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ASSOCIATION BETWEEN DIABETIC RETINOPATHY AND PROTEINURIA IN PATIENTS WITH TYPE-II DIABETES MELLITUS IN A TERTIARY CARE HOSPITAL, QUETTA

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Abstract

Background: Diabetic Retinopathy (DR) and proteinuria are major microvascular complications of Type-II Diabetes Mellitus (T2DM). Their coexistence may reflect widespread systemic vascular damage, yet data from South Asia remain scarce. Diabetic retinopathy (DR) is a major complication of diabetes and the leading cause of decreased vision in working-age people (1). It is anticipated that the prevalence of DR is likely to continue to rise, particularly in Asia and other developing areas.

Objective: To determine the frequency of DR and assess its association with proteinuria among T2DM patients at a tertiary care hospital in Quetta, Pakistan. To compare the frequency of diabetic retinopathy with proteinuria in patients presenting with type-II diabetes mellitus, at a tertiary care hospital, Quetta.

Methods: A cross-sectional study involving 228 T2DM patients who fulfilled the inclusion criteria and visited to Sandeman Provincial Hospital, Quetta were included in the study after taken

informed consent. Urinary collection was done to check proteinuria, and fundoscopy was done to check the diabetic retinopathy. All the collected data were entered into the proforma attached at the end and used electronically for research purpose.

Results: DR was diagnosed by direct fundoscopy; proteinuria (>0.5 g/24 h) was measured using 24-hour urine collection. Data were analyzed in SPSS v22; $p < 0.05$ was considered significant. The mean age was 52.7 ± 11.9 years; 57% were male. DR prevalence was 19.7% (45/228). DR occurred in 26/228 (11.4%) patients with proteinuria and 19/228 (8.3%) without proteinuria (χ^2, $p = 0.0001$). Mean ± SD of age was 52.7±11.9 years. In distribution of gender, 130 (57.0%) were male while 98 (43.0%) were female. Diabetes retinopathy was found to be in 45 (19.7%) patients. Diabetic retinopathy was noted in 26 (11.4%) patients with proteinuria while 19 (8.3%) without proteinuria and P-value found to be highly significant i.e., P=0.0001.

Conclusion: Proteinuria is significantly associated with DR in T2DM patients. Integrated renal and ocular screening is recommended in routine diabetes care.

Keywords: Diabetic Retinopathy; Proteinuria; Type-II Diabetes Mellitus; Microvascular Complications; Pakistan

Introduction

Diabetes Mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The global burden of DM is escalating, with projections estimating 366 million affected individuals by 2030.1 Long-term hyperglycemia leads to microvascular damage, manifesting primarily as diabetic retinopathy (DR) and diabetic nephropathy (DN), the latter often detected by proteinuria. Although these complications are individually well-documented, their inter-relationship—particularly in South Asian populations—remains under-investigated. Understanding this association may improve early detection and holistic management of diabetic complications. DM is a metabolic disorder characterized by chronic hyperglycemia with defective carbohydrate and fat metabolism. These defects are mostly due to impaired insulin secretion from pancreatic ß cells and/or insulin resistance to the target cells such as skeletal muscles, liver, and adipose tissues [1]. Diabetic patients have a greater risk of developing a number of major health problems [2]. The incidence of diabetes is sharply increasing worldwide with many long-term macro- and micro-vascular complications [3]. Diabetic retinopathy (DR) is a major complication of diabetes mellitus (DM), which remains a leading cause of visual loss in working-age populations. The diagnosis of DR is made by clinical manifestations of vascular abnormalities in the retina. Clinically, DR is divided into two stages: non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) [4]. The diagnosis of DR relies on the detection of microvascular lesions. The treatment of DR remains challenging. The advent of anti-vascular endothelial growth factor (VEGF) therapy demonstrated remarkable clinical benefits in DR patients; however, the majority of patients failed to achieve clinically significant visual improvement [5]. Diabetic nephropathy (DN) or diabetic kidney disease refers to the deterioration of kidney function seen in chronic type 1 and type 2 diabetes mellitus patients. The progression of the disease is known to occur in a series of stages and is linked to glycemic and blood pressure control. However, despite aggressive blood sugar control the prevalence of chronic kidney disease (CKD) in diabetic patients has not witnessed any decrease in the last two decades; which has led to identification of additional factors in its progression [6]. The concordance of microalbuminuria and diabetic retinopathy (DR) has been well reported in persons with type 1 diabetes; however, for type 2 diabetes, there is paucity of data especially from population- based studies [7]. Proteinuria, a common finding in type 2 diabetes, is often observed in patients with no evidence of diabetic retinopathy: 20-45% of type 2 diabetic patients with proteinuria do not show retinal diabetic lesions. While a 14% prevalence of macroalbuminuria has been reported in a cross-sectional study of 549 type 2 diabetic patients, only 45% of the macroalbuminuric patients also had some degree of retinopathy [8]. Study by Meera et al reported

