

Prevalence and Risk Factors of Chronic Kidney Disease among Palestinian Diabetic Patients: a Cross Sectional Study

Zaher Nazzal (✉ znazzal@najah.edu)

An-Najah National University <https://orcid.org/0000-0002-2655-6109>

Zakaria Hamdan

An-najah National University Faculty of Medicine and Health Sciences

Donia Masri

An-najah National University Faculty of Medicine and Health Sciences

Oday Abu-Kaf

An-najah National University Faculty of Medicine and Health Sciences

Mohammad Hamad

An-najah National University Faculty of Medicine and Health Sciences

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Abstract

Background

Chronic kidney disease (CKD) is a worldwide public health problem and diabetes is one of major risk factor for its development and progression. The aim of this study is to assess the prevalence of chronic kidney disease in a cross-sectional population of patients with type 2 diabetes treated in primary health care centers in North West Bank.

Methods

Patients' data including patient characteristics, creatinine level, blood pressure, HbA1c, and hypertension and diabetes duration was collected from primary health care centers. eGFR was calculated using the CKD-EPI equation. CKD was staged according to the Kidney Disease Improving Global Outcomes System (KDIGO) 2012 guidelines. Both univariate and multivariate statistical analysis was conducted using SPSS.

Results

The prevalence of chronic kidney disease among diabetic adults in North West Bank was found to be 23.6% (95% CI: 19.4%-28.1%) distributed as follows: 19.7% had stage 3 CKD, 2.6% had stage 4 CKD and 1.3% had stage 5 CKD. In multivariate logistic regression, CKD was significantly associated with hypertension [adjusted OR= 4.43, P value=0.005], smoking [adjusted OR= 2.1, P value=0.01], and age [adjusted OR= 1.1, P value <0.001]

Conclusions

CKD is highly prevalent among Palestinian diabetic adults. Co-morbid hypertension, smoking and older age were found to increase the probability of developing this condition. Intensive screening for diabetic patients to detect CKD at earlier stages and implementation of more aggressive treatment modalities for diabetes as well as other important risk factors, especially hypertension and smoking are recommended.

Background

Non-communicable diseases, such as diabetes and kidney disease, are the leading cause of mortality and morbidity worldwide [1]. Diabetes Mellitus (DM) is recognized as the world's fastest growing chronic condition. Worldwide, 1 in each 11 adults has DM, 90% of whom have Type 2 Diabetes Mellitus (T2DM). This number has actually increased tremendously in the last three decades owing to the increasing rates of sedentary lifestyle, unhealthy diet, smoking and alcohol consumption [2]. Unfortunately, all Arab states in The Middle East and North African region are burdened with the second highest diabetes prevalence rate [3]. Among the Palestinians living in the West Bank, the prevalence of T2DM was 15.3% in 2010 and it is predicted to increase up to 20.8% and 23.4% in the years 2020 and 2030 subsequently[4].

The chronic hyperglycemia of DM is known to be, besides hypertension (HTN), one of the leading causes of Chronic Kidney Disease (CKD); which is defined as a progressive loss in renal function over a period of more than three months, where kidney's ability to filter blood or perform other activities is impaired. This is usually associated with a reduction in glomerular filtration rate (GFR) and proteinuria[5].

CKD is a worldwide public health problem, both for its high morbidity and cost of treatment. Outcomes of CKD include not only progression to kidney failure but also complications of reduced kidney function and increased risk of cardiovascular disease and all-cause mortality overall[6]. The Global Burden of Disease 2015 study estimated that, in 2015, 1.2 million people died from kidney failure, an increase of 32% since 2005[7]. Unfortunately, renal disease in its mild form is commonly under-diagnosed and undertreated, especially in the Arab, world resulting in lost opportunities for prevention [8].

Many of the complications of CKD can be prevented or delayed by early detection and treatment. As well, early diagnosis of kidney disease can slow down or avert worsening of kidney functions by inexpensive interventions, several of which are on the WHO's so-called best buys list for noncommunicable disease management [9].

In the Middle East, there is a lack of data about the prevalence of CKD among diabetic patients. However, the prevalence of CKD among the general population was 6.8% in Jordan, 5.7% in Saudi Arabia[10] &14.9% in Iran[11].

