Original Article

Screening for Renal Function Impairment in Patients with Chronic Type II Diabetes Mellitus in a Tertiary Care Hospital of Pakistan

Rafiq Ahmad Siddiqui,[1] Shamim Akram,[2] Emaan Fatima,[3] Zoofishan Imran,[4] Muhammad Mustansar,[5] Saadia Liaqat[6]

Abstract

Objective: The objective of the present study was to detect early biochemical changes, in type II diabetics, indicating renal function impairment leading to Chronic Kidney Disease (CKD).

Methodology: This study was conducted in the Department of Biochemistry at Shaikh Zayed FPGMI, Lahore during September 2016 to April 2017. It was a cross-sectional analytical study and was done through nonprobability convenient sampling The study comprised of 50 diagnosed patients of type II diabetes mellitus (for the last 10 years) and 50 healthy subjects. Both male and female participants in equal number between the age of 35-75 were included in the study. Blood glucose level (random), blood urea, serum creatinine, urinary albumin and urinary creatinine were estimated and albumin to creatinine ratio (ACR) in mg/g was calculated. eGFR was also calculated using S/creatinine. The lab values of the study parameters were recorded on the designed proforma after getting proper written consent from the participants. SPSS 20.0 was used for data entry and analysis.

Results: Mean values of random plasma glucose level, blood urea, serum creatinine, urine albumin, urine creatinine, ACR and eGFR of patients when compared with those of healthy group showed significant p-values (≤0.05).

Conclusion: There was a significant difference in renal laboratory parameters between diabetic patients and healthy controls indicating the presence of CKD. In a developing country like Pakistan type II diabetes mellitus is an incidental finding due to lack of regular health monitoring and it is very difficult to determine the exact duration of the disease. Patients of type II DM develop CKD (Chronic Kidney Disease) due to persistent high plasma glucose levels. Therefore good control of DM and regular monitoring of renal parameters will be helpful in preventing the development of CKD.

Key Words: Diabetes Mellitus, Nephropathy, Chronic Kidney Disease, Urinary Albumin to Creatinine ratio.

How to cite: Siddiqui RA, Akram S, Fatima E, Imran Z, Mustansar M, Liaqat S. Screening for Renal Function Impairment in Patients with Chronic Type II Diabetes Mellitus in a Tertiary Care Hospital of Pakistan. *MedERA-Journal of CMH LMC and IOD. 2023; 5(2): 63-68*

DOI: *https://doi.org/10.61982/medera.v5i2*

1. *Assistant Professor, Department of Biochemistry, Services Institute of Medical Sciences, Lahore*
2. *Associate Professor, Department of Biochemistry, Rashid Latif Khan University Medical College, Lahore*
3. *MBBS Student (2022-2027), Agha Khan University, Karachi*
4. *Assistant Professor, Department of Community Medicine, Rashid Latif Khan University Medical College, Lahore*
5. *Professor, Department of Biochemistry, Pak Red Crescent Medical College, Lahore*
6. *Senior Demonstrator, Department of Anatomy, Services Institute of Medical Sciences, Lahore*

Correspondence:
Dr. Rafiq Ahmad Siddiqui, *Assistant Professor of Biochemistry, Services Institute of Medical Sciences, Lahore. E.mail: rafiqsiddiqui66@gmail.com*

Submission Date: 30-09-2023
1st Revision Date: 07-10-2023
2nd Revision Date: 26-10-2023
Acceptance Date: 14-11-2023

Introduction

Diabetes mellitus (DM) is a rapidly increasing problem for human health worldwide and it has got a huge burden on healthcare system. It was estimated that in 2017 there were 451 million (age 18–99 years) people with diabetes worldwide. These figures were expected to increase to 693 million by 2045.[1] In the developing countries the prevalence of DM is increasing very rapidly. 7% of the population is affected by type 2 DM. Out of total number of diabetic patients more than 90% belong to type II diabetes mellitus.[2] Diabetic renal disease is one of the major chronic complications of type II diabetes and is the main reason of end stage renal disease throughout the world.[3] Type II DM is a disease of miscellaneous causes marked by high blood glucose level, resulting from flaws in the action of insulin, secretion of insulin or both.[4] Type II DM causes destruction, loss of function and failure of different organs specially blood vessels, heart, kidneys and nerves. [5]