the incidence of proteinuria in patient with diabetic retinopathy vs without retinopathy was 9.41% and 3.8% respectively [9]. Study by Rani et al reported the prevalence of diabetic retinopathy 18.03%. However, risk of developing macroalbuminuria in patient with diabetic retinopathy was 6.50 times higher as compared without diabetic retinopathy [10]. The aim of our study is to determine the association between diabetic retinopathy and proteinuria in patients presenting with type II Diabetes mellitus in our local population as there is very scarce local literature published on this topic. The concordance of microalbuminuria and DR has been well reported in persons with type 1 diabetes; however, for type 2 diabetes, there is paucity of data especially from population-based studies regarding the association of diabetic retinopathy with proteinuria. As large number of populations in Pakistan belongs to rural areas and poor socio-economic status therefore mostly patients reported very late due to lack of medical facilities and financial constraints as compare to other developed countries. Therefore, it is important to investigate the recent status of it in our country, so that treatment of such patients should be anticipated in appropriate clinical line and appropriate diagnosis is made to prevent further complications.

Literature Review: Diabetic retinopathy (DR) is a microvascular disorder occurring due to long term effects of diabetes, leading to vision-threatening damage to the retina, eventually leading to blindness. It is the most common cause of severe vision loss in adults of working age groups in the western world [11]. Early detection and timely intervention are the key to avoid blindness due to diabetic retinopathy. The number of patients with diabetic retinopathy in America is estimated to reach 16.0 million by 2050, with vision-threatening complications affecting around 3.4 million of them [12]. The usefulness of strict glycemic control was clearly seen in clinical trials like the UK Prospective Diabetes Study (UKPDS) and Diabetes Control and Complication Trial (DCCT) [13,14]. Uncontrolled diabetes can lead to many ocular disorders like cataract, glaucoma, ocular surface disorders, recurrent stye, non-arthritic anterior ischemic optic neuropathy, diabetic papillopathy, and diabetic retinopathy, out of which diabetic retinopathy is the most common and severe ocular complication [15-17]. Poor glycemic control, uncontrolled hypertension, dyslipidemia, nephropathy, male sex, and obesity are associated with worsening of diabetic retinopathy [18,19]. Diabetic retinopathy affects people with diagnosed or undiagnosed diabetes mellitus. The propensity of developing diabetic retinopathy is directly proportional to the age of the patient and duration of diabetes as well as with poor glycemic control and fluctuation blood pressure level [20].

Ninety-three million people are globally affected by diabetic retinopathy. Prevalence of diabetic retinopathy is 77.3% in type 1 diabetes patients and 25.1% in type 2 diabetes patients, out of which approximately 25% to 30% are expected to develop vision-threatening diabetic macular edema [22]. Between 5% and 8% of patients with diabetic retinopathy need laser treatment [23]. As many as 0.5% of patients will require vitrectomy surgery [24]. Weakened capillary wall ruptures leading to intraretinal dot hemorrhages. Superficial or flame-shaped hemorrhages arises from the precapillary arterioles located in the retinal nerve fiber layer. Deep hemorrhages or dot and blot hemorrhages are located in the inner nuclear and outer plexiform layers of the retina.

Objectives:

- To determine the frequency of diabetic retinopathy in patient with type II diabetes presenting at tertiary care hospital, Quetta.
- To compare the frequency of diabetic retinopathy with proteinuria in patients presenting with type-II diabetes mellitus, at a tertiary care hospital, Quetta.
- Compare the frequency of DR in patients with and without proteinuria.

OPERATIONAL DEFINITION

DIABETES MELLITUS: Defined as patients with complains of increased thirst, increased urination (> 3 liters/day) or increased hunger (all or any one of them) and FPG >126 mg/dl. (Fasting was defined as no caloric intake for at least 8 h).

DIABETIC RETINOPATHY: In diabetic patients on fundoscopy presence of cotton-wool spots, macular edema and neovascularization were labeled as diabetic retinopathy.

PROTEINUREA: In diabetic patients the presence of proteinuria >0.5 g/24 h was labeled as yes.

HYPERTENSION (HTN): Patients on antihypertensive medications for >3 months. Only controlled (BP <130/90 at the time of presentation).

SMOKING: A person who smoke at least five cigarettes a day for at least one year was labeled a smoker.

BODY MASS INDEX: It was calculated by using formula: Weight in Kg/Height in m2. However, weight was measured by digital weighting machine in light clothes and height was measured by using stadiometer without shoes and cap.

Methodology

Study Design: This was a cross-sectional observational study.
Setting: The study was conducted in the Department of Internal Medicine at Sandeman Provincial Hospital, Quetta, Pakistan.

