ORIGINAL ARTICLE

FREQUENCY OF NON-DIABETIC RENAL DISEASE IN TYPE 2 DIABETES MELLITUS PATIENTS UNDERGOING RENAL BIOPSY

Muhammad Zeeshan Khan[1], Mudassar Hussain[1], Azhar Ali Khan[2], Usman Hassan[1], Noreen Akhter[1], Maryium Hameed[1], Sajid Mushtaq[1], Usman Ayub Awan[1]

[1]Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, [2]Nephrology Department, Shaikh Zayed Hospital Lahore-Pakistan

Background: Diabetes mellitus has become a major emerging health concern. Its burden, estimated to be 451 million in 2017, has been projected to rise to 693 million by 2045. This will bring a rise in the prevalence of its associated complications. There is a wide spectrum of non-diabetic renal disease (NDRD) known to be present in diabetic patients with variable prevalence. However, the majority of diabetes mellitus (DM) patients with renal disease are yet not biopsied and the diagnosis of diabetic nephropathy (DN) is presumed on clinical grounds. **Methods:** It is a retrospective cross-sectional study. We selected a total of 126 cases of renal biopsies with a history of type 2 diabetes mellitus. Demographic data was collected from the medical records and pathology reports while all cases were evaluated by reviewing the archived slides. **Results:** Patients were categorized into group 1 with isolated NDRD, group 2 showing NDRD mixed with DN and group 3 with isolated DN. Thirty-four (27%) cases had isolated NDRD (group 1), 14 (11%) had NDRD mixed with DN and 78 (62%) patients had isolated DN. NDRD, either alone or in combination with DN, was found to be present in 48 patients with an overall prevalence of 38%. **Conclusion:** Our study concludes that NDRD is frequent in type 2 diabetes mellitus patients. Renal biopsy remains the key diagnostic tool in such cases, providing crucial information for proper management of the underlying pathology.

Keywords: Type 2 diabetes mellitus; Diabetic nephropathy (DN); Non-diabetic renal disease (NDRD); Renal biopsy

Citation: Khan MZ, Hussain M, Khan AA, Hassan U, Akhter N, Hameed M, *et al*. Frequency of non-diabetic renal disease in type 2 diabetes mellitus patients undergoing renal biopsy. J Ayub Med Coll Abbottabad 2021;33(Suppl. 1):757–62.

INTRODUCTION

Diabetes mellitus (DM) has become a major emerging health concern and is the seventh leading cause of death worldwide as it carries a significant risk of cardiovascular disease. Its burden was estimated to be approximately 171 million in 2000 which increased to 382 million in 2013 and later to 451 million in 2017. This has been projected to further rise up to 693 million by 2045,[1] which will ultimately lead to an upsurge in the prevalence of its associated complications. Diabetic nephropathy (DN) is the most common renal pathology and the leading cause of chronic kidney disease (CKD), finally culminating into end-stage renal disease (ESRD).[2–4] CKD is defined clinically as a persistently raised urinary albumin excretion of ≥30 mg/g, a reduction in estimated glomerular filtration rate of less than 60 ml/min/1.73 m2 or both.[5–7] DN is not the only cause of CKD in the type 2 diabetes population. Non-diabetic renal disease (NDRD) comprises a heterogeneous group and is known to be present in diabetic patients with variable prevalence reported in different studies.[8–13] Multiple studies have suggested that NDRD has a better prognosis than classic DN but this information can only be fruitful if it is timely diagnosed.[14–16] Most patients with T2DM are not formally evaluated with a renal biopsy, as it is an invasive procedure. The diagnosis is generally presumed on clinical grounds and the nephrologists reserve the option of renal biopsy in DM when NDRD is suspected or when diabetic nephropathy is questionable. This results in a proportion of patients with NDRD being inaccurately classified as having DN. Renal biopsy is the only approach to a definite diagnosis. Previously, only two studies have been carried out in Pakistan to evaluate the prevalence of NDKD among T2DM patients. Both were done in the centers located in city of Karachi and only those patients were selected who presented at their centers for renal biopsy.[10,14] The study period of both of these studies is more than 10 years old now. At our center, we receive renal biopsies from various medical hospitals and nephrology centers from Lahore as well as other cities from all over Punjab. Our aim is to study the recent trend in the frequency and nature of NDRD in the T2DM population who underwent a renal biopsy.

