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Research Article

Frequency of Type 2 Diabetes and Associated Comorbidities Frequency of Type 2 Diabetes and Associated Comorbidities in Elderly Saudi Population

Khalid Aljabri, S. J.[1*], Samia Bokhari, A.[1], Muneera Alshareef, A.[1], Patan Khan, M.[1] & Bandari Aljabri, K.[2]

[1]*Department of Endocrinology, King Fahad Armed Forces Hospital, Jeddah, Kingdom of Saudi Arabia*

[2]*College of medicine, Um Al Qura University, Makkah, Kingdom of Saudi Arabia*

[*]**Correspondence to:** Dr. Khalid Aljabri, S. J., Department of Endocrinology, King Fahad Armed Forces Hospital, Jeddah, Kingdom of Saudi Arabia.

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Abstract

Background and Objective

The prevalence and incidence of type 2 diabetes mellitus (T2DM) are increasing worldwide. T2DM was the second common chronic disease diagnosed among elderly patients. This study aims to determine the frequency of type 2 diabetes and associated comorbidities in elderly Saudi population.

Methods

For the present study, we analyzed participants who are older than or equal to 60 years old. A total of 1022 were selected to be enrolled for the present study. All patients were from the population of the Primary health and Diabetic Centres at King Fahad Armed Forces Hospital. Participants were defined as having T2DM according to self-report, clinical reports, use of antidiabetic agents

and HbA1c (≥6.5). Laboratory assessments included HbA1c, lipids, creatinine and urinary microalbumin.

Main results

Of the 1012 participants analyzed, 538 were men (53.2%). Age was 68.5 ± 6.9. Obesity was present in 432(46.7%) with female to male ratio 1.2:1. Blood measurements revealed the following values: total cholesterol levels 4.7 ± 1.1mmol/L, high density lipoprotein 1.2 ± 0.3mmol/L, triglyceride levels 1.7 ± 0.8 and low density lipoprotein 2.8 ± 0.9mmol/L. There were significant higher values of total cholesterol, low density lipoprotein and high density lipoprotein for female in comparison to male, p<0.0001, p=0.002 and p<0.0001 respectively. High triglyceride was found to be higher in male, p=0.004. Of the overall 1012 analyzed participants, chronic renal failure and DN were present in 128(12.8%) and 261(37.6%) respectively. T2DM had been diagnosed in 730 (72.1%) with no significant difference between both gender, p=0.4. 530(83.9%) was diagnosed with HTN and T2DM with significant difference favoring female gender (52.1% vs. 47.9%) with female to male ratio 1.1:1, p<0.0001. Obesity was present in 328(49.8%) of patients with T2DM with female to male ratio 1.5:1. Patients with T2DM has significantly lower total cholesterol, high density lipoprotein and low density lipoprotein and higher triglyceride. Chronic renal failure and DN were present in 254(14.0%) and 101 (39.2%) respectively. Patients with T2DM have a HbA1c of 8.3 ± 2.2. The older the patients with T2DM, the lower the HbA1c; r = - 0.07,p=0.05. Patients with T2DM with HTN has higher HbA1c than those without HTN, 8.2 ± .2 vs. 7.6 ± 2.1, P<0.0001 respectively. The older the patients with T2DM and HTN, the lower the HbA1c; r = - 0.07,p=0.1. There were no significant difference when comparing T2DM in relation to different BMI categories and different age groups. There was a significant difference between T2DM and HTN and different BMI categories, p<0.0001. When comparing T2DM associated with HTN in relation to different BMI categories, there was a significant difference between T2DM associated with HTN and different BMI categories, p<0.0001. T2DM subjects were more likely to have hypertension when subjects have higher BMI, p=0.001, Figure 2. Only significant difference was found between gender in obese cases with T2DM associated with HTN, p=0.04.

Introduction

Diabetes mellitus is a major cause of excess mortality and morbidity and have a higher risk of developing microvascular and macrovascular disease than the general population [1-4]. The prevalence of type 2 diabetes mellitus (T2DM) are increasing worldwide [5]. Statistics regarding the increasing trend of diabetes in the world have also been observed in Saudi Arabia. In Saudi Arabia, primary epidemiological diabetes features are not different. As per the WHO country profile 2016, 14.4% of Saudi population has diabetes, while prevalence in males is 14.7% [6]. The diabetes mellitus prevalence among adult Saudi population has reached 23.7%, a percentage being the highest across the globe [7-10]. A National Community Based Survey in the Saudi Arabia found that the prevalence of diabetes among elderly population aged 60-70 years was 36.5 [8]. Diabetes mellitus was the second common chronic disease (57.3%) diagnosed among elderly patients [11].