Diabetes mellitus has been linked to microvascular complications such as nephropathy, neuropathy and retinopathy. These microvascular complications ultimately lead to kidney damage.[6] Diabetic nephropathy (DN) is a clinical diagnosis and its presentation can vary in patients with type II DM. In initial phase the process starts with glomerular hyperfilteration followed by albuminuria (microalbuminuria/ macroalbuminuria), hypertension and gradually increasing loss of glomerular filtration rate (GFR) that results in end stage nephropathy.[7] DN is characterized by persistent albuminuria (or albuminuria excretion rate of >300 mg/d or 200 μg/min) measured at least twice within three to six months interval with progressive decrease in glomerular filtration rate (GFR). [8]

The rate and incidence of diabetic nephropathy is not assessed properly in type II DM mainly due to onset belonging to various ages and difficulty in detecting the time of onset. The risk of gradual development and progress of diabetic nephropathy lies mainly on bad glycemic and blood pressure control, obesity, dyslipidemia, lack of exercise, elevated uric acid levels, and chronic inflammation.[9] It develops in approximately 40% of patients with diabetes, after 10 years of type 2 diabetes mellitus was diagnosed. [10]

Microalbuminuria is an early symbol of diabetic nephropathy. In clinical practice the microalbuminuria is assessed as a routine for screening but the damage to the kidneys might be there even without microalbuminuria. It is important to use different methods for early assessment of diabetic nephropathy. This may allow earlier diagnosis and treatment which minimize diabetic nephropathy or slow down its progress thereby raising life expectancy among people with DM.[11] Diabetic nephropathy is now considered as the leading cause of CKD and end-stage kidney disease (ESKD) worldwide and it is linked to an increase in cardiovascular (CV) risk. Diabetic nephropathy increases morbidity and mortality in patients of DM.[12] In Pakistan also, it is the main cause of CKD due to the increasing prevalence of DM. Chronic kidney disease (CKD), a progressive chronic disorder, is affecting almost 13% population of America.[13] Its prevalence is more in South Asia including Pakistan. Along with diabetes hypertension is also a major risk factor of CKD.[14] A minimum of two elevated ACR levels (ratio of urine albumin to creatinine ≥ 30 mg/g) and similarly two eGFR values below 60 ml/min/1.73 m^2 at least 90 days apart are required to make a diagnosis of CKD.[15]

Methodology

After approval of the institutional ethics committee (Ref no. F-38/ NHRC/ADMIN/ IRB/ 204) and by conforming it to the Helsinki Declaration this study was carried on ten years old diagnosed type II diabetic patients. IRB approval letter . Patients were taken from the Department of Nephrology and Diabetic Clinic of Shaikh Zayed Hospital, Lahore.

The biomarkers used in this study include random

plasma glucose, blood urea, serum creatinine, urine albumin and creatinine (in mg/dl), albumin to creatinine ratio (in mg/g) and creatinine clearance (eGFR). The lab. tests were performed on all the participants to obtain the fresh data.

The total sample size was one hundred individuals. Group1 comprised of 50 healthy participants having no diabetes and Group 2 having 50 patients of type II DM diagnosed for the last 10 or more years. Besides age and gender, the height, weight, blood pressure and pulse of the participants were recorded. Individuals on steroids or anti-oxidant drugs or having active infection, neoplasia and any serious disease were not included in the study. Similarly alcoholics and pregnant women were also excluded from the study.