MATERIAL AND METHODS

It is a retrospective cross-sectional study. After the approval from the hospital ethical committee, we

searched the computerized database for percutaneous renal biopsies received for reporting from January 1, 2016 to June 30, 2019. The demographic and clinical data of the selected patients were collected from the pathology reports and requisition slips.

All renal biopsy cases with a clinical history of type 2 diabetes mellitus, reported between January 1, 2016 and June 30, 2019, were included.

Cases with inadequate renal biopsy, history of renal transplant and malignancy or second / follow-up biopsy were excluded. Cases in which a definite diagnosis was not possible due to unavailability of electron microscopic examination were also excluded. Type 1 diabetes mellitus patients have not been included in the study.

Archived slides from formalin-fixed paraffin-embedded tissue stained with haematoxylin & eosin (H&E), periodic acid-Schiff (PAS), Jones methenamine silver and Masson trichrome were retrieved and reviewed, under light microscopy, by two pathologists with a special interest in renal pathology. Diabetic nephropathy was diagnosed and classified by the presence of mesangial expansion with or without the Kimmelstiel-Wilson nodules, glomerular basement membrane thickening, capsular drops, and fibrin drops.[15–18] Electron microscopic examination was not possible due to the unavailability of this facility at our institute.

Patients were categorized into the following three groups on the basis of the pathological findings:

Group 1: Isolated NDRD

Group 2: NDRD mixed with Diabetic nephropathy

Group 3: Isolated DN

Statistical analysis was carried out using Microsoft Excel for Windows platform version 2013. Simple descriptive statistics such as mean and standard deviation were used for variables such as age and duration of diabetes. Percentages were used for categorical data.

RESULTS

A total of 126 cases were selected in our study. An overall mean age at the time of biopsy was 47.8±11.4 years with a male to female ratio of 3:1. Clinical parameters of the three groups have been summarized in table-1. The results show thirty-four (27%) cases had isolated NDRD (group 1) while 14 (11%) cases had DN complicated with NDRD (group 2). Isolated diabetic nephropathy (group 3) was found in 78 (62%) cases. Thus, NDRD was present in 48 cases, either alone or mixed with DN, with an overall prevalence of 38%.

Indications of renal biopsy in our study population included worsening proteinuria with less than 5 years history of type 2 diabetes mellitus, active urinary sediment (microscopic haematuria & RBC casts), rapidly declining renal functions/AKI, laboratory markers of systemic diseases (low complements, ANA, ANCA, Cryoglobulins, HbsAg, Anti HCV) and heavy proteinuria in the absence of diabetic retinopathy. These have been summarized in table 2 with respective frequencies.

The mean age at the time of biopsy was 49±4.2 years with a male to female ratio of 1.6:1. Patients in this group presented with an average duration of diabetes of 7.14 years (SD±4.58). Among the 34 cases with isolated NDRD, membranous glomerulonephritis was the predominant pattern, present in 12 (35.3%) cases. It was followed by focal segmental glomerulosclerosis (FSGS) involving 6 (17.7%) cases and acute interstitial nephritis involving 4 (11.8%) cases. Other non-diabetic renal diseases with their respective frequencies are listed in table-3. One of the cases showed cortical infarction with no sign of glomerulopathy or interstitial nephritis. Twenty (58.8%) cases showed mild and 7 (20.6%) showed moderate interstitial fibrosis and tubular atrophy (IFTA) in this group. There was no or minimal IFTA in 7 (20.6%) cases. Twenty (58.8%) cases had a concomitant history of hypertension.

Patients in this group presented with a mean age of 42.7±8.6 years and male to female ratio of 1.3:1. The average duration of diabetes in this group was 10.78 years (SD±5.14). A total of 14 (11%) cases belonged to this group. Acute interstitial nephritis was the predominant NDRD in this group, involving 5 (35.8%) cases. Membranous nephropathy, IgA nephropathy and focal segmental glomerulosclerosis each represented 14.3% of the non-diabetic renal disease with mixed DN. Membranoproliferative glomerulonephritis, C3 glomerulopathy and diffuse proliferative glomerulonephritis each involved 1 (7.1%) of the total NDRD in this group. IFTA was moderate in 12 (85.7%) while mild in 2(14.3%) cases in this group. Out of a total of 14 cases in this group, 7 (50%) had a concomitant history of HTN.

