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Chronic Kidney Disease and Associated Risk Factors Among Patients with Type-2 Diabetes Mellitus in a Tertiary Care Hospital

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ABSTRACT

Objective: To determine the frequency of chronic kidney disease and its associated risk factors in patients with type 2 Diabetes Mellitus.

Study Design: Cross-sectional study.

Place and Duration of Study: Combined Military Hospital Malir Cantt, Karachi, from Jan to Jun 2019.

Methodology: A total of 203 adult patients with Type 2 Diabetes Mellitus were included in the study after taking informed consent on the justification of inclusion/exclusion criteria. The estimated Glomerular filtration rate was calculated for each patient using Creatinine based chronic kidney disease epidemiology collaboration (CKD-EPI) equation. Chronic kidney disease was defined as decreased glomerular filtration rate of <60 mL/min per 1.73m2. In addition, risk factors for developing chronic kidney disease, including Body Mass Index and blood pressure, were clinically determined.

***Results*:** Out of 203 patients with type 2 diabetes mellitus, 65(32%) had Chronic kidney disease. Most of them, 34(52.30%), were in Chronic kidney disease stage 3, while 21(32.30%) were in stages 4 and 10(15.40%) were having stage 5. Increasing age, smoking, female gender and higher body mass index were positively correlated with the development of chronic kidney disease in diabetes patients.

Conclusion: Chronic kidney disease is a frequently observed complication in diabetes patients. Early detection and appropriate treatment can help in retarding progression to advanced stages of chronic kidney disease. Regular screening of diabetes patients for chronic kidney disease and associated risk factors is therefore recommended.

Keywords: Chronic kidney disease, Glomerular filtration rate, Type-2 diabetes mellitus.

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INTRODUCTION

Chronic Kidney Disease (CKD) is prevalent worldwide, with an estimated global prevalence of 13.4%(11.7-15.1%).[1] It is defined as Glomerular Filtration Rate (GFR) <60ml/min/1.73m2 for more than three months and/or other markers of kidney damage as evident on renal imaging, urine microscopy or histopathology.[2,3] Diabetes is a major cause of End-stage renal disease (ESRD) worldwide. Furthermore, with the emergence of the Type2 Diabetes mellitus (T2DM) epidemic, the incidence of CKD is also increasing. Early detection and appropriate management of diabetes-related renal complications can retard the progression of decline in renal functions.[4] Similarly, timely interventions to modify risk factors associated with the development of CKD in T2DM can help retard the incidence of this complication.[5] Therefore patients suffering from T2DM should be actively searched for the presence of CKD and its risk factors.[6]

Studies in Pakistan mostly focused on microalbuminuria as a manifestation of diabetic kidney disease. An estimated prevalence of diabetic nephropathy is 28% in our country.[6,7] However, data on the extent of this problem in our patients are still being determined. This study aimed to determine the frequency of CKD based on estimated GFR values in patients with T2DM and to determine associated risk factors in patients attending a tertiary care hospital in Pakistan. Determining the frequency of CKD in T2DM and its associations will help increase awareness among patients and treating physicians regarding this potentially dreadful complication. It will also result in early diagnosis and timely management to retard the progression of the disease.

METHODOLOGY

The cross-sectional study was conducted at the Department of Medicine, Combined Military Hospital (CMH) Malir Cantt Karachi from January to June 2019. Research and Ethics Committee CMH Malir approved the study (No 1440/2019/trg/adm dated 15 Nov 2019). The sample size was calculated using single population proportion formula considering 15.3% CKD prevalence in Pakistan.[7]

Inclusion Criteria: Adult patients (age 18 years or above) with Type 2 diabetes mellitus attending routine

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medical OPD were included using a non-probability consecutive sampling technique.

Exclusion Criteria: Patients having pregnancy, acute febrile illness, renal transplant, structural abnormality of kidneys, acute glomerulonephritis, obstructive uropathy and concomitant hepatic or cardiac failure were excluded from the study.

