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ORIGINAL ARTICLE

PREVALENCE OF RISK FACTORS OF DIABETIC NEPHROPATHY AND THEIR ASSOCIATION WITH ESTIMATED GFR IN PATIENTS OF TYPE 2 DIABETES MELLITUS

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ABSTRACT

Background: Diabetic nephropathy is the leading cause of Chronic renal disease and thus end stage renal disease (ESRD). Early detection of glomerular changes along with strict glycemic control and management of different risk factors can help reduce risk of diabetic kidney disease (DKD). That's why this study was planned in order to investigate the association between risk factors and estimated GFR in patients of diabetes mellitus type 2.

Materials & Methods: An analytical study was conducted at KRL hospital Islamabad during November 01, 2021 - February 28, 2022. A total of 74 T2DM patients coming to hospital for Checkup were selected which were divided in two groups of 37 participants in each and data was obtained on a structured questionnaire. Normality of data was checked through Kolmogorov-Smirnov (K-S) test. Means of two groups was compared through an independent sample T-test. To determine the association of variables, regression was applied and p-value < 0.05 was considered statistically significant.

Results: In group 1 (eGFR >90ml/min) there were 62.5% females and 37.5% males while in group 2 (eGFR<90ml/min) there were 88.9% female and 11.1% were males. Duration of diabetes also affected eGFR as only 5.4% of the population in Group 1 (eGFR >90ml/min/1.73m2) was suffering from T2DM for more than 10 years whereas this percentage was 37.8% in Group 2 (eGFR 90-30ml/min/1.73m^2) with the same duration of diabetes. Respondents in group 1 having HbA1C <7% were only 12.5% while those who had >7 were 87.5% while in group 2 there were 100% respondents with HbA1C of >7 and those with uncontrolled BSR (>200 mg/dl) were 66.7%.In concordance with these results duration of diabetes, smoking, control of DM, Hypertension, BMI and total cholesterol has significant effect on eGFR.

Conclusion: It was concluded that duration of DM, control of DM, hypertension control, obesity, hypercholesterolemia and smoking were associated with increased risk of developing DKD and thus lowering eGFR. Similarly reduced physical activity, increasing age, female gender and positive family history had the effect of reducing eGFR significantly as reported in group 2.

KEY WORDS: Diabetes Mellitus; ESRD; Prevalence; Diabetic nephropathy; chronic kidney disease.

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INTRODUCTION

Diabetes mellitus (DM) type-2 is a chronic disorder of carbohydrate metabolism caused by a combination of hereditary and environmental factors. Diabetes is a major health problem worldwide that has reached alarming levels, it is estimated that 537 million people have diabetes in a recent survey of international diabetes federation.[1] According to WHO, about 422 million people worldwide have diabetes, the majority living in low and middle-income countries, and 1.5 million deaths are directly related to diabetes each year.[2] Other studies conducted in Pakistan in between 1995 and 2014 have shown the prevalence of T2DM to be between 8.0% and 14.0%, depending on regional variations data collected from urban and rural areas and diagnostic crieteria.[3]

T2DM is a slowly progressive disorder which affects the vascular system including small and major vessels of the human body. It is mostly asymptomatic and disease goes undetected for the number of years

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which can cause poor outcomes in populations. One of the most common and major complications of T2DM is diabetic nephropathy. Prevalence of diabetic nephropathy in Pakistan is 29.52%.[4] Multiple risk factors including duration of diabetes, degree of hyperglycemia, blood pressure control, dyslipidemia, and individual lifestyle can contribute to progression and severity of disease. Diabetic nephropathy (DN), also known as diabetic kidney disease (DKD), is one of the most important microvascular complication of T2DM, affecting 30–45% patients, with a peak incidence in the population having 10–20 years duration of T2DM.[5] Renal impairment in diabetic patients can be manifested as a decrease in the estimated glomerular filtration rate (eGFR) and the progression from microalbuminuria and macroalbuminuria to proteinuria, or both.[4] Estimation of GFR is important to detect initial derangements in kidney functions in these patients.[6] It is the most common cause of Chronic kidney disease (CKD) leading to end stage renal disease (ESRD).

