ORIGINAL ARTICLE

HISTOLOGICAL PATTERN OF NON-DIABETIC RENAL DISEASE IN TYPE 2 DIABETES MELLITUS. A STUDY IN A TERTIARY CARE HOSPITAL

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ABSTRACT

OBJECTIVE: To determine the histological pattern of non-diabetic renal disease in type 2 diabetes mellitus.

MATERIAL AND METHODS: This descriptive, cross-sectional study was conducted in the Nephrology department MTI Lady Reading Hospital Peshawar from January 2018 to January 2021. All type 2 diabetic patients with normal fundi were included in the study irrespective of time duration. A total of 30 patients were registered. Their biodata was entered in a prescribed proforma. Those having normal fundi were included in the study and were then exposed to renal biopsy. Those patients having diabetic retinal changes were excluded from the study.

RESULTS: Out of 30 patients, males were 20 and females were 10 with a ratio of 2:1 with a mean age of 55.5±13.3SD years. Pure diabetic nephropathy (DN) was noted in 9 (30%) cases, Non-Diabetic Renal Disease (NDRD) in 13 (43.3%) cases, and NDRD on DN in 8 (26.7%) cases. Among the Non-Diabetic Renal Disease (NDRD), Membranous Glomerulonephritis (MGN) was present in 9 (30%) cases, Acute Tubular Necrosis (ATN) in 5 (16.6%) cases, Focal Segmental Glomerulosclerosis (FSGN) in 4 (13.33%.) cases, Mesangiocapillary Glomerulonephritis (MCGN) in 2 (6.7%) cases and Hemolytic Uremic Syndrome (HUS) in 1 (3.3%) cases.

CONCLUSION: It was concluded from the study that the absence of diabetic retinopathy does not exclude diabetic nephropathy. Renal biopsy should be done in all patients with type 2 DM irrespective of time duration especially with normal fundi and atypical renal involvement.

KEYWORDS: Renal biopsy, Fundoscopy, Non-diabetic renal disease, Glomerulonephritis

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INTRODUCTION

Diabetic nephropathy (DN) has been reported as the leading cause of chronic kidney diseases and End-Stage Renal Disease (ESRD). [1, 2] Diabetes has been reported as one of the most important causes of ESRD in Europe and Asia, contributing to 20–30% of the incident ESRD patients in Europe and up to 40–55% in certain parts of Asia. [3-6]

The development of chronic complications of diabetes is closely related to diabetic control. Micro and macrovascular complications of diabetes can result in significant morbidity and mortality. [7] The diagnosis of DN is almost always based on clinical grounds in type 1 diabetes but not in those with type 2 diabetes mellitus. [8] Diabetic retinopathy is a screening and diagnostic clinical finding for DN in type 2 diabetic patients. Proliferative diabetic retinopathy may be a highly specific indicator for diabetic nephropathy. [9] Non-diabetic renal diseases (NDRD) either isolated or superimposed on an underlying DN, have been reported. The prevalence of biopsy-proven NDRD in patients with diabetes varies from 10–85% among different reports. [10-13] These differences may be due to set criteria or the populations being studied.[14, 15]

Better kidney survival has been reported in the early diagnosis and appropriate therapy of patients with non-diabetic renal disease. [16] The indication of renal biopsy in patients with type 2 DM in absence of diabetic retinopathy has been reported, in atypical clinical features of renal involvement with short duration, acute onset of nephrotic syndrome, proteinuria with active urine sediment, and acute kidney injury of unknown cause. [17, 18]

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Treatment of NDRD is completely different from DN. Immunosuppressive therapy is the mainstay of the treatment in NDRD apart from angiotensin-converting enzyme inhibitors or angiotensin receptor blockers and statins. Thus, it is important to diagnose NDRD very early and for that, kidney biopsy is necessary to confirm the diagnosis. This study was aimed to determine the frequency of NDRD with or without DN in type 2 DM patients who have an atypical presentation of diabetic renal involvement. NDRD is defined as a kidney disease that is not associated with diabetes mellitus and with the absence of changes in the target organs (retinopathy) caused by long-term diabetes mellitus.

MATERIALS AND METHODS

This descriptive, cross-sectional study was carried out in the Nephrology Department, Lady Reading Hospital Peshawar from January 2018 to January 2021. This study comprised of 30 patients having nephropathy with a history of type 2 diabetes mellitus at the time of diagnosis irrespective of duration. Male and female patients of all age groups were included. Renal biopsy was performed in all those cases who had unexplained rapidly increasing proteinuria, active urine sediment and rapidly rising creatinine, and proteinuria with rising creatinine and renal involvement with the normal funduscopic examination. Fundoscopy was done and fundal photographs were taken of all patients. Patients having type 1 diabetes mellitus and those who have diabetic retinopathy were excluded from the study. Institutional ethical approval was granted for this research work.

Written consent was taken from all patients and biodata was entered on prescribed proforma. Variables were entered in SPSS 20.0. Variables like name, age, sex, duration and type of diabetes, proteinuria, urea and creatinine, ultrasound, Fundoscopy, and renal biopsy findings were recorded. Fundoscopy findings were broadly categorized into normal, non-proliferative, and proliferative diabetic retinopathy. All renal biopsies were sent to Ziauddin Hospital Karachi for histopathology and immunofluorescence.