Common risk factors including greater duration of DM, HTN, poor metabolic control, smoking, obesity and hyperlipidemia had been suggested to increase the risk of developing diabetic complications. Blood pressure (BP) and glycemic control are shown to cause more kidney damage and subsequent decrease in kidney function. Similarly, some background variables proved to be positively associated with CKD such as age, smoking, and BMI [12–14].

In North West Bank, a study was conducted in 2008 on diabetic hypertensive patients, reported that 35.5% of DM and HTN patients had reduced renal function that is significantly associated with patients age, duration of DM and the number of chronic diseases[15].

GFR is the best measure of kidney function since it accounts for age, race and sex. Currently the two most common methods for determining GFR are creatinine clearance and estimated GFR (eGFR)[16]. Formula-derived eGFR results have become widely used in clinical practice and have been recommended by the National Service Framework for Renal Services in the U.K in the annual evaluation of all patients with diabetes (Department of Health Renal Team [17]).

It is important to identify the risk factors of renal function deterioration for development of prevention interventions in diabetic patients' management and to prevent its complications. The aim of this study is to estimate the prevalence of CKD among Palestinian diabetic patients, and to assess the associated risk factors.

Methods

Study design and population

This is a cross-sectional study targeted Palestinian diabetic adult patients from the West Bank. In Palestine, all patients diagnosed with DM are referred to primary health care (PHC) directorates, in their cities, where they receive their diabetes care, treatment and follow up on regular basis. Patients with T2DM and age > 18 were included in the study. However, type 1 diabetes mellitus, gestational diabetes mellitus, pregnant women and patients who didn't have at least 2 serum creatinine readings at least 3 months apart were excluded from the study.

The Cochran's sample size formula was used to calculate the sample size [Necessary Sample Size = $(Z\text{-score})^2 * \text{Std Dev} * (1 + \text{Std Dev}) / (\text{margin of error})^2$]. A sample size of 385 patients was calculated assuming a 95% confidence level, 0.5 standard deviation and a margin of error $\pm 5\%$.

Patients were randomly selected as they attended their PHC clinics. The data were collected between September 2018 and December 2018 by personal interviews and from the electronic records of the patients.

Serial serum creatinine data were collected and eGFR was determined using Chronic Kidney Disease Epidemiology Collaboration formula based on serum creatinine (CKD-EPI_{Cr}). CKD was defined as having a decreased eGFR (< 60 ml/min per 1.73 m²) for 3 months. CKD stage was defined in accordance with the guideline of National Kidney Foundation [5], which stage 1, 2, 3, 4, and 5 had a eGFR of ≥ 90 , 60 to 90, 30 to 59, 15–29, and < 15 ml/min per 1.73 m² or commencement of dialysis therapy, respectively. Prevalence of CKD was determined using the National Kidney Foundation Kidney Disease Outcomes Quality Initiative Classification of CKD based on eGFR alone. Albuminuria marks CKD stages 1 and 2, however, it was missing most of enrolled patients and thus it was not considered to determine CKD stages.

Participants were considered diabetics if they already had a diagnosis of T2DM or were taking insulin or oral hypoglycemic agents. We defined patients as hypertensive if they were previously diagnosed with HTN or taking antihypertensive medications. Obesity was defined as BMI ≥ 30 .

Measures

Blood pressure measurements were taken by a trained nurse using an electronic sphygmomanometer. The height and weight were taken at the time of interview and were used to calculate the BMI. Creatinine readings were obtained from the medical records using at least 2 readings at least 3 months apart and the CKD-Epi formula was used to calculate eGFR. Patients with eGFR < 60 ml/min/1.73m² were considered to have CKD. The last available HbA1c reading was used.

Approvals from Al-Najah National University Institutional Review Board (IRB) and the Palestinian Ministry of Health were taken. All subjects approached for the study were invited to participate voluntarily after being explained the study aim, risk and benefit of participation. Informed consent was obtained from all individual participants included in the study.