DN, microscopically, is characterized by glomerular basement membrane (GBM) thickening, glomerular mesangial matrix expansion, and formation of glomerular nodular sclerosis in its advanced stages. Clinically, DN is defined by proteinuria occurrence or declined renal function e.g reduced glomerular filtration rate (GFR).[5] It has been also described as a main cause of morbidity and mortality in patients with diabetes and in adults persistent microalbuminuria is the best marker of consequent risk for its development.[4-5] Early detection of pathological glomerular changes along with strict glycemic control and management of different risk factors can be helpful in reducing progression to End stage renal disease.[4,6] That's why we planned this study in order to explore the association between risk factors and estimated GFR in patients of diabetes mellitus type 2.

MATERIAL AND METHODS

An analytical study was conducted at the Medicine department, KRL hospital Islamabad Pakistan (November 2021 - February 2022) after getting approval from the ethical committee at the hospital. A total of 74 T2DM patients coming to KRL for Checkup were selected and data was obtained on a structured questionnaire after informed consent. Patients included were having eGFR from 30-90 ml/min/1.73m^2 and more.

Sample size was calculated through WHO calculator by using power 80%, confidence level 5%, anticipated GFR = 55.5±27.4 ml/min/1.73 m2.[7] Calculated sample size was 70 individuals. To overcome the possibility of dropouts, we inducted 74 patients. Sampling technique used was non- probability convenient Sampling.

Our inclusion criteria included T2DM having (CKD stage 1-3) eGFR ranging from >90 ml/min/1.73m^2 and further <90 up to 30ml/min/1.73m^2 and individuals of 30 – 60 years of age both male and female gender were included. Exclusion Criteria included: T2DM patients having Acute myocardial infarction (AMI), Acute Renal Failure, Severe trauma, Hyperglycaemic crisis, Hypertensive crises, CKD of Stage 4 & 5 (eGFR <30 ml/min/1.73m^2 or on Dialysis), Type-1 DM, Gestational Diabetes and other rare causes.

Patient's history was taken through performa. Their height and weight was measured. BMI was calculated (weight in kg / height in m^2). Total 3ml blood was taken in a gel tube. Serum was separated. Spot urine sample was collected in a plastic urine container. HDL was analyzed through CHOD-PAP method, total cholesterol through enzymatic cholesterol oxidase method, creatinine through jaffe method, triglyceride through quinoneimine aminoantipyrine method, HbA1C through latex enhanced immunoturbidimetric assay, microalbuminuria through solid-phase, non-competitive, double-antibody reaction. LDL was calculated through formula: Total Cholesterol-HDL-Triglycerides/5. HbA1c and microalbuminuria were analyzed on LAB -100. Lipid profile and serum creatinine was measured on automated chemistry analyzer, Selectra pro M. eGFR was estimated using Cockcroft and gault equation *(140-age years*weight kg*K serum creatinine (µmol/l).*

BMI was calculated through formula: *weight in kg/ Height in meter square.*

Data was analyzed by SPSS software version 21. Mean and SD was calculated for quantitative variables. Number and percentage was calculated for qualitative variables. Normality of data was checked through Kolmogorov-Smirnov (K-S) test. Means of two groups was compared through an independent sample T-test. Logistic regression was applied to assess the predictors. Our dependent variable was eGFR and independent variables were blood glucose, HbA1c, blood pressure, lipid profile, BMI, smoking status, duration of diabetes and physical inactivity. Odds ratio and 95% confidence interval was calculated. P-value ≤ 0.05 was considered statistically significant.

Data was entered into Ms Excel software and exported to SPSS software for analysis. Relationships between eGFR and risk factors were analyzed.

RESULTS

Of 74 individuals participating in the study there were 45 females (60.81%) and 29 (39.18%) were males, prevalence of risk factors of DN was assessed and their effect on eGFR was checked. Population included was 30-60 years of age in which 40 individuals (54%) fell in 4th and 5th decade of life. Studied population was divided in two groups according to their eGFR to simplify expression of results, in group 1 eGFR was >90ml/min/1.73m2 whereas in group 2 individuals had eGFR (90-30ml/min/1.73m2).The demographic characteristics of both groups are shown in table:1.

