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Research Article

Complications and Associated Conditions among Omani Type 2 Diabetes Patients at Sultan Qaboos University Hospital, Muscat, Oman

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Abstract

Objective: To estimate the prevalence of type 2 diabetes (T2D) complications and associated conditions among Omani patients at Sultan Qaboos University Hospital (SQUH).

Methods: A total of 986 T2D Omani patients was included in this study. Data were collected from June 2010 to February 2012. Data include demographic, anthropometric and biochemical investigations. Complications among patients were recorded.

Results: Thirty-six percent of the patients were overweight and 51% were obese. Thirty-five percent of the patients had high serum total cholesterol, 63% had high LDL cholesterol, 38% had high serum triglycerides, while 50% and 48% of the males and females, respectively, had low HDL cholesterol. Half of the patients had at least one T2D complication, while 86% had a complication or associated condition. Twenty percent had coronary artery disease, 5% had a stroke, 66% had hypertension, 10% had documented retinopathy, 15% had microalbuminuria, 31% had nephropathy, 9% had neuropathy and 2% had peripheral vascular disease.

Conclusion: The prevalence of diabetes complications and associated conditions among Omani T2D patients was not different from other populations. However, prevalence of retinopathy and neuropathy was lower and this indicates the need for a proper assessment and documentation.

Keywords: Type 2 Diabetes; Omani; Complications; Associated conditions; Prevalence

Abbreviations

T2D: Type 2 Diabetes; SQUH: Sultan Qaboos University Hospital; BP: Blood Pressure; CVD: CardioVascular Dseases; PVD: Peripheral Vascular Disease; IGT: Impaired Glucose Tolerance; MI: Myocardial Infarction; ESRD: End Stage Renal Disease; BMI: Body Mass Iindex; ACR: Urine MicroAlbumin/Creatinine Ratio; ADA: American Diabetes Association; EGFR: Estimated Glomerular Filtration Rate; CKD: Chronic Kidney Disease; CAD: Coronary Artery Disease; HDL: High Density Lipoprotein cholesterol; LDL: Low Density Lipoprotein cholesterol; NSTEMI: Non-ST segment Elevation Myocardial Infarction; STEMI: ST segment Elevation Myocardial Infarction.

Introduction

Type 2 diabetes mellitus (T2D) is associated with acute and chronic metabolic consequences, where the frequency of events varies according to the level of glycemic control, blood pressure (BP) and dyslipidemia. Acute fluctuations in serum glucose may lead to emergency situations (e.g. Diabetic ketoacidosis, hyperosmolar hyperglycemic syndrome or severe hypoglycemia). Longer-term follow up is required to promote better blood glucose regulation and avoidance of diabetic emergencies. Glucose dysregulation is also associated with damaging effects on tissues, leading to complications. Diabetes increases the risk of microvascular and macrovascular diseases. Microvascular diseases include retinopathy, nephropathy, neuropathies, and the consequences that stem from these (e.g. congestive heart failure, diabetic foot). Macrovascular diseases include cardiovascular diseases (CVD), cerebrovascular disease or "stroke" and peripheral vascular disease (PVD). These complications are associated with considerable morbidity, reduced quality of life, disability, premature mortality and high economic costs.

Diabetes and impaired glucose tolerance (IGT) increase CVD risk three-to eightfold. Thus, over 40% of patients hospitalized with acute myocardial infarction (MI) have diabetes and 35% have IGT. In addition, new blood vessel growth in response to ischemia is impaired in diabetes, resulting in the decreased collateral vessel formation in ischemic hearts, and in non-healing foot ulcers. DM is also now the leading cause of new blindness in people 20 – 74 years of age and the leading cause of end stage renal disease (ESRD) in the developed world. Survival of patients with diabetic ESRD on dialysis is half that of those without diabetes. More than 60% of patients with diabetes are affected by neuropathy, which includes distal symmetrical polyneuropathy, mononeuropathies and a variety of autonomic neuropathies causing erectile dysfunction, urinary incontinence, gastroparesis and nocturnal diarrhea. Diabetes accelerated lower extremity arterial disease in conjunction with neuropathy accounts

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Table 1: Characteristics of Omani T2D patients (*n*= 986).