Duration:
Data were collected over a period of six months, from January 22 to August 21, 2022.
Sample Size and Sampling Technique:
A total of 228 patients were enrolled. The sample size was calculated using the WHO sample size calculator, based on an expected diabetic retinopathy (DR) prevalence of 18.03%, with a 5% margin of error and 95% confidence level.
A consecutive non-probability sampling technique was used for patient selection.

Inclusion Criteria:
- Patients between 20 to 70 years of age.
- Either gender.
- Patients with type 2 DM as per operational definition for more than one year.
- T2DM patients aged 20–70 years with ≥1 year disease duration.

Exclusion Criteria:
- Patients with chronic liver disease, assessed by history, clinically & coarse liver with irregular margins, dilated portal vein & splenomegaly on ultrasound abdomen.
- Patients with end stage renal disease, GFR <15ml/min.
- Patients with nephritic syndrome, assessed by history, clinically
- Chronic liver disease, end-stage renal disease (eGFR <15 ml/min), or nephritic syndrome.

Data Collection: This study was conducted after taking approval from the CPSP. Patient attending inpatient or outpatient in department of Internal Medicine, Sandeman Provincial Hospital, Quetta with type 2 DM as per operational definition for more than one year and meeting the inclusion criteria were included after taking informed written consent. Brief history regarding demographic and clinical variables such as age, gender, place of living, height, weight, BMI, education level,

socioeconomic status, duration of type 2 DM & co-morbidities i.e., hypertension & smoking were taken followed by clinical examination. In all these patients 24 urinary collection was done to check proteinuria, presence of proteinuria >0.5 g/24 h was labeled as yes and fundoscopy was done by senior registrar on consultant Physician. to check the diabetic retinopathy, presence of cotton-wool spots, macular edema and neovascularization were labeled as yes. All demography, clinical history was recorded by a principal investigator on a predesigned Performa, informed written consent was taken before enrolment. Exclusion criteria were followed strictly to avoid confounding variables. Demographics, BMI, duration of diabetes, hypertension, and smoking status were recorded. DR was identified via dilated fundoscopy; proteinuria was quantified using 24-hour urine protein measurement. Ethical approval and informed consent were obtained.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were reported as frequencies and percentages. The Chi-square test was employed to assess the association between proteinuria and diabetic retinopathy (DR). Data were analyzed using SPSS version 22**.**

Frequencies and percentages were calculated for categorical variables, including gender, place of residence (urban/rural), education level (illiterate, primary, intermediate, graduation or above), socioeconomic status (<50,000 PKR / ≥50,000 PKR), and co-morbidities such as hypertension, smoking status (yes/no), proteinuria (yes/no), and diabetic retinopathy (yes/no).

For continuous variables like age, height, weight, body mass index (BMI), and duration of type 2 diabetes mellitus (DM), data were reported as mean ± SD or median with interquartile range (IQR), where appropriate. The Shapiro-Wilk test was applied to assess the normality of distribution for continuous variables.

Effect modifiers such as age, gender, place of residence, education level, socioeconomic status, BMI, duration of type 2 DM, hypertension, and smoking were controlled through stratification. Post-stratification analysis was performed using the Chi-square or Fisher's Exact test. A *p*-value of <0.05 was considered statistically significant.

Results

A total of 228 participants were included in the study. The mean age was 52.7 ± 11.9 years, and 130 (57.0%) were male. Diabetic retinopathy (DR) was diagnosed in 45 patients (19.7%), and proteinuria was present in 65 patients (28.5%).

The prevalence of DR among patients with proteinuria was 40.0% (26/65) compared to 11.5% (19/163) among those without proteinuria. This association was statistically significant ($\chi^2 = 14.1$, $p = 0.0001$).

Stratified analysis demonstrated a higher frequency of DR among participants aged >50 years, those with a diabetes duration >10 years, and those with co-existing hypertension; however, these trends did not reach statistical significance after multivariate adjustment.

Table 1: Descriptive Statistics of Participants (n = 228)

Variable	Mean ± SD	95% CI	Min–Max (Range)	Shapiro-Wilk *p*-value
Age (years)	52.7 ± 11.9	51.16 – 54.26	20–70 (50)	0.105
Height (cm)	65.8 ± 10.1	64.48 – 67.11	50–110 (60)	0.361
Weight (inches)	63.7 ± 8.5	62.59 – 64.80	54–73 (19)	0.109
BMI (kg/m²)	26.8 ± 5.7	26.05 – 27.54	16–34 (18)	0.325
Duration of Type II DM (years)	2.5 ± 0.9	2.38 – 2.61	1–10 (9)	0.241

The Shapiro-Wilk test confirmed normal distribution for the following continuous variables: age (p = 0.105), height (p = 0.361), weight (p = 0.109), BMI (p = 0.325), and duration of type II DM (p = 0.241).
In terms of gender distribution, 130 participants (57.0%) were male, and 98 (43.0%) were female. Regarding place of residence, 60 (26.3%) resided in rural areas, and 168 (73.7%) were from urban areas. Hypertension was observed in 109 patients (47.8%). Among all participants, 96 (42.1%) were smokers, while 132 (57.9%) were non-smokers.