Five ml of the venous blood was drawn for biochemical analysis. A wide mouth bottle was used for the collection of urine sample. Tests for random plasma glucose, blood urea, serum creatinine, urinary albumin and creatinine (spot) were performed on all the participants. Creatinine clearance (e-GFR) was calculated by using serum creatinine and with the help of CG (Cock croft and Gault) formula.[16] Urine albumin to creatinine ratio was calculated in mg/g. The tests were performed in the biochemistry lab of Shaikh Zayed Hospital Lahore.

By using SPSS 20.0 the biochemical parameters of group 1 and 2 were compared. Two tailed t test was used to calculate p value.

Results

The results of these two groups were compared with each other. Results of the groups are shown in the table given below.

In Group 1 and 2, the p-value for age was non-significant. However, the p values for blood glucose (random), blood urea, S/creatinine, U/albumin, U/creatinine, urine albumin creatinine ratio and eGFR were highly significant in group 2 as compared to group 1. These parameters indicate Chronic Renal Disease in group 2 diabetic patients.

Table 1: *Comparison of variables of two study groups*

Sr. No.	Variable	Group 1 (n= 50) Mean ± SD	Group 2 (n= 50) Mean ± SD	P-Value
1	Age (Years)	49.6 ± 7.7	52.3 ± 8.7 w	0.103
2	Random Plasma Glucose (mg/dl)	118.4 ± 8.5	316.7 ± 28.9	0.001
3	Blood Urea (mg/dl)	26.7 ± 4.9	179.3 ± 30.5	0.001
4	Serum Creatinine (mg/dl)	0.87 ± 0.15	3.61 ± 1.14	0.001
5	Urine Albumin (mg/dl)	1 ± 0.0	141.54 ± 54.32	0.001
6	Urine Creatinine (mg/dl)	104.5 ± 11.2	87.3 ± 27.3	0.001
7	Albumin Creatinine Ratio(mg/g)	9.7 ± 1.1	1875.1 ± 164.5	0.001
8	e GFR (ml/min/1.73m^2)	116 ± 18.2	22.8 ± 10.4	0.001

p-values < 0.05 were considered as significant.
Group 1 – Healthy Subjects
Group 2 – Type II DM (chronic)

In this study the participants having normal blood pressure and normal weight were included. Mean values of the laboratory results were taken for comparison between the two groups.

Discussion

Type II Diabetes Mellitus is one of the main reasons of mortality and morbidity throughout the world and is a serious problem for human health.[17] This disease has got an association with both macrovascular and microvascular complications. Proteinuria is detected in diabetic kidney disease in chronic cases of DM.[18]

In this study there was no significant difference of age between the two groups as shown in the Table. The duration of DM in patients was 10 years or more. This criteria matches with the study conducted earlier by Selvi V S et al. [19]

The blood glucose (random) in group 2 was determined to be higher significantly than that of group 1 (healthy controls) (p-value < 0.001) (Table). It reveals

that, usually, there is poor glycemic control in complicated cases of DM. J Jitraknatee drew similar conclusions in their studies. [20]

The median level of B/urea and S/creatinine in group 1 (healthy controls) was found to be significant than that of group 2.

The median level for serum creatinine in group 1 and 2 showed a significant difference (p-value 0.001). These differences have also been highlighted by Oluba OM and Festuso. They stated that diabetic nephropathy was observed in approximately one third patients of type 2 DM.[21]

The median urine albumin level in group 1 and 2 showed a significant difference (p-value 0.001). Similarly, the mean values for urine creatinine and albumin creatinine ratio were also significantly different.

Studies described that early markers of diabetic neph-ropathy are microalbuminuria and increased urinary albumin to creatinine ratio. For diagnosing diabetic nephropathy microalbuminuria is considered as the main and gold standard. Most guidelines suggest annual screening with ACR to detect microalbumin-uria in all people with diabetes.[22] However, it cannot catch almost half of the patients of early diabetic nephropathy. The presence of albuminuria, diabetic retinopathy and poor glycaemic control are inde-pendent risk factors for the development of CKD among type II DM patients. [23]

In diabetic kidney disease albuminuria is taken as the first sign and is used for screening traditionally. However according to the available evidence, the natural history of diabetic kidney disease has changed and considerable portion of patients are normal albuminuric, despite having low eGFR.[24] eGFR in group 2 was significantly decreased as compared to that in group 1 (p-value 0.001).