Patients' demographic data were collected using a structured proforma, which included separate sections for medical history and clinical data. Roche analysed serum creatinine by the Modified Jaffe Endpoint Kinetic method on Cobas C-501 Chemistry Autoanalyzer. The Chronic Kidney Disease Epidemiology (CKD-EPI) collaboration equation (Creatinine based) was used to determine estimated GFR (eGFR). In the Kidney Disease: Improving Global Outcomes (KDIGO) 2012 CKD Guidelines, CKD was defined by decreased GFR <60 mL/min per 1.73m2 and/or kidney damage as indicated by other markers for three months. As we excluded other damage markers, we restricted our study to define CKD based on eGFR <60 mL/min per 1.73 m2. Patients having CKD were classified into five stages according to the Kidney Disease: Improving Global Outcomes (KDIGO) classification system as follows: Stage 1: eGFR of ≥90 ml/min/1.73m2 (with structural, biochemical or radiological evidence of renal damage), stage 2: eGFR of 60-89 ml/min/1.73m2 (with structural, biochemical or radiological evidence of renal damage), stage 3: eGFR of 30-59 ml/min /1.73m2, stage 4: eGFR of 15-29 ml/min/1.73m2 and stage 5 (kidney failure): eGFR of <15ml/min/1.73m2.[8] Body mass index (BMI) was calculated as weight divided by height squared (kg/m2). BMI >25 kg/m2 was considered overweight.[9] Blood pressure was measured by nurses using calibrated standard equipment. Measurements were taken from the upper arm while placing the hand at the heart level after the patient had been sitting for more than 5 minutes. Systolic blood pressure ≥140mmHg and/or diastolic blood pressure ≥90mmHg or current uses of blood pressure-lowering medication were used to define hypertension.[10]

Statistical Package for Social Sciences (SPSS) version 23.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Univariate and multivariate binary logistic regression was conducted to determine the relationship of different risk factors with CKD. These included age, gender, hypertension, smoking, duration of diabetes and obesity. The *p*-value of ≤0.05 was set as the cut-off value for significance.

RESULTS

A total of 203 patients with T2DM were investigated for CKD. The mean age was 51.72±15.46 years. Males were 128(63.05%), while 75(36.95%) were females. CKD was present in 65 patients, and hence the frequency of CKD was 32%. Stage-wise stratification of CKD patients revealed that 34 cases (52.3%) had eGFR between 30 to 59ml/min (Stage 3), 21(32.3%) had eGFR between 15 to 29 ml/min (stage 4), and 10(15.4%) were having eGFR less than 15 ml/min (stage-5) (Figure).

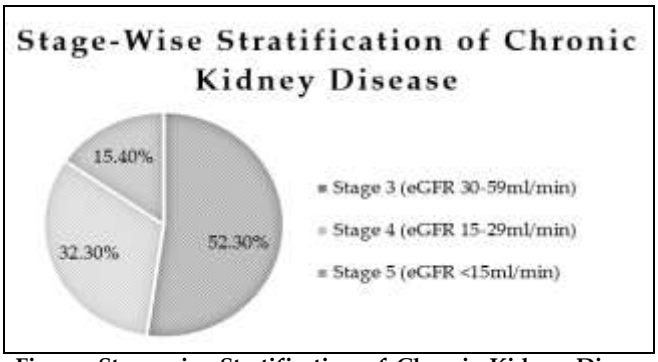

Figure: Stage-wise Stratification of Chronic Kidney Disease (n=203)

The results of binary logistic regression are shown in Table-I. CKD could be predicted by increasing age (112% increased risk for every year increase in age), female gender (16.5 times increased risk as compared to males), smoking (33 times increased risk as compared to non-smokers) and obesity (nearly six times increased risk as compared to non-obese people).

DISCUSSION

Chronic kidney disease (CKD) is increasingly recognized as a major global public health problem globally.[9] It increases the risk of all-cause mortality, cardiovascular mortality, and end-stage renal disease (ESRD) progression. To establish better prevention strategies and enable early detection, much effort has been made to identify risk factors associated with CKD development. The commonest risk factor for the development of CKD has been described as Diabetes mellitus, and we have demonstrated CKD as a frequently observed complication as almost one in every three diabetes patients has this complication. In contrast to other local studies which specifically investigated microalbuminuria as a manifestation of diabetic kidney disease, it is evident from our results that extent of low GFR is more common than

proteinuria. World-over prevalence of CKD in diabetes mellitus has been estimated between 16.2 to 34.1% (Table-II).

