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Study of Frequency of Primary Open Angle Glaucoma in Type-2 Diabetes Mellitus.

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ABSTRACT

Background: Primary open angle glaucoma (POAG) is a silent disease that may result in irreversible bilateral blindness if not identified and treated effectively. Diabetes mellitus (DM) is a group of metabolic disorders characterized by hyperglycemia. Evidence demonstrates that vascular disturbances to the optic nerve's anterior portion are responsible for optic nerve head changes, which can result in glaucomatous optic neuropathy. Diabetes mellitus as a microangiopathy itself affects the ocular circulation. Studies studying diabetes as a risk factor for development of glaucoma have given conflicting results. This study was therefore planned to see the frequency of primary open angle glaucoma and in diabetics. **Methods:** It was an observational cross-sectional study. The present study consisted of 100 types 2 diabetes mellitus patients and 100 controls without diabetes between 40-70 years of age of either sex. The patients from both groups were thoroughly examined for the diagnosis of Primary Open Angle Glaucoma (POAG) after applying the diagnostic criteria. **Results:** The frequency of Primary open angle Glaucoma was significantly more among Diabetics (20.0%) in comparison to Non-Diabetics (12.0%). **Conclusion:** A public health awareness approach is recommended in all patients of type 2 diabetes mellitus patients regarding Primary Open Angle Glaucoma in the study area.

Keywords: Primary open angle glaucoma,Type 2 diabetes mellitus.

INTRODUCTION

Glaucoma affects more than 70 million people worldwide with approximately 10% being bilaterally blind,[1] making it the leading cause of irreversible blindness in the world. Evidence demonstrates that vascular disturbances to the optic nerve's anterior portion are responsible for optic nerve head changes, which can result in glaucomatous optic neuropathy.[2]

Diabetes Mellitus (DM) is a group of metabolic disorders characterized by hyperglycemia.[3] There is considerable evidence that type T2D is a risk factor for POAG.[4] Microvascular damage from diabetes could impair blood flow to the anterior optic nerve, resulting in optic nerve damage.[5,6] Diabetes also impairs the autoregulation of posterior ciliary circulation, which may exacerbate glaucomatous optic neuropathy.[7]

A recent summary of the results of 47 studies that collectively included nearly 3 million people concluded, "diabetes, diabetes duration, and fasting glucose levels were associated with a significantly increased risk of glaucoma, and diabetes and fasting glucose levels were associated with slightly higher IOP.[4]

The studies that have been done thus far have shown a mix bag of results regarding association between diabetes mellitus and Primary Open Angle Glaucoma.[8-13] Also Indian studies regarding this association are few and far between. This study was planned to not only evaluate the correlation between Primary Open Angle Glaucoma and type 2 diabetes mellitus but also to find the frequency of such correlation in an Indian population of western UP.

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MATERIALS AND METHODS

It was an observational cross-sectional study to find the frequency of POAG among patients with type 2 diabetes mellitus. The present study was conducted in the Department of Ophthalmology, Teerthanker Mahaveer Medical College & Research Centre, Moradabad. A well informed consent was taken from all the patients included in the study.

Inclusion criteria

The study involved 200 patients which were selected for the study as follows.

Group 1 - 100 type 2 diabetic patients between 40-70 years of age, of either sex, were selected from

diabetic clinic of medicine OPD by systematic random sampling irrespective of duration of diabetes. Group 2- 100 Non –Diabetic patients of either sex of comparable age group as above were selected from those attending the OPD of department of Ophthalmology by systematic random sampling.

Exclusion Criteria

Age below 40 and above 70 years, ocular hypertension, pregnant patients, history of trauma that is directly related to glaucoma, any preexisting ocular surgery and pathology, patient with any other systemic illnesses, patient refusal/ unco-operative patient.

Methodology

A well informed consent was taken from all patients recruited for the study.

