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IDENTIFYING RISK FACTORS ASSOCIATED WITH DIABETIC KIDNEY DISEASE IN TYPE 2 DIABETICS: A SINGLE-CENTER STUDY

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Abstract

Objective: To determine and assess the risk factors for diabetic kidney disease in individuals with type 2 diabetes.

Methodology: The prevalence of risk factors for diabetic kidney disease (DKD) was examined in this cross-sectional study, which used data collected in the duration from January, 2018 to July, 2018 among type 2 diabetes mellitus (T2DM) patients of 18 years or above age, pursuing medical treatment at the Medicine Department of Medical B Unit, Lady Reading Hospital Peshawar, Pakistan. Excluded were patients with incomplete data, end-stage renal disease (ESRD) on dialysis, and other etiologies of chronic kidney disease (CKD) or proteinuria. Informed consent was obtained, and the study adhered to ethical standards. Data on medical history, comorbidities, glycemic control, medication use, lifestyle factors, physical measurements, and laboratory parameters were collected. DKD was defined as per established criteria. SPSS version 23.0 was used for the statistical analysis, with a significance level of $p < 0.05$.

Results: Of the 163 T2DM patients in this study, 42.94% had DKD. DKD was significantly associated with age over 50 (82.86% vs. 48.39% in non-DKD patients), female gender (68.57% vs. 31.43% in males), diabetes duration over 10 years (57.14% vs. 30.11%), hypertension (82.86% vs. 55.91%), and peripheral neuropathy (57.14% vs. 21.51%). DKD patients had higher BMI (50.00% vs. 19.35% in non-DKD patients) and waist circumference (mean 37.8 cm vs. 33.8 cm in non-DKD patients), along with insulin therapy (64.29% vs. 32.26% in non-DKD patients) and elevated HbA1c levels (85.71% with HbA1c ≥7% vs. 46.24%). Adverse lipid profiles were observed in DKD patients, with higher LDL and triglycerides, and lower HDL levels. DKD patients exhibited elevated serum creatinine (1.7± 0.7mg/dL vs. 1.2± 0.5mg/dL in non-DKD patients), lower serum albumin (3.5± 0.4g/dL vs. 4.0± 0.5g/dL in non-DKD patients), higher ACR (42.86% with ACR ≥300 mg/g vs. 16.13%), and low eGFR (71.43% vs. 19.35%).

Conclusion: According to our research, diabetic people have a notable tendency to develop diabetic kidney disease (DKD) (42.94%), with older age, longer diabetes duration, hypertension, peripheral neuropathy, and dyslipidemia as key associated factors. Elevated HbA1c levels, reduced eGFR, and high albuminuria prevalence underscore DKD severity. This emphasizes the critical need for

comprehensive management, including stringent glucose control, blood pressure regulation, and lipid management, with regular kidney function monitoring. These proactive measures can potentially curb DKD progression and improve health outcomes for diabetic patients in Pakistan.

Keywords: Hypertension, Obesity, Diabetes, Diabetic Kidney Disease, ACR, eGFR.

Introduction

Diabetes mellitus (DM) poses a growing healthcare challenge worldwide, with Pakistan facing a significant problem due to its growing pervasiveness and associated complications. The vast majority of cases of diabetes worldwide are caused by type-2 diabetes (T2DM), and Pakistan is no exception, experiencing a rising number of T2DM diagnoses, particularly in urban areas.[1-2] This surge in T2DM prevalence, coupled with inadequate healthcare infrastructure and limited resources, exacerbates the challenge of managing diabetes-related complications, including diabetes related kidney damage.