A mean age of 48.8±9.8 years was noted in this group. The male to female ratio was 6:1. The average duration of diabetes was 9.62 years (SD±5.35). A concomitant history of hypertension was present in 42.3% of these cases. The glomerular lesions were further classified as follows: 33 (42.3%) cases in class IV showing advanced glomerulosclerosis with more than 50% globally sclerosed glomeruli, 30 (38.5%) cases in class III with at least one Kimmelstiel-Wilson nodular lesion and less than 50% globally sclerosed glomeruli, 9 (11.5%) in class IIb showing severe mesangial expansion and 6 (7.7%) in class IIa with mild mesangial expansion. Interstitial fibrosis and tubular atrophy were found to be severe in 16 (20.5%), moderate in 40 (51.3%) and mild in 19 (24.4%) cases. No or minimal IFTA was noted in 3 (3.8%) cases.

Table-1: Clinical parameters in different groups of patients

Parameters	Group 1 Isolated NDRD n=34	Group 2 NDRD with DN n=14	Group 3 Isolated DN n=78
Mean age at time of biopsy (years)	49±4.2	42.7±8.6	48.8±9.8
Male/Female	21/13	8/6	67/11
Duration of diabetes (years)	7.14 years (SD± 4.58)	10.78 years (SD± 5.14)	9.62 years (SD± 5.35)
HTN	20 (58.8%)	7 (50%)	33 (42.3%)

Table-2: Indications of renal biopsy in the study population

Indication	Number of patients	Percentage
Active urinary sediment (microscopic haematuria, RBC Cast)	43	34.12
Worsening proteinuria with less than 5 years duration of diabetes	38	30.16
Rapidly declining renal functions/AKI	33	26.20
Heavy proteinuria in the absence of diabetic retinopathy	12	9.52
Total	126	100

Table-3: Frequency and nature of non-diabetic renal diseases in groups 1 and 2

Pathology	Isolated NDRD n (%)	NDRD with DN n (%)
Membranous nephropathy	12 (35.3)	2 (14.3)
Focal segmental glomerulosclerosis	6 (17.7)	2 (14.3)
Acute interstitial nephritis	4 (11.8)	5 (35.8)
Amyloidosis	3 (8.8)	-
Pauci-immune (ANCA associated) crescentic glomerulonephritis	3 (8.8)	-
Cryoglobulinemic glomerulonephritis	2 (5.9)	-
IgA nephropathy	2 (5.9)	2 (14.3)
Lupus nephritis	1 (2.9)	-
Cortical infarct	1 (2.9)	-
Membrano-proliferative glomerulonephritis	-	1 (7.1)
Diffuse proliferative glomerulonephritis	-	1 (7.1)
C3 Glomerulonephritis	-	1 (7.1)
Total	34 (100)	14 (100)

Table-4: Comparison of NDRD and DN prevalence in different parts of world

Country	% Isolated NDRD	% NDRD with DN	% Isolated DN
United States (Pham *et al*) [22]	53.2	19.3	27.5
United States (Sharma *et al*) [23]	36	27	37
United States (Nzerue *et al*) [24]	19.4	38.7	41.9
China (Wong *et al*) [17]	46	19	35
China (Mak *et al*) [25]	16	17	67
Japan (Harada *et al*) [26]	34.5	10.9	54.5
Japan (Akimoto *et al*) [27]	26	6	68
Japan (Tone *et al*) [28]	16.5	47.5	36
India (Prakash *et al*) [29]	30.5	13	56.5
India (Soni *et al*) [11]	27.5	30	42.5
India (Moger *et al*) [30]	23.1	42.3	34.6
Pakistan (Yaqub *et al*) [10]	52	17	31
Pakistan (Arif *et al*) [14]	41.1	8.22	27.3

DISCUSSION

The global burden of T2DM, with its associated complications, is increasing worldwide.[1] Diabetic nephropathy is the most common renal complication and the leading cause of ESRD in T2DM.[2–4] Furthermore, survival of ESRD patients on regular dialysis is lower than non-diabetic ESRD patients undergoing maintenance dialysis. It is also among the chief renal pathology demanding renal replacement therapy. The diagnosis of DN is generally presumed on clinical grounds with support from certain laboratory analyses. The supportive features include persistent proteinuria, progressive and slow decline in kidney function and hypertension.[18] However; it is not the only form of the renal pathology present in this group of patients.

