ORIGINAL ARTICLE

Diabetic Nephropathy: Duration and Glycemic Control Affect the Outcome

Robina Mushtaq[1], Ambreen Ansar[2], Anwar Bibi[3], Musarat Ramzan[4]

ABSTRACT

Objective: The aim was to find out frequency of Nephropathy in subjects having type 2 Diabetes Mellitus; and to determine the effect of disease duration and blood glucose levels on the development of Diabetic nephropathy.

Study Design: Cross-sectional.

Place and Duration of Study: POF Hospital Wah Cantt, 1st January to 30th June 2018.

Materials and Methods: Two hundred and ten subjects were enrolled having Type-2 Diabetes for more than 5 years. A closed ended questionnaire was used to record information on disease duration, glycosylated hemoglobin level, blood pressure and albuminuria. The data was analyzed by SPSS v-19 and significance of results was studied by Chi-square test.

Results: Among 210 patients 126 were male and 84 were female. Out of 210 people under study 54.76% had Diabetic Nephropathy. Significantly a greater number of Diabetic Nephropathy was recorded among subjects having Diabetes for more than 10 years (p-values 0.03), and whose blood sugar levels were never controlled (p-values 0.000).

Conclusion: The frequency of Diabetic Nephropathy was found to be quite high. It was significantly higher among subjects having diabetes for longer duration and uncontrolled blood sugar levels. Therefore, it is essential to monitor these patients regularly to prevent complications and improve their health.

Key Words: *Albuminuria, Diabetes Mellitus, Diabetic Nephropathy, Glycated Hemoglobin A, Hypertension, Risk factors.*

Introduction

Diabetes mellitus is progressively becoming a worldwide epidemic, about 8% (350 million) people are having DM, and this would rise to above 550 million by 2035.[1] Diabetes Mellitus (DM) is a disease in which the body's ability to produce or respond to the hormone insulin is impaired, resulting in abnormal metabolism of carbohydrates and elevated levels of glucose in the blood. Type-1 Diabetes is due to autoimmune damage of pancreatic islets cells, while Type 2 diabetes develops when the body becomes resistant to insulin or when the pancreas is unable to produce enough insulin.[2,3]

Over time, high blood glucose can damage the body's blood vessels, both tiny and large. Damage to tiny blood vessels causes micro vascular complications; damage to large vessels causes macro vascular complications. Long-standing blood glucose level is responsible for impairment of different organs leading to visual, neurological, renal, and cardiovascular problems.[4,5]

DN remains an important common complication of diabetes. It is characterized by gradually increasing urine albumin excretion, accompanied by slowly rising blood pressure; the decline in glomerular filtration rate occurs late.[6,7] Diabetes harms the kidneys by causing damage to tiny blood vessels of filtering units. With time, high blood sugar levels cause these vessels to become narrow and clogged. Once the nephrons are damaged and reduction of functional renal mass reaches a certain point, the remaining nephrons begin a process of irreversible sclerosis leading to ESRD.[8,9] ESRD is the final stage of nephropathy, where kidney function has declined to the point that they can no longer function on their own; Patients will need expensive procedures to live.[10,11] The possibility of cardiac diseases increases as urine albumin excretion increases and as GFR decreases.[6] ESRD and cardiac problems lead to decreased life expectation in these patients.[7,12]

Department of Community Medicine
Wah Medical College, Wah Cantt

Correspondence:
Dr. Robina Mushtaq
Department of Community Medicine
Wah Medical College, Wah Cantt
E-mail: robina.mushtaq@yahoo.com

Funding Source: NIL; Conflict of Interest: NIL
Received: January 19, 2021; Revised: November 08, 2021
Accepted: February 24, 2022

