Original Article

Clinical Study of Association of Diabetic Retinopathy with Diabetic Nephropathy

Diabetic Retinopathy with Diabetic Nephropathy

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ABSTRACT

Objective: To determine whether or not patients with diabetic retinopathy (DR) have nephropathy or neuropathy, and to establish a link between the severity of DR and the presence or absence of either.

Study Design: Prospective, hospital-based, non-interventional study

Place and Duration of Study: This study was conducted at the Peoples University of Medical Sciences for Women Shaheed Benazir Abad Sindh, from January 2019 to November 2020.

Materials and Methods: Patients with diabetes mellitus (DM) for at least five years who gave their informed consent to participate in the research were eligible to participate were included in this study. According to Early Treatment Diabetic Retinopathy Study categorization, the patient was diagnosed with DR. Urine albumin creatinine ratio and estimated glomerular filtration rate were used to determine the severity of diabetic nephropathy. Diabetic neuropathy severity was determined by the speed of nerve conduction.

Results: A total of 70 patients were enrolled in this study. DR severity appears to be linked to DN severity. There was a statistically significant ($P<0.05$) link between the severity of DR and the stage of DN (U ACR staging). There was a statistically significant correlation ($P<0.05$) between the severity of diabetes and the severity of diabetic nephropathy. Diabetic neuropathy was found to be unrelated to the severity of DR.

Conclusion: An indicator of future renal disease development as well as an indicator of neurological outcomes in diabetic patients may be found in the relationship between DR severity and the severity of both diabetic nephropathy and diabetic neuropathy.

Key Words: Diabetic nephropathy, diabetic neuropathy, diabetic retinopathy

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INTRODUCTION

Many metabolic illnesses have the phenotype of hyperglycemia, and they include diabetes mellitus (DM). Different forms of DM are produced by a complicated interplay of genetic and environmental variables.

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On the basis of the pathogenic mechanism that causes hyperglycemia,[1] DM is classified. Type 1 and Type 2 DM are the two most common types of DM. An autoimmune to insulin-producing beta cells causes complete or near-complete insulin insufficiency in Type 1 DM. Variable levels of insulin resistance, decreased insulin secretion, and increased hepatic glucose production characterize type 2 DM.[1] The disease's morbidity and death can be attributed to a single DM affecting numerous organ systems. Both type 1 and type 2 diabetes suffer from a variety of diabetes-related problems, which can be separated into vascular and nonvascular complications. Microvascular consequences such as retinopathy, nephropathy, and neuropathy, as well as macrovascular complications such as coronary artery disease, peripheral arterial disease, and cerebrovascular disease, are all examples of DM's vascular complications. Skin changes, infections, and hearing loss are all examples of nonvascular consequences. Type 2 diabetes may raise a person's risk of dementia and cognitive decline, according to some research.

Diabetic retinopathy: More than 7% of the global population is affected by diabetes, and around half of those people have some DR at any given moment.[2,3]

WHO estimates that DR is to blame for 3%–7% of all cases of blindness in Asia.[4] DR's onset and progression have been linked to a variety of risk factors. Factors that put people at risk at the overall level include the length of time a person has lived with diabetes, how well their blood sugars are being controlled, how old they are as well as the type of diabetes they are dealing with. The longer a person has diabetes and the better their glycemic control, the more likely they are to develop retinopathy.[5] Early treatment diabetic retinopathy study (ETDRS) classification is the most commonly used DR classification.[6]

Diabetic nephropathy: Chronic proteinuria, high blood pressure, and a poor glomerular filtration rate are all symptoms of DN (GFR).[7] Nephropathy affects 25–45% of Type 1 DM patients during the course of their lives.[8] Nephropathy is most likely to manifest itself 10–15 years after the commencement of the disease. Type 2 diabetes patients have a decreased incidence of nephropathy, according to research. Approximately 50% of diabetics with type 2 diabetes developed nephropathy.[9]

Diabetic neuropathy: Diabetes' most prevalent and difficult consequence is peripheral neuropathy.[10] Diabetics with diabetes for more than 25 years have a 50 percent higher risk of developing diabetic neuropathy than those who are diagnosed within the first year of their condition.[11] Patients with subclinical neuropathic disorders could account for as much as 90% of the total population. It is estimated that DPN and cardiac autonomic neuropathy are the two most frequent diabetic neuropathies. Consequently, DPN first affects the lower extremities' distal regions. The classic "stocking and glove" sensory loss occurs as the disease progresses, when the loss of sense in the lower limbs progresses to the hand. Study participants with DR were evaluated for the presence of kidney and nerve damage, with an eye toward finding out if their condition was worsened by diabetes-related kidney damage or diabetic neuropathy, respectively.

