.397	1.33(0.89-1.99)	0.154
Gender				
Male	1		1	
Female	0.75(0.58-0.97)	0.03	2.41(1.34-4.34)	0.003
Education				
Primary	1		1	
Below 12 grade	0.96(0.58-1.56)	0.874	0.51(0.35-0.75)	0.001
Undergraduate	0.77(0.36-1.64)	0.502	0.54(0.29-1.00)	0.05
Graduate	1.14(0.82-1.59)	0.412	0.44(0.18-1.06)	0.059
Postgraduate	1.84(1.33-2.54)	<0.001	0.60(0.38-0.93)	0.024
Area				
Urban	1		1	
Rural	1.07(0.83-1.39)	0.577	0.78(0.57-1.06)	0.114
Family history				
Positive	1		1	
Negative	0.96(0.73-1.26)	0.795	0.89(0.64-1.22)	0.468
Ethnicity				
Urdu	1		1	
Punjabi	0.83(0.62-1.13)	0.245	1.50(0.79-2.85)	0.208

Sindhi	0.59(0.36-0.97)	0.041	1.56(0.85-2.84)	0.146
Balochi	0.71(0.41-1.23)	0.228	1.28(0.60-2.72)	0.511
Kashmiri	0.52(0.30-0.89)	0.018	1.22(0.55-2.70)	0.624
BMI				
Normal weight = 18.5–23	1		1	
Overweight = 23–27.5	0.29(0.19-0.44)	<0.001	16.2(8.015-33.1)	<0.001
Obesity = > 27.5	0.49(0.31-0.78)	0.003	1.86(1.08-3.20)	0.025
Underweight = <18.5	0.61(0.37-1)	0.05	0.94(0.58-1.51)	0.812
Socioeconomic status				
Medium Status	1		1	
Low Status	0.782(0.51-1.196)	0.256	0.77(0.490-1.22)	0.278
High Status	0.525(0.28-0.97)	0.041	0.58(0.3-1.12)	0.107
Marital status				
Single	1		1	
Married	2.62(2.00-3.44)	<0.001	2.35(0.00)	1.00
Others	1.27(0.66-2.46)	0.468	5.75(0.00)	1.00
Duration of diabetes, years				
Lesser than 5 years	1		1	
Greater or equal to 5 years	0.48(0.33-0.70)	<0.001	1.30(0.79-2.13)	0.291
Health-related behaviors				
Adherence to medication				
No	1		1	
Yes	0.93(0.73-1.2)	0.612	1.05(0.80-1.38)	0.688
Adherence to diet				
No	1		1	
Yes	0.64(0.49-0.85)	0.002	1.35(1.00-1.83)	0.046
Adherence to physical activity				
No	1		1	
Yes	0.83(0.64-1.07)	0.155	1.06(0.81-1.41)	0.665
Essential health service-related practices				
Regular scheduled visit to diabetic center				
No	1		1	
Yes	1.02(0.79-1.31)	0.848	0.81(0.62-1.07)	0.14
Practicing self-monitoring of blood glucose				
No	1		1	
Yes	0.75(0.58-0.97)	0.030	0.80(0.61-1.05)	0.115
Rely on alternative treatment				
No	1		1	
Yes	1.44(1.08-1.91)	0.012	1.12(0.82-1.54)	0.009

P-value < 0.05 is significant.

Prevalence of comorbidities in T2DM

The pattern of comorbidity prevalence among patients with T2DM is shown in Figure-1A. All asked comorbidities were found to be more prevalent in male T2DM participants. Among T2DM patients, 15.8 % were found to have CKD (10 % male; 5.8 % female), 14.4 % were reported to suffer from a GAD including depression (18.4 % male; 6 % female, 14 % were having Bone diseases (8.8 % male; 5.2 % female). 12.6 % of T2DM population were informed of having CVD (7% male; 5.6 % female) 11 % and 9 % were distressed with Eye (6.4 % male; 4.6 % female) and food diseases respectively (7.6 % male; 1.4 % female). Participants of the age group, 41-50 years, showed a high prevalence of these comorbid conditions (Figure 1B). When assessing the subgroups of BMI, CKD, CVD, GAD, bone diseases, and eye diseases were found to be the most prevalent comorbidities in each group. Results of this study indicate higher occurrence (39.6 %) of asked comorbidities in T2DM individuals having normal BMI. 6 % reported having Kidney diseases; 6 % Heart diseases; 6 % Psychological disorders; 4.8 % Eye diseases; 4.4 % Bone diseases. The more prevalent disease among the underweight, overweight and obese sub-group was kidney disease.