The patients from both groups were thoroughly examined for the diagnosis of POAG.All patients thus selected were examined as follows. Chief complaint with their duration was noted, a detailed history of diabetes, glaucoma was taken. History of anti-glaucoma medications, their dosage, duration and side effects were noted. Systemic medications for diabetes were noted. Visual acuity of each participant was recorded on Snellen's chart. Adenexa were examined. Ocular movements were recorded. Anterior Segment examination (using the Slit Lamp). Intraocular pressure was measured using Goldmann applanation Tonometer in both eyes. Gonioscopy was done using the Goldmann 2 mirror goniolens. Fundus examination was done using a 90D and indirect ophthalmoscope and optic nerve head changes were noted with respect to superior or inferior notching, cupping and vertical cup disc ratio, thinning of neuroretinal rim changes with special reference to temporal pallor, focal atropy, concentric atropy, saucerisation, pallor / cup discrepancy, asymmetry of the cup:disc ratio>0.2 between the two eyes, deepening of the cup and bean pot cupping. Splinter haemorrhage and tortuosity of retinal vessels, nasal shifting of blood vessels, bayonetting sign, baring of circumlinear vessels were also noted. Peripapillary changes were also observed. Perimetry was also performed using the Zeiss Humphrey Visual Field Analyser. We used 24 -2 pattern SITA strategy and 10-2 for extremely depressed fields. Visual field changes were noted. We applied the following criteria.

Diagnostic Criteria Of Primary Open Angle Glaucoma Patients were as follows:[14]

1. I.O.P 21 mm Hg
2. Glaucomatous Optic Nerve damage
3. An open anterior chamber angle.
4. Characteristic visual field loss.
5. Absence of signs of secondary glaucoma or a non-glaucomatous cause of optic neuropathy.

Data obtained were analysed with appropriate statistical software SPSS version 21.0

RESULTS

The study population consisted of 94 (47.0%) males and 106 (53.0%) females. Among diabetics, there were 50 (50.0%) males and 50 (50.0%) females and among non-diabetics, there were 44 (44.0%) males and 56 (56.0%) females.The distribution of males and females was compared between diabetics and non-diabetics. There was no significant distribution of males and females between diabetics and non-diabetics. [Table 1] shows gender wise distribution in between groups.

Table 1: Gender wise distribution in between groups

Gender	Group1(Diabetic)	Group 2(Non-Diabetic)	Total
Male	50	44	94
	50.0%	44.0%	47.0%
Female	50	56	106
	50.0%	56.0%	53.0%
Total	100	100	100
	100.0%	100.0%	100.0%

Chi-square test * Non-significant difference

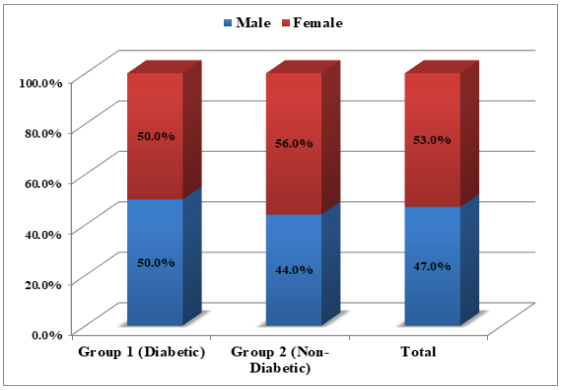

Figure 1: Gender wise distribution.

The distribution of males and females was compared between Diabetics and Non-Diabetics. The frequency of Primary open angle Glaucoma (POAG) was significantly more among Diabetics (20.0%) in comparison to Non-Diabetics (6.0%). [Table 2] frequency of primary open angle glaucoma in between groups.

Table 2: frequency of primary open angle glaucoma in between groups.