One of the main long-term consequences of type 2 diabetes is diabetic kidney disease (DKD), which is the primary cause of both end-stage renal disease (ESRD) and chronic kidney disease (CKD).[3-4] Despite the gold standard for diagnosing diabetic nephropathy being renal biopsy, its limited availability and invasive nature hinder its widespread use. Consequently, many patients with diabetes are diagnosed with DKD based on clinical presentations and laboratory assessments, potentially leading to underdiagnosis or misclassification.[5]

Effective therapy and preventative efforts for T2DM patients require an understanding of the occurrence and associated risks related with DKD.[6] However, similar to global trends, the incidence and progression of DKD in the context of T2DM in Pakistan are not fully elucidated, partly due to challenges in defining disease onset and assessing associated comorbidities. Moreover, there exist significant racial and ethnic differences in the DKD epidemiology, influenced by differences in healthcare access, environmental factors, dietary habits, and smoking prevalence.[7-8]

As the prevalence of T2DM continues to rise, driven by urbanization, lifestyle changes, and genetic predispositions, the need to address DKD becomes increasingly urgent.[9] Projections suggest that by 2030, Pakistan will see a substantial increase in the diabetic population, elevating the risk of complications caused by diabetes, including the renal impairment.[10]

The purpose of this study is to look into the risk factors, features, and prevalence of DKD among T2DM patients in Pakistan. By examining these factors, the study seeks to inform healthcare policies, enhance patient education, and guide clinical decision-making to mitigate the burden of DKD. Furthermore, the study will explore the implications of its findings for healthcare providers and patients, offering insights into potential interventions and strategies to improve outcomes for individuals with diabetes-related kidney disease in the country.

Objective

To determine and assess the risk factors for diabetic kidney disease in individuals with type 2 diabetes.

Study Design and Methods

The prevalence of risk factors for diabetic kidney disease (DKD) was examined in this cross-sectional study, which used data collected in the duration from January, 2018 to July, 2018 among type 2 diabetes mellitus (T2DM) patients of 18 years or above age, pursuing medical treatment at the Medicine Department of Medicine Department of Medical B Unit, Lady Reading Hospital Peshawar, Pakistan. Patients with incomplete data (fewer than two serum creatinine or urine albumin protein readings within six months), end-stage renal disease (ESRD) on dialysis, and other etiologies of chronic kidney disease (CKD) or proteinuria were omitted. Informed consent was attained from study participants, and the Ethical Review Committee of the institute provided the approval.

Data Collection and Assessment

A research assistant identified and confirmed those who had type 2 diabetes mellitus (T2DM) during hospital visits using health records. Interviews with patients and an examination of their medical

documents were used to gather data. The collected data included past medical history and co-morbidities such as hypertension, stroke, myocardial infarction, diabetes onset, and peripheral neuropathy. Glycemic control was assessed using the latest hemoglobin A1c (HbA1c) values. Medication use was documented, including anti-diabetics, anti-hypertensives, statins, and other medicines.

Lifestyle factors were also recorded, focusing on smoking status. Physical measurements included blood pressure, with abnormal readings defined as more than 140/90mmHg, body mass index (BMI) with obesity demarcated as BMI over 30kg/m², and waist circumference, considering more than 35cm in females and more than 40cm in males as abnormal. Laboratory data collected within 3 to 6 months of the visit included HbA1c, fasting lipid profile (HDL, triglycerides, LDL), and serum albumin levels. Urinary albumin excretion and serum creatinine levels obtained within three months intervals were used to evaluate kidney function.

Standardized levels of creatinine in the serum and the CKD-EPI formula were used to compute the estimated glomerular filtration rate, or eGFR. The two types of albuminuria were identified as macroalbuminuria (ACR ≥300 mg/g) and microalbuminuria (albumin-to-creatinine ratio [ACR] ≥30 and ≤300 mg/g). Urinary samples positive for leukocytes, nitrites, erythrocytes, or hemoglobin levels ≥5 counts/μL were excluded to avoid false positives due to infections or hematuria.

When combined with long-standing diabetes and the rule out other causes of chronic kidney disease (CKD), diabetic kidney disease (DKD) was defined as an eGFR of less than 60 mL/min/1.73 m² and/or urine albumin excretion of 30 mg/g creatinine or more, enduring for at least three months.

Data Analysis:

The SPSS version 23.0 was used to analyze the data. For numerical data, the mean and standard deviation were calculated; for categorical data, frequencies and percentages were shown. When utilizing the chi-square test to compare data, a p-value of less than 0.05 was deemed significant.