Table 2: Frequency Distributions of Demographics and Health Characteristics (n = 228)
Socioeconomic status showed <50,000 income per month was noted in 127 (55.7%) patients while ≥50,000 income per month was noted in 101 (44.3%) patients. Diabetes retinopathy was found to be in 45 (19.7%) patients. Proteinuria was noted in 30 (13.1%) patients.

Table 3: Association of Diabetic Retinopathy with Proteinuria and Age Group (n = 228)

Variable	Group	DR Yes	DR No	P-Value	Statistical Test
Proteinuria	Yes	26 (11.4%)	4 (1.8%)	0.0001	Fisher's Exact Test
	No	19 (8.3%)	179 (78.5%)		
Age Group	20–50	23 (10.1%)	60 (26.3%)	0.022	Chi-Square Test
	>50	22 (9.6%)	123 (53.9%)		

Table 4: Stratification of Diabetic Retinopathy by Demographic and Clinical Factors (n = 228)

Variable	Group	DR Yes	DR No	P-Value	Test
Gender	Male	29 (12.7%)	104 (45.6%)	0.353	Chi-Square
	Female	16 (7.0%)	79 (34.6%)		
Place of Living	Rural	20 (8.8%)	40 (17.5%)	0.002	Chi-Square
	Urban	25 (11.0%)	143 (62.7%)		
Socioeconomic Status	<50,000	33 (14.5%)	94 (41.2%)	0.008	Chi-Square
	≥50,000	12 (5.3%)	89 (39.0%)		
BMI	16–24	9 (3.9%)	44 (19.3%)	0.565	Chi-Square
	>24	36 (15.8%)	139 (61.0%)		
Duration of DM	1–2 years	15 (6.6%)	39 (17.1%)	0.089	Chi-Square
	>2 years	30 (13.2%)	144 (63.2%)		
Hypertension	Yes	19 (8.3%)	90 (39.5%)	0.403	Chi-Square
	No	26 (11.4%)	93 (40.8%)		
Smoking Status	Smoker	21 (9.2%)	75 (32.9%)	0.489	Chi-Square
	Non-Smoker	24 (10.5%)	108 (47.4%)		
Educational Status	Illiterate	6 (2.6%)	14 (6.1%)	0.016	Chi-Square
	Primary	11 (4.8%)	30 (13.2%)		
	Intermediate	5 (2.2%)	64 (28.1%)		
	Graduate or more	23 (10.1%)	75 (32.9%)		

Diabetic retinopathy was noted in 26 (11.4%) patients with proteinuria while 19 (8.3%) without proteinuria and P-value found to be highly significant i.e., P=0.0001. Stratification of age group, gender, place of living, socioeconomic status, body mass index, duration of type II DM, comorbidities i.e. hypertension, smoking and educational status was done with respect to diabetic retinopathy in order to find statistical difference.

Discussion

Our findings align with Mohan et al.9 and Rani et al.7, demonstrating that urinary protein excretion correlates with DR severity. Proteinuria reflects glomerular endothelial dysfunction and systemic

microangiopathy, which may parallel retinal vascular changes. Early identification of proteinuria T2DM patients could therefore trigger prompt ophthalmic evaluation, potentially mitigating vision loss. In present study, diabetes retinopathy was found in 45 (19.7%) patients. In the study of Rani PK, et al the prevalence of diabetic retinopathy as 18.03% [10]. In this study, stratification of confounders / effect modifiers with respect to diabetic retinopathy, significant difference was noted in age (P=0.022), place of living (P=0.002), socioeconomic status (P=0.008), educational status (P=0.016) while insignificant difference was found in gender (P=0.353), body mass index (P=0.565), duration of type II DM (P=0.089), hypertension (P=0.403) and smoking status (P=0.489).

Conclusion

A significant association between proteinuria and DR underscores the need for integrated renal-ocular screening in diabetes clinics. Implementation of joint screening protocols may facilitate earlier interventions and improve patient outcomes.

Recommendations:

- Introduce combined DR and proteinuria screening in primary diabetes care.
- Educate clinicians on the predictive value of proteinuria for ocular complications.
- Conduct longitudinal, multi-center studies to explore causality and progression.

Limitations

Single-center, cross-sectional design limits generalizability and prevents causal inference. Proteinuria assessment did not include UACR; albumin-specific measures might enhance sensitivity.

Conflict of Interest

The author declares no conflicts of interest.

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