RESULTS

The total number of patients was 30. Male were 20 (70%) while females were 10 (30%). The age range was 25 years to 88 years with a mean age of 55.5±13.3SD (table 1). Pure Diabetic Nephropathy (DN) was present in 9 (30%) cases, NDRD on DN in 8 (26.69%) cases, and NDRD in 13 (43.4%) cases (Table 2). The most common histological pattern was membranous GN (09 cases, 30%) followed by ATN (05 cases, 16.6%), FSGS (4 cases, 13.33%), and Keimel Stiel Lesions were seen in 9 (30%) patients. MSGN was present in 2 (6.6%) cases and HUS in 1 (3.4%) cases (Table 3). Different variables were correlated with nephrotic range proteinuria and a p-value was calculated. A P-value less than 0.05 was considered significant (table 4).

Table 1: Age Distribution

	N	Minimum	Maximum	Mean	Std. Deviation
Age	30	25.00	83.00	55.5000	13.27105

Table 2: Prevalence of NDRD with or without DN

Variables	Frequency	Percent
DN	9	30.0
NDRD	13	43.3
NDRD on DN	8	26.7
Total	30	100.0

Table 3: Renal Biopsy Findings

Variables	Frequency	Percent
Acute tubular necrosis	5	16.7
Diabetic nephropathy	9	30.0
Focal Segmental Glomerulosclerosis	4	13.3
Hemolytic uremic syndrome	1	3.3
Mesangiocapillary glomerulonephritis	2	6.7
Membranous glomerulonephritis	9	30
Total	30	100

Table 4: Correlation of variables with Proteinuria >3gm

Variable	P-value
DN (n=09)	0.031*
NDRD (n=13)	0.004*
NDRD on DN (n=08)	0.001*
Duration of Diabetes (years)	0.335
Gender of Patients	0.770
Age of Patient (years)	0.717
Hypertension	0.783
Level of Creatinine	0.284

DISCUSSION

Diabetes Mellitus is one of the fastest-growing chronic diseases worldwide. [27] Diabetic nephropathy is the leading cause of ESRD requiring dialysis. [19] Although patients with T2DM often end up in DN, but they can also experience other renal diseases, unrelated to diabetes and known as NDRD.[11] In this study, three groups were made. The aim was to determine the prevalence of DN, NDRD and NDRD superimposed on DN in type 2 diabetic patients with atypical renal involvement. In the present study, the mean age was 55.5 years ±13.27 SD with male (n=20) outnumbering the female (n=10) with male to fe-

male ratio of 2:1. Unnikrishnan et al, covering the south Indian population reported the average age of patients as 51 ± 12 years. [20] Mak et al reported average age was 57 ± 1.8 years in patients having DN and 50 ± 1.9 years in patients having mixed lesions in their study. [21] Yip- Boon Chong et al also showed a mean age of 53.8 ± 9.7 years with male predominance. [22] Thus, our study was similar to other studies in terms of age and gender.

In our study, NDRD with 13 cases (43.3%) was the most common entity followed by DN with 9 cases (30%) and NDRD on DN with 8 cases (26.7%). In this regard, our study has similarities with a study conducted by Prakash J et al in which NDRD was 41.9%, DN 38.7%, and NDRD superimposed on DN 19.4%. [23]

The most common pathology in the NDRD group was Membranous GN with 9 (30%) cases followed by FSGS with 04 cases (13.33%). In the DN+NDRD group, ATN was the most common entity. This finding is correlating with the results of other studies. [17, 18, 24, 25] Another Iranian study conducted by Tayebeh et al also favors the same finding. [26] while another study by Pham TT contradicts our study in which FSGS was the most entity. [25]

In this study, the duration of diabetes before the biopsy was significantly shorter among the NDRD patients. However, the lack of diabetic retinopathy was the only independent predictor of NDRD. The literature review shows that in many studies, the short duration of diabetes was an indicator of NDRD.[14, 16] In our study, the mean duration of diabetes mellitus was 11±7.12 SD years. In contrast, Mak SK et al mentioned in their study that DN could not be distinguished from NDRD by the presence of diabetic retinopathy, age of onset, and duration of diabetes. [21] This correlates with our findings as well. We found that diabetic retinopathy was absent among all groups. Similarly, the NDRD and DN groups of patients were having a higher rate of proteinuria and were frankly nephrotic. The majority of the Patients with NDRD and DN were having acute kidney injury. Similar findings were also reported by Taybeh et al. [26] As this is a single-center study on a small population of patients, so care should be taken to generalize the results on all diabetic populations. Large center studies involving different institutions need to be carried out for this purpose.

CONCLUSION

On basis of our study, it is suggested that routine presumption of type 2 diabetes as the cause of diabetic nephropathy may not be correct because NDRD or mixed lesions may develop in these patients as seen in our study. Therefore, in selected patients with unusual renal involvement, renal biopsy should always be considered because disease-specific therapies may prolong renal survival.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Muhammad N: Concept/ Idea, Literature, review, Drafting & Final Review

Khan Z: Concept/ Idea, Analysis & Interpretation of Data, References

Khan MW: Manuscript Writing, Literature review, Analysis & Interpretation of Data

Muhammad S: Manuscript Writing, Literature review, Analysis & Interpretation of Data

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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.