In a study carried out in King Fahd hospital, it was found that, the prevalence of diabetes was 34.1% in males and 27.6% in females, however, prevalence of diabetes decreased in patients older than 70 years [12].

T2DM is known to affect quite a few body systems and thereby affect the individual's health in different ways such as having coronary artery disease (CAD), renal failure, diabetic retinopathy, etc. Therefore, many countries attempted to study the consequences of diabetes on the population. However, it is interesting to note that the prevalence of DM is extremely variable among different populations though it increases with aging [8]. Spence in 1920 was the first to document impairment of glucose metabolism in subjects over the age of 60 years [13]. The cause for increased occurrence of T2DM in the elderly population remains to be clearly defined. A better understanding of the underlying mechanisms responsible for diabetes in old age is critical to develop strategies to treat elderly with diabetes and to prevent the disease. The management of older people with diabetes requires special care and attention. Although it is obvious that it is important to know the true magnitude of the major disease such as T2DM, reliable data on its prevalence are lacking for most countries. Previous studies in Saudi Arabia have been not been based on representative population samples, and have used fasting glucose values only.

Current recommendations for diabetes screening by the American Diabetes Association focus nearly exclusively on adults who are overweight or obese as defined by body mass index (BMI) until the patient meets the age-oriented screening at 45 years [14]. Further, the recently released recommendation from the US Preventive Services Task Force regarding screening for abnormal glucose levels and T2DM limits screening to individuals who are overweight or obese [15]. This focus on obese or overweight individuals, Although obesity and diabetes have shown trends of increasing prevalence. "United States Preventive Services Task Force" has recommended screening of diabetes in adults devoid of precise symptoms and in individuals with BP higher than 135/80mmHg [21]. Elderly are vulnerable group in any population. Determining the prevalence of diabetes mellitus in any community is important to for planning and implementation of control services. This study aims to determine the frequency of type 2 diabetes and associated comorbidities in elderly Saudi population.

Methods

For the present study, we analyzed participants who are equal to or older than 60 years old. A total of 1022 were selected to be enrolled for the present study. All patients were from the population of the Primary health and Diabetic Centres at King Fahad Armed Forces Hospital. Participants were defined as having T2DM according to self-report, clinical reports, use of antidiabetic agents and HbA1c (≥6.5) [14]. All data were collected by personal interview and on the basis of a review of electronic medical data. Weight (kg) and height (cm) were measured by physician and nurse interviewers and recorded. Overweight and obesity were defined as BMI 25-29.9 and ≥ 30.0kg/m^2 respectively [16]. Blood Pressure readings were within a gap of 15 minutes using a mercury sphygmomanometer by palpation and auscultation method in right arm in sitting position. Two readings were taken 15min apart and the average of both the readings was taken for analysis. Hypertension (HTN) was also diagnosed based on anti HTN medications or having a prescription of antihypertensive drugs and were classified as Hypertensive irrespective of their current blood pressure reading or if the blood pressure was greater than 140/90mmHg i,e systolic BP more than 140 and diastolic BP more than 90mm of Hg -Report of the American College of Cardiology/American Heart Association

Task Force on Clinical Practice Guidelines [17]. Laboratory assessments included HbA1c, lipids, creatinine and urinary microalbumin. HbA1c was expressed as percentage. High performance liquid chromatography was used. Fasting serum lipids were measured on a sample of blood after fasting for 14 hours. We used the Enzmatic method for determining the cholesterol and trigylcerides levels. Diabetic nephropathy (DN) was assessed by measurement of mean albumin excretion rate (AER) on timed, overnight urine collections. We use a polyclonal radioimmunoassay for albumin measurement. DN is defined as an albumin excretion rate of > 20g/min in a timed or a 24-hr urine collection which is an equivalent to > 30mg/g creatinine in a random spot sample. Chronic renal failure was documented as per the medical records, self reporting by the patient or compatible biochemical values (upper serum creatinine for our laboratory 106Umol/l.