Statistical analysis

Statistical analysis was conducted using the SPSS version 20.0. Categorical data were expressed as number (percentage) and continuous data as means \pm standard deviation unless otherwise stated. Differences in patient's characteristics and risk factors for CKD were studied using chi-square test and T-test, as appropriate. Statistical significance is taken at p value of < 0.05 . Additionally, multivariate logistic regression was conducted to control for possible confounders.

Results

Study population:

The study recruited 386 patients with T2DM from PHC clinics in North West Bank. Almost half the participants were male (49.7%) and their mean age was 60.6 ± 10.4 years. HTN was reported in 278 (75.3%) participants, with a mean duration of 6.78 ± 7.7 years. The mean duration of diabetes was 12.4 years (3.9 years to 20.9 years) and their HbA1c level ranged from 6.39–10.47% with an average of $8.4\% \pm 2.0$. The majority of the participants was obese and 30.4% were smokers. Table 1 presents the clinical and background data of the patients.

Table 1
Clinical and Background characteristics of the participants (n = 386)

Characteristics	Frequency	Percentage
Gender		
Male	192	49.7%
Female	194	50.3%
Hypertension		
Yes	278	75.3%
No	91	24.7%
Smoker		
Yes	113	30.4%
No	259	69.6%
Systolic BP mmHg (Mean ± SD)	137.7 ± 18.2	
Diastolic BP mmHg (Mean ± SD)	77.3 ± 11.1	
Age years(Mean ± SD)	60.7 ± 10.4	
BMI (Mean ± SD)	32.7 ± 5.8	
HbA1c % (Mean ± SD)	8.4 ± 2.04	
Estimated GFR(ml/min/1.73m ²)	75.3 ± 24	
DM Duration (years) (Mean ± SD)	12.4 ± 8.5	
HTN Duration (years) (Mean ± SD)	6.8 ± 7.7	

Frequency Of Chronic Kidney Disease

Using the CKD-EPI equation, the eGFR mean (± SD) for the all participants was 75.3 ± 24. Estimated GFR ≥ 60 ml/min/1.73 m² was reported among 295 (76.4%) diabetes patients. CKD Stages 3, 4, and 5 were present in 19.7%, 2.6%, and 1.3% of the participants, respectively. In total, the prevalence of Impaired Renal Function (CKD stages 3–5) among T2DM patients was 23.6% (95% CI: 19.4%-28.1%) (Fig. 1).

Table 2 shows the average eGFR in relation to clinical and background variables. A significant decrease in eGFR was noted as the age, SBP, duration of HTN, and duration of DM increases (p value < 0.001).

Table 2
Clinical and background variables of each eGFR category

eGFR Stage (n)	GFR ≥ 90 (n = 127)	GFR = 60–89 (n = 168)	GFR = 30–59 (n = 76)	GFR = 15–29 (n = 10)	GFR < 15 (n = 5)	P value*
eGFR (Mean ± SD)	(100.2 ± 7.8)	(75 ± 8.5)	(45.5 ± 7.9)	(20.4 ± 3.5)	(10.8 ± 1.8)	
Age (years)(Mean ± SD)	53.1 ± 9.4	63.2 ± 8.9	67.2 ± 7.3	62.1 ± 9.8	65 ± 12.5	< 0.001
Systolic BP (mmHg)(Mean ± SD)	133 ± 16.5	139.3 ± 17.7	139.2 ± 19.9	153 ± 15.6	154 ± 22	< 0.001
Diastolic BP (mmHg)(Mean ± SD)	77.7 ± 11.4	76.5 ± 11.2	77.5 ± 10.5	80.1 ± 14	81.4 ± 6.8	0.883
Hypertension Duration (years) (Mean ± SD)	6.5 ± 5	9.0 ± 7.4	11.0 ± 9	11.6 ± 13.3	12.6 ± 6.8	0.013
HbA1c (%) (Mean ± SD)	8.58 ± 2	8.38 ± 1.98	8.57 ± 2.2	7.3 ± 1.7	6.4 ± 1.14	0.057
Diabetes Duration (years) (Mean ± SD)	9.3 ± 6.6	12.9 ± 8.4	14.9 ± 8.8	16.8 ± 13.2	21.4 ± 9.8	0.007
*Kruskal Wallis test. BP = Blood Pressure. eGFR = estimated glomerular filtration rate.						

