Original Article

Diabetic Retinopathy as a Risk for Primary Open Angle Glaucoma

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ABSTRACT

Purpose: To evaluate diabetic retinopathy as a risk factor for open-angle glaucoma.

Study Design: Case control study.

Place and Duration of Study: Munawar Memorial Hospital Chakwal from December 2021 to April 2022.

Methods: A sample of 206 eyes of 103 diabetic patients, 40 to 65 years of age and either gender were included in the study. The eyes were divided into two groups on the basis of presence and absence of diabetic retinopathy. Data included age, gender, visual acuity, intraocular pressure, type, and duration of diabetes mellitus. Fundus examination was carried out using a 90 Diopters lens. Diabetic retinopathy was graded according to the early treatment diabetic retinopathy scale (ETDRS). Primary open angle glaucoma was diagnosed on the basis of optic nerve head changes, defective visual field and raised intraocular pressure. Data was analyzed by IBM SPSS Statistics for Windows, Version 20.0.

Results: Of 103 subjects, 52 subjects were male and 51 were female. Of the 206 eyes of 103 subjects, 100 eyes had no signs of diabetic retinopathy while 106 eyes had signs of diabetic retinopathy. Fifty six eyes had primary open angle glaucoma. Chi-square and a multivariate regression model were used for analysis. The odds ratio of diabetic retinopathy for primary open angle glaucoma was 1.50.

Conclusion: In conclusion, Diabetic retinopathy was found to be a significant risk for developing primary open angle glaucoma in addition to other contributing factors like age, duration of diabetes mellitus, increased intraocular pressure, Ocular Perfusion pressure and cup disc ratio.

Key Words: Diabetic Retinopathy, Primary open angle Glaucoma, Intraocular pressure, Ocular Perfusion pressure.

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INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder characterized by raised blood sugar levels due to abnormalities in secretion or action of insulin or both.[1] DM is a major etiological factor for prolonged ill health and premature death. Increased life expectancy and limited access to health care facilities are contributing factors to the accelerated rise in the diabetic population.[2] Diabetic retinopathy (DR) is an angiopathic ocular complication due to un-controlled diabetes which can result in irreversible vision loss.[3]

Thus, DR constitutes a major cause of visual loss around the world.[4] Pooled Prevalence of vision-threatening diabetic retinopathy (VTDR) in Pakistan is reported as 28.2%.[5]

Glaucoma is an optic neuropathy and one of the major causes of irreversible blindness globally.[6] It is estimated that the population of glaucoma subjects will rise to 111.8 million in 2040.[7] Limited access to eye care services is associated with an increased incidence of glaucoma-related visual loss.[8]

DM is a common risk for incidence of primary open angle glaucoma and diabetic retinopathy.[9] Diabetes results in increased lipid glycation and disturbs lipid metabolism. This promotes oxidative stress and apoptosis of retinal ganglion cells.[10] Diabetes also promotes apoptosis by chronically elevated intraocular pressure.[11]Increased aqueous humor glucose levels may increase the production and storage of fibronectin in trabecular meshwork (TM). This depletion of TM cells may suggest a common metabolic link between incidence of primary open angle glaucoma and diabetic retinopathy.[12]It is suggested that retinal tissue ischemia contributes to retinal ganglion cell loss in glaucoma by the accumulation of free radicals.[13] This suggests that diabetes is a risk for neuronal damage.[14] Some studies report that neuro-degeneration resulting from diabetes may manifest earlier than incidence of other vascular abnormalities.[15]

In a tele retinal screening program to find association between glaucoma and DR, the prevalence of glaucoma in diabetics ranged from 1% to 2.7%. However, this study failed to prove any significant link between DR and glaucoma.[16]

Very limited work has been done in Pakistan regarding association between these diseases. This study was planned to find the association of DR and Primary open angle glaucoma (POAG).

