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ORIGINAL ARTICLE

Prevalence and risk factors for diabetic nephropathy in type 2 diabetic patients, Taif City, Saudi Arabia

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ABSTRACT

Background: Diabetes mellitus (DM) is increasing dramatically throughout the world as the number of affected adults has quadrupled since 1980 to be 422 million adults in 2016. Diabetic nephropathy (DNP) is one of the severe complications of DM and the leading cause of end-stage renal disease (ESRD) in the USA, microalbuminuria considered to be an early stage of diabetic nephropathy.

Methodology: A cross-sectional study was conducted in outpatient clinics of the diabetic center in Prince Mansour Military Hospital. Diabetes type 2 patients above the ages of 25 years who attended the clinic between November 2017 and April 2018 were included in this study. Data were collected by questionnaire and medical records were reviewed for demographic and disease-related variables. DNP was detected by measuring the albumin to creatinine ratio and diagnosed if this ratio was between 30 and 299 mcg/mg of creatinine as microalbuminuria and > 300 mcg/mg of creatinine as macroalbuminuria. ESRD was defined as GFR less than 15 ml/minute/1.73 m^2.

Results: The prevalence of DNP was 56 (18.9%) out of 296 patients. A statistically significant correlation was found between DNP and duration of diabetes and hypertension, neuropathy, HbA1c%, serum creatinine, and high-density lipoproteins. No statistical significance was found for gender, age, body mass index, retinopathy, and smoking.

Conclusion: The prevalence of DNP in patients with type 2 diabetes in Taif city was lower than in most studies conducted in our region. The study reported the need to screen for DNP in Saudi society and to improve patient's education about management of modifiable risk factors like maintaining good glycemic control and adherence to hypertension treatment to reduce the burden of future ESRD.

Keywords: Nephropathies, diabetic, Kingdom of Saudi Arabia, diabetes mellitus, noninsulin-dependent.

Introduction

Diabetes mellitus (DM) is increasing dramatically throughout the world as the number of affected adults has quadrupled since 1980 to be 422 million adults in 2016; it was mainly due to the increase in type 2-DM prevalence [1]. Also, the World Health Organization has predicted that the number of type 2-DM alone will increase by 2030 to 366 million [2]. Diabetic nephropathy (DNP) is one of the severe complications of DM and the leading cause of end-stage renal disease (ESRD) in the USA [3] and it occurs in 25%–40% of type 2-DM patients [4].

In the Middle East region, diabetes prevalence is very high averaging 10.9%, and among six Middle Eastern countries in the top 10 countries in diabetes prevalence, Saudi Arabia was ranked 2 [5]. Therefore, there is a massive increase in both diabetes mellitus and diabetic nephropathy in the last decades and it is becoming a significant cause for economic burden in the health care system in Saudi Arabia [6].

American Diabetic Association stated that screening for DNP in type 2-DM must start at the time of diagnosis,

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while type 1-DM must be screened in the first year after diagnosis [3]. There are many quantitative methods for screening of DNP in diabetic patients which include; random albumin/creatinine ratios (ACR) and the results are divided into three categories according to the American Diabetes Association; normal albumin excretion: <30 mcg/mg of creatinine, microalbuminuria: 30–299 mcg/mg of creatinine, and macroalbuminuria: >300 mcg/mg of creatinine [7]. Other methods are a 24-hour collection with creatinine and measurement of creatinine clearance or timed overnight urine collection for protein [8].

DNP is a progressive disease which starts at early stages characterized by microalbuminuria known as incipient DNP and progresses to macroalbuminuria or proteinuria and the more advanced stage known as overt DNP with or without a reduction in glomerular filtration rate (GFR) [9]. There are many risk factors for developing DNP and enhancing the development of its progression. The most affecting risk factor is the poor glycemic control that leads to microalbuminuria and progresses to later stages; other risk factors include hypertension and hypercholesterolemia [10].

There are few studies about DNP in the region despite the magnitude of the problem, so we conducted our study to assess the prevalence of DNP and to assess the common risk factors that may contribute to this issue in Taif City.

Methodology

This study was a randomized cross-sectional hospital-based study that was applied on type 2-DM patients who attended outpatient clinics of diabetic center in Prince Mansour Military Hospital (PMMH) in Taif City to assess the prevalence and risk factors of DNP.