Primary open angle Glaucoma(POAG)	Group 1(Diabetic)	Group 2(Non-Diabetic)	Total
Absent	80	94	174
	80.0%	94.0%	87.0%
Present	20	6	26
	20.0%	6.0%	13.0%
Total	100	100	100
	100.0%	100.0%	100.0%
Chi-square value = 22.000, p-value < 0.001*			

Chi-square test * Significant difference

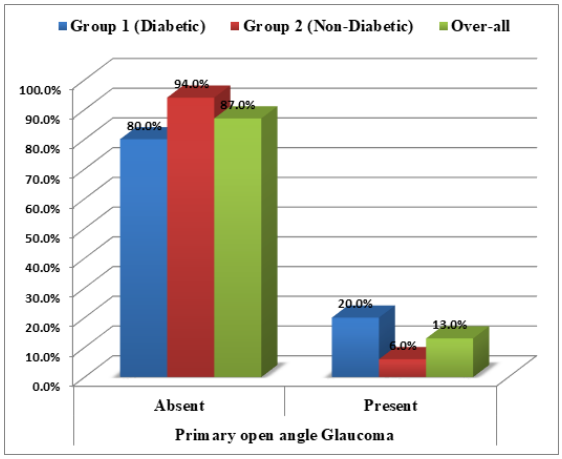

Figure 2: Frequency of primary open angle glaucoma in between groups.

The comparison of mean right and left eye intraocular pressure (iop) by applanation tonometry was compared using the unpaired t-test. the mean right and left eye intraocular pressure by applanation tonometry was significantly more among diabetics (28.60±5.66 and 28.04±4.79 respectively) in comparison to non-diabetics (16.76±4.80 and 16.56±3.48 respectively). [Table 3] shows the intraocular pressure (iop) by applanation tonometry of right eye and left eye in between the groups.

Table 3: Intraocular pressure (iop) by applanation tonometry of right eye and left eye in between the groups.

	Group 1(Diabetic)		Group 2(Non-Diabetic)				
IOP by Applanation Tonometry	Mean	Std. Deviation	Mean	Std. Deviation	Mean Difference	t-test value	p-value
Right eye	28.60	5.66	16.76	4.80	3.84	3.66	< 0.001*
Left Eye	28.04	4.79	16.56	3.86	3.48	4.00	< 0.001*

Unpaired t-test * Significant difference

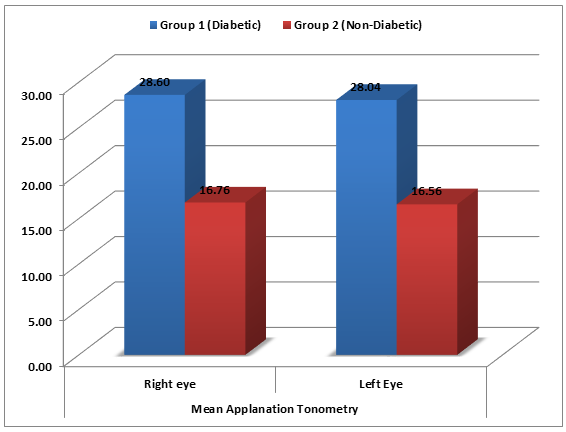

Figure 3: Iop by applanation tonometry of right eye and left eye in between the groups

The comparison of mean fundus (CD ratio) was compared using the Unpaired t-test. The mean fundus (CD ratio) was significantly more among diabetics (0.50±0.20 and 0.48±0.19 respectively) in comparison to non-diabetics (0.25±0.15 and 0.24±0.12 respectively). [Table 4] shows cup disc (C:D) ratio in between the groups.

Table 4: C:D ratio in between the groups.

	Group 1 (Diabetic)		Group 2 (Non-Diabetic)				
Fundus (CD ratio)	Mean	Std. Deviation	Mean	Std. Deviation	Mean Difference	t-test value	p-value
Right eye	0.50	0.27	0.25	0.18	0.24	6.98	< 0.001*
Left Eye	0.48	0.28	0.24	0.18	0.24	7.55	< 0.001*