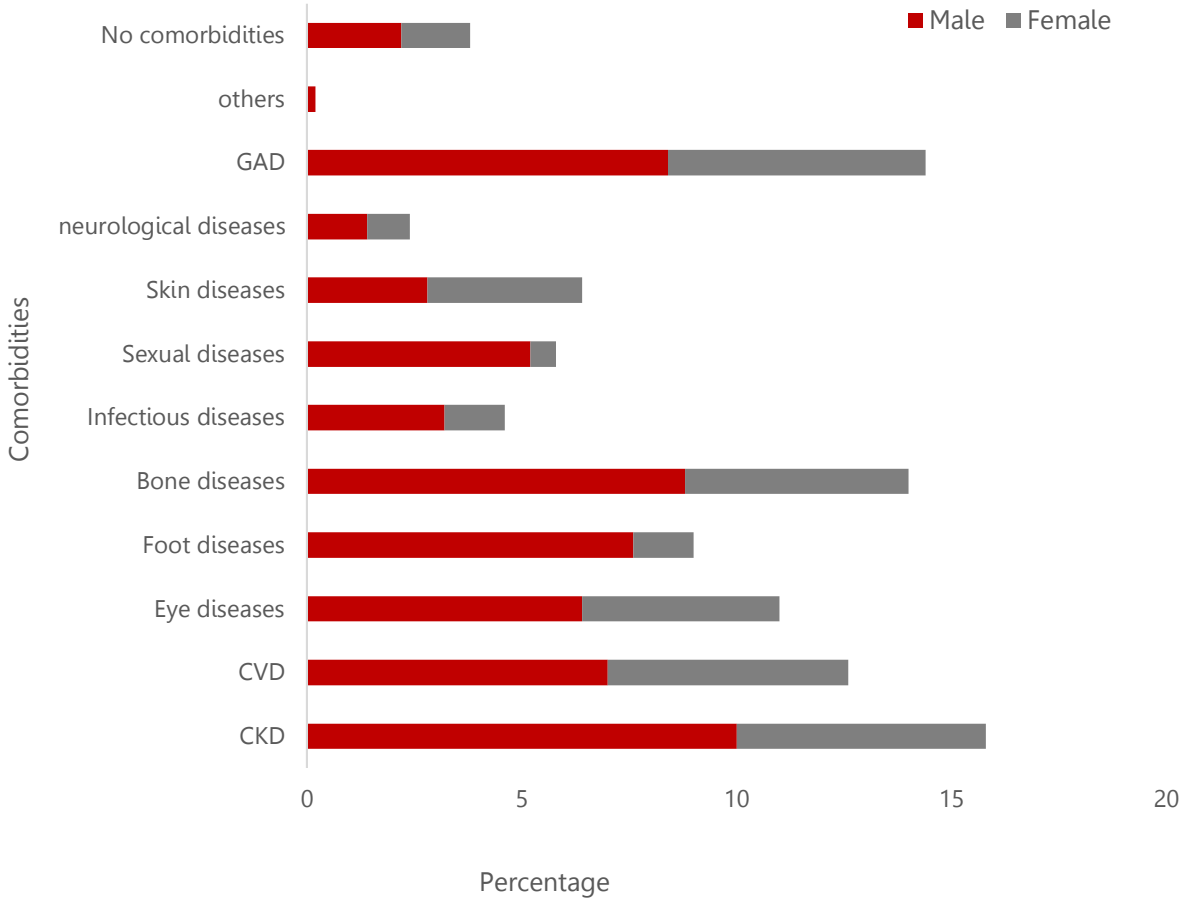

Figure 1A: Prevalence of comorbidities among T2DM participants and a fraction of T2DM subjects based on their gender