Statistical Analysis

Univariate analysis of demographic and clinical laboratory were accomplished using unpaired t-test between variables, to estimate the significance of different between groups where appropriate. Chi square (X^2) test were used for categorical data comparison. In order to evaluate the adjusted association of aforementioned factors on being diabetic in relation to the nondiabetic subjects, a multinomial logistic regression model was fit, in which the categorical dependent variable was T2DM (with "T2DM" as the reference category), and significant variables in bivariate analyses were included as explanatory variables. The adjusted odds ratio (OR) with a 95% confidence interval (CI) was calculated. All statistical analyses were performed using SPSS Version 22.0. The difference between groups was considered significant when $P<0.05$.

Results

Of the 1012 participants analyzed, 538 were men (53.2%). Age was 68.5 ± 6.9, table 1. Obesity was present in 432(46.7%) with female to male ratio 1.2:1. Blood measurements revealed the following values: total cholesterol levels 4.7 ± 1.1mmol/L, high density lipoprotein 1.2 ± 0.3mmol/L, triglyceride levels 1.7 ±0.8 and low density lipoprotein 2.8 ± 0.9mmol/L. There were significant higher values of total cholesterol, low density lipoprotein and high density lipoprotein for female in comparison to male, $p<0.0001$, $p=0.002$ and $p<0.0001$ respectively. High triglyceride was found to be higher in male, $p=0.004$. Of the overall 1012 analyzed participants, chronic renal failure and DN were present in 128(12.8%) and 261(37.6%) respectively. Table 2 showed the characteristic of patients with T2DM. T2DM had been diagnosed in 730 (72.1%) with no significant difference between both gender, $p=0.4$. 530(83.9%) was diagnosed with HTN and T2DM with significant difference favoring female gender (52.1% vs. 47.9%) with female to male ratio 1.1:1, $p<0.0001$. Obesity was present in 328(49.8%) of patients with T2DM with female to male ratio 1.5:1. Patients with T2DM has significantly lower total cholesterol, high density lipoprotein and low density lipoprotein and higher triglyceride. Chronic renal failure and DN were present in 254(14.0%) and 101 (39.2%) respectively. Patients with T2DM have a HbA1c of 8.3 ± 2.2. The older the patients with T2DM, the lower the HbA1c; $r = - 0.07$,$p=0.05$. Patients with T2DM with HTN has higher HbA1c than those without HTN, 8.2 ± .2 vs. 7.6 ± 2.1, $P<0.0001$ respectively. The older the patients with T2DM and HTN, the lower the HbA1c; $r = - 0.07$,$p=0.1$. There were no significant difference when comparing T2DM in relation to different BMI categories and different age groups, figure 1. There was a significant difference between T2DM and HTN and different BMI categories, $p<0.0001$. When comparing T2DM associated with HTN in relation to different BMI categories, there was a significant difference between T2DM associated with HTN and

different BMI categories, p<0.0001, figure 2. T2DM subjects were more likely to have hypertension when subjects have higher BMI, p=0.001, Figure 2. Only significant difference was found between gender in obese cases with T2DM associated with HTN, p=0.04.

Table 1: *Characteristics of patients (means ± SD or number (%))*

Parameters		Total	Male	Female	P value
n (%)		1012	538(53.2)	474 (46.8)	
Age (years)		68.5 ± 6.9	68.3 ± 6.5	68.8 ± 7.2	0.2
Body mass index (kg/m²)	<25.0	191(20.6)	111(58.1)	80(41.9)	<0.0001
	25.0-29.9	302(32.6)	203(67.2)	99(32.8)	
	≥30	432(46.7)	194(44.9)	238(55.1)	
Diabetes		730(72.1)	382(52.3)	348(47.7)	0.4
Hypertension		632(62.5)	313(49.5)	319(50.5)	0.003
Total cholesterol (mmol/l)		4.7 ± 1.1	4.5 ± 1.1	4.9 ± 1.1	<0.0001
Low density lipoprotein (mmol/l)		2.8 ± 0.9	2.7 ± 0.9	2.9 ± 0.9	0.002
Triglyceride (mmol/l)		1.7 ± 0.8	1.8 ± 0.9	1.6 ± 0.7	0.004
High density lipoprotein (mmol/l)		1.2 ± 0.3	1.0 ± 0.2	1.3 ± 0.3	<0.0001
Renal failure		128(12.8)	101(78.9)	27(21.1)	<0.0001
Diabetic nephropathy		261(37.6)	152(58.2)	109(41.8)	<0.0001