Results

Among the 163 patients enrolled in the study, 70 (42.94%) were diagnosed with diabetic kidney disease (DKD), while 93 (57.06%) were not. Patients over 50 years old were significantly more likely to have DKD, with 82.86% of DKD patients falling into this age group compared to 48.39% of non-DKD patients ($p < 0.001$). DKD was more common in women (68.57%) than in men (31.43%), according to a gender study ($p = 0.012$).

The duration of diabetes was also a significant factor, with 57.14% of DKD patients having had diabetes for more than 10 years compared to 30.11% in the non-DKD patients($p < 0.001$). Hypertension was more common in the DKD patients (82.86%) versus non-DKD patients (55.91%) ($p < 0.001$). Peripheral neuropathy was predominantly associated with DKD, affecting 57.14% of DKD patients compared to 21.51% of non-DKD patients ($p < 0.001$).

There was no discernible variation in the groups' smoking status. In terms of BMI, a higher percentage of DKD patients had a BMI over 30 kg/m² (50.00%) compared to non-DKD patients (19.35%) ($p < 0.001$). Waist circumference was considerably higher in the DKD group, with a mean of 37.8 ± 5.1 cm in contrast to 33.8 ± 4.8 cm in the non-DKD group ($p < 0.001$).

Medication use showed that insulin therapy was more prevalent among DKD patients (64.29%) than non-DKD patients (32.26%) ($p < 0.001$). The non-DKD group used metformin at a higher rate (86.02%) than the DKD group (71.43%) ($p = 0.014$). The non-DKD group had a substantially higher frequency of combination therapy with empagliflozin (32.25%) compared to the DKD group (14.28%) ($p < 0.001$). The use of ACE inhibitors or ARBs was similar between the groups. Table 1 illustrate these findings which highlight the significant associations of advanced age, female sex, longer duration of diabetes, hypertension, peripheral neuropathy, higher BMI, and specific medication use with the presence of DKD.

Table 1: Study Population baseline characteristics

Variable	Sub-groups	Total N=163 (100%)	DKD Present N=70 (42.94%)	DKD Not Present N=93 (57.06%)	p-value
Age	Below 50 years	60 (36.81%)	12 (17.14%)	48 (51.61%)	<0.001
	Above 50 years	103 (63.19%)	58 (82.86%)	45 (48.39%)	
Gender	Male	70 (42.94%)	22 (31.43%)	48 (51.61%)	0.012
	Female	93 (57.06%)	48 (68.57%)	45 (48.39%)	
Duration of Diabetes	1-5 years	40 (24.54%)	8 (11.43%)	32 (34.41%)	<0.001
	5-10 years	55 (33.74%)	22 (31.43%)	33 (35.48%)	
	More than 10 years	68 (41.72%)	40 (57.14%)	28 (30.11%)	
Co-morbidities	Hypertension	110 (67.48%)	58 (82.86%)	52 (55.91%)	<0.001
	Stroke	15 (9.20%)	6 (8.57%)	9 (9.68%)	0.824
	Myocardial infarction	20 (12.27%)	10 (14.29%)	10 (10.75%)	0.504
	Peripheral Neuropathy	60 (36.81%)	40 (57.14%)	20 (21.51%)	<0.001
Smoking Status	Non-Smoker	90 (55.21%)	38 (54.29%)	52 (55.91%)	0.829
	Ex-Smoker	30 (18.40%)	15 (21.43%)	15 (16.13%)	0.420
	Active Smoker	43 (26.38%)	17 (24.29%)	26 (27.96%)	0.624
BMI	<24.9 kg/m^2	50 (30.67%)	10 (14.29%)	40 (43.01%)	<0.001
	25- 29.9 kg/m^2	60 (36.81%)	25 (35.71%)	35 (37.63%)	0.769
	>30 kg/m^2	53 (32.52%)	35 (50.00%)	18 (19.35%)	<0.001
Waist circumference	Cm (Mean ± SD)	35.6 ± 5.2	37.8 ± 5.1	33.8 ± 4.8	<0.001
Antidiabetic Medications	Insulin	75 (46.01%)	45 (64.29%)	30 (32.26%)	<0.001
	Metformin	130 (79.75%)	50 (71.43%)	80 (86.02%)	0.014
	Combination therapy with Empagliflozin	40 (24.54%)	10 (14.28%)	30 (32.25%)	<0.001
	Combination therapy with sulfonylurea	30 (18.40%)	10 (14.29%)	20 (21.51%)	0.225
RAAS blockers	ACEi/ARBs	110 (67.48%)	50 (71.43%)	60 (64.52%)	0.325