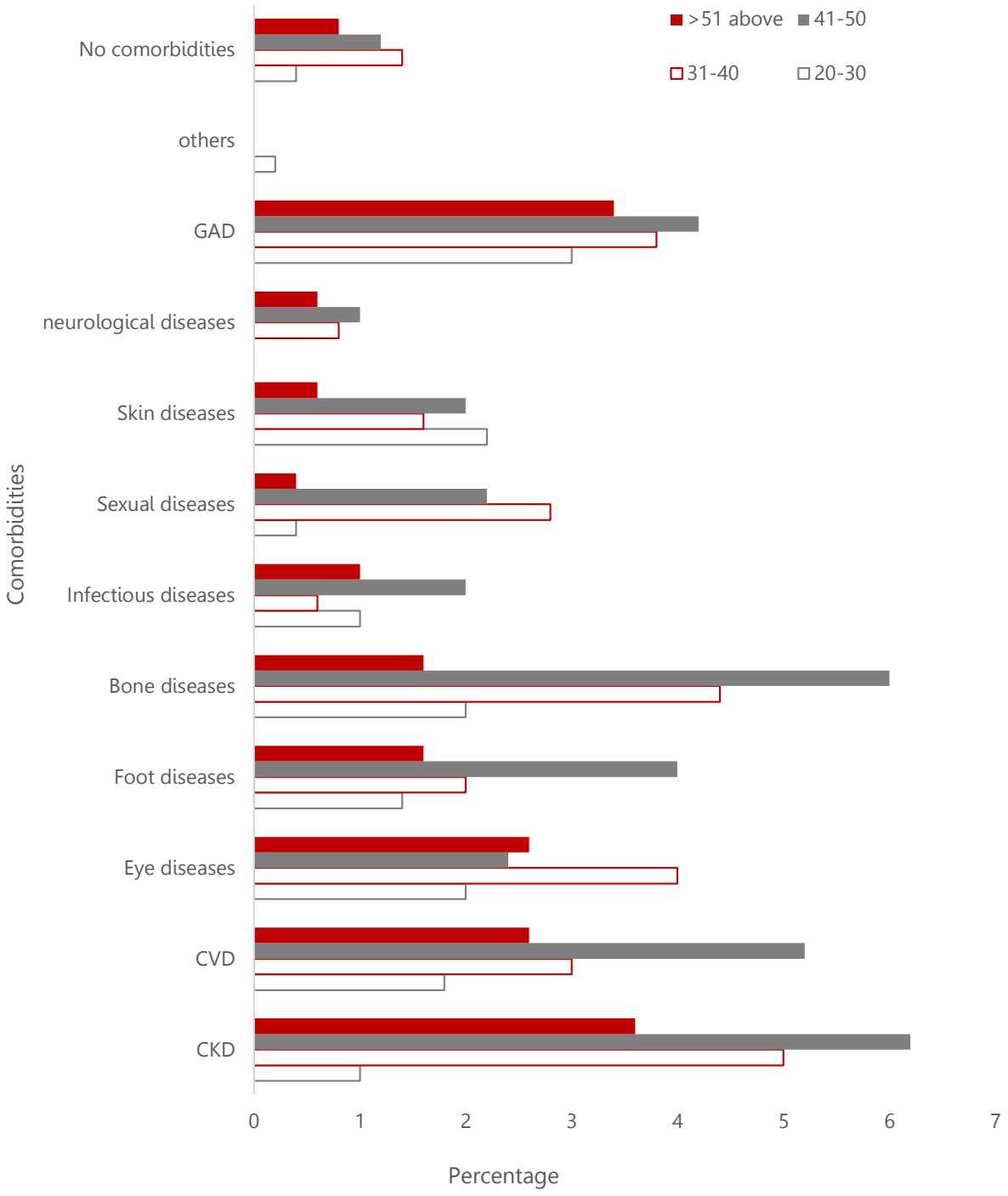

Figure 1B: Prevalence of comorbidities among fraction of T2DM subjects based on their ages