Univariate analysis was conducted to explore the factors associated with the development of CKD. The results showed that CKD is significantly associated with HTN ($p < 0.001$), smoking ($p = 0.022$), age ($p < 0.001$), DM duration ($p < 0.001$) and HTN duration ($p < 0.001$). However, HbA1c and BMI showed no significant relation with CKD, as shown in Table 3.

Table 3
Comparison between patients with Chronic Kidney Disease and preserved GFR (n = 386)

Variables	Chronic Kidney Disease		P Value
	Yes (n = 91)	Yes (n = 91)	
	Frequency (%)	Frequency (%)	
Gender			
Female	43 (22%)	151 (78%)	0.550**
Male	48 (25%)	144 (75%)	
Hypertension			
Yes	85 (30.6%)	193 (69.4%)	< 0.001**
No	05 (5.5%)	86 (94.5%)	
Smoker			
Yes	36 (31.85%)	77 (68.14%)	0.022**
No	55 (21.2%)	204 (78.76%)	
Age (Mean ± SD)	66.5 ± 7.9	58.8 ± 10.4	< 0.001*
BMI (Mean ± SD)	33 ± 5.82	32.5 ± 5.84	0.508*
Diabetes duration (Mean ± SD)	15.46+/-9.4	11.43+/-7.96	< 0.001*
Hypertension duration (Mean ± SD)	10.54+/-9.38	5.57+/-6.68	< 0.001*
HbA1c (Mean ± SD)	8.31 ± 2.2	8.47 ± 2	.527*
SD = standard deviation, *Independent t-test, ** chi-square, BMI = Body Mass Index, HbA1c = glycosilated hemoglobin			

To control for cofounders, multivariate logistic model was conducted. All variables with P value < 0.10 in the univariate analysis were included in the multivariate regression model. Older age (OR: 1.1, 95% CI: 1.05–1.12), HTN (OR: 4.43, 95% CI: 1.59–12.39) and smoking (OR: 2.10, 95% CI: 1.2–3.7) are found to increase the risk of CKD.

Table 4
Multivariable model of factors independently associated with Chronic
Kidney Disease

Variables	P Value	Adjusted OR (95% CI)
Hypertension		
Yes No ¹	0.005	4.4 (1.59–12.39)
Smoker		
Yes No ¹	0.010	2.1 (1.12–3.72)
Age (Mean ± SD)	< 0.001	1.1 (1.05–1.12)
Diabetes duration (Mean ± SD)	0.075	1.1 (0.99–1.06)
Hypertension duration (Mean ± SD)	0.156	1.1 (0.99–1.06)
SD = standard deviation, OR = Odds Ratio, CI = Confidence Interval		

Discussion

Worldwide, over 200 million people are estimated to suffer from CKD that are susceptible to develop End-stage Renal Disease (ESRD) if no action is done to diagnose and treat them in early stages[18]. ESRD represents the tip of the iceberg and the actual number of patients with CKD is a lot more. Studying the prevalence of CKD in Palestine is important as it helps in early detection and thus prevention and control diabetic nephropathy.

To the best of our knowledge, this study was the first epidemiological investigation on CKD prevalence among Palestinian diabetic patients attending primary care consults. It showed that 23.6% (95%CI 19.1–28.4) of diabetic patients in the North West Bank have CKD. Sweileh et al reported a prevalence of 35.5% of CKD in Palestine in 2008[15]. However, this study was carried out among diabetic hypertensive patients and targeted hospitalized diabetic patients, which explain the difference in the prevalence rate. Additionally, it used only one creatinine reading which would have been probably representing acute rather than chronic kidney injury.

Results on the prevalence of CKD among diabetic patients are variable; like Finland (16.2%) [19], Southern Ethiopia (23.4%) [20] Spain (27.9%)[21]. Unfortunately, similar data from the surrounding countries is lacking. This variation on the prevalence of CKD among Diabetic patients is attributed to difference in the definitions adopted and the characteristics of the studied populations.