MATERIALS AND METHODS

The Peoples University of Medical Sciences for Women Shaheed Benazir Abad Sindh, undertook this prospective, hospital-based, non-interventional study from January 2019 to November 2020. All 70 people who came to the eye OPD with symptoms of diminished vision were included in this study. There was an ethics committee's clearance, which was granted in February 2019. Patients with diabetes mellitus for at-least five years who gave their informed consent to participate in the research were included. Diabetes was not considered a factor in the exclusion of patients with preexisting nephropathy and neuropathy at the time of presentation.

All patients were given written informed consent before to participating in the study. Examination of the eyes after a thorough clinical examination, standard diagnostic criteria were followed, and tests like as fundus photography, OCT, and ophthalmoscopy were carried out. ETDRS classification was used to classify the instances with DR-like characteristics in the fundus. The presence or absence of clinically significant macular edoema further divided patients with DR into two groups (CSME). For nephropathy, use the following treatment options: For example, the following is an estimate of U.A.C.R: 1. For chronic kidney disease (CKD), the U.A.C.R. value staging was done as normal or moderate (less than 30 mg/24 h), microalbuminuria (30-300 mg/24 h), and macroalbuminuria (more than 300 mg/24 h). In order to arrive at an accurate estimate of GFR, the serum creatinine value is used (using CKD epidemiology collaboration equation): 2. A patient with stage 1 CKD (eGFR value >90 mL/min) is classified as having advanced kidney disease, while those with stage 2 CKD (eGFR value 60–89 mL/min) or stage 3A CKD (eGFR value 45–59 mL/min) are classified as having stage 3B CKD (eGFR value 30–44mL/min), and those with stage 4 CKD (15–29 ml/min).

Nerve conduction study (NCS): Tibial nerve NCV values were used to classify diabetic neuropathy as either nonexistent (>5 mv), mild (2.5–5 mv), or severe (2.5–5 mv). Mann–Whitney and Chi-square tests were used to assess numerical data and categorical variables, respectively. A statistically significant difference was defined as one with a P value lower than 0.05.

RESULTS

A total of 70 patients were enrolled in this study. As may be shown in Table 1, participants were distributed according on the severity of their DR. Thirty-six (51.42%) of the 70 patients had mild nonproliferative diabetic retinopathy (NPDR), 20 (28.57%) had moderate NPDR, 12 (17.14%) had severe NPDR, and 2 (2.85%) had proliferative diabetic retinopathy (PDR), according to the study.

In this study, 43 patients had DM for less than 10 years, 19 patients had DM for 11-20 years, and 8 patients had DM for 21-30 years. The eye with the most severe DR was considered in patients with bilateral DR.

As shown in Table 2, the severity of DR is distributed according to the CSME. There were a total of 36 individuals with mild NPDR, 30 of whom had no CSME and 6 of whom had CSME. Only 3 of the total 20 patients with significant NPDR had CSME. The CSME was used in all cases of NPDR and PDR that were severe. There was a statistically significant difference in the severity of DR based on the CSME.

Table 3 indicates the correlation between DR and DN severity (eGFR staging). Seventeen of the 36 individuals with mild NPDR had already reached stage 2 of kidney disease. CKD stage 3A was found in 8 of the 20 patients with moderate NPDR. A stage 3A

kidney disease was found in five of the 12 patients with severe NPDR. One of the two PDR patients had CKD stage 3B. We found that there was a statistically significant correlation between the severity of DR and the severity/stage (eGFR staging) of the DN.

DR severity appears to be linked to DN severity in Table 4. (U ACR staging). There were 21 patients with mild micro albuminuria and 16 individuals with moderate micro albuminuria in the NPDR group. Macroalbuminuria was seen in 9 patients with severe NPDR and 1 patient with severe PDR. There was a statistically significant (P=0.05) link between the severity of DR and the stage of DN (U ACR staging).

Table No.1: Distribution of study population according to the severity of DR (n = 70)

Severity of DR	Frequency	Percentage
Mild NPDR	36	51.42%
Moderate NPDR	20	28.57%
Severe NPDR	12	17.14%
PDR	2	2.85%
TOTAL	**70**	**100%**

Table No.2: Distribution of severity of DR according to CSME (n = 70)

Severity of DR	Without CSME	With CSME	Total
Mild NPDR	30	6	36
Moderate NPDR	17	3	20
Sever NPDR	0	12	12
PDR	0	2	2
Total	**47**	**23**	**70**
X^2 value	**33.412**		
***P*-value**	**0.0001***		

Table 3: Association of severity of DR with severity/ staging of diabetic nephropathy (eGFR staging) (n = 70)

Nephropathy (EGFR staging)	Mild NPDR	Moderate NPDR	Severe NPDR	PDR
1	10	2	0	0
2	17	6	4	0
3A	4	8	5	0
3B	2	3	2	1
4	0	1	1	1
5	3	0	0	0
Total	**36**	**20**	**12**	**2**
X^2 value	**25.512**			
***P* value**	**0.009***			

Table 4: Association of severity of DR with severity/ staging of nephropathy (UACR staging) (n = 70)

Nephropathy (UACR staging)	Mild NPDR	Moderate NPDR	Severe NPDR	PDR
Normal (A1)	9	0	0	0
Microalbuminuria (A2)	21	16	3	1
Macroalbuminuria (A3)	6	4	9	1
Total	**36**	**20**	**12**	**2**
X^2 value	**19.724**			
***P*-value**	**0.003***			

DISCUSSION

The primary goal of this study was to investigate the relationship between DR and DN and diabetic neuropathy and the severity of retinopathy. Males made up 78.95 percent of the participants in this study, while females made up 21.05 percent.