Unpaired t-test * Significant difference

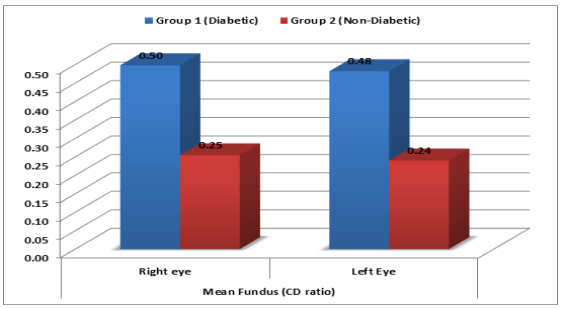

Figure 4: C:D ratio in between the groups

DISCUSSION

Various studies have been done to examine the relationship between diabetes and glaucoma with variable results. Some of these discrepancies may be related to the study sample, sample size, patient drop-out, detection bias, reverse causation, and variations in the diagnostic criteria and methods for defining glaucoma and diabetes. In addition, these studies were not designed with a primary endpoint of evaluating the association between glaucoma and diabetes. For example, the Ocular Hypertension Treatment Study, a randomized trial that examined the safety and efficacy of IOP lowering medications in delaying or preventing the development of POAG, initially reported that diabetes was protective against the conversion from ocular hypertension (elevated IOP without optic neuropathy) to glaucoma.[15] However, the diagnosis of diabetes was made by patient self-report and further analysis showed that the study sample was underpowered to find an effect of diabetes on the development of glaucoma.[16] Despite these discrepancies, the majority of the evidence suggests an increased risk of POAG in persons with diabetes.

In our study, the frequency of Primary open angle Glaucoma was significantly more among Diabetics

(20.0%) in comparison to Non-Diabetics (6.0%) which was similar to the study by Chopra et al,[17] the positive, independent association between T2DM and OAG. This sample population had a high prevalence of both T2DM and OAG. The prevalence of OAG was 40% higher in participants with T2DM than in those without which was much more than reported in our study. In the study by Bamashmus et al,[18] Glaucoma was noted in 8.6% of patients with DM and a study in Oman reported that 8.9% of patients with DM were suffering from glaucoma which was lesser than the present study.[19] This is in line with other large population-based cross-sectional studies of predominantly whites, including the Beaver Dam Eye Study, Blue Mountains Eye Study, and NHS, all of which found that persons with DM have an independent higher risk of having OAG than those without DM.[8-10] In particular, the Blue Mountains Eye Study also reported a significant and consistent association between DM and OAG, independent of level of IOP.[17]
This also concurs with the studies by Jayanta et al,[20] POAG was diagnosed among 7.0% diabetic patients in the age group of 15-75 years, which was more than that as compared to general population (1-2%),[21] but similar to the findings by Neilsen (6%).[22] and Grecoet al(9.26%).[23] In the Blue Mountains Eye Study,[9] the entire study population underwent a detailed eye examination including automated perimetry, stereo optic disc photographs, and applanation tonometry to establish a diagnosis of glaucoma or ocular hypertension. The age-sex adjusted odds ratio (OR) for glaucoma in diabetics compared with those without diabetes was 2.12 (95% confidence intervals (CI) 1.18–3.79), and the authors concluded that there was a real association between glaucoma and diabetes. On the other hand, the Baltimore Eye Study,[11] which was conducted similarly to the Blue Mountains Eye Study, found an age-race adjusted odds ratio of 1.03.

In contrast, unlike these previously reported studies of primarily white populations, the Baltimore Eye Survey examined a more varied population (45% black) and found no association between primary OAG and history of T2DM.[11] The variance in results between our study and Baltimore Eye Survey may be related not only to their different populations, but also to their differing definitions of DM.[17] The definition of DM in the Baltimore Eye Survey was limited to positive history of diabetes elicited from the patient during a personal interview.[11] Proyecto VER also found no association between primary OAG and a history of T2DM after adjusting for age.[13] These genetic and hereditary differences between the 2 populations of Proyecto VER and our study, along with differences in study design and recruitment methodology and variations in definitions of T2DM and OAG, may help explain the variability in reported results.[17]

