Original Article

The Frequency of Preclinical Nephropathy in Patients of Type II Diabetes Mellitus with Diabetic Retinopathy

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ABSTRACT

OBJECTIVE: To determine the frequency of preclinical nephropathy in patients with diabetic retinopathy and its correlation to the severity of retinopathy.
STUDY DESIGN: Prospective case study.
PLACE AND DURATION OF STUDY: Department of Ophthalmology, Military Hospital (MH), Rawalpindi for six months
METHODS: Ninety (90) diabetic patients (thirty in each grade of retinopathy i.e. background, preproliferative and proliferative) with no known renal dysfunction were included in the study. They were investigated for albumin/creatinine ratio of a spot urine sample. The outcome of renal function was described as either positive or negative. The cutoff value for albumin creatinine ratio was 300 mg/g. The various grades of retinopathy were compared to the values of urine albumin creatinine ratio, to find the correlation.
RESULTS: Five (17%) patients with background diabetic retinopathy had preclinical nephropathy. Seventeen (60%) patients with preproliferative diabetic retinopathy and 27 (90%) of patients with proliferative diabetic retinopathy had preclinical nephropathy. The frequency of nephropathy correlated to the severity of retinopathy (correlation co efficient, r value: 0.630) and p value of <0.001.
CONCLUSION: It is important for ophthalmologists to carefully consider the renal status of any patient with retinopathy as this can influence the progression of retinopathy and its response to treatment.

KEYWORDS: Diabetes mellitus, Diabetic nephropathy, Diabetic retinopathy, preproliferative, proliferative.

INTRODUCTION

Diabetic retinopathy (DR) is the leading cause of acquired and permanent blindness in the United States and the United Kingdom. [1] Although in much of the developing world, the main causes of blindness has been cited as cataract and trachoma, the increased trend towards sedentary life styles, obesity, lack of exercise and unfavorable eating habits has recently and dramatically increased the incidence of diabetes and its complications in our country. [1] DR has been found to be the most common complication of diabetes mellitus in many studies [2] thus making it a significant cause of acquired permanent blindness in our setup as well. The medical, social and financial impact of this disease is substantial. [3]

With the advent of new and improved treatment modalities that can effectively deal with diabetic retinopathy, the emphasis today lies on early detection of retinopathy and the recommendation is to greatly adhere to the treatment strategies outlined after extensive research.

The importance of this study is twofold. First, it is important to know how many of the patients presenting to our clinics in Pakistan with diabetic retinopathy also have renal dysfunction. Renal disease stays quiescent until it has progressed to a stage of marked and often irreversible damage to the renal tissue. At this stage, not only is the treatment less effective but also very costly for the patient as well as the health care system. On the other hand, Diabetic macular edema (DME) can lead to blurred vision at a very early stage in the course of diabetic eye disease and assure that the patient seek consultation. Here, knowledge of the probability of having occult nephropathy determined by the severity of the retinopathy can lead to prompt and early referral to nephrologists and curb this preclinical renal disorder at a stage where it is not only reversible but also cost effective. Secondly, it has been highlighted above that the presence of nephropathy in a diabetic patient is a risk factor for the development as well as the progression of diabetic retinopathy. Moreover studies have also shown that the long term benefit of pan retinal photocoagulation is

adversely affected by the concomitant existence of diabetic nephropathy.

It will also be interesting to know how results of a study of this nature conducted in Pakistan compares with the data from studies carried out abroad. Here, unfortunately, patients generally present at a later stage principally due to lack of awareness about their disease, low literacy levels and poor socioeconomic status compared with societies with more developed healthcare systems and educational backgrounds.

The purpose of this study was to determine the frequency of pre clinical diabetic nephropathy in patients with diabetic retinopathy (DR) and to determine the correlation of preclinical diabetic nephropathy to the grade of diabetic retinopathy. The results of this study may aid in developing a protocol for early detection of diabetic nephropathy for its effective management.

MATERIALS AND METHODS

The study was conducted at The Department of Ophthalmology, Military Hospital (MH) Rawalpindi. The duration of the study was 06 months. A total of 90 diabetic patients were selected by non-probability purposive sampling technique. It was a prospective case study. Inclusion criteria was type 2 diabetes diabetic retinopathy of any severity while exclusion criteria was ocular pathology obscuring proper visualization of the fundus e.g. dense cataracts, vitreous hemorrhage, vitritis, corneal opacities and any comorbidity of chronic diseases that could impair renal function e.g. pyelonephritis, hypertension and cardiac failure.

All diabetic patients presenting to the ophthalmology out patient department of the Military Hospital, underwent a dilated fundus exam. Those having retinopathy were graded according to international criteria (Eva Kohner's classification) as follows:-

Background (Grade I): Hard exudates, dot and blot haemorrhages.

Preproliferative (Grade II): Cotton wool spots and intraretinal microvascular abnormalities.