Studying the risk factors associated with CKD, especially the modifiable factors, is important to develop prevention and control interventions. The prevalence rate of HTN reported in this study among patients

with type 2 diabetes (75%) was high. It is more than what have been reported in the neighboring countries; Jordan (72.4%)[22], Qatar (64.5%)[23] and Saudi Arabia (53%)[24]. This relatively higher rate of HTN could be related to the fact that most diabetic patients included in the study were obese and aged > 60 years.

This study showed a significant relation (P Value < 0.001) between BP and the kidney damage, reflected by decreased eGFR as systolic BP increases (Table 2). Diabetic patients with HTN are 4.4 more times prone to develop CKD compared to diabetic patients with normal BP. These findings are consistent with literature from different countries [14, 19, 21]. This risk of CKD and kidney damage can be further increased as the age increases. There is a great overlap between HTN and impaired renal function. The patient goes into a vicious cycle where decreased kidney function causes an elevation in BP and this elevation will cause further kidney damage and subsequent decrease in the kidney function.

The high prevalence of HTN among our patients is alarming and should be taken into consideration, as many studies reported the relation between high BP and development of ESRD. A study in Japan showed that patients with high BP have 15 times more chances of developing ESRD in comparison to patients with controlled BP (= 110/70) [25]. This is important and more attention should be focused toward a better BP control among diabetic patients.

In this study, 30.4% of the patients were smokers; higher proportion of them among the CKD group (39.6%). Smoking did correlate with renal function progression in this study (P value = 0.022). The association between smoking and presence of CKD among diabetic patients is clearer, with most of the studies showing a significant relationship between these two variables. Recently two meta-analysis suggested evidence for cigarette smoking as an independent risk factor for CKD[13, 26]. Xia et al reported that compared with never-smokers, the risk of incident CKD were 1.27 (95% CI 1.19–1.35) for ever-smokers, 1.34 (95% CI 1.23–1.47) for current smokers and 1.15 (95% CI 1.08–1.23) for former smokers [13]. The not well understood nephrotoxic effect of smoking that includes endothelial cell dysfunction and the increased insulin resistance regardless of the diabetic status can explain this finding[13].

Regarding age, it was found to be a significant risk factor (P value < 0.001). This can be explained by the steady decline in GFR with normal aging; a process that is accelerated by superimposing factors like diabetes. Many studies reported age as a risk factor for CKD among diabetic patients [11, 14, 19, 20]. Additionally, as noted in Table 2, a significant decrease in eGFR was reported as the age increases. These results indicate the need for robust screening of diabetic patients with focusing on elderly patients.

The average BMI of diabetic patients, in this study, was 32.5 kg/m² (± 5.8) without significant correlation with the renal function (P value = 0.508). There are inconsistent results regarding the relationship between obesity and CKD, where many studies, like Framingham study [27], show a positive association between BMI and CKD. Another study in UK showed that there is an increasing risk of CKD with increasing the weight [18]. In the other hand, a study in Thailand found a negative association between BMI and CKD, with which was owed to reverse causality where patients with advanced CKD may have a reduced BMI due to their disease [14]. These variations in results question the reliability of BMI for predicting CKD

among diabetic patients. However, it should be noted that the BMI in the whole sample was high, which means that patients should be advised and counseled to lose more weight in the primary health care clinics.

HbA1c is a recommended standard of care to monitor diabetes. In this study, the mean HbA1c was 8.31%, but it was not significant to the presence of CKD (P value = 0.527). Increasing evidence shows a link between the glycemic environment and the renal damage. As in obesity, there are conflicting data regarding this association. A study in Spain showed that HbA1c levels were significantly higher among CKD diabetic patients (OR = 1.011, 95% CI 1.005–1.017, P < 0.001) [21]. However, other studies showed no significance increase in HbA1c level among CKD diabetic patients [20]. This results can be partially explained by the physiologic improvement of HbA1c due to the decreased insulin excretion by the kidneys in patients with impaired renal function [29].

