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ORIGINAL PAPER

Prevalence of Glaucoma Amongst Diabetic Patients Attending a Tertiary Health Care in North Eastern India

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ABSTRACT

Introduction: Glaucoma and the angiopathy of Diabetes Mellitus (DM) constitute a significant amount of blinding diseases of human beings. DM has been suggested as risk factors for Primary Open Angle Glaucoma (POAG) and Neovascular Glaucoma (NVG). Thus, with the alarming rise in Diabetes prevalence globally; the establishment of DM as a major risk factor for POAG and NVG and the matter of blindness following glaucoma and its management are of grave concern. Methods: The present study was conducted on 1200 diabetic patients between 15 - 75 years of age attending the Endocrinology and Ophthalmology departments. Systemic, routine ophthalmic examination and laboratory investigations were done in all cases. Applanation tonometry, slit lamp biomicrocopy, gonioscopy and disc evaluation using Goldman 3 -mirror lens, +90 D lens and visual field examination (using Humphrey visual field analyzer utilizing SITA standard strategy program 30-2) was performed. Results and Discussions: Among 1200 patients, POAG was found in 7.0% (n=84), Ocular hypertension (OHT) in 3.33% (n=40) and NVG in 2.33% (n=28). The prevalence of POAG in this study was nearly 5-6 times higher than that as seen in the general population. All the patients with NVG had PDR. Pupillary margin neovascularization preceded anterior chamber angle neovascularization in all these patients. POAG was seen to be more prevalent amongst OHA treated diabetics (8.25%), neovascular glaucoma amongst insulin treated (3.18%) and ocular hypertension showed no relationship to treatment pattern. Conclusion: POAG was found to be more prevalent amongst patients suffering from diabetes mellitus as compared to the general population and NVG was found in a significant proportion of diabetics with proliferative diabetic retinopathy.

***Keywords:** Diabetes Mellitus, Primary Open Angle Glaucoma, Neovascular Glaucoma*

INTRODUCTION

Glaucoma is a potentially blinding, multifactorial optic neuropathy with an estimated prevalence of around 60.5 million people worldwide in 2010 and is expected to increase to 79.6 million by 2020.[1] With 6 million people blind and millions more suffering from visual disability, it accounts for 13.5% of global blindness, third only to cataracts and trachoma. It is estimated to affect 12 million Indians: accounting for 12.8% of the total blindness in the country and is considered to be the third most common cause of blindness in India as well. The prevalence of glaucoma in India ranges from 2.6% to 4.1%. [2] Glaucoma and the angiopathy of Diabetes mellitus constitute a significant amount of blinding diseases of human beings. Thus, the matter of blindness following glaucoma and its management is of grave concern.

The general incidence of Diabetes mellitus is high for it affects between 1.4% and 1.7% of the population of the western world. As per the global estimate of the prevalence of diabetes mellitus in the above 15 years Indian population was an alarming 7.8%.[3]

The prevalence of primary open angle glaucoma (P.O.A.G.) is several times higher in the diabetic population than in the general population.[4,5] The prevalence of rubeosis iridis among patients with diabetes mellitus ranges from 0.25-20%. The reported incidence of neovascular glaucoma (NVG) in diabetic patients with rubeosis iridis is also high.[6]

Objectives: To find out (1) the prevalence of primary open angle glaucoma and neovascular glaucoma amongst diabetic patients attending this tertiary eye care hospital. (2) A relationship between diabetes mellitus and the above mentioned types of glaucoma.

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METHODS

This study was conducted at the RIO, GMCH, and Guwahati, Assam on 1214 patients of Diabetes Mellitus over a period of 4 years from 01.04.2012 to 31.03.2016. Eight patients were lost to follow up after the initial work-up. Six patients who only allowed fundoscopic examination but refused IOP measurements and visual field analysis were excluded from the study.

Hence, the 1200 patients between 15 – 75 years of age attending the Endocrinology and Ophthalmology departments (both OPD and Indoor) were finally chosen on fulfillment of the following criteria for Diabetes Mellitus as advocated by the National Diabetes Data Group and WHO (adopted from the American Diabetes Association, 2007)

- Symptoms of Diabetes Mellitus plus Random Blood Glucose concentration >/= 11.1 m mol/L (200 mg/dl) OR
- Fasting plasma glucose >/= 7.0 m mol/L (126 mg/dl) on at least two occasions OR
- Two hour plasma glucose >/= 11.1 m mol/L (200 mg/dl) during an oral glucose tolerance test (i.e., after ingestion of 75 gm of anhydrous glucose dissolved in water).