	Mean ± SD	Median (range)*
Age (years)	56 ± 11	
Gender (M: F)	470: 516	
Weight (kg)	77 ± 17	
Height (cm)		157 (135 - 182)
BMI (kg/m²)		30 (15 - 58)
Systolic BP (mmHg)		137 (57 - 229)
Diastolic BP (mmHg)	76 ± 11	
Fasting glucose (mmol/l)		8.8 (3 - 25)
HbA_{1C} (%)		8.2 (4.1 - 18.6)
Serum creatinine (µmol/L)		63 (27 - 673)
Total cholesterol (mmol/l)		4.7 (1.6 - 11.0)
LDL cholesterol (mmol/l)		2.8 (0.70 - 8.4)
Triglycerides (mmol/l)		1.4 (0.40 - 32)
HDL cholesterol (mmol/l)		1.2 (0.11 - 6.1)

*Median (range = minimum - maximum) displayed in the table when the variable does not follow a normal distribution pattern.

for 50% of all non-traumatic amputations in the USA [1].

Hypertension is also one of the most significant secondary risk factors for the development of microvascular diabetic complications. In both retina and glomerulus, reduction of the vascular surface area appears to occur first in microvessels with high perfusion pressure. Tight control of blood pressure delays the progression of retinopathy and nephropathy, while elevated blood pressure accelerates the onset of nephropathy and its progression [2]. The term diabetic dyslipidemia refers to the lipid abnormalities typically seen in persons with T2D. It is characterized by elevated serum triglyceride and LDL cholesterol concentrations and low serum HDL cholesterol concentrations.

T2D is also associated with the "metabolic syndrome," a collection of cardiovascular risk factors (abdominal obesity, hyperinsulinemia, hypertension, dyslipidemia, proinflammatory and procoagulant states). These factors increase the likelihood of developing additional risks, and with each added risk, predispose one to an increasing risk of atherosclerotic vascular disease events and mortality [3].

If diabetes is treated properly, the mortality from acute and chronic hyperglycemia is reduced. Patients and resources (e.g. Hospital facilities, experience of staff, etc.) characteristics may also modify the outcomes. Inadequate therapeutic instruments and medication, and insufficient numbers of trained staff result in poor glycemic control and higher risk of mortality.

This is a retrospective study aimed at estimation of the prevalence of microvascular and macrovascular complications of T2D as well as the prevalence of diabetes associated conditions among Omani patients. Information provided by this study will allow the clinicians to draw appropriate plans for reduction and prevention of diabetes complications among the Omani population.

Materials and Methods

Sample size calculation

Sampsize website was used for calculating the sample size. Using precision of 2%, a prevalence of 11%, population size of 2 million and 95% confidence interval, a minimum of 940 patients should be used in this study.

Sample collection

A total of 986 T2D Omani patients was included in this study. T2D patients were recruited from the Diabetes Clinic (*n*= 523), Family Medicine Clinic (*n*= 150) and as inpatients (*n*= 313) at Sultan Qaboos University Hospital (SQUH), a countrywide tertiary referral center in Oman. A history of T2D among patients was ascertained from the diagnosis and medical history deposited in the electronic records of the hospital information system. The inclusion criteria were Omani T2D patients, over 18 years old. Exclusion criteria included: patients diagnosed with type 1 diabetes; positive antibodies (islet cell antibodies and glutamic acid decarboxylase antibodies) or patients diagnosed with any type of cancer. Data were collected from June 2010 to February 2012. Participants were informed about the project and written consent was obtained. The study was approved by the Ethics and Research Committee of the College of Medicine, Sultan Qaboos University, Muscat, Oman.

Anthropometric and Biochemical data

Data on demographic, anthropometric and biochemical investigations were collected from the hospital information system, electronic records, and summarized in Table 1. Patient's weight and height were collected and body mass index (BMI) was calculated [weight (kg) /height² (m^2)]. Obesity status was defined according to the international classification of an adult's weight, [Normal BMI: 18.5 - 24.99 kg/m^2, overweight: 25.00 - 29.99 kg/m^2 and obese ≥ 30.00 kg/m^2]. Blood pressure and duration of diabetes among patients were documented. The biochemical investigations included: serum fasting glucose, HbA_{1C} level, serum creatinine, serum total cholesterol, LDL-cholesterol, serum HDL-cholesterol, serum triglycerides and urine microalbumin/creatinine ratio (ACR). American Diabetes Association (ADA) criteria for diabetes lipid control were used to define hyperlipidemia, and summarized in Table 2 [4]. Estimated glomerular filtration rate (eGFR) was calculated from serum creatinine. ACR and eGFR were used to assess kidney function among patients (Normal kidney function: normal urine ACR (men ≤ 2.5 mg/mmol, women ≤ 3.5 mg/mmol) and normal eGFR (≥90 ml/min/1.73m^2); Microalbuminuria: Urine ACR: 2.6-29 mg/mmol (men) and 3.6 - 29 mg/mmol (women); chronic kidney disease (CKD) stage 2: eGFR= 60 - 89 ml/min/1.73m^2; CKD stage 3: eGFR= 30 - 59 ml/min/1.73m^2; CKD stage 4: eGFR= 15 - 29 ml/min/1.73m^2 and CKD stage 5: eGFR < 15 ml/min/1.73m^2 or on dialysis [5].