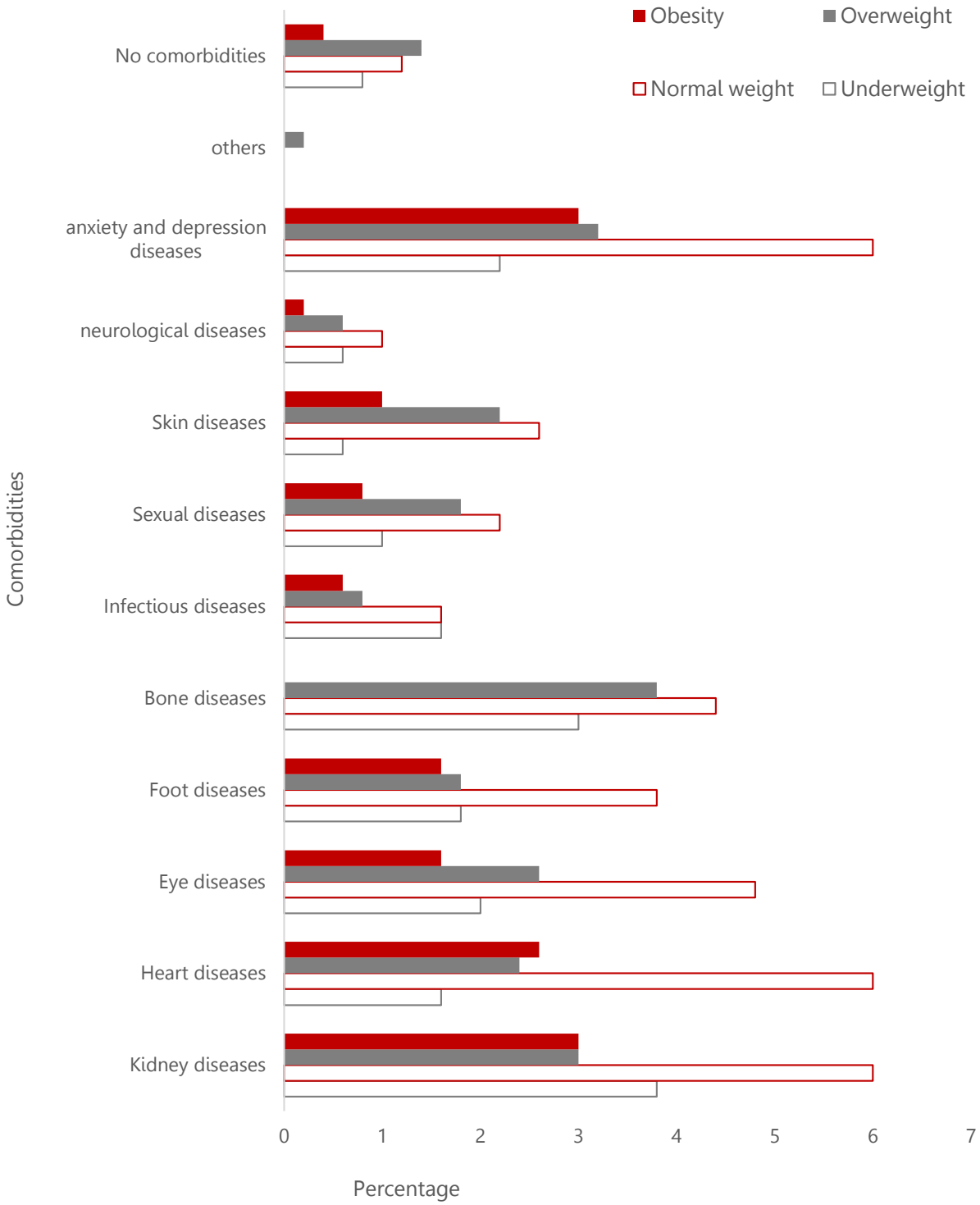

Figure 1C: Prevalence of comorbidities among fraction of T2DM subjects based on their BMI

Discussion

Various modifiable and non-modifiable risk factors have been attributed to the management of Diabetes Type 2, leading to a higher risk of morbidity and mortality[21]. Simple day-to-day modifications, including recommended diet, regular physical activity, or treatment management, can significantly decrease the incidence of diabetes in high-risk populations and delaying the onset of T2DM[22].

The present study assessed patient-level information gathered on a structured questionnaire based on the Michigan survey. Along with the basic demographic data of study subjects, the study included a range of non-modifiable risk factors (age, gender, urbanization and education) and modifiable risk factors (BMI, dietary intake, health surveillance and associated comorbidities). The data were analyzed through a statistical approach. In univariate logistic regression analysis, a significant association between gender, BMI, duration of diabetes, visits to the diabetic center, practicing self-monitoring of blood glucose and T2DM was observed.

Our findings indicate that the disease is managed by a range of factors, including age, gender, BMI and education of the individual. In our study group, the male population was at a significantly higher risk of developing T2DM as compared to females. Our findings are consistent with recent studies that showed men had a higher prevalence of DM than women across Asian and African subgroups[23]. However, contradictory data was reported by Aamir, 2019, where the prevalence of T2DM was higher in females as compared to males[4]. Previous studies have reported an established co-relation of increasing age with T2DM. According to previous studies, the global prevalence of diabetes reported that most diabetic patients were aged 50 years and above. However, this perception has revised but accumulating data suggest that it is also the case for children and adolescents with T2DM when a growing number of young people aged 20–40 years are diagnosed with the disease, which indicates that Type 2 diabetes has long been considered a condition which affects both young and elder population[24]. Our study suggested an alarming rate of 15 % of young diabetic patients below the age of 30 years. Glycemic control among young individuals with T2DM is often poor and requires frequent education regarding disease management[25]. Urbanization is one of the predictors of diabetics and prediabetes. Our comprehensive data further suggests that the highest prevalence of individual belong to urban areas compared to rural areas. Overall, our results are in accordance with the worldwide prevalence of diabetic populations, which are expected to occur lower than in rural areas or less urbanized communities[26]. Education is a profound tool, and formal education has been often linked with increased awareness regarding the development and management of the disease. Our data have reported that the highest number of diabetic individuals have below primary level education. Similar data have been reported previously where a low education profile has been positively associated with decreased knowledge of one's medical condition and increasing T2DM frequency[4,27]. The contradictory data can be supported by a range of different factors including the clinical settings in which the data was collected as well as the psychosocial stress and major life events.