According to the International Diabetes Federation (IDF), currently 7.5 million Pakistani populations are affected with DM[13], and almost 20% to 40% diabetics in the long run have kidney disease.[1] Lots of diabetics with impaired renal function are ignorant of their condition, resulting in delayed management and increased morbidity due to ESRD and cardiac diseases.[8] Only a few studies have been conducted in our country to establish the effect of diabetes duration and glycemic control on kidney functions. Well-timed testing of renal functions in patients having DM for longer duration would delay the development of kidney disease.[14] Early detection and management holdup the disease process and lessen the risk of ESRD, thus reducing the burden on health care delivery system. An easy approach to avoid or interrupt DN is adopting healthy way of living and good glycemic control. The aim was to find out frequency of Nephropathy in subjects having type 2 Diabetes Mellitus; and to determine the effect of disease duration and blood glucose levels on the development of Diabetic nephropathy.

Materials and Methods

A Cross-sectional study was conducted at POF Hospital Wah Cantt during 1st January to 30th June 2018. Sample size was 210 based on 95% confidence level, 5% precision and 16.4% [6] anticipated proportion, subjects were selected by purposive sampling. Prior permission to conduct this study was taken from the institutional review board. Informed consent was taken from patients before data collection. Patients having Diabetes for more than 5 years were included. Information regarding blood urea and creatinine levels, duration of Diabetes, HbA1c levels, family history, blood pressure and albuminuria was taken from the documents of selected patients by the researchers. A diabetic person having albuminuria and Hypertension for the last 6 months (confirmed from patients record file) was labeled as having Diabetic Nephropathy. Patients having blood pressure above 130/90 mmHg during last 6 months were labeled as having Hypertension. On the basis of HbA1c levels three categories of glycemic control were formed; always control (HbA1c level < 7% during last 6 months), sometime control (HbA1c level 7% - 8% during last 6 months) and never control (HbA1c level > 8% during last 6 months). The data analysis was done by SPSS v-19 and Chi-square test was applied to find out the relationship of diabetes duration and blood sugar levels with diabetic nephropathy (level of significance was 0.05).

Results

Mean age in this study was 55.77 ± 13.68 years. Out of 210 patients 126 (60%) and 84 (40%) were male and female respectively. Ninety-eight (46.7%) patients had Diabetes for 5-10 years and 112 (53.3%) patients had for >10 years. One hundred and thirty-seven (65.2%) patients had positive family history while 73 (34.8%) had no family history of Diabetes Mellitus. Sixty-two (29.5%) had HbA1c level below 7%, 123 (58.6%) had HbA1c level between 7% and 8% while HbA1c level of 25 (11.9%) patients was above 8%. One hundred and forty-six (69.5%) patients had blood pressure above 130/90 mmHg on average during last 6 months. One hundred and fifteen (54.8%) patients had albuminuria and Hypertension for the last 6 months (Fig. 1).

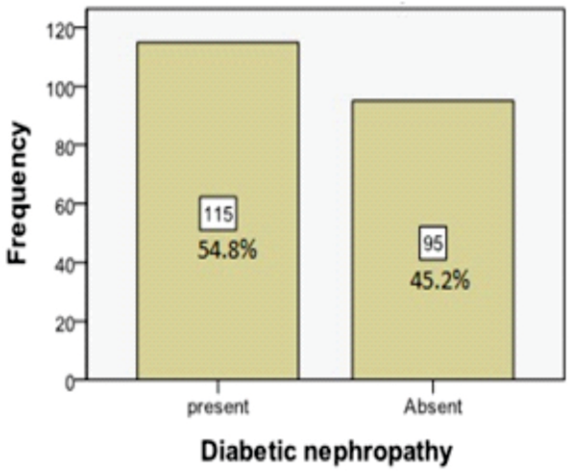

Fig. 1: Frequency (%) of Diabetic Nephropathy

Mean blood creatinine and urea levels were 1.99±1.65 mg/dL and 65.26 ± 29.62 mg/dL respectively. Frequency of diabetic nephropathy among male was 70 (55.5%) and females was 45 (53.5%) which is statistically insignificant (p-value 0.7). Seventy-nine (57.6%) patients with Diabetic nephropathy had family history of DM as compared to 36 (49.3%) who had no family history (statistically insignificant p-value 0.24). Nephropathy was reported notably more [69 (61.6%)] among patients having DM for more than 10 years, while frequency among those having DM for 5-10 years was [46 (46.9%), (p-value 0.033)]. The patients whose blood sugar levels were never controlled had high rate of