Diabetes complications and associated conditions

Diabetes complications and associated conditions among patients were taken from the medical history and diagnosis of patients deposited in the electronic records of the hospital information system. Complications were divided into microvascular and macrovascular complications. Microvascular complications included retinopathy, microalbuminuria, diabetic nephropathy and diabetic neuropathy. Diabetic retinopathy was defined by the presence of proliferative and non proliferative retinopathy. Nephropathy was defined by the presence of proteinuria, CKD and ESRD. Neuropathy was defined by presence of peripheral neuropathy symptoms or nerve conduction study findings, after exclusion of other causes. Macrovascular

Table 2: Lipids profile analysis among Omani T2D patients seen at SQUH.

Lipids	T2D patients (*n*)	*n* (%)
Total cholesterol (mmol/L)	908	
Desirable (<5.2)		591 (65)
Borderline high (5.2 - 6.2)		235 (26)
High (>6.2)		82 (9)
LDL cholesterol (mmol/L)	895	
Optimal (<2.59)		330 (37)
Near optimal (2.59 - 3.34)		296 (33)
Borderline high (3.35 - 4.12)		180 (20)
High (4.13 - 4.89)		57 (6)
Very high (>4.90)		32 (4)
Triglycerides (mmol/L)	907	
Normal (0.4 - 1.8)		642 (71)
High (>1.8)		265 (29)
HDL cholesterol (mmol/L)	900	
Males (n= 430)		
Low (<0.9)		121(28)
Moderately low (0.9 - 1.45)		257 (60)
Desirable (>1.45)		52 (12)
Females (n= 470)		
Low (<1.15)		171 (36)
Moderately low (1.15 - 1.68)		238 (51)
Desirable (>1.68)		61 (13)

complications included PVD, coronary artery disease (CAD), other heart related diseases, and stroke. PVD included diabetic foot, claudication symptoms, ischemic limb and gangrene. CAD included the diagnosis of acute coronary syndrome, including NSTEMI/STEMI/angina, post percutaneous coronary intervention (PCI), and post coronary artery bypass graft (CABG). Other cardiovascular diseases included diabetic cardiomyopathy, hypertensive heart disease, valve diseases and arrhythmias. Cerebrovascular disease was defined by the presence of transient ischemic attack or stroke in the past medical history. Associated conditions such as hypertension, obesity and dyslipidemia were taken as defined. Associated endocrine diseases included Cushing's disease, acromegaly and polycystic ovarian disease, which are known to be associated with diabetes. However, endocrine diseases included all endocrine diseases other than the diabetes associated diseases. Thyroid diseases were defined as any disease involving the thyroid such as hypothyroidism, hyperthyroidism or thyroid nodules.

Drugs used by the patients

Data on the drugs used by the patients were collected from the patient's medical history deposited in the hospital information system.

Statistical analysis

The SPSS statistical package software (v20.0) was used for statistical analysis of measured parameters. The measured anthropometric and biochemical parameters were tested for normal distribution using one sample Kolmogorov-Smirnov test. The mean ± SD was reported for variables following normal distribution, while the median (range) was reported for variables with skewed distribution.

Results

Demographic, anthropometric and biochemical characteristics of all participants were summarized in Table 1. In this cohort of Omani T2D patients, the mean age (±SD) was (56 ± 11) years and 48% of the patients (*n*= 470) were males. The median (range) for BMI was 30 (15 - 58) kg/m^2, for fasting plasma glucose level was 8.8 (3 - 25) mmol/L, and for HbA_{1C} was 8.2 (4.1 - 18.6) %. For lipid profile, the median (range) for serum total cholesterol was 4.7 (1.6 - 11.0) mmol/l, LDL cholesterol was 2.8 (0.7 - 8.4) mmol/l, triglycerides was 1.4 (0.4 - 32) mmol/l, and HDL cholesterol was 1.2 (0.11 - 6.1) mmol/l.

Duration of diabetes was documented for only 64% (*n*= 630) of the T2D Omani patients. Thirty four percent (*n*= 212) had diabetes for 1 - 5 years, 27.6% (*n*= 174) for 6 - 10 years, 15.6% (*n*= 98) for 11 - 15 years, 16.7% (*n*= 105) for 16 - 20 years and 6.5% (*n*= 41) had diabetes for more than 20 years.