It is important to adopt different methods for early assessment of diabetic nephropathy. This may allow earlier diagnosis and treatment, which minimize diabetic nephropathy or turn down the development of diabetic nephropathy leading to CKD.

Conclusion

There was a significant difference in renal laboratory parameters between diabetic patients and healthy controls indicating the presence of CKD. In our community due to lack of regular health monitoring patients of type II DM are diagnosed incidently and it is very difficult to determine the exact duration of the disease. Type II diabetics develop nephropathy as a complication due to persistent high plasma glucose levels.

It is recommended that proper control of DM and regular monitoring and control of the aforesaid biochemical parameters indicating nephropathy are utmost important. Healthy changes in life style including control of diet, weight and stress as well as adopting habit of regular exercise can delay the development and progress of nephropathy which may give rise to CKD.

Conflict of interest: *None*

Funding disclosure: *None*

References

1. Cho NH, Shaw JE, Karuranga S, Huang Y, da Rocha Fernandes JD, Ohlrogge AW, et al. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract. 2018; 138(1):271-281. doi: 10.1016/ j.diabres. 2018. 02.023.
2. Unnikrishnan R, Mohan V. Diabetes and the WHO model list of essential medicines. The Lancet Diabetes Endocrinol. 2022;10(1):19-20. doi: 10.1016/S2213-8587(21)00321-1.
3. Maggiore U, Budde K, Heemann U, Hilbrands L, Oberbauer R, Oniscu GC, et al. ERA-EDTA DESCARTES

working group. Long-term risks of kidney living donation: review and position paper by the ERA-EDTA DESCARTES working group. Nephrol Dial Transplant. 2017;32(2):216-223. doi: 10.1093/ ndt/ gfw 429.