METHODS

The study was carried out at eye department of Munawar Memorial Hospital and College of Optometry Chakwal. It was a cross-sectional study to find out association of diabetes with POAG. Informed consent was taken from the participants and were divided into two groups (with and without diabetic retinopathy). All patients with either type I or type II, both genders, age of 40 to 65 years were included in the study. Data were collected through self-designed proforma. Subjects with cataract, corneal disease and other ocular pathologies were excluded from the study. After complete ocular and systemic history, visual acuity was assessed using Snellen visual acuity chart. All subjects underwent detailed ocular examination including anterior and posterior segments. IOP was measured using a Goldmann applanation tonometer. Other diagnostic tests like pachymetry and perimetry were performed to confirm diagnosis of primary open angle glaucoma. Secondary cause of glaucoma was ruled out. Tropicamide 1% was used to dilate pupils. Fundus examination was carried out using 90 Diopters lens to assess stage of Diabetic retinopathy and cup-disc ratio. DR was graded according to Early Treatment Diabetic Retinopathy system (ETDRS) grading scale into mild, moderate, severe non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR). POAG was diagnosed on the basis of characteristic optic nerve head signs, defective visual field and associated intraocular pressure. These findings were confirmed by the ophthalmologist.

Blood pressure was measured in the sitting position after 5 minutes of rest with mercury sphygmomanometer in accordance with the hospital protocol. Two readings were obtained with the difference of 5 minutes. The mean of these two readings was taken as blood pressure. Mean arterial pressure (MAP) was calculated by using systolic blood pressure (SBP) and diastolic blood pressure (DBP) using following formula:

MAP = mean arterial pressure = 0.333 (SBP – DBP) +DBP.

Ocular perfusion pressure (OPP) was calculated using following formula:

$$OPP = 0.666\ MAP - IOP$$

Data was analyzed by IBM SPSS Statistics for Windows, Version 20.0. Independent sample t test and chi square was used to compare characteristics between two groups. Multivariate logistic regression model was employed to calculate risk of POAG.

RESULTS

One hundred and three diabetic patients included 52 males and 51 females. Thirty one were using insulin while 72 were suffering from NIDDM. Of 206 eyes of 103 subjects, 100 eyes had no signs of DR while 106 eyes had DR. Out of all, 56 eyes had POAG. Independent sample t test was used for comparative analysis of characteristics between subjects with and without DR. Mean IOP in subjects with DR was 16.70 ± 7.98 while mean IOP in subjects without DR was 16.48 ± 7.3. This difference between two groups was not statistically significant. Out of total, 127 eyes had cup-disc ratio (CDR) equal to or less than 0.4 while 15 eyes had CDR equal to greater than 0.8 (Table 1). Chi square analysis was performed to establish association between DR and POAG. On bivariate analysis 26.41% eyes with DR had POAG compared with 28% eyes

without DR. Chi square statistics = 0.65, p = 0.798 (Table 2).

Table 1: *Characteristics of sample.*

Variable	DRGroup	Group with No DR	P value
Age	58.86 ± 10.107	59.85 ± 13.353	0.29
Duration of DM	14.33 ± 11.015	9.88 ± 6.869	0.38
CDR	0.42 ± 0.183	0.41 ± 0.19	0.261
IOP	16.70 ± 7.99	16.48 ± 7.297	0.488
SYSTOLE	140.0 ± 10.0	142.3 ± 20.54	0.082
DIASTOLE	96.67 ± 5.77	92.70 ± 13.62	0.102
BSR	259.33 ± 101.7	246.40 ± 71.43	0.491
OPP	78.03 ± 16.43	78.06 ± 16.64	0.6

Table 2: *Bivariate analysis of diabetic retinopathy and glaucoma status.*

	Glaucoma	No Glaucoma	Total
DR	28 (26.41%)	78 (73.58%)	106 (100%)
No DR	28 (28%)	72 (72%)	100 (100%)
Total	56	150	206

In multivariate regression model, risk factors for the development of POAG were DR, age, IOP, OPP, increased CDR and longer duration of diabetes mellitus (p = 0.05; confidence interval 0.50 – 3.727). Table 3 and 4 depict the details.

Table 3: *Multivariate analysis of ocular and systemic factors of POAG.*

Parameter	P value	Odd's Ratio	Confidence Interval
DR	0.05	1.50	0.50 – 3.727
Age	0.122	1.027	0.993 – 1.063
Males	0.18	0.88	0.331 – 2.383
Duration of DM	0.18	1.03	0.67 – 1.58
OPP	0.007	1.19	1.03 – 1.21
IOP	0.24	1.05	0.883 – 1.03
IDDM	0.15	2.116	0.748 – 5.982
CDR	0.53	2.004	0.11 – 1.23

Table 4: *Risk Factors Associated with Glaucoma after adjusting for age and gender.*

Parameter	P value	Adjusted Odd's Ratio	Confidence Interval
DR	0.04	1.33	0.50 – 3.727
Age	0.123	1.036	0.991 – 1.083
Male sex	0.9	0.65	0.31 – 2.4