In this study there was no association between gender and CKD (P value = 0.384). The relation between gender and CKD among diabetic patients is inconsistent in the literature. Many studies showed the female gender as a risk factor [11, 14, 19]; however, others reported the male gender as a risk factor[21]. This may be due the distribution of risk factors, like obesity and T2DM control status, between genders.

There were some limitations in this study. First, being a cross sectional study, not longitudinal, precludes any causal relationship between impaired renal function and their risk factors. Secondly, due to the low resources in the primary care settings there is a lack of data regarding proteinuria and renal biopsy which made it difficult to diagnose stage 1 CKD.

Including the diagnosis of CKD based on eGFR on multiple measures to establish chronicity, and conducting the study in PHC centers where almost all diabetic patients in Palestine receive, for free of charge, their preventive and curative services are the main strengths of our study.

Conclusions

This study demonstrates a high prevalence (23.6%) of CKD among diabetic patients in Palestine. The rate is higher among hypertensive patients and increase with age. We recommend intensive screening for diabetic patients to detect CKD at earlier stages and implement more aggressive treatment modalities for diabetes as well as other important risk factors, especially HTN and smoking. We also recommend studying the effect of anti-diabetic and anti-hypertensive medications on the rate of renal function deterioration and to check treatment compliance in these patients, in addition to assessing the mortality rate and progression to ESRD and dialysis in each eGFR category.

List Of Abbreviations

CKD	Chronic Kidney Disease
BP	Blood Pressure
DM	Diabetes Mellitus
ESRD	End-stage Renal Disease
eGFR	estimated GFR
GFR	Glomerular Filtration Rate
HTN	Hypertension
PHC	Primary Health Care
T2DM	Type 2 Diabetes Mellitus

Declarations

Ethics and Consent

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study was approved by the Institutional Review Board of Al-Najah National University. All subjects included in the study were invited to participate voluntarily after being explained the study aim, risk and benefit of participation. Informed consent was obtained from all individual participants included in the study.

Consent for Publication:

Not applicable

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request

Competing Interest

The authors declare that they have no competing interests in this section.

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Author contributions

ZN and ZH Participated in conceiving and study design, supervised data collection, data analysis, manuscript writing. ZN, DM, MH, and OA performed the material preparation, data collection and analysis. All authors interpreted the results. The first draft of the manuscript was written by [Dunia Masri] and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript

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Figures

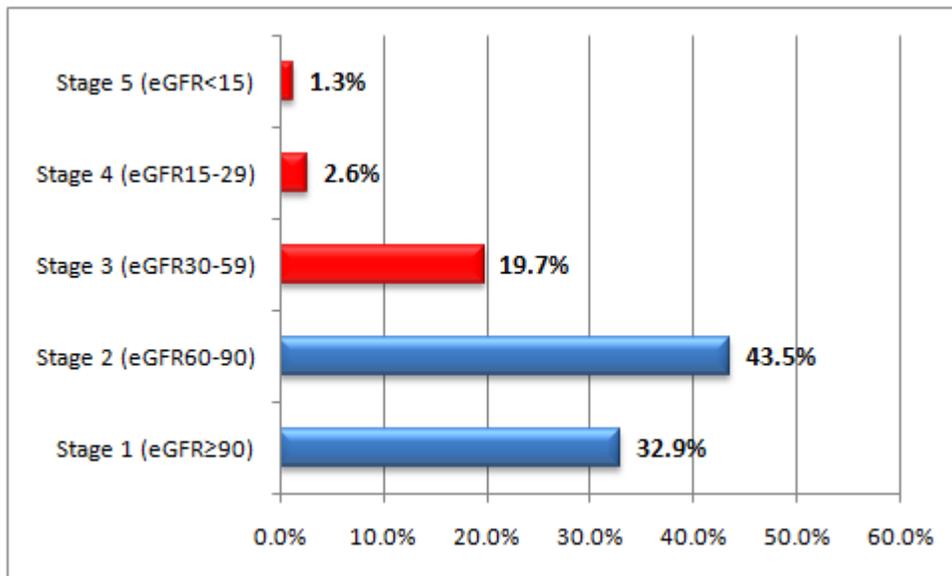


Figure 1

Frequencies of CKD stages based on eGFR (n=386).