Table 2 depicts the trends observed in laboratory investigations in both the patients' groups. Patients with DKD (42.94%) had significantly higher HbA1c levels, with 85.71% having HbA1c ≥7% compared to 46.24% in the non-DKD group ($p < 0.001$). Lipid profiles showed elevated LDL and triglycerides and lower HDL levels in the DKD group, with mean LDL at 140 ± 20 mg/dL and triglycerides at 190 ± 40 mg/dL, in contrast to 120 ± 25mg/dL and 150 ± 45 mg/dL respectively in the non-DKD group($p < 0.001$ for all). HDL levels were on the lower side in the DKD group (40 ± 8mg/dL vs. 50 ± 10mg/dL, $p < 0.001$). Renal function tests revealed higher serum creatinine levels in DKD patients (1.7 ± 0.7 mg/dL) versus non-DKD patients (1.2 ± 0.5 mg/dL, $p < 0.001$), and decreased serum albumin levels in the DKD group (3.5 ± 0.4g/dL vs. 4.0 ±0.5 g/dL, $p < 0.001$). Albumin-to-creatinine ratio (ACR) was substancially higher in DKD patients, with 42.86% having ACR ≥300 mg/g compared to 16.13% in the non-DKD group ($p < 0.001$). Furthermore, 71.43% of DKD patients had an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m² compared to 19.35% of non-DKD patients ($p < 0.001$). These results demonstrate the correlation between the prevalence of DKD in T2DM patients and poor glycemic control, unfavorable lipid profiles, and compromised renal function.

Table 2: Laboratory investigations of both the study groups

Lab tests	Sub-groups	Total N=163 (100%)	DKD Present N=70 (42.94%)	DKD Not Present N=93 (57.06%)	p-value
HbA1c%	Below 6.9%	60 (36.81%)	10 (14.29%)	50 (53.76%)	<0.001
	7% and above	103 (63.19%)	60 (85.71%)	43 (46.24%)	
Lipid Profile	LDL (mg/dL)	130 ± 25	140 ± 20	120 ± 25	<0.001
	HDL (mg/dL)	45 ± 10	40 ± 8	50 ± 10	<0.001
	Triglycerides (mg/dL)	170 ± 45	190 ± 40	150 ± 45	<0.001
Renal function tests	Serum creatinine	1.4 ± 0.6	1.7 ± 0.7	1.2 ± 0.5	<0.001
	Serum Albumin (g/dL)	3.8 ± 0.5	3.5 ± 0.4	4.0 ± 0.5	<0.001
ACR	≥30 and ≤300 mg/g	55 (33.74%)	20 (28.57%)	35 (37.63%)	0.159
	≥300 mg/g	45 (27.61%)	30 (42.86%)	15 (16.13%)	<0.001
eGFR	<60 mL/min/1.73 m²	68 (41.72%)	50 (71.43%)	18 (19.35%)	<0.001
	>60 mL/min/1.73 m²	95 (58.28%)	20 (28.57%)	75 (80.65%)	

Discussion

We discovered that 42.94% of the diabetic individuals who visited the hospital were estimated to have DKD. Age, gender, length of diabetes, concurrent medical conditions, smoking history, BMI, waist circumference, and the use of medications were all strongly linked with the occurrence of DKD.