Table 2: *Characteristics of patients with type 2 diabetes mellitus (means ± SD or number (%))*

Parameters		Type 2 diabetes		P value
		Present	Absent	
n (%)		382(52.3)	348(47.7)	
Age (years)		68.3 ± 6.8	69.0 ± 7.0	0.1
Gender	Male	382(71.0)	156(29.0)	0.4
	Female	348(73.4)	126(26.6)	
Body mass index (kg/m²)	<25.0	117(61.3)	74(38.7)	0.001
	25.0-29.9	214(70.9)	88(29.1)	
	≥30	328(75.9)	104(24.1)	
Hypertension		530(83.9)	102(16.1)	<0.0001
Total cholesterol (mmol/l)		4.6 ± 1.1	4.9 ± 1.0	<0.0001
Low density lipoprotein (mmol/l)		2.7 ± 0.9	3.0 ± 0.9	<0.0001
Triglyceride (mmol/l)		1.7 ± 0.9	1.5 ± 0.7	<0.0001
High density lipoprotein (mmol/l)		1.1 ± 0.3	1.2 ± 0.3	0.002
Renal failure		101(78.9)	27(21.1)	0.07
Diabetic nephropathy		254(97.3)	7(2.7)	0.001

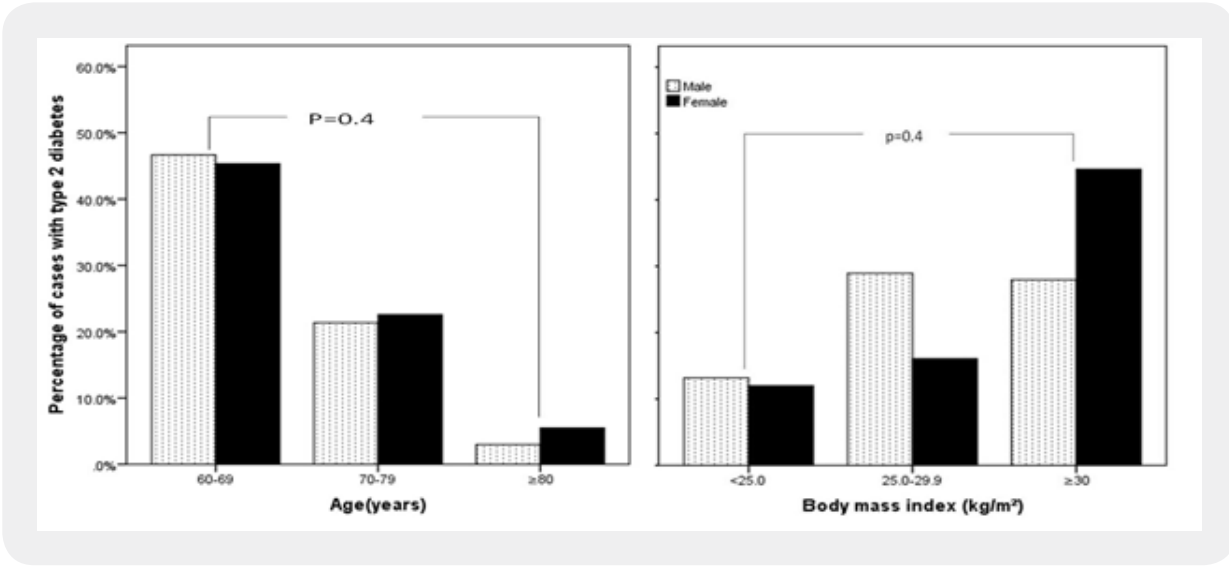

Figure 1: *Percentage of patients with type 2 diabetes mellitus in relation to body mass index and age categories*