Nephropathy 21 (84%), in contrast to those having sometime [75 (61%)] and always controlled sugar levels [19 (30.6%)] (statistically significant p-value 0.000). Nephropathy occurred more in Hypertensive subjects [Table I].

Table I: Relationship of Diabetic Nephropathy with Different Variables

Variable	Attributes	Diabetic Nephropathy Frequency (%)	p-value
Gender	Male Female	70 (55.5%) 45 (53.5%)	0.7
Blood Glucose Level	Always control Sometime control Never control	19 (30.6%) 75 (61%) 21 (84%)	0.000
Duration of Diabetes Mellitus	5 – 10 years > 10 years	46 (46.9%) 69 (61.6%)	0.033
Hypertension	Yes No	88 (60.2%) 27 (42%)	0.015

Discussion

Diabetic Nephropathy is diagnosed if albuminuria and impaired renal functions persist for at least 3 months. Nephropathy is related to high mortality in common people as well as among diabetics. Early findings will let insistent actions to be taken to impede the progression of disease to ESRD.

The number of diabetics is constantly rising in Pakistan. Type 2 Diabetes can occur at any stage of life, even in children. However, it occurs most often in middle-aged and older people. In our study mean age of subjects was around 56 years, more than fifty percent subjects were having Diabetic Nephropathy; male and female were almost equally affected. The subjects having HbA1c levels persistently above 8% and diabetes for more than 10 years had significantly high frequency of Nephropathy.

The mean age of subjects was comparable to other studies made in Shanghai[15] (56 year), Pakistan[4] (55.2 year), and Tanzania[5] (45-60 year). In diabetics the organs are exposed to hyperglycemia. Intracellular hyperglycemia causes collection of unstable oxygen radicals, resulting in damage to blood vessels. Even with proper management and check on glucose level, diabetics can still develop renal pathological changes like glomerulosclerosis and chronic kidney disease. The first sign of nephropathy is presence of albumin in urine. Frequency of Diabetic Nephropathy (54.76%) was found similar to other studies by Khalid (43%)[10], Machingura (45%)[16], Wu (40%)[17], Parving (39%)[18] and Hasabi (45%) [19] this frequency was high as compared to the studies conducted in Pakistan[4] (20 %), Mediterranean region[6] (16.4%), China[15] (30.9%), USA[8] (33%), Saudi Arab[9] (10.8%), and India[20] (26.9%). The high rate in our setting may be because the patients are diagnosed late due to shortage of medical facilities, high expenditure, low health risk awareness among populations and more priority is given to communicable diseases.

Type 2 diabetes is now equally prevalent among men and women in most populations and the effect of sex on nephropathy is not well established. In our study male and female were almost equally affected, while in a study by Zhou et al[15] females had a significantly high rate of Diabetic Nephropathy. Uncontrolled Diabetes had increased the risk of development of Nephropathy. There was some evidence that improved glucose control delayed the progression of albuminuria. With decrease of 1% HbA1c level, there was a 37% decreased possibility of nephropathy [21]. In this study, the subjects having HbA1c levels persistently above 8% had significantly high frequency of Nephropathy (p-value 0.000). These results were consistent with other studies showing a relation of high HbA1c levels to the progression of Nephropathy; China[15] (P <0.001), USA[8] (P< 0.001), Ethiopia[3] (P< 0.002), Saudi Arab[9] (OR 1.17), India[22] (OR 11.8), and Zimbabwe[16] (OR 1.20).