The Rotterdam study had previously reported a positive association between DM and OAG,[24] with a relative risk of 3.11 (95% CI, 1.12–8.66) of prevalent high-tension OAG in participants with DM using a subset of their baseline data. However, the authors changed their definition of OAG used in the baseline analysis (now excluding IOP as part of the diagnosis of OAG) for the subsequent longitudinal data analysis. Using the newer definition of OAG, the Rotterdam study reported that diabetes was not a risk factor for incident OAG in their prospective population-based cohort study of whites.[24] Furthermore, they reported that the recalculated relative risk of the baseline group in their final analysis had also become non significant (OR, 1.40), based on their revised OAG definition. When deciding on the criteria for glaucomatous optic nerve damage, the cut-off value for bilateral C/D ratio was chosen as 0.6 because when C/D ratio equals or exceeds 0.6, the probability of abnormality increases dramatically.[25] The side difference in C/D ratio was set at ≥0.2 because 88% of normal subjects have a C/D vertical ratio side difference equal or less than 0.1.[26] The appearance of the optic nerve head was not used as a restriction criterion for the entry of subjects into either the normal or glaucoma.[27] Early detection of chronic and blinding eye conditions such as glaucoma and Diabetic Retinopathy (DR) are recommended for timely intervention and treatment.[28] However, universal screening as a public health measure is recommended only if the prevalence of the individual eye disease is high.[29] Nearly 30% of individuals with open angle glaucoma have diabetes.[30] Therefore, DR screening among diabetics is recommended.[28] Global public health policy for preventing visual disabilities due to glaucoma has been proposed by experts to the World Health Organization.[31] Combined screening for DR and glaucoma should depend on the magnitude of both of these potentially blinding conditions, and it should be implemented at that country/sub-regional level despite global policies.[32] Although population based glaucoma screening is not recommended, periodic comprehensive eye assessment of all patients older than 40 years (including diabetics) could be an alternative strategy for early detection of glaucoma.[30]
Our study had a few restrictions. With a limited sample of patients visiting one institution, the results should be estimated with caution. This type of institution-based case selection could have brought health-seeking bias. Most importantly, a longitudinal study is required to study the risk factors for glaucoma. Our cross-sectional study reports trends only.

CONCLUSION

The frequency of Primary open angle Glaucoma was significantly more among Diabetics (20.0%) in

comparison to Non-Diabetics (12.0%). The study population consisted of 47.0% males and 53.0% females. Among diabetics, there were 50.0% males and 50.0% females and among non-diabetics, there were 44.0% males and 56.0% females.The mean age of the Non-Diabetics was 51.50±8.72 years and Diabetics was 56.82±9.79 years. The mean Right and Left eye iop by Applanation Tonometry was significantly more among Diabetics (28.60±5.66 and 28.04±4.79 respectively) in comparison to Non-Diabetics (16.76±4.80 and 16.56±3.48 respectively).The mean Fundus (CD ratio) was significantly more among Diabetics (0.50±0.20 and 0.48±0.19 respectively) in comparison to Non-Diabetics (0.25±0.15 and 0.24±0.12 respectively).

In conclusion, the frequency of primary open angle glaucoma was found to be higher in our study especially among the type 2 diabetes mellitus patients in comparison to nondiabetics. A public health awareness approach is recommended in all patients of type 2 diabetes mellitus patients regarding primary open angle glaucoma in the study area. Information on co-morbidities in the eye and visual disabilities among patients with DM should be further verified by studies with a larger sample.In short, the occurrence of type 2 diabetes mellitus (T2DM) and a longer duration of T2DM were found to be associated with a higher risk of open angle glaucoma (OAG). Our study had a few limitations. With a limited sample of patients visiting one institution, the results should be extrapolated with caution. The institution-based case selection could have introduced health-seeking bias. Ideally, a longitudinal study is required to study the risk factors for glaucoma. Our cross-sectional study reports trends only. During the study we came across several shortcomings in our study. This study included only those patients who presented in the OPD and therefore the study group was a subset of the general population and we could not accurately relate the frequency of primary open angle glaucoma (POAG) in diabetics and its association. Further studies need to be carried out with in general population the relatively high frequency of DM and OAG in this group presents enormous public health implications. Screening programs and health care planning may be affected by this association found between POAG and DM, likely with the need for additional testing for OAG. To emphasize, this current report is a step toward resolving the controversy regarding whether DM is a risk factor for OAG. Future longitudinal data should provide a more strong assessment of the risk of developing OAG in persons with T2DM.

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