Proliferative (Grade III): Neovascularisation. Although stereoscopic fundus photography is more reliable and was employed in many similar international studies but it is costly and time consuming. Therefore, the expertise of a senior ophthalmologist of our department was used for diagnoses and grading of the severity of retinopathy.

Those that met the selection criteria were then informed about the study. An informed written consent was obtained from all patients participating in the study for further investigation and using this data for research.

Demographic information was collected i.e. name, age, sex and address.

The clinical history, symptoms, their severity and duration was recorded. They were asked for the presence / absence of visual deterioration, floaters and flashes of light, pain, night blindness and alterations in colour perception. The past ocular and systemic history regarding cataracts and cataract extraction, ocular surgeries, glaucoma, optic neuropathies was noted. The findings of ophthalmic examination i.e. visual acuity and intraocular pressures and grade of retinopathy were also noted. They were then investigated for the presence of preclinical nephropathy by evaluating the spot urine sample and determining the albumin to creatinine ratio. Preclinical nephropathy was defined as the range of albumin hyper-excretion that exceeds the normal range but fall short of detection by standard proteinuria test. The cutoff value was taken as 300mg/g. This test is more convenient and better for screening of preclinical nephropathy than 24 hour urinary sample collection for microalbuminuria. All information was collected on a proforma

Data analysis

SPSS version 11 was used to analyze the data. The variables of clinical assessments have been described as frequencies and proportions. The outcome of renal function has been described as either positive or negative with 300mg/g as the cut off value. The outcome of various retinopathy grades were compared with the urine albumin/creatinine ratio to find the correlation. The effect of confounders was eliminated by stratification. An 'r' value (coefficient of correlation) was calculated. P value of less than .05 was taken as significant.

RESULTS

A total of 50 (55.6%) male patients and 40 (44.4%) female patients completed the data **(Figure I).** The mean age was 58.3±9.7 yrs (range 35 to 79 yrs). The mean duration of diabetes was 12.7±3.7 yrs.

Forty-nine (54%) patients with retinopathy had underlying preclinical renal dysfunction **(Figure II)**. Five (17%) diabetics with background diabetic retinopathy (BGDR) had preclinical nephropathy. Seventeen (60%) with non-proliferative diabetic retinopathy (NPDR) and 27 (90%) with proliferative diabetic retinopathy (PDR) had preclinical nephropathy **(Figure III)**.

The frequency of nephropathy highly correlated with the severity of retinopathy (r value 0.630) and this correlation was statistically significant ($P < 0.001$).

FIGURE I: GENDER DISTRIBUTION

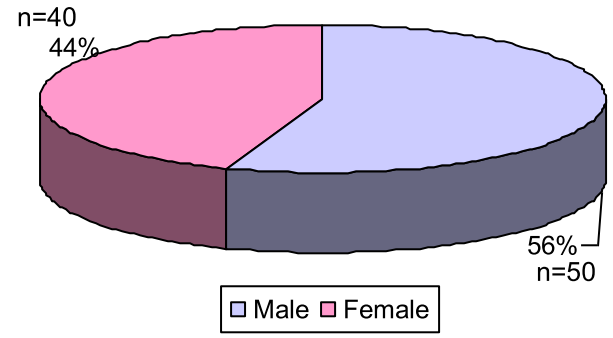


FIGURE II: FREQUENCY OF PRECLINICAL NEPHROPATHY IN 90 PATIENTS OF DIABETIC RETINOPATHY

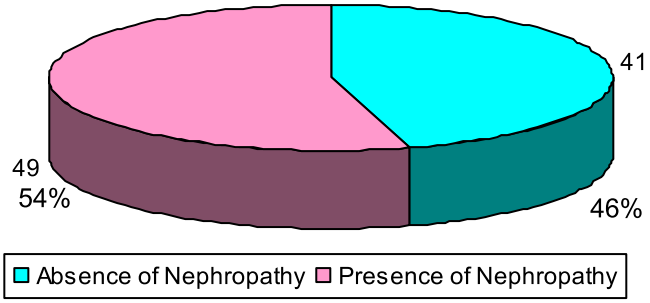
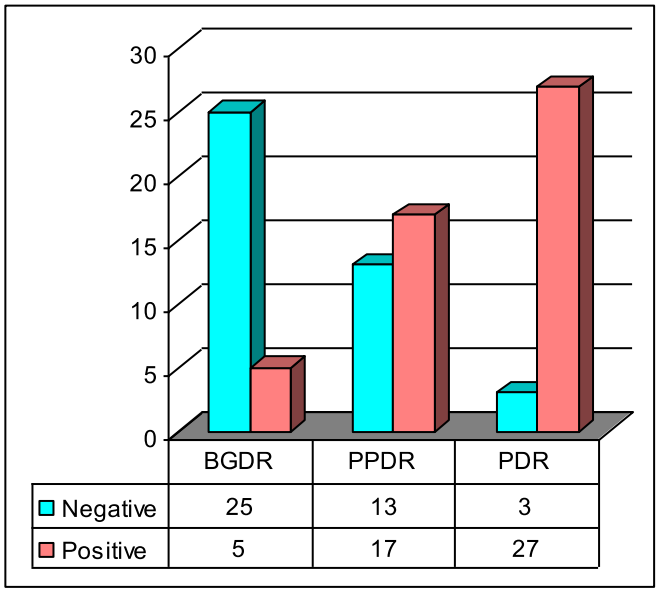