Table:1. Demographic charateristics of two groups.

		eGFR > 90 (Group 1)		eGFR < 90 (Group 2)	
	Variables	N	Percent	N	Percent
Age of the Respondents	26-35	12	32.4	-	-
	36-45	10	27.0	7	18.9
	46-55	10	27.0	9	24.3
	55+	5	13.5	21	56.8
Gender of the Respondents	Male	16	43.2	13	35.1
	Female	21	56.8	24	64.9
Duration of Diabetes	0-2	5	13.5	8	21.6
	3-5	18	48.6	4	10.8
	6-8	7	18.9	11	29.7
	9-10	5	13.5	-	-
	10+	2	5.4	14	37.8
Family History of Diabetes	Yes	26	70.3	34	91.9
	No	11	29.7	3	8.1
Family History of Renal Disease	Yes	8	21.6	7	18.9
	No	29	78.4	30	81.1
Type of Physical Activity	Walk	21	56.8	12	32.4
	Exercise	5	13.5	25	67.6
	No Physical Activity	11	29.7	37	100.0
Sugar Levels	<126 mg/dl	4	10.8	9	24.3
	126-200 mg/dl	14	37.8	4	35.1
	>200 mg/dl	11	29.7	24	64.8
Smoking	Yes	13	35.1	24	64.9
	No	24	64.9	13	35.1
Blood Pressure	<=140/90	31	83.8	13	35.1
	>140/90	6	16.2	24	64.9
HbA1C (%)	<7	22	59.5	-	-
	>7	15	40.5	37	100.0
Cholesterol	<180	16	43.2	11	29.7
	180-200	14	37.8	7	18.9
	200-250	7	18.9	19	51.4
BMI	Normal	24	64.9	15	40.5
	Overweight	9	24.3	19	51.4
	Obese	4	10.8	3	8.1

The Kolmogorov-Smirnov (K-S) test was applied to check the normality of data and it showed data was normally distributed among group1 and group 2 (P-value >0.05).

An independent sample T Test was conducted to see whether there is significant difference in duration of T2DM, Smoking, Blood pressure, HbA1C, cholesterol, type of physical activity, family history of renal disease and BMI for group 1 and 2. P-value for these parameters was found to be <0.05 which means there is significant difference between the two groups.

Regression Analysis					
Model	R	R Square	Adjusted R Square	Sig.	Standardized Coefficients (Beta)
1	.562a	.315	.306	.000	-.562

As it is visible that R square value is 0.315 which means that our independent variables (duration of T2DM, Smoking, Blood pressure, HbA1C, cholesterol, type of physical activity, family history of renal disease and BMI) have a 31.5% effect on the dependent variable (eGFR). As the ANOVA results show that the P-value is 0.000 hence we can say there is significant relation between our dependent and independent variables. As indicated by the coefficient results that the beta value is -0.562 which means that the change in independent variable by one unit will bring about a change of 0.562 units in dependent variable, further as a beta value is negative that implies A negative relation between the two variables. In concordance with these results gender, age, duration of diabetes, smoking, physical activity, control of DM, Family history of DM, Hypertension, BMI and total cholesterol has significant effect on eGFR.

DISCUSSION

Good glycemic control, blood pressure control, physical activity and cessation of smoking are important factors which can slow the progression of DKD. Literature has evidence of controlling these risk factors and effects on early stages of DN. In present study it was found that **hyperglycemia** (High BSR and HbA1C >7) had significant effect on eGFR and higher the glucose levels more will be the risk for developing DN. As in group 2, 64.8% respondents had BSR >200mg/dl and HbA1C >7 was present in 100% of the individuals whereas in group 1 population having BSR >200mg/dl were 29.7% and HbA1c >7 were 40.5% respondents only this was supported by the study conducted by Hussain et.al which showed that intensive glycemic control can delay the onset and progression of DN.[8] This was also supported by study by Acharya K et.al which showed higher the levels of HbA1C >8 resulted in developing albuminuria in 50% of the population and thus diabetic kidney disease.[9] This was in concordance with a case controls study which showed that controls (n=60) had average FBS of 87.5 in contrast to 162.5 in cases. Similarly controls had mean HbA1C 5.1 as compared to 6.86 in cases.[10]

Our study showed that **duration** of T2DM significantly affected eGFR such that 37.8% of group 2 had duration of >10 years which is also supported by study conducted by Acharya K et.al which showed that population having duration of >15 years was 66% and thus developing nephropathy.[9] Our study showed that 64.9% of the group 2 individuals were **hypertensive** and had increased risk of developing DN which is in concordance with Russo GT et.al study which stated that uncontrolled HTN can increase the risk of DN by 23%.[11] Another meta-analysis by Hussain et.al showed that hypertension is a prime risk factor for developing DN.[8] This was also supported by a study conducted by Alwakeel JS et.al showed that hypertension was documented in 92.2% of the population having diabetic nephropathy.[12] Another study by Russo GT et.al stated that increase blood pressure 54% of the population was associated with development of diabetic kidney disease.[13]