4. Brijesh M, Saurav P. Comparative study of significance of serum cystatin-C, serum creatinine and microalbuminuria estimation in patients of early diabetic nephropathy. J Diabetes Metab. 2015; 6(490): 2. doi: 10.4172/2155-6156.1000490.
5. Bereda G. Differences Between Hyperglycemic Hyperosmolar Non-Ketotic Syndrome and Diabetic Ketoacidosis. BOHR Inter J Curr Res Diabetes Prevent Med. 2022;1(1):21-24. https:// doi. org/ 10.54646/ bijrdpm.003
6. Beckman JA, Creager MA. Vascular complications of diabetes. Circ Res. 2016;118(11):1771-1785. doi: 10.1161/CIRCRESAHA.115.306884.
7. Eknoyan G, Lameire N, Eckardt K, Kasiske B, Wheeler D, Levin A, et al. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney int. 2013;3(1):5-14. doi: 10. 7326/ 0003-4819-158-11-201306040-00007.
8. Selby NM, Taal MW. An updated overview of diabetic nephropathy: Diagnosis, prognosis, treatment goals and latest guidelines. Diabetes, Obes Metab. 2020; 22(1):3-15. doi: 10.1111/dom.14007.
9. Wang CP, Lu YC, Hung WC, Tsai IT, Chang YH, Hu DW, et al. Inter-relationship of risk factors and pathways associated with chronic kidney disease in patients with type 2 diabetes mellitus: a structural equation modelling analysis. Public Health. 2021 ; 17(2) 182-190. doi:10.7150/ijms.40417
10. Alicic RZ, Rooney MT, Tuttle KR. Diabetic kidney disease: challenges, progress, and possibilities. Clin J Am Soc Nephrol: CJASN. 2017;12(12):2032-2045. doi: 10.2215/CJN.11491116.
11. Thornton Snider J, Sullivan J, van Eijndhoven E, Hansen MK, Bellosillo N, Neslusan C, et al. Lifetime benefits of early detection and treatment of diabetic kidney disease. PLoS One. 2019;14(5):0217487. https:// doi.org/10.1371/journal.pone.0217487
12. Pelle MC, Provenzano M, Busutti M, Porcu CV, Zaffina I, Stanga L, et al. Up-date on diabetic nephropathy. Life. 2022;12(8):1202. doi: 10.3390/life12081202.
13. Coresh J, Selvin E, Stevens LA, Manzi J, Kusek JW, Eggers P, et al. Prevalence of chronic kidney disease in the United States. Jama. 2007; 298(17):2038-2047. doi: 10.1001/jama.298.17.2038.
14. Ullah K, Butt G, Masroor I, Kanwal K, Kifayat F. Epidemiology of chronic kidney disease in a Pakistani population. Saudi J Kidney Dis Transpl. 2015; 26(6): 1307-1310. doi: 10.4103/1319-2442.168694.
15. Cockcroft DW, Gault H. Prediction of creatinine clearance from serum creatinine. Nephron. 1976 ; 16(1): 31-41. doi: 10.1159/000180580.
16. Aldukhayel A. Prevalence of diabetic nephropathy among Type 2 diabetic patients in some of the Arab countries. Inter J Health Sci. 2017;11(1):1-4. doi: 10.1159/000382028.
17. Thipsawat S. Early detection of diabetic nephropathy in patient with type 2 diabetes mellitus: A review of the literature. Diab Vasc Dis Res. 2021; 18(6): 14791641211058856. doi: 10.1177/14791641211058856.
18. Selvi VK, Fathima MW, Sivakumar N, Prabhu K. Estimation of serum ferritin level in type 2 diabetes mellitus with chronic kidney disease. Journal of Chemical and Pharmaceutical Research. 2015; 7(10): 246-249. https://www.jocpr.com/articles/ estimation-of-serum-ferritin-level-in-type2-diabetes-mellitus-with-chronic-kidney-disease.pdf
19. Jitraknatee J, Ruengorn C, Nochaiwong S. Prevalence and risk factors of chronic kidney disease among type 2 diabetes patients: a cross-sectional study in primary care practice. Sci Rep. 2020 Apr 10;10(1): 6205. doi: 10.1038/s41598-020-63443-4.
20. Idonije BO, Festus O, Oluba OM. Plasma glucose, creatinine and urea levels in type 2 diabetic patients attending a Nigerian teaching hospital. Res J Med Sci. 2011;5(1):1-3. doi: 10.3923/RJMSCI.2011.1.3
21. Cosentino F, Grant PJ, Aboyans V, Bailey CJ, Ceriello A, Delgado V, et al. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: The Task Force for

diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and the European Association for the Study of Diabetes (EASD). Eur Heart J. 2020 ;41(2):255-323. doi: 10. 1093/eurheartj/ehz486.

22. Russo GT, De Cosmo S, Viazzi F, Mirijello A, Ceriello A, Guida P, et al. AMD-Annals Study Group. Diabetic kidney disease in the elderly: prevalence and clinical correlates. BMC Geriatr. 2018; 18(1):1-1. doi: 10. 1186/s12877-018-0732-4.
23. Liyanage PL, Lekamwasam S, Weerarathna TP, Srikantha DW. Prevalence of normoalbuminuric renal insufficiency and associated clinical factors in adult onset diabetes. BMC Nephrol. 2018; 19(1):1-6. doi: 10.1186/s12882-018-1001-7.
24. Care D. Standards of medical care in diabetes 2019. Diabetes Care. 2019; 37(1):11-34. doi: 10.2337/cd18-0105.

Authors Contribution

RAS: Conceptualization of study
EF, ZI: Literature Search
EF: Statistical Analysis
SL: Data Collection and Analysis
MM: Writing of Manuscript
SA: Drafting, Revision

All authors are equally accountable for accuracy, integrity of all aspects of the research work.