Daily life management plays a significant role in the management of T2DM. Patients experiencing multiple chronic conditions need to administer their self-care and treatment. It was also observed during the present study that the majority of diabetic individuals enrolled in this do not do enough daily physical activity and follow the diet recommended for disease management. We further observed that in our study population, patients who visit the diabetic clinic regularly and practice self-monitoring of the glycemic index were significantly correlated with better diabetes management. These findings were similar to previous data, which suggest that self-monitoring of glucose with record-keeping behavior was helpful in the management of diabetes[28]. BMI is another important factor that affects the susceptibility towards developing T2DM and also

plays an important role in disease management. Previously, a higher BMI has been associated with an increased risk of developing T2DM. We also found a strong association of all BMI classes with diabetes, which suggests that BMI is a significant risk factor for T2DM. Our study observed that more than 56 % of individuals having BMI above the healthy range (>23) were diabetic compared to non-diabetic individuals. Evidence from several studies indicates that obesity and weight gain are associated with an increased risk of diabetes[4].

Multiple chronic conditions play a significant role in the treatment administration of T2DM patients, which includes determining the correct diabetes course of treatment. Previous studies have reported that the presence of multiple comorbidities affects the quality of life associated with a patient's health and can lead to secondary complications[27,29]. Our data suggest that 80% of diabetic patients had at least one comorbidity, whereas 59 % had more than two or more comorbidities. Similar data were reported by Iglay et al[27]. Our study also found a significant prevalence of diabetic nephropathy, coronary artery disease and sexual dysfunctions by increasing age and male gender. Similar data were reported by previous studies where researchers have reported an increasing prevalence of male diabetic patients developing secondary health complications[4,26]. The order of comorbid prevalent in our study was CKD, GAD, Bone diseases and CVD, respectively. Besides these, less frequent diseases were retinopathy, Foot disease, skin disease and neurological diseases.

T2DM is one of the leading causes of CKD worldwide[30]. Globally, the overall prevalence of CKD among T2DM patients varied from 6.0–39.3 %[31]. In our study group, CKD was the most prevalent comorbidity amongst all T2DM patients affecting a large number of males of age group 41-50 years as compared to females (16 %; 10 % in males and 6 % in females). Similar to our studies, Hasan et al., reported CKD prevalence in Pakistan 12-30 %, with a higher prevalence in male patients in comparison to females[32]. GAD is among the most prevalent mental health conditions and is characterized by unmanageable distress[33]. In Pakistan, the mean overall prevalence of anxiety and depression is 27 % affecting more females than males[34]. The current study also found a higher GAD risk in female T2DM patients as compared to male subjects, which is in accordance with previously published data[33]. Altered bone metabolism is profound comorbidity associated with T2DM. Patients with T2DM have a 40–70 % increased risk for fractures, despite having a normal increased bone mineral density[35]. In the present study, the reported bone disease is the third most prevalent comorbidity in T2DM patients and accounts for approximately 15 % of total comorbidities reported. CVDs are one of the most common diseases reported in diabetic individuals. Several studies have been reported in this regard where hypertension and dyslipidemia are the most prevalent comorbidity reported in T2DM patients[23,27]. The data is contradictory to our findings, where CVDs are not as frequently observed as have been reported previously.

A range of contributing factors is involved in the disease pattern and prevalence of associated aspects of T2DM. Most importantly, the clinical setting from which the data was collected and the number of participants recruited in the study may result in data variability. The present study has a substantial sample size with comparable non-diabetic Individuals. However, the data was collected from a single center and is representative of the individuals attending the clinic. Accordingly, the generalizability of our finding to other T2DM populations and healthcare settings other than in diabetic clinics is uncertain and warrants further study.

Conclusion

The present study represents the modifiable and no-modifiable risk factors associated with T2DM management. Our study reported that males of age group 41-50 and having T2DM diagnosed in less than five years attend the diabetic clinic more frequently as compared to females. Our data further suggest that most of the T2DM patients have at least one comorbidity, which increases the

disease management complication of the patients as well as the clinicians. The study further highlights the increasing risk of T2DM associated kidney disorders and psychological stress in diabetic individuals, and CVD is not the most prevalent comorbidity among the patients who attend the diabetic clinic frequently.

Conflicts of Interest

The authors declare no conflict of interest.

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