In present study it has been proven that **BMI** can have significant effect on eGFR as frequency of overweight individuals was 51.4% in group 2 as compared to 24.3% in group 1 and thus significant derangements in renal functions, supported by Hussain et.al study which stated that 264 patients suffering from diabetic kidney disease were obese and can lead to DN by glomerular injury, hyperfiltration and proteinuria.[8] This was in contrast to the study conducted by Akhtar et.al which suggested that obesity has no role in onset or progression of DN.[4] This was also supported by study published in BMC geriatric journal which showed 42.5% population were obese those with having T2DM, 23% and 31.8% of the population having eGFR <60ml/min were obese in another study.[13]

Smoking was found to have significant effect on progression of DN as it was reported that 64.9% of the group 2 participants were smokers as compared to 35.1% of the group 1 this can be confirmed by meta-analysis including nine cohorts which showed that there was significant risk of developing diabetic nephropathy in diabetic smokers.[8] This was in contrast to a study conducted by Thakur SK et.al which showed that population progressing towards DKD were 27.3% of the smokers and 72.7% of the non-smokers among them thus no significant effect of smoking was found on DKD.[14] Results of our study were supported by a study published in BMC geriatric journal which showed that people who were smoking that is 20.4% (3941 out of 54,297) of the study population developed early albuminuria as compared to non-smokers and thus DKD.[13] In anoth-

er study conducted by Sivasubramanian V et.al in South India showed that only 12% of the respondents were smokers while 60% never smoked thus having negative correlation between HbA1C and eGFR.[15]

In our study it was shown that 25% of the group 2 people and only 11% of the group 1 people were having sedentary life style which was in concordance with the Thakur SK et.al study which showed that 77.3% of the Type 2 diabetics developing micro-albuminuria were having sedentary life style.[14] In addition health screening and education, lifestyle modification, early intervention and prevention can also help reduce the risk of development of DN.[15]

It was found that **gender** difference was a significant risk factor in developing DN as there were 64.9% females with T2DM in group 2 as compared to group 1 where only 21% of the gender was female in contrast to a study conducted in china showed the pooled prevalence of diabetic nephropathy were higher in the male dominated studies 27.7% as compared to female dominated studies where it was only 17.6%.[16] In contrast to this a study conducted by Russo GT et.al reported that 58.4% of the male gender as compared to females were more prone to development of DKD in T2DM.[13]

In our study higher **cholesterol** levels were associated with increase risk for DN as in group 2 51.4% of the population were having high cholesterol levels as compared to 18.9% of the group 2 only. In another study published in BMC geriatric journal it was concluded that population having low eGFR that is 52.0% were having high levels of triglycerides and low HDL had increase the risk of DN along with hyperglycemia and hypertension.[13] In another study a retrospective analysis conducted by Zeng Y qin et.al showed that 86.4% of the people who had DKD were having dyslipidaemias.[17]

In this study age had significant association with derangements in renal functions as in group 2 most of the population were 55+ that is 56.8%. Similar results were reported in study conducted in Pakistan by Aamir AH et.al which showed majority that is 26.03% of the population were in age group 50-60 years.[18] This was also supported by a study by Thakur SK et.al which showed that 49.8% of the population fell in 40-60 years of age.[14]

It was also found that **family history** of T2DM was present in 91% of the group 2 participants. This was in concordance with the study by Aamir AH et.al which stated that family history of DM was present in 31.29% of the population.[18] Differences in different studies as compared to our study could be explained by racial and ethnic factors along with different lifestyles in regions of the world. In order to refrain from complications of T2DM patient education, healthy lifestyle and better health policies can help prevent progression of DN. Timing of proteinuria DN is variable and may be present at the time of diagnosis.

CONCLUSION

It was concluded that duration of DM, control of DM, hypertension control, obesity, hypercholesterolemia and smoking were associated with increased risk of developing DKD and thus lowering eGFR. Similarly reduced physical activity, increasing age, female gender and positive family history had the effect of reducing eGFR significantly as reported in cases. In Asian region and in Pakistan we need more measures to control progression of risk factors and our study could have potential in order to influence policies and further plan of control and prevention of T2DM and its complications**.**

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	AA, AK
Acquisition, Analysis or Interpretation of Data:	AA, AK, ARB
Manuscript Writing & Approval:	AA, AK, ARB

All the 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.