We included all patients above 25-year-old who are pre-diagnosed with type 2-DM by their physicians and following up in the PMMH. On the other hand, we excluded patients who are diagnosed with type 1-DM, gestational diabetes, and patients who have any conditions that lead to increase in albuminuria such as acute febrile illness, urinary tract infection, hematuria, and vigorous exercise.

The ethical approval was obtained by the research ethics committee of Alhada military hospitals. The participants were randomly selected from those who are included in the study through the period from November 2017 to April 2018. The Consent form was signed from all participants after explaining the objectives of the study, and the data will be used for the research. The data were collected with the assistance of well-trained data collectors.

The questionnaire contained two parts. The first part was obtained by interview to get the demographic data, some individual characteristics, and information regarding diabetic status. Retinopathy defined using a patient's medical records documentation and we used the Douleur Neuropathique-4 questionnaire (DN4), which is a valid 10-items survey to assess the presence of diabetic neuropathy [11]. The second part is regarding some laboratory data such as random ACR, HbA1c%, and serum creatinine which were attained from the patients' files using their medical record numbers.

ACR is the amount of albumin in urine divided by the amount of creatinine in urine and used for DNP diagnosis according to the US National Kidney Foundation criteria [12]. Results were divided into three categories; normal albumin excretion <30 mcg/mg of creatinine,

Table 1. *Total participants characteristics.*

Variables		*n* (%)
Gender	Male	111 (37.5%)
	Female	185 (62.5%)
Age	Mean ± SD = 59 ± 11	
	25–44	24 (8.1%)
	45–65	175 (59.1%)
	>65	97 (32.8%)
DM duration	Mean ± SD = 13 ± 8	
	<5	27 (9.1%)
	5–10	61 (20.6%)
	10–15	109 (36.8%)
	>15	99 (33.4%)
BMI	Mean ± SD = 30.89 ± 5.92	
	Underweight = <18.5	2 (0.7%)
	Normal = 18.5–24.9	29 (9.8%)
	Overweight = 25–29.9	106 (35.8%)
	Obese = >30	159 (53.7%)
Neuropathy	Yes	161 (54.4%)
	No	135 (45.6%)
Retinopathy	Yes	174 (58.8%)
	No	122 (41.2%)
Hypertension	Yes	153 (51.7%)
	No	143 (48.3%)
Smoking	Yes	26 (8.8%)
	No	270 (91.2%)
History of myocardial infarction	Yes	42 (14.2%)
	No	254 (85.8%)
Family History of DNP	Yes	39 (13.2%)
	No	257 (86.8%)
HbA1c%	Mean ± SD = 9.09 ± 2.21	
Creatinine mol/l	Mean ± SD = 77 ± 26	
Triglycerides/mg	Mean ± SD = 148.97 ± 82.97	
Total cholesterol/mg	Mean ± SD = 174.38 ± 42.73	
High-density lipoproteins/mg (HDL)	Mean ± SD = 41.40 ± 9.29	
Low-density lipoproteins/mg (LDL)	Mean ± SD = 103.49 ± 35.89	

SD = standard deviation.

Table 2. *Comparison between participants DNP versus non-DNP demographic and clinical characters.*

Variables		Non-DNP *n* (%)	DNP *n* (%)	*p*-value
Gender	Male	85 (76.6%)	26 (23.4%)	0.125
	Female	155 (83.8%)	30 (16.2%)	
Age (years)	Mean ± SD	58.9 ± 11.3	60.2 ± 10.5	0.435
	25–44	19 (79.2%)	5 (20.8%)	
	45–65	141 (80.6%)	34 (19.4%)	
	>65	80 (82.5%)	17 (17.5%)	
Type 2-DM Duration (years)	Mean ± SD	12.6 ± 7.4	17.0 ± 7.5	0.000**
	<5	26 (96.3%)	1 (3.7%)	
	5–10	55 (90.2%)	6 (9.8%)	
	10–15	90 (82.6%)	19 (17.4%)	
	>15	69 (69.7%)	30 (30.3%)	
BMI (kg/m^2)	Mean ± SD	30.7 ± 5.7	31.6 ± 6.6	0.264
	Underweight = <18.5	1 (50.0%)	1 (50.0%)	
	Normal = 18.5–25	24 (82.8%)	5 (17.2%)	
	overweight = 25–30	86 (81.1%)	20 (18.9%)	
	Obese = >30	129 (81.1%)	30 (18.9%)	
Neuropathy	Yes	122 (75.8%)	39 (24.2%)	0.011**
	No	118 (87.4%)	17 (12.6%)	
Retinopathy	Yes	136 (78.2%)	38 (21.8%)	0.126
	No	104 (85.2%)	18 (14.8%)	
Hypertension	Yes	109 (71.2%)	44 (28.8%)	0.000**
	No	131 (91.6%)	12 (8.4%)	
Smoking	Yes	20 (76.9%)	6 (23.1%)	0.571
	No	220 (81.5%)	50 (18.5%)	
History of myocardial infarction	Yes	30 (71.4%)	12 (28.6%)	0.085
	No	210 (82.7%)	44 (17.3%)	
Family History of DNP	Yes	33 (84.6%)	6 (15.4%)	0.545
	No	207 (80.5%)	50 (19.5%)	