The natural history of kidney involvement is variable in both T1DM & T2DM patients, with disease course more precise in the former group but on the other hand, it is not well characterized in the T2DM population on the account of uncertain onset of diagnosis before the presentation. A number of patients having T2DM already manifest micro albuminuria or even macro albuminuria by the time they pay first visit to a nephrologist. Since only a few numbers of diabetic patients undergo renal biopsy, the term diabetic kidney disease should be reserved for the patients in whom diabetic nephropathy is suspected on clinical parameters. On the other hand, diabetic nephropathy should be mentioned only for those patients with the histological evidence of renal involvement typical of diabetes.

The literature has provided sufficient evidence that despite having macro albuminuria in diabetic patients, there is still high probability of NDRD especially in the absence of diabetic retinopathy. Roughly about 30% of proteinuric diabetic patients without diabetic retinopathy will display either normal histology or pattern of renal diseases other than diabetic nephropathy. NDRD encompasses all the other renal pathologies occurring in T2DM patients. Different clinical features are atypical for the clinical presentation of diabetic nephropathy & are predictive of NDRD. These include worsening proteinuria or proteinuria in the absence of diabetic retinopathy, rapidly declining renal function, active urinary sediment and short duration of diabetes.[11,20] However, there is significant heterogeneity in clinical presentation of diabetic nephropathy and NDRD. This result in diagnostic difficulties in the clinical differentiation between DN and NDRD in certain cases.[8,9,21] The correct diagnoses of these diseases have significant influence on the selection of a proper treatment plan. It is difficult to reverse diabetic nephropathy whereas some NDRD's can be readily treated with favourable outcomes.[16,17] No uniform criteria are in practice to select diabetic patients for renal biopsy and a significant number of patients with potential NDRD are frequently overlooked.[20]

There is a wide variation of the prevalence of NDRD among type 2 diabetes patients, undergoing renal biopsy, in the published literature.[8–13] The reason for this fact is due to the variable renal biopsy policies in different medical setups. We found a total prevalence of NDRD, alone or mixed with diabetic nephropathy, to be 38% in the patients undergoing renal biopsy with a history of type 2 diabetes. It was found to be 69% (n=64) and 49% (n=73) in the other two studies conducted in Pakistan.[10,14] A comparison of the prevalence of NDRD in T2DM patients reported in literature has been provided in the table-4.

In our study, there was a male predominance in all the three groups with a significantly higher male: female of almost 6:1 in isolated DN patients. However, it was 1.6:1 in group 1 and 1.3:1 in group 2. Patients with mixed NDRD and DN were relatively younger than the other two groups. Isolated NDRD group showed a significantly shorter duration of diabetes compared to the other two groups. It has previously been shown by Lee *et al* that there is significant association between shorter duration of diabetes at the time of renal biopsy and NDRD.[15] Due to the retrospective nature of the study, important data regarding the accurate measurements of proteinuria, HbA1c and lipid profile were not found in minority of the cases.

We found membranous nephropathy to be the most common pathology in the isolated NDRD group, followed by focal segmental glomerulosclerosis, acute interstitial nephritis and amyloidosis. Among group 2 patients, acute interstitial nephritis was found to be the most common NDRD and was followed by membranous nephropathy and IgA nephropathy. Soni *et al* also found membranous nephropathy to be the most frequent pathology in the isolated NDRD group while acute interstitial nephritis was the predominant non-diabetic pathology mixed with DN.[11] However, Yaqub *et al* found acute interstitial nephritis to be the most frequent NDRD in the isolated NDRD group.[10] Minimal change disease was found to be the commonest NDRD in the study by Das *et al*.[9]

In our study, isolated diabetic nephropathy was present in 62% of the cases. Major proportion of these cases displayed advanced disease with classes III and IV, collectively comprising approximately 81% of isolated DN. Duration of diabetes was higher in this group as compared to the isolated NDRD as shown in table-1.

Various studies have highlighted the absence of diabetic retinopathy, haematuria, acute kidney injury and rapid worsening of renal function to be the indicators of NDRD.[11,20] However, its differentiation from DN is still difficult on clinical and laboratory criteria and a number of cases can be overlooked by too strict selection criteria for renal biopsy in T2DM patients.[8,9,21] The renal function can be preserved by modifying the treatment according to the nature of NDRD's.[8,16,17] Thus it is essential that a uniform and flexible selection criteria must be formulated.