The likelihood of Nephropathy among diabetics also increases with the duration of disease.[8] Regardless of check on blood glucose and Blood Pressure the incidence of albuminuria increases as a consequence of increasing survival and duration of diabetes. The frequency of DN was found to be significantly higher among patients having diabetes for more than 10 years (p-value 0.033). The relationship of long-standing DM and Nephropathy had been proved by many studies; from USA (p-value 0.001)[8], Pakistan (p-value 0.05)[4], Saudi Arab (p< 0.0001)[9], Zimbabwe (OR= 1.03),[16] and India (p = 0.046) [20] (OR = 4.69).[22] Hypertension is an invariable accompaniment of ESRD and control of hypertension reduces the risk of developing albuminuria. A substantial association was found between presence of albuminuria and

hypertension (p = 0.015); similar association had been studied by Shera et. al.[4] (p = 0.05), Al-Rubeaan[9] (p < 0.0001), Parving[18] (OR = 1.10), and Akheel[22] (OR = 2.06). Educating patients on health risks associated with Diabetes and changing their mode of living for better glycemic control can impede the disease process and lower the burden on health system of country.

Conclusion

The frequency of Diabetic Nephropathy is found to be quite high. It is significantly higher among subjects having diabetes for longer duration and uncontrolled blood sugar levels. Careful monitoring of diabetic patients can prevent complications and improve their quality of life. Educating patients regarding the risk factors can reduce the burden of kidney diseases.