Prevalence of T2D complications and associated conditions among Omani patients, Table 3

In a total of 986 T2D Omani patients and from the patient's medical history, half of the patients (*n*= 461) had at least one microvascular or macrovascular T2D complication, while 86% (*n*= 852) had a complication or associated condition.

Hypertension: Sixty six percent of the patients were reported to have hypertension. However, 50% (478 patients out of 964 patients) had controlled BP of <140/80 mmHg. The median (range) for systolic BP was 137 (57 - 229) mmHg, while mean diastolic BP (±SD) was 76 ± 11 mmHg. Sixty nine percent (*n*= 676) was prescribed with antihypertensive drugs, 24% (*n*= 239) were not given any antihypertensive drugs, while no drug documentation was found for the rest (*n*= 71). In those prescribed with antihypertensive drugs, 44% (*n*= 300) were prescribed with one drug, 37% (*n*= 248) with two drugs, 15% (*n*= 99) with three drugs and 4% (*n*= 29) with four drugs.

Obesity: From BMI calculation, 36% (*n*= 253) were overweight and 51% (*n*= 356) were obese, while 14% (*n*= 96) were under-weight or of normal-weight.

Dyslipidemia: From lipids profile analysis, and according to ADA criteria, 35% (*n*= 317) of these patients had high serum total cholesterol (≥ 5.2 mmol/l), 63% (*n*= 565) had high LDL cholesterol (≥ 2.6 mmol/l), 38% (*n*= 347) had high serum triglycerides (≥ 1.7 mmol/l), while, 50% and 48% of males and females, respectively, had low serum HDL cholesterol (male < 1.0 mmol/l, female <1.3 mmol/l). Statins (simvastatin and rosvastatin) were prescribed to 70% (*n*= 686) of patients.

Retinopathy: Ten percent (*n*= 99) of all patients (*n*= 986) was reported to have retinopathy. However, only 45% (*n*= 109) of those patients visiting the Diabetes Clinic at SQUH (*n*= 241), were referred to an ophthalmologist for investigations and 13% (*n*= 14) of those

Table 3: Prevalence of T2D complications and associated conditions among Omani T2D patients seen at SQUH.

T2D complications and associated conditions	Prevalence %
Hypertension	66 %
Obesity (overweight & Obese)	87 %
Nephropathy	31 %
CAD	20 %
Micro albuminuria	15 %
Retinopathy	10 %
Neuropathy	9 %
Stroke & Cerebrovascular diseases	5 %
PVD	2 %

referred to ophthalmologists were reported to have retinopathy. Many patients had an ophthalmology follow-up outside SQUH.

Microalbuminuria and nephropathy: Urine ACR and eGFR of patients indicated that 15% (*n*= 146) of Omani T2D patients had microalbuminuria and 31% (*n*= 304) had nephropathy. Fifteen % (*n*= 147) had CKD stage 2, 12% (*n*= 120) had CKD stage 3, 2.3% (*n*= 23) had CKD stage 4 and 1.4% (*n*= 14) had CKD stage 5. Twenty six percent (*n*= 253) of patients (*n*= 986) received an angiotensin converting enzyme inhibitor (ACE-I), while 36% (*n*= 355) received an angiotensin receptor blocker (ARB) [79% (*n*= 280) using one drug; 21% (*n*= 75) using two drugs].

Diabetic neuropathy: Nine percent (*n*= 90) of the 986 Omani T2D patients were reported to have neuropathy, and only 5% (*n*= 48) received neuropathy drugs (Amitriptyline, Gabapentin, Pregabalin and Duloxetine). Sixty-nine percent (*n*= 33) of those 48 patients were treated with Amitriptyline, 21% (*n*= 10) with Gabapentin and 8% (*n*= 4) with Pregabalin. Only one patient was treated with Duloxetine. However, 10% (*n*= 97) of the total 986 diabetic patients were prescribed supplements (Neurorubin and Multivitamin).

Macrovascular complications: From patients' medical records, 2% (*n*= 20) had PVD, 20% (*n*= 197) had CAD, 5% (*n*= 48) had a stroke and cerebrovascular diseases. Nine patients out of the twenty patients with PVD and diabetic foot, had an amputation. Sixty two percent (*n*= 609) of the patients were prescribed Aspirin.

Endocrine diseases: Three percent of the patients (*n*= 26) had endocrine dysfunction and 0.5% (*n*= 5) had associated endocrine diseases, while 13% (*n*= 130) had thyroid diseases.