Our data showed that older age (>50 years) was notably linked with a higher prevalence of DKD, with 82.86% of DKD patients being above 50 years old compared to 48.39% without DKD ($p<0.001$). This is consistent with the physiological decay in renal functions with aging, leading to a gradual decline in eGFR as highlighted by Coresh J. et al..[11]

Gender differences were also notable, with females showing a higher prevalence of DKD (68.57%) compared to males (31.43%), suggesting potential gender-specific risk factors or differences in disease progression ($p=0.012$).

Another important effect was the length of diabetes. Individuals who had diabetes for longer than ten years were more likely to get DKD (57.14%) than those who had the disease for less time ($p<0.001$). This aligns with the chronic nature of diabetes and its cumulative impact on kidney function, as discussed by Adler A.I. et al..[12]

Comorbid conditions like hypertension (82.86% in DKD patients) and peripheral neuropathy (57.14%) were significantly more prevalent in the DKD group ($p<0.001$), highlighting the interplay between these conditions and kidney disease progression. These findings are consistent with studies by Adler A.I. et al. and Afkarian M. et al..[12-13]

Dyslipidemia was prominent among DKD patients, with higher LDL (140 ± 20 mg/dL) and triglycerides (190 ± 40 mg/dL) and lower HDL levels (40 ± 8 mg/dL) compared to non-DKD patients ($p<0.001$). This supports findings from the ADVANCE study[14] and the FIELD study[15], which identified dyslipidemia as a significant risk factor for DKD.

Serum creatinine levels in DKD patients (1.7 ± 0.7 mg/dL) were substantially higher than in those without DKD (1.2 ± 0.5 mg/dL) according to renal function tests ($p<0.001$). Furthermore, DKD patients had lower serum albumin (3.5 ± 0.4 g/dL) than non-DKD patients (4.0 ± 0.5 g/dL) ($p<0.001$). These markers reflect impaired kidney function and proteinuria, aligning with findings from Brenner B.M. et al..[16]

Those with DKD had a substantially greater degree of albuminuria (ACR ≥300 mg/g) at 42.86% than those with no DKD (16.13%) ($p<0.001$). This result emphasizes the significance of albuminuria as a precursor to renal injury, as suggested by the American Diabetes Association (2020).[17]

Our study also disclosed that DKD patients had a markedly lower eGFR (<60 mL/min/1.73 m² in 71.43% of DKD patients) compared to non-DKD patients (19.35%) ($p<0.001$). This supports the need for regular monitoring of eGFR alongside albuminuria to identify DKD, in line with Coresh J. et al..[11]

Drugs like RAAS blockers and metformin have been linked to a decreased risk of advanced chronic kidney disease. Compared to patients who were not taking metformin (86.02%), those who were on it (71.43%) had a decreased prevalence of DKD ($p=0.014$). This supports the preventive benefits of metformin that have been seen in a number of studies (UKPDS Group).[18] Similar to this, RAAS blockers were linked negatively to advanced stages of CKD and albuminuria, which corroborated findings from large-scale trials such as the Irbesartan Diabetic Nephropathy Trial (Lewis E.J. et al.) and the Angiotensin Antagonist Losartan study (Brenner B.M. et al.)16.[19]

Our study identifies several key factors associated with DKD in Pakistani diabetic patients. These include age, duration of diabetes, comorbidities, dyslipidemia, and specific medications. These findings are consistent with regional and global studies and underscore the need for comprehensive management strategies targeting these risk factors to prevent or delay the progression of DKD.

Conclusion

Our study reveals that a sizeable proportion of diabetic patients (42.94%) suffer from diabetic kidney disease (DKD), with older age, longer diabetes duration, hypertension, peripheral neuropathy, and dyslipidemia being key associated factors. Elevated HbA1c levels, reduced eGFR, and high albuminuria prevalence further emphasize the severity of DKD. These findings highlight the critical need for comprehensive management strategies, including stringent glucose control, blood pressure regulation, and lipid management. Regular monitoring of kidney function through eGFR and albuminuria screenings should be an integral part of diabetic care. By adopting these proactive measures, we can potentially curb the progression of DKD and improve health outcomes for diabetic patients in Pakistan.

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