In the Chennai urban rural epidemiology study Eye study, a similar male predominance was found.[12] The study population was comprised of people ranging in age from 31 to 81, with a mean age of 58.86 years and a standard deviation of 9.85 years. 94.74% of the 57 individuals had NPDR and 5.266% had PDR. A similar study in Sikkim was conducted by Bhutia et al.[13] who found similar results. There were 22 (38.60%) patients with mild NPDR, 14 (24.56%) with moderate NPDR, 18 (31.58%) with severe NPDR, and 3 (5.26%) with PDR in our study sample. There were 30 (52.63%) patients of DR who did not have CSME, and 27 (47.37%) patients who did. According to CSME, the distribution of DR severity was shown to be statistically significant (P value 0.0001). Only 2 of the 22 patients with mild NPDR had CSME, while 20 of the patients without CSME had mild NPDR. Only four of the 14 individuals with moderate NPDR who were evaluated had CSME. All patients with significant NPDR and PDR showed up with CSME. As a result of this strong correlation, it appears that a higher proportion of people with a severe form of diabetes mellitus (DR) have CSME, compared to the proportion who don't. After microalbuminuria and macroalbuminuria, there were five individuals in our study who had no albuminuria at all, accounting for 56.14% of the participants in our study.

Both EGFR staging and U ACR staging were found to be statistically highly significant in our study, which indicates that with growing severity of the disease, the severity of the DN will also increase in proportion to the severity of the disease. As DR and DN share many of the same pathogenic mechanisms, the development and progression of both are intertwined. As a result, the severity of DR and DN worsening were found to be inversely proportional in our research. Wajid et al.[14] found that 20% of patients and 25.6% had retinopathy, in a similar study. The micro albuminuria rate was 90%

and the retinopathy rate was 100% in patients with diabetes who had been on medication for more than 15 years.

Lunetta et al[15] and Manaviat et al[16] found a similar link. A number of studies have shown that DR may be a powerful predictor of the advancement of renal impairment in people with diabetes mellitus who have microalbuminuria. According to El-Asrar et al[17], the prevalence of DN increased as the severity of DR increased. Our research reveals that the severity of DR increases with the level of albuminuria, which is statistically significant. Patients with macroalbuminuria were more likely to have proliferative retinopathy than those with microproteinuria. Proliferative retinopathy is associated with an increase in urine albumin excretion, according to Singh et al.[18]

NCSs are the most objective and noninvasive markers of nerve function available to researchers.

When it comes to assessing structural changes, NCS are the most objective and dependable benchmark.[19] NCV is a method for determining the rate at which electrical impulses travel through a nerve by measuring the NCV. This process is used to detect if nerves are normal or if they have been damaged or destroyed.[20] We discovered that 13 (61.14%) of the 21 patients who had NCV scans to detect subclinical neuropathy had abnormalities, while 8 (38.10 percent) of the patients had normal NCV studies. We found no statistically significant link between the degree of neuropathy and the severity of DR in our research (P value 0.532). Two patients with mild NPDR were among four with mild neuropathy. Three of the nine individuals with severe neuropathy had mild NPDR, while the other three had PDR. The lack of NCV testing at our facility during the COVID 19 pandemic may have contributed to the lack of a meaningful correlation in the study's small sample size (n = 21). As a result, a large sample size is required to draw firm conclusions and prove a link between DR and neuropathy. Out of 13 diabetic neuropathy sufferers, 12 had diabetic nephropathy, suggesting a possible link and similar pathophysiologic pathways for the development of these conditions**.**

CONCLUSION

For diabetic nephropathy patients, even if there is no evidence of proteinuria, we can accurately anticipate the presence of subclinical disease and make appropriate referrals to the nephrologist. There was no correlation between the severity of DR and diabetic neuropathy in our study. It is necessary to conduct extensive research. Neuropathy and nephropathy are often found together in patients with retinopathy. Patients with diabetes should be evaluated by an ophthalmologist, endocrinologist, nephrologist, and neurologist as part of comprehensive treatment.

Author's Contribution:

Concept & Design of Study:	Arif Rabani
Drafting:	Muhammad Khalid, Attaullah Shah Bukhari
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