DISCUSSION

We compared frequency of POAG in diabetics with and without DR. Both groups were similar in age, gender and duration of DM. Frequency of DR was 51% in the whole sample. Similar results were reported by an earlier study from Pakistan.[17] Comorbidity of DR and POAG is reported to be 4.5%.[18] The increased prevalence of comorbid retinal disease can double the chances of low vision indicating that coexistence of these two vision-threatening diseases is an important public health challenge. Overall frequency of glaucoma in both groups was reported to be 27%, a bit higher than previous research which showed this percentage as 20%.[19] In this particular study, on bivariate analysis, the frequency of POAG in DR group was 26% while in the other group without DR was 28%. These results were not statistically significant**.** However, DR was identified as a strong risk factor for development of POAG in multivariate regression analysis after adjusting for other factors.

Gangwani et al, reported glaucoma in diabetic population in range of 1% to 2.7%. Results were reported on basis of increased cupping of optic disc in a tele retinal screening program.[16] Bhutia et al., reported this percentage as 20%.[19] Corresponding figures for this study are 27%. This discrepancy in results can be explained on the basis of different study population and study design. It is noteworthy that in the works of Bhutia, all types of glaucoma were included.

In this study diabetic retinopathy was indicated as a significant risk (p value < 0.05) for development of POAG (OR = 1.5 Confidence Interval 0.50 – 3.727). After adjusting for age and gender, adjusted odds ratio was not significantly affected. Literature also suggests increase odds for development of open-angle glaucoma for patients of 40 years of age with DR.[20] However, the authors used only DR cases which explains the difference in results. A recent study reported lack of association between DR and POAG.[21] This variation in results can be explained on basis of type of DM. Majority of subjects included in this research were suffering from NIDDM. Age, gender, ethnicity and duration of diabetes may be contributing factors causing this disparity.

Other risk factors for development of POAG were age, longer duration of DM, IOP and CDR. Earlier studies also reported that the increased age and increased intraocular pressure (IOP) were associated with higher risk of open angle glaucoma. Contribution of other risk factors to the development of POAG was also confirmed in literature.[22] Male gender was found

to be protective against development of POAG even after adjusting for confounding factors like age. Contradicting this, the previous studies indicated that females were at higher risk of developing open angle glaucoma.[23] A strong association was also found between OPP and POAG (OR = 1.19, CI = 1.03 – 1.21). These results were highly significant (p value < 0.05). Literature supports this finding. Chronic fluctuation in OPP can cause optic disc ischemia which further aggravates glaucoma progression.[24] This finding implies need for deeper understanding to link the effect of intraocular pressure and blood pressure in diabetics. Combined DR and glaucoma screening programs should be conducted for cost effectiveness. It will aid the clinicians and policy makers to optimize capacity planning for resource management. Early screening of DR and glaucoma can prevent visual loss and reduce burden of disability. Further studies both descriptive and prospective including survival data with longer duration and large sample size are required to establish the consensual relationship between DR and POAG.

Strength of the current study was comparative analysis of POAG in subjects with and without DR. Most of the previous studies were cross sectional and observational. We have included POAG and diabetic patients on the basis of clinical examination of the patient and detailed anterior and posterior segment evaluation. Certain limitations are to be considered while interpreting these results. Some systemic risk factors like hematocrit and HBA1C were not assessed due to cost implications. Both types of diabetic subjects i.e. IDDM and NIDDM were included in this study which can be separately investigated.

CONCLUSION

DR is a significant risk for development of POAG despite other contributing factors like age, duration of DM, increased IOP, OPP and CDR.

Conflict of Interest: Authors declared no conflict of interest.

Ethical Approval

The study was approved by the Institutional review board/Ethical review board **(TUF/IRB/041/2022).**

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Author's Designation and Contribution

Iqra Khalil; Optometrist: *Concepts, Design, Literature Search, Data Acquisition, Data analysis, Statistical Analysis, Manuscript Preparation, Manuscript Editing, Manuscript Review.*

Ayesha Kiran; Optometrist: *Data Analysis, Statistical Analysis, Manuscript Preparation.*

Sajjad Haider; Consultant Ophthalmologist: *Data Analysis, Manuscript Editing, Manuscript Review.*

Bushra Kanwal; Optometrist: *Data Analysis, Manuscript Preparation, Manuscript Editing.*