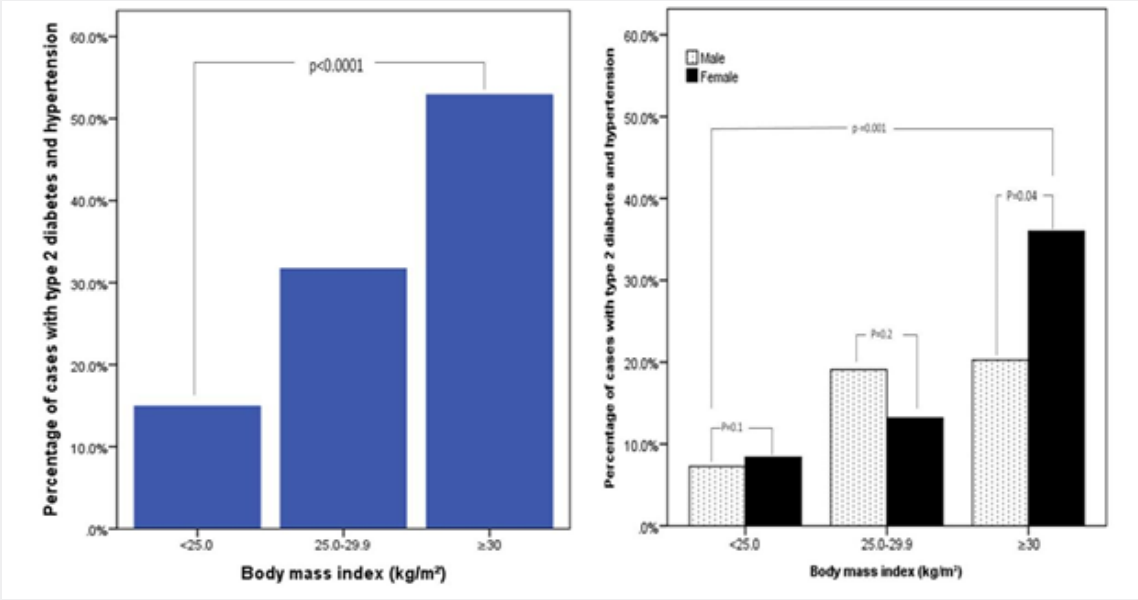

Figure 2: *Percentage of patients with type 2 diabetes mellitus associated with hypertension stratified by gender in relation to body mass index categories*

Discussion

This study showed that the frequency of T2DM in elderly Saudi population is high. Generalization to all population could not be due to regionalized characteristics. In addition, it does not evaluate the healthcare services offered in our city. The size of our sample and the cross section type of the study should be of consideration.

T2DM is a major health concern worldwide and is increasing in parallel with the HTN and obesity epidemic [18]. Prevalence of T2DM has increased dramatically with 1 million people reported to have been diagnosed with T2DM in 1994, increasing to 382 million by 2013, and with prediction of 592 million by 2035 [19]. Given that both genetic and environmental factors contribute to T2DM progression, it has been proposed that amongst increasing globalization, Asian ethnicities including Saudi Arabia have been unable to adapt to food and lifestyle related aspects of westernized culture [20]. Hence when matched for the same gender, age, and body weight, those with Asian ethnicity appear to have a greater risk of poor metabolic health than Caucasian counterparts including Europeans people [21]. This increased risk for T2DM has been reported in both Asians and Saudi Arabia [8-12,22].

Our study showed the frequency of T2DM was 72.1% and 68% in individuals aged >60 years (60-105 years) and in individuals aged 60-79 years respectively. In the DECODE study (Diabetes Epidemiology: Collaborative analysis of Diagnostic criteria in Europe), DECODE which measured plasma glucose in 13 European cohorts, in accordance with WHO recommendations for the diagnosis of diabetes, the prevalence of diabetes was 10-20% in individuals aged 60-79 years [23]. In other studies, conducted in subjects aged >60 years in Spain, the overall prevalence of diabetes was 16.1-16.8%, lower than ours (13.1%) [24,25]. This variation maybe related to the methodology used to collect the information as well as the variability of results when they are self reported by the patient. In a study in people older than65 years in the United States using data from Medicare, the prevalence was 24.8% [26]. Also in discordance with other studies. we found that most cases of diabetes were not occurred in the oldest individuals [27,28]. One possible explanation for this could be a progressively greater awareness of diabetes on the part of both patients and medical professional. Although most studies in the general population have found a higher prevalence of diabetes in men, some have found that the prevalence in people over age 65 is higher in women which in concordance with our results [24,29,30]. The DECODE study has reported diabetes prevalence rates of 8.5% in men and 9.3% in women between the ages of 60 and 69years, increasing to 12.4% in men and 15.4% in women between age 70 and 79 years, and to 12.9% in men and22.4% in women between age 80 and 89 [23]. Our results are consistent with the prevalence in men but not women. The frequency of T2DM was 39.5% in men and 33.8% in women between the ages of 60 and 69years, increased to 36.9% in men and 34.3% in women between age 70 and 79 years and 25.0% in men and 40.6% in women > age 80 years. The differences by sex found in different age groups in relation to gender are not statistically significant, p=0.04, figure 1. In discordance to our result, in recent national study, diabetes prevalence using 10-year succession for men and women showed significant increase in its total prevalence and significant difference between the two genders before 70 years of age, but a significant decrease in the total prevalence in the age group ≥70 years compared with the preceding age group (P = 0.02) with no significant difference between the two genders.