Table-I: Factors Associated with Chronic Kidney Disease (n=203)

Factors	Study Parameter CKD		Univariate Logistic Regression			Multivariate Logistic Regression		
	Present	Absent	*p*-value	Un-adjusted OR	95% CI for UOR	*p*-value	Adjusted OR	95% CI for AOR
Age								
Mean+/-SD	63.69+/-11.65	46.09+/-12.04	<0.001	1.125	1.087-1.163	<0.001	1.120	1.068-1.174
Gender								
Male	34(52.31)	94(68.11)	0.031	1.948	1.065-3.564	<0.001	16.452	3.969-68.190
Female	31(47.69)	44(31.88)						
Hyertension (BP >140/90 mmHg)								
Present	43(66.15)	50(36.23)	<0.001	3.440	1.850-6.395	0.133	2.143	0.793-5.789
Absent	22(33.85)	88(63.77)						
Smoking								
Smoker	35(53.85)	17(12.32)	<0.001	8.304	4.107-16.788	<0.001	33.811	7.043-162.324
Non-Smoker	30(46.15)	121(87.68)						
Duration of Diabetes								
<10 yrs	27(41.54)	119(86.23)	<0.001	8.815	4.416-17.596	0.145	2.201	0.761-6.366
>10 yrs	38(58.46)	19(13.77)						
Obesity (BMI >30)								
Obese	36(55.38)	23(16.67)	<0.001	6.207	3.198-12.045	<0.001	5.971	2.198-16.219
Non-Obese	29(44.61)	115(83.33)						

Table-II: Chronic Kidney Disease in Diabetes Mellitus Patients in Other Studies

Study/Country	Chronic Kidney Disease Prevalence (%)
Low *et al.*/Singapore[10]	21.4
Damtie *et al.*/Ethiopia[11]	21.8
Ullah K *et al.*/ Pakistan[6]	28
Rodriguez-Poncelas *et al.*/ Spain[12]	18
Zhang *et al.*/China[13]	21.8
Coll-de-Tuero *et al.*/ Mediterranean region[14]	34.1
Thomas *et al.*/Australia[15]	23.1
Metsärinne *et al.*/ Finland[16]	16.2
Our Study	32

Our results are consistent with findings elsewhere. A large variety of estimates in different studies is likely due to the method of classifying CKD. Per KDIGO guidelines, we classified CKD as eGFR<60 ml/ min. However, some studies identified CKD as being eGFR <120ml/min, resulting in more affected patients.[17]

Our study results reiterated that major traditional risk factors (e.g., smoking, obesity and increasing age) are associated with the development of CKD in T2DM patients. Several landmark clinical trials have provided strong evidence regarding the causal effects of these risk factors and have also suggested that active control of these risk factors can retard renal progression.[17] This study established a significant association between CKD and older age (AOR: 1.120, 95% CI: 1.068-1.17). This result is consistent with other studies.[18]

Another important association of CKD is with the female gender in our study. Interestingly, the increased duration of diabetes and the presence of hypertension were related to CKD in univariate regression but lost their statistical significance in multivariate regression analysis. Although they are important and proven risk factors, [11,12,19] we could not establish them in this study population. This variation may be due to a need for more insight among patients regarding the duration of DM and the presence of hypertension, as most of our patients rely on their distant memories of symptoms rather than an actual diagnosis. In addition, a small sample size may affect the statistical tool to show the association between hypertension, duration of DM and CKD.

The findings have established a baseline profile of CKD amongst patients with T2DM for future management and preventive strategies. This will help physicians to appreciate the magnitude of CKD among patients with T2DM and to exercise vigilance in diabetes care. Our study will likely stimulate further research on renal complications in DM patients to improve clinical outcomes. Analysis of renal biopsy findings in diabetic patients will help to establish the mechanism of various non-proteinuric renal injuries leading to low GFR.

LIMITATIONS OF STUDY

There are limitations to this study. First, we restricted our study to patients with Type2DM visiting hospital

settings. Hence findings cannot be generalized to general diabetes patients, including Type1DM. Furthermore, the study population was small to draw substantial results indicating the actual extent of the problem in our population.

CONCLUSION

In conclusion, this study identified a high frequency of chronic kidney disease among diabetes patients. Therefore, the estimated glomerular filtration rate should be determined in such patients at regular intervals for earlier diagnosis. Prompt recognition of CKD and its associated risk factors can lead to timely interventions and can help retard the progression of this potentially fatal complication.

Conflict of Interest: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

FI & HJS: Concept, critical review, approval of the final version to be published.

AK & GF: Data acquisition, data analysis, data interpretation, , approval of the final version to be published.

SY & AA: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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