Discussion

The risk of developing micro- or macrovacsular complications of diabetes depends on both the duration and the severity of hyperglycemia. In this study, half the Omani T2D patients, referred to SQUH, had microvascular or macrovascular T2D complication, while 86% had a complication or an associated condition. This high prevalence of complications is expected since 66% of the investigated subjects had diabetes for more than five years, and the median for fasting glucose and HbA_{1C} indicates uncontrolled glucose level.

T2D typically occurs in the setting of the metabolic syndrome, which also includes abdominal obesity, hypertension, hyperlipidemia and increased coagulability. In this study, 66% of the investigated cohort had hypertension, 36% were overweight and 51% were obese. Thirty five percent had high total serum cholesterol, 63% had high LDL cholesterol, 38% had high serum triglycerides, while 50% and 48% of the males and females respectively had low serum HDL cholesterol. Compared to diabetic patients in other populations, hypertension was reported at 44 - 75%, over-weight and obesity at 71 - 91%, high total cholesterol at 69 - 77%, high LDL cholesterol at 63-92%, low HDL cholesterol at 22 - 84% and 72 - 83 % had high TG [6- 11].

T2D also acts as an independent risk factor for the development of ischemic disease, stroke, and death [12]. In our study, 20% of the Omani T2D patients had CAD, 5% had a stroke and cerebrovascular disease and 2% had PVD. Nine patients out of twenty with PVD and diabetic foot had an amputation. According to the World Health Organization, the prevalence of CVD in diabetic patients ranges from 26 to 36% [13]. From different studies among diabetics, cardiovascular complications were reported at 10 - 27 % [6, 14-16], coronary heart disease was reported at 5 - 19% [15, 17-19], PVD was reported at 3 - 18% [15] and cerebrovascular accident was reported at 7% [15].

Diabetic retinopathy may be the most common microvascular complication of diabetes. The prevalence of diabetic retinopathy demonstrates wide variations between countries, ranges from 10 to 30% among diabetic patients at the time of diagnosis [20]. In this study, retinopathy was documented in only 10% of the investigated Omani T2D patients, which is consistent with previous studies among Omani diabetic patients that reported it at 6 - 14% [21, 22]. However, our results are inconsistent with studies among other populations, which found higher prevalence of retinopathy among T2D patients that ranged from 29% to 54% [17, 20, 23-25]. Compared to Arab countries, it was reported at 11% to 19% [19, 26-28]. In addition, diabetic retinopathy in member countries of the Eastern Mediterranean region was estimated between 10 - 64% [29]. The substantial heterogeneity in reported prevalence of retinopathy may be due to differences in the age structure of different population and to differences in study methodology and a population sample. The low frequency of retinopathy in this study is probably due to the fact that patients referred to opthalmology clinics in other Hospitals.

In this study, urine ACR and eGFR values showed that 15% and 31% of the patients had microalbuminuria and nephropathy, respectively. Twenty six percent of the Omani T2D patients were prescribed ACE-I, while 36% were prescribed ARBs. A previous study conducted in Oman reported the prevalence of microalbuminuria at 27% [30]. This is high compared to our study and that might be due to different screening procedures. However, a recent study in Oman also reported a high rate of diabetic nephropathy at 43% (microalbuminuria and macroalbuminuria) [31]. Another study conducted among 3 Arabian Gulf countries indicated that the prevalence of albuminuria was 29 to 43% [32]. Our findings are in agreement with other studies among different populations, which reported high rates of diabetic nephropathy at 31% to 53% [17, 18, 27, 33-35].

Diabetic neuropathy is recognized by the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes. As with other microvascular complications, risk of developing diabetic neuropathy is proportional to both the magnitude and duration of hyperglycemia [36]. In this study, only 9% of the Omani T2D patients was reported to have diabetic neuropathy. However, it was reported at 21% to 46% in other populations [17-19, 27, 37, 38]. Another study in Canada reported a prevalence of 15% for neuropathy in patients with established diabetes [39]. However, all these studies used different diagnostic methods to diagnose neuropathy. In our study, 5% of the 986 patients were prescribed neuropathy drugs and 10% prescribed supplements.

In general, the prevalence of diabetes micro- and macrovascular complications; and diabetes associated conditions among Omani T2D patients were not different from what was reported in other populations. However, the prevalence of retinopathy and neuropathy were lower and this could be attributed to the fact that those two complications were not documented properly in the patient's medical records.

Conclusions

Detailed clinical data from even small cohorts may enhance our understanding of the extent and nature of these conditions. In addition, proper assessment and documentation of diabetes associated conditions and complications may enhance the development and expansion of the services provided for such important cohort of patients. Therefore, comprehensive care and detailed electronic recording of diabetic patient's complications should be adopted at SQUH.

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