The participants in our study with T2DM had higher BMI, more frequent HTN, higher trigLyceride, frequent renal failure and DN than those without diabetes. logistic regression analysis showed no significant association of any of the covariables except for hypertriglyceridemia and DN with T2DM subjects. Previous cross-sectional studies have reported that multiple risk factors are related to T2DM, such as increased age, overweight, obesity, blood pressure, and dyslipidemia [31-33]. Our study showed the age of subjects had lower odds of being T2DM (p=0.9, OR: 0.99, 95% CI (0.95-1.04) in concordance with earlier reports [31,34]. Odds of being in the diabetic group gets multiplied by 1.16 for each unitary increase in male gender (p =0.1, OR: 1.16, 95% CI 0.54-2.51). The reason for such an observation has not been completely elucidated but is proposed to be associated with obesity which is highly prevalent in the populations worldwide [35,36]. Since obesity is closely linked to increased insulin resistance and decreased insulin sensitivity and higher risk of diabetes, arresting the obesity pandemic among our population should be a priority [33,35]. Special, culturally oriented community-based intervention programs need to be implemented. Due to our small sample size, this is inconclusive and needs to be verified by extending our study to more of our communities.

As seen in this study, majority of the female participants were obese (43.1 % vs. 32.9 for male, p=0.2). There Odds of being in the T2DM gets multiplied by 1.08 for each unitary increase in overweight group (OR = 1.08, 95% CI = 0.48–2.45, p=0.8). Previous studies have reported that overweight and obesity were the mainly factors contributing to insulin resistance, and insulin resistance was the basis of diabetes and other chronic diseases [36,37]. Increasing evidence suggests that the excess body fat in overweight/obese people might lead to increased degradation of fat, which resulted in the production of large amounts of free fatty acids (FFAs). When the level of FFAs was higher in blood, the capacity of liver tissue for insulin-mediated glucose uptake and utilization was lower, so the blood glucose level was high in circulation [38]. In other words, high FFAs in the blood was one of the important pathogenic factors of obesity caused by insulin resistance [39].

A high level of triglycerides was significantly associated as a risk factor for developing T2DM (OR = 2.54,95% CI = (1.21-5.34), P=0.01). High level of triglycerides could increase the fat deposition in muscle, liver, and pancreas, and it could damage the function of mitochondria and induce oxidative stress which, in turn, could cause insulin resistance, but also lead to impaired islet B cell function [40]. Some studies suggested an interrelation between hypertriglyceridemia and insulin resistance and that they promote each other's development [41,42]. In concordance with our result, in some epidemiological studies, for instance, the Framingham Heart Study, hypertriglyceridemia was more prevalent in type 2 diabetes mellitus patients than in the normal population, suggesting that hypertriglyceridemia is a causal factor of type 2 diabetes mellitus [43]. However, this paper was a cross-sectional study, thus it was impossible to determine the causal relationship between hypertriglyceridemia and pre-diabetes and T2DM.

Hypertension was found to be a nonsignificant risk factor for T2DM in our study (OR = 1.11, 95% CI =0.54-2.30, p=0.8). A possible mechanism is that the activity of angiotensin II is increased in the circulatory system of patient with hypertension. Angiotensin II activates renin-angiotensin-aldosterone system and affects the function of the pancreatic islets, resulting in islet fibrosis and reduced synthesis of insulin, and ultimately leading to insulin resistance [44,45]. Insulin resistance can also aggravate the condition of hypertension. Directly or indirectly through the activity of renin-angiotensin-aldosterone system, insulin promotes renal tubular to reabsorb Na+ and water, leading to the increased blood volume and cardiac output; this is

considered as one of reasons for the development of hypertension [46]. Interactions between abnormal glucose tolerance, hypertension, and dyslipidemia could impair endothelial cell and result in atherosclerosis or other cardiovascular complications. Therefore, the management of daily diet of people with T2DM and the monitoring of body weight, blood lipids, and blood pressure is very important.