It is worth mentioning here that renal biopsy should also be considered in the selection criteria of the clinical trials aimed to modify the clinical course of diabetic nephropathy.[31] It will ensure that isolated DN patients are selected for the study and will avoid confounding effects of NDRD on the outcome of the clinical trials.

Limitations:

Retrospective nature of study and the absence of electron microscopy limit the scope of this study. A small proportion of T2DM patients were excluded owing to unavailability of electron microscopy to make a definite diagnosis. Minimal change disease or class I diabetes could have been the possible pathologies in those patients.

CONCLUSION

Our study concludes that non-diabetic renal disease is frequent in type 2 diabetic patients undergoing renal biopsy, either alone or in combination with diabetic nephropathy. Renal biopsy remains the key diagnostic tool in such cases, providing crucial information for a proper management of the underlying pathology.

AUTHORS' CONTRIBUTION

MH & UH: Conceptualized and devised the study design. MH, MZK & AAK: Literature search and data collection. MZK & MC: Drafting of the manuscript with input from all authors. UAA: Data analysis and interpretation. SM & NA: Proofreading and drafting of the final manuscript.

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;138:271–81.
2. Ritz E, Rychlik I, Locatelli F, Halimi S. End-stage renal failure in type 2 diabetes: A medical catastrophe of worldwide dimensions. Am J Kidney Dis 1999;34(5):795–808.
3. Atkins R. The epidemiology of chronic kidney disease. Kidney Int 2005;67:S14–8.
4. Saran R, Robinson B, Abbott KC, Agodoa LYC, Bragg-Gresham J, Balkrishnan R, *et al*. US Renal Data System 2018 Annual Data Report: epidemiology of kidney disease in the United States. Am J Kidney Dis 2019;73(3 Suppl 1):A7–8.
5. Thomas MC, Weekes AJ, Broadley OJ, Cooper ME, Mathew TH. The burden of chronic kidney disease in Australian patients with type 2 diabetes (the NEFRON study). Med J Aust 2006;185(3):140–4.
6. Dwyer JP, Parving HH, Hunsicker LG, Ravid M, Remuzzi G, Lewis JB. Renal dysfunction in the presence of normoalbuminuria in type 2 diabetes: results from the DEMAND study. Cardiorenal Med 2012;2(1):1–10.
7. Thomas MC, Cooper ME, Zimmet P. Changing epidemiology of type 2 diabetes mellitus and associated chronic kidney disease. Nat Rev Nephrol 2016;12(2):73–81.
8. Tan J, Zwi LJ, Collins JF, Marshall MR, Cundy T. Presentation, pathology and prognosis of renal disease in type 2 diabetes. BMJ Open Diabetes Res Care 2017;5:e000412.
9. Das U, Dakshinamurty KV, Prayaga A, Uppin MS. Nondiabetic kidney disease in type 2 diabetic patients: A single center experience. Indian J Nephrol 2012;22:358–62.
10. Yaqub S, Kashif W, Hussain SA. Non-diabetic renal disease in patients with type-2 diabetes mellitus. Saudi J Kidney Dis Transpl 2012;23:1000–7.
11. Soni SS, Gowrishankar S, Kishan AG, Raman A. Non diabetic renal disease in type 2 diabetes mellitus. Nephrology (Carlton). 2006;11:533–7.
12. Fiorentino M, Bolignano D, Tesar V, Pisano A, Biesen WV, Tripepi G, *et al*. Renal biopsy in patients with diabetes: a pooled meta-analysis of 48 studies. Nephrol Dial Transplant. 2017;32:97–110.
13. Gonzalez Suarez ML, Thomas DB, Barisoni L, Fornoni A. Diabetic nephropathy: Is it time yet for routine kidney biopsy? World J Diabetes 2013;4(6):245–55.
14. Arif M, Arif MK, Arif MS. An evaluation of renal biopsy in type-II diabetic patients. J Coll Physicians Surg Pak 2009;19(10):627–31.
15. Lee YH, Kim KP, Kim YG, Moon JY, Jung SW, Park E, *et al*. Clinicopathological features of diabetic and nondiabetic renal diseases in type 2 diabetic patients with nephrotic-range proteinuria. Medicine (Baltimore) 2017;96(36):e8047.
16. Byun JM, Lee CH, Lee SR, Moon JY, Lee SH, Lee TW, *et al*. Renal outcomes and clinical course of nondiabetic renal diseases in patients with type 2 diabetes. Korean J Intern Med 2013;28(5):565–72.
17. Wong TY, Choi PC, Szeto CC, To KF, Tang NL, Chan AW, *et al*. Renal outcome in type 2 diabetic patients with or without coexisting nondiabetic nephropathies. Diabetes Care 2002;25(5):900–5.
18. Tervaert TW, Mooyaart AL, Amann K, Cohen AH, Cook HT, Drachenberg CB, *et al*. Pathologic Classification of Diabetic Nephropathy. J Am Soc Nephrol 2010;21(14):556–63.
19. Saran R, Robinson B, Abbott KC, Agodoa LYC, Bhave N, Bragg-Gresham J, *et al*. US Renal Data System 2017 annual data report: epidemiology of kidney disease in the United States. Am J Kidney Dis 2018;71(3 Suppl 1):A7.
20. Serra A, Romero R, Bayes B, Lopez D, Bonet J. Is there a need for changes in renal biopsy criteria in proteinuria in type 2 diabetes? Diabetes Res Clin Pract 2002;58(2):149–53.
21. Liang S, Zhang XG, Cai GY, Zhu HY, Zhou JH, Wu J, *et al*. Identifying parameters to distinguish non-diabetic renal diseases from diabetic nephropathy in patients with type 2 diabetes mellitus: A meta-analysis. PLoS One 2013;8(5):e64184.
22. Pham TT, Sim JJ, Kujubu DA, Liu IL, Kumar VA. Prevalence of nondiabetic renal disease in diabetic patients. Am J Nephrol 2007;27(3):322–8.
23. Sharma SG, Bomback AS, Radhakrishnan J, Herlitz LC, Stokes MB, Markowitz GS, *et al*. The modern spectrum of renal biopsy findings in patients with diabetes. Clin J Am Soc Nephrol 2013;8(10):1718–24.
24. Nzerue CM, Hewan-Lowe K, Harvey P, Mohammed D, Furlong B, Oster R. Prevalence of non-diabetic renal disease among African-American patients with type II diabetes mellitus. Scand J Urol Nephrol 2000;34(5):331–5.
25. Mak SK, Gwi E, Chan KW, Wong PN, Lo KY, Lee KF, *et al*. Clinical predictors of non-diabetic renal disease in patients with non-insulin dependent diabetes mellitus. Nephrol Dial Transplant 1997;12(12):2588–91.
26. Harada K, Akai Y, Sumida K, Yoshikawa M, Takahashi H, Yamaguchi Y, *et al*. Significance of renal biopsy in patients with presumed diabetic nephropathy. J Diabetes Investig 2013;4(1):88–93.
27. Akimoto T, Ito C, Saito O, Takahashi H, Takeda S, Ando Y, *et al*. Microscopic hematuria and diabetic glomerulosclerosis--clinicopathological analysis of type 2 diabetic patients