SD = standard deviation.
** = statistically significant (*p* value = <0.05).

microalbuminuria 30–299 mcg/mg of creatinine, and macroalbuminuria > 300 mcg/mg of creatinine [12]. ESRD was defined as GFR less than 15 ml/minute/1.73 m^2 [13].

The data were entered by Microsoft Office 2016 and analyzed using the Statistical Package for the Social Sciences (SPSS) program, version 21, developed by International Business Machines (IBM®) Corporation statistical program for analysis. Chi-squared test (χ^2) was used to look for a statistically significant association between DNP and different categorical characteristics and *t*-test for numerical variables, a *p*-value of <0.05 was considered as statistically significant.

Results

The total study sample was composed of 296 patients. The overall prevalence of diabetic nephropathy was 56 (18.9%) out of 296 patients, including [microalbuminuria 45 (15.2%), macroalbuminuria 11 (3.7%), ESRD = 0 (0%)] male participants = 111 (37.5%) and female participants = 185 (62.5%). Table 1 shows the rest characteristics of participants.

Table 2 shows 26 (23.4%) of male patients were having DNP and 30 (16.2%) of females were having DNP. Type 2 diabetic patients with nephropathy appeared to be older, with the mean of ages equals 60.29 ± 10.593 years for DNP versus 58.99 ± 11.339 years for non-DNP and had significantly longer diabetes duration as DNP = 17.00 ± 7.58 years versus non-DNP = 12.64 ± 7.464 years, Obese patients with body mass index (BMI) above 30 in DNP patients were 30 out of 56, 18.9% of all obese patients in the study.

Diabetic neuropathy was significantly associated with DNP with 39 out of 56 and 24.2% of all neuropathic patients. Hypertension was significantly correlated

Table 3. *Laboratory characteristic comparison (Mean ± SD).*

Variables	Non-DNP	DNP	*p*-value
HbA1c%	8.7 ± 2.0	10.3 ± 2.4	0.000**
Creatinine (mg/dl)	73.3 ± 22.3	90.3 ± 36.5	0.000**
Triglycerides (mg/dl)	144.7 ± 76.3	167.0 ± 105.7	0.069
Total cholesterol (mg/dl)	173.9 ± 41.3	176.2 ± 48.6	0.720
HDL (mg/dl)	41.9 ± 9.4	38.9 ± 8.1	0.027**
LDL (mg/dl)	102.4 ± 34.1	107.9 ± 42.4	0.610

SD = standard deviation.
** = statistically significant (*p* value = <0.05).

with DNP, 44 patients out of 56 DNP patients were hypertensive.

Table 3 shows the laboratory characteristic of DNP and non-DNP. The mean of HbA1c% in DNP = 10.3 ± 2.4 was significantly higher than non-DNP patients. Serum creatinine in DNP was significantly higher 90.36 ± 36.546 mg/dl *versus* 73.33 ± 22.300 mg/dl in non-DNP. Decreased high-density lipoproteins (HDL) show a statistical association with DNP with *p*-value = 0.027.