FIGURE III: CORRELATION OF PRECLINICAL DIABETIC NEPHROPATHY TO THE GRADE OF DIABETIC RETINOPATHY



DISCUSSION

A relationship between renal and retinal angiopathy in diabetes has been studied internationally[4]. Many studies can be found in international literature based on different research designs (i.e. cross sectional, [5,6,7] and longitudinal,[8,9,10] studies) that support a relationship between diabetic retinopathy and nephropathy. Possible confounders like hypertension probably intervening between a direct relationship between our two study parameters have also been sought and it seems that this relationship is complex and is indicative of a common end pathophysiology stemming from microangiopathy. Many side risk associations of both retinopathy and nephropathy independently have been found like longstanding hyperglycemia, high HbA1c levels, duration of diabetes and hypertension[11,12,13]. Still other studies negate a direct relationship between the two i.e. retinopathy and nephropathy like the microalbuminuria collaborative study group repo [14] in opposition to those that support it. [15]

Conversely, there are studies in which nephropathy has been used as a predictor of retinopathy [16] and in a prospective study involving 211 patients with type I Diabetes mellitus (DM), the prevalence of PDR increased from 7% at onset of microalbuminuria to 29% four years after the onset of microalbuminuria as compared with 3% and 8%, respectively, in patients without persistent microalbuminuria. Similar studies done on other ethnic groups have also come up with consistant results but no such study was found in local literature[17,18]. Wisconson Epidemiology Study of Diabetic Retinopathy (WESDR) stated that gross proteinuria at baseline increases the risk of developing microalbuminuria as well.

The clinical relevance of this study is beneficial to both the ophthalmologist and an internist in their approach to a patient with diabetes and its complications as discussed below.

The results of this study agree with other related studies published in international literature. Renin Angiotensin System Study (RASS) [19] stated the correlation of severity of retinopathy to the renal anatomical abnormalities. RASS study concludes that even renal anatomical dysfunction can be compared and correlated to the severity of retinopathy. Another remarkable observation is that RASS commented that the occurrence of kidney dysfunction in individuals with diabetic retinopathy is more frequent when we consider it in terms of anatomical dysfunction rather than functional dysfunction. Our results show a similar frequency of nephropathy to each grade of retinopathy even though a renal functional parameter was employed. This might indicate that had an anatomical criterion been employed to assess renal pathology in our set up, the frequencies would have been much higher.

Factors like poverty, difficult access to ophthalmic health care, lack of awareness, the silent nature of diabetes, all seem to explain the striking results of this study and highlight the importance of using one ab-

normality as a tool to predict the presence of another diabetic complication.

Ahmed et al [15] in their study conducted in Saudia Arabia determined the predictive value of retinopathy with the rationale that this particular diabetic complication can be easily detected on a routine ophthalmic visit making it a cost effective, non invasive and convenient tool for predicting the presence of other diabetic complications. The results of the study in our setup are comparable to the findings of the above-mentioned study but again the respective percentages of nephropathy in this setup were much higher. Furthermore Ahmed et al [15] also concluded that retinopathy can serve as a valuable predictor for the presence of other diabetic complications such as neuropathy and cerebrovascular disease.

Rema et al [21] conducted a study on the risk factors influencing the long term results of panretinal photocoagulation in patients with diabetic retinopathy. This study was conducted in Chennai, India. It concluded that the duration of diabetes, the pre-treatment visual acuity and the presence of proteinuria significantly affected the visual acuity at one year following PRP. It appears that the presence of underlying undiagnosed and untreated nephropathy in patients being treated with PRP may be negatively influencing the benefit of this modality of treatment in Pakistan.

CONCLUSION AND RECOMMENDATIONS

The results of this study indicate that diabetic retinopathy shows a state of generalized vascular damage and supports the views for a common pathogenesis of retinopathy and other diabetic complications. Moreover, the frequency of nephropathy rose with increased severity of retinopathy. These results suggest that retinopathy (especially PDR) can be considered a risk indicator for preclinical nephropathy.

DM is a systemic disease with numerous complications in organs other than the eye. The presence and severity of retinopathy highly correlates with the presence of nephropathy. Since this relationship can have important clinical bearing in the treatment of diabetic patients it is therefore recommended that the renal status of any patient with diabetic retinopathy be assessed as it can influence the progression of retinopathy and its response to laser treatment.

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