REFERENCES

1. Gheith O, Farouk N, Nampoory N, Halim MA, Al-Otaibi T. Diabetic kidney disease: worldwide difference of prevalence and risk factors. J Nephropharmacol. 2016; 5(1): 49–56.
2. Magee C, Grieve DJ, Watson CJ, Brazil DP. Diabetic Nephropathy: a Tangled Web to Unweave**.** Cardiovasc Drugs Ther. 2017; 31(5): 579–592.doi: 10.1007/s10557-017-6755-9
3. Hintsa S, Dube L, Abay M, Angesom T, Workicho A. Determinants of diabetic nephropathy in Ayder Referral Hospital, Northern Ethiopia: A case-control study. PLoS One. 2017; 12(4): e0173566.doi: 10.1371/journal.pone.0173566
4. Shera AS, Jawad F, Maqsood A, Jamal S, Azfar M, Ahmed U. Prevalence of Chronic Complications and Associated Factors in Type 2 Diabetes. JPMA. 2004; 54(2): 54-9
5. Janmohamed MN, Kalluvya SE, Mueller A, Kabangila R, Smart LR, Downs JA et al. Prevalence of chronic kidney disease in diabetic adult out-patients in Tanzania. BMC Nephrology. 2013; 14:183.Doi:10.1186/1471-2369-14-183
6. Coll-de-Tuero G, Mata-Cases M, Rodriguez-Poncelas A, Pepio JMA, Roura P, Benito B et al. Chronic kidney disease in type 2 diabetic patients: prevalence and associated variables in a random sample of 2642 patients of a Mediterranean area. BMC Nephrology.2012;13:87. doi:10.1186/1471-2369-13-87
7. Tziomalos K, Athyros VG. Diabetic Nephropathy: New Risk Factors and Improvements in Diagnosis. Rev Diabet Stud. 2015; 12(1-2): 110–118.doi: 10.1900/RDS.2015.12.110
8. Wall BM, Hardison RM, Molitch ME, Marroquin OC, McGill JB, August PA. High Prevalence and Diversity of Kidney Dysfunction in Patients with Type 2 Diabetes Mellitus and Coronary Artery Disease: The BARI 2D baseline data. Am J Med Sci. 2010; 339(5): 401-410.
9. 9. Al-Rubeaan K, Youssef AM, Subhani SN, Ahmad NA, Al-Sharqawi AH, Al-Mutlaq HM, et al. Diabetic Nephropathy and Its Risk Factors in a Society with a Type 2 Diabetes Epidemic: A Saudi National Diabetes Registry-Based Study. PLoS One. 2014; 9(2): e88956.doi: 10.1371/journal.pone.0088956
10. Al-Rubeaan K, Siddiqui K, Al-Ghonaim MA, Youssef AM, AlNaqeeb D. The Saudi Diabetic Kidney Disease study (Saudi-DKD): clinical characteristics and biochemical parameters. Ann Saudi Med. 2018; 38(1): 46–56.doi: 10.5144/0256-4947.2018.03.01.1010
11. Zhuo L, Zou G, Li W, Lu J, Ren W. Prevalence of diabetic nephropathy complicating non-diabetic renal disease among Chinese patients with type 2 diabetes mellitus. European Journal of Medical Research. 2013; **18**:4. doi.org/10.1186/2047-783X-18-4
12. de Boer IH, Rue TC, Hall YN, Heagerty PJ, Weiss NS, Himmelfarb J. Temporal Trends in the Prevalence of Diabetic Kidney Disease in the United States. JAMA. 2011; 305(24):2532-2539
13. Uddin F, Ali B, Junaid N. Prevalence of diabetic complications in newly diagnosed type 2 diabetes patients in Pakistan: findings from national registry. J Ayub Med Coll Abbottabad. 2018; 30(4 Suppl 1):652–8.
14. Inassi J, Vijayalakshmy R. Role of duration of diabetes in the development of nephropathy in type 2Diabetic patients. National Journal of Medical Research. 2013; 3(1): 5-8
15. Zhou Y, Echouffo-Tcheugui JB, Gu J, Ruan X, Zhao GM, Zhang H et al. Prevalence of chronic kidney disease across levels of glycemia among adults in Pudong New Area, Shanghai, China. BMC Nephrology. 2013; 14:253. doi:10.1186/1471-2369-14-253
16. Machingura PI, Chikwasha V, Okwanga PN, Gomo E. Prevalence of and Factors Associated with Nephropathy in Diabetic Patients Attending an Outpatient Clinic in Harare, Zimbabwe. Am J Trop Med Hyg. 2017; 96(2): 477–482.doi: 10.4269/ajtmh.15-0827
17. Wu AYT, Kong NCT, de Leon FA, Pan CY, Tai TY, Yeung VTF et al. An alarmingly high prevalence of diabetic nephropathy in Asian type 2 diabetic patients: the Micro Albuminuria Prevalence (MAP) Study. Diabetologia. 2005; 48(1): 17-26. doi.org/10.1007/s00125-004-1599-9
18. Parving HH, Lewis JB, Ravid M, Remuzzi G, Hunsicker LG. Prevalence and risk factors for microalbuminuria in a referred cohort of type II diabetic patients: A global perspective. Kidney International. 2006; 69:2057–2063. doi:10.1038/sj.ki.5000377
19. Hasabi IS, Kardkal BL, Bande US. The role of duration of Diabetes in the development of nephropathy. Journal of Evidence Based Medicine and Healthcare. 2017; 4: 6017-6021. DOI - 10.18410/jebmh/2017/1212
20. Unnikrishnan R, Rema M, Pradeepa R, Deepa M, Shanthirani CS, Deepa R, et al. Prevalence and Risk Factors of Diabetic Nephropathy in an Urban South Indian Population. Diabetes Care. 2007; 30(8):2019–2024
21. Stratton IM, Adler AI , Neil HA , Matthews DR , Manley SE , Cull CA , et al. Association of glycemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. Br Med J. 2000; 321: 405 – 412

22. Ahmed MA, Kishore G, Khader HA, Kasturirangan MN. Risk Factors and Management of Diabetic Nephropathy. Saudi J Kidney Dis Transpl. 2013; 24(6):1242-1247

CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

GRANT SUPPORT AND FINANCIAL DISCLOSURE

Authors have declared no specific grant for this research from any funding agency in public, commercial or nonprofit sector.

DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.