Discussion

Based on the results of this study, the total prevalence of diabetic nephropathy in type 2 diabetic patients was 18.9% (microalbuminuria = 15.2%, macroalbuminuria = 3.7%, and ESRD = 0%), which is similar to Huraib et al. [14] in Riyadh, Saudi Arabia 16.8% , Ansar et al. [15] (north of Iran) 17.2% , more than Gatling et al. [16] and Marshall and Alberti [17] (United Kingdom) 7%–9% and less than Haffner et al. [18] (Mexican Americans) 31%, Gupta et al. [19] (north India) 27%, Bamashmoos and Ganem [20] (Sana'a, Yemen) 33.5%, Alrawahi et al. [21] (Oman) 42.5%.

Variations in the prevalence can be explained by genetic susceptibility to nephropathy and prolonged diabetic duration, differences in age groups and population, the definition of diabetic nephropathy, methods of measurement, and urine collection. In the present study, a statistically significant correlation was found between diabetic nephropathy and the duration of diabetes and hypertension, neuropathy, HbA1c%, serum creatinine, and HDL.

There was no statistical significance to age in this study, which was supported by multiple studies [22],which was contrary to other studies that provided statistical significance to age [23]. It is implied due to the variations in the prevalence of DNP and the mean of patients' ages that were reported in these previous studies.

Prevalence of DNP shows no statistical significance with genders in this study. Similar to Lutale et al. [22] and some other studies [23], in contrast, the prevalence of DNP was statistically significant among male like in Mather et al. [24], and in other studies among female as in Alfehaid [25]. This could be due to different ways of samples selection or certain differences in population or behaviors.

Our study found that the mean duration of diabetes in DNP patients was 17 ± 7.59 years and non-DNP was 12.64 ± 7.46 years, and this was significantly higher and associated with nephropathy with a p-value < 0.05, this was similar to previous different studies [26]. While there are studies that showed no association with duration [22,23] that may have explained by late diagnosing of DM as the diagnose established with present complication. Hence, early screening of DM should be performed, as following of American Diabetes Association recommendations [27].

In this study, hypertension shows a highly significant association with nephropathy with a p-value < 0.000, as in most other studies [18], which suggest that the increase in systemic blood pressure the systolic pressure can cause intra renal damage that affects glomerular circulation leading to albuminuria [28].

In this present study, poor glycemic control was indicated by HbA1c% and the mean value of HbA1c% for DNP group was 10.33 ± 2.49 and non-DNP was 8.79 ± 2.03, this was significantly higher in nephropathic compared to the non-DNP group with p-value ≤ 0.000. This finding was similar to other studies [29], prolonged hyperglycemia can effect on glomeruli and mesangial cells, ends by thickening the glomerular basement membrane and mesangial cell expansion; hence, DNP appears to be a complication to poor glycemic control [30].

In this present study, serum creatinine is significantly higher in DNP patients compared to non-DNP with p-value = 0.000, the mean value in DNP = 90.36 ± 36.54 mg/dl *versus* 73.33 ± 22.30 mg/dl for non-DNP. High serum creatinine is a sign of renal damage and indicates to low kidney function; many studies show the same result where diabetic patients with high albuminuria have high serum creatinine [22,23].

Our study failed to show a significant difference in lipid profile for diabetic nephropathy patients, except for HDL. The mean in triglycerides, total cholesterol, and LDL was higher in the DNP group but not statistically significant, other study mentions that the dyslipidemia is a predictor for microalbuminuria or nephropathy [22], this variant result may occur due to differences in level of health care and physical activity, BMI, eating habits, and using of statins.

Limitations

Although this study was well prepared, it is still considered with some limitations. The study was conducted in a single hospital in Taif City. The sample size was somewhat smaller to be generalized on the population of the region due to time restrictions and limited data collectors. Further studies need to be conducted with

a larger sample size to apply investigation on and generalize its result.

Conclusion

In conclusion, diabetic nephropathy prevalence is 18.9%, prolonged duration of diabetes, hypertension, poor glycemic control, dyslipidemia, especially in HDL were significant associated risk factors. Screening for diabetes should be performed for early diagnosis. Diabetic patients have to be educated about the modifiable risk factors for primary prevention. Maintaining good glycemic control, adherence to hypertension treatment, early detection of low kidney function can decrease the prevalence of diabetic nephropathy.

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Declaration of conflicting interests
None.

Consent for Publication
Informed consent was obtained from all the participants.

Ethical Approval
The study was approved by Ethical Committee, Armed Forces Hospital, Taif region via Ref: PTRC #H-02-T-001 17-10-301, dated 23 Nov 2017.

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