associated with overt proteinuria. Nephron Clin Pract 2008;109(3):c119–26.
28. Tone A, Shikata K, Matsuda M, Usui H, Okada S, Ogawa D, *et al*. Clinical features of non-diabetic renal diseases in patients with type 2 diabetes. Diabetes Res Clin Pract 2005;69(3):237–42.
29. Prakash J, Lodha M, Singh SK, Vohra R, Raja R, Usha. Diabetic retinopathy is a poor predictor of type of nephropathy in proteinuric type 2 diabetic patients. J Assoc Physicians India 2007;55:412–6.
30. Moger V, Kumar SK, Sakhuja V, Joshi K, Walker R, Kohli HS, *et al*. Rapidly progressive renal failure in type 2 diabetes in the tropical environment: a clinico-pathological study. Ren Fail 2005;27(5):595–600.
31. Espinel E, Agraz I, Ibernon M, Ramos N, Fort J, Serón D. Renal biopsy in type 2 diabetic patients. J Clin Med 2015;4(5):998–1009.

Submitted: June 4, 2020	*Revised: September 11, 2020*	*Accepted: May 2, 2021*

Address for Correspondence:

Muhammad Zeeshan Khan, Histopathology Department, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore-Pakistan
Cell: +92 334 718 4000
Email: dr.zeeshan.afip@gmail.com