DN is the leading cause of end-stage renal disease and the care of patients with T2DM and DN contributes significantly to health care costs. DN patients are a problem at the interface between general medicine, primary care physician, diabetology and nephrology. Of patients with T2DM, about 10%-20% will eventually develop DN [47]. The earliest clinical evidence of DN is the appearance of low but abnormal levels of albumin in the urine, referred to as microalbuminuria (MA), and patients with MA are referred to as having incipient DN. A higher proportion of individuals with T2DM are found to have overt nephropathy and MA shortly after diabetes diagnosis, because diabetes is actually present for many years before the diagnosis is made and as shown by biopsy studies, the presence of albuminuria may be less specific for the presence of diabetic nephropathy. MA is a marker of increased cardiovascular morbidity and mortality for patients with T2DM. Thus, possible vascular disease could be indicated by the finding of MA and it is an indication for aggressive intervention to reduce all cardiovascular risk factors.

We have shown DN frequency in T2DM to be 39.2%. Reports from various epidemiological and cross sectional studies have shown marked variation in the prevalence of MA [48-53]. In Saudi Arabia, the rate of MA among Type 2 diabetic patients attending the diabetic clinic of King Abdulaziz University Hospital during the period of September 2004 to April 2005 was 45.6% [54]. About 54.3% of patients with Type 2 DM attending a primary care center in Ssouthern Saudi Arabia, had proteinuria [55]. A cross-sectional study, where 54.670 Saudi Type 2 diabetic patients were selected from Saudi National Diabetes Registry found that the prevalence of MA was 1.2% [56]. MicroAlbuminuria Prevalence Study is a large multicentre epidemiological study in Asia to determine the prevalence of MA in T2DM patients with hypertension [57]. In a population of 5,549 patients, 39.8% have MA. This is higher than the prevalence rates, reported by us (33.2%) and in population-based studies for Western diabetic patients (17% to 21%) [58]. In another Asian study, in southern India, MA was detected in 36.3% of T2DM [59]. These variations in the prevalence rate of proteinuria can be attributed to differences in several factors such as; study design, source of study population, sample selection, race, age, sex structure of the study population, diagnostic criteria, as well as the methods of measurement of proteinuria and urine collection, diabetic duration, diabetic treatment, and presence of hypertension [60].

One of the limitations of this study is that we used self-reported data to assess diabetes. Several authors point out that self-reported data could underestimate diabetes prevalence. 24,26 Although this underestimation is possible, other authors have confirmed that self-reported diabetes is a reasonably reliable surrogate for diagnosed diabetes, based on their studies of the accuracy of patients' self-reportscompared with medical records [61,62]. In health care systems where general practitioners have a complete vision of their patients' medical status and in which patients have easy and frequent access to medical services, patients are more likely to be well informed about their diseases, especially in the case of chronic diseases like diabetes [63]. This is the case in our hospital, where every community-dwelling person is registered in the patient list of a general practice, and access to other health care facilities, including outpatient clinics, is only possible through referral by a general practitioner [64]. Our sample was drawn from a hospital based patients, therefore this

study may not be comparable to other population studies and cannot strictly be generalized to the whole older Sausi population. Results of our investigation must be interpreted in light of some limitations such as the cross-sectional design, which does not let to establish any causal relation with respect to T2DM state and only provides mere associations. Considering the goal population, a larger cohort would have probably provided a greater power of the statistical analyses [65,66].

Conclusion

This study found the major clinical differences between prediabetic and T2DM pateints were the higher hypertension and hypertriglyceridenia in the T2DM pateints. Clearly, despite the small sample size, this study has posed important public health issues that require immediate attention from the health authority. Unless immediate steps are taken to contain the increasing prevalence of obesity, diabetes, prediabetes, the health care costs for chronic diseases will pose an enormous financial burden to the country.

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