Diagnostic Criteria Of Primary Open Angle Glaucoma Patients: The criteria adopted were based on the Beaver Dam Eye Study.

1. I.O.P. >/= 22 mm Hg by Applanation tonometry.
2. Glaucomatous cupping and pallor of the optic disc. The cup to disc ratio >/= 0.8 or a difference of >/= 0.2 in the involved eye.
3. Visual field defect typical of glaucoma.
4. A gonioscopially open angle.

DIAGNOSTIC CRITERIA OF NEOVASCULAR GLAUCOMA PATIENTS:

1. Intraocular Pressure (I.O.P.) >/= 22 mm Hg by Applanation tonometry.
2. Neovascularization of iris or anterior chamber angle.

CASES NOT INCLUDED IN THIS STUDY:

1. Pregnant patients.
2. Patients on diabetogenic drugs.
3. History of trauma that is directly related to glaucoma.
4. Patients with visually disabling cataracts.

Patient Work Up: (The findings were recorded in the proforma prepared for the study)

1. History: Chief complaints, duration and medications of diabetes, glaucoma; dosage, duration and side effects; surgical treatment for glaucoma, if any were noted.

2. Physical Examination: General and Systemic examination done.

3. Laboratory Investigations: Blood sugar– Fasting and Post prandial Urine sugar, Glycosylated hemoglobin, Lipid profile, Blood urea, Serum creatinine were estimated.

4. General Ophthalmic Examination: (a) The visual acuity was recorded using the Snellen's chart after full correction of refractive errors and crosschecked with a pinhole. (b) Ocular adnexa and lids, ocular movements, lacrimal passage patency were noted. (c) Anterior segment examination, using slit lamp biomicroscope was done.

Cornea: contour, diameter, any opacities or oedema is looked for.

Anterior Chamber: Reaction, central and peripheral depth (Van Herrick method)

Pupil: Size, shape, border, reaction to light, exfoliation etc.

Iris: Rubeosis, atrophy, iridectomy, heterochromia, and granuloma were looked for.

Lens: Position, opacities lens were noted.

5. Special Examinations: (a) IOP was measured using a Goldmann Applanation tonometer with a Haag- Streit slit lamp. Three readings were taken in each eye and the mean value was used. Both eyes were subjected to measurement. (b) Gonioscopy was done using the Goldmann 3-mirror lens. The Shaffers classification was used to grade the angle of anterior chamber. He suggested using the angular width of the recess as the criterion for grading and attempted to correlate this with the potential for angle closure (**Table 1**). A high risk of angle closure is associated with grade I or II iridocorneal angles.[7]

Table 1 Grading (Shaffer)

Numerical	Angle	Clinical interpretation
Grade 0	Complete or partial closure	Closure present
Grade I narrow	10° angle at recess	Closure possible
Grade II narrow	20° angle at recess	Closure possible
Grade III narrow	30° angle at recess	Closure impossible
Grade IV open	40° or more angle at recess	Closure impossible

Presence of peripheral anterior synechiae, pigment exfoliation, angle recession, and angle neovascularization were looked for. All the four quadrants of both the eyes were examined.

A. Fundus examined using Direct Ophthalmoscope, Indirect Ophthalmoscope and slit lamp biomicroscopy using +90 D lens to observe the optic disc stereoscopically to note the following points.

i. Optic nerve head evaluation with special reference to temporal pallor, saucerization, peripapillary atrophy, splinter haemorrhage.

ii. Cup: disc ratio, superior or inferior notching, laminar dot sign.

iii. Blood vessels showing nasal shifting, bayoneting, baring of circumlinear vessels, neovascularization.

iv. Nerve Fibre layer defects (using red filter light)

v. Rest of the fundus was examined for the presence of retinopathy, neovascularization with the help of indirect ophthalmoscope.

B. Visual Fields: The visual field assessments were done with the help of Automated Perimetry using the Humphrey's Visual Field Analyzer utilizing SITA standard strategy program 30-2.

RESULTS

The present study was conducted on 1200 diabetic patients (644 male and 556 female) satisfying the patient selection criteria mentioned earlier. The mean age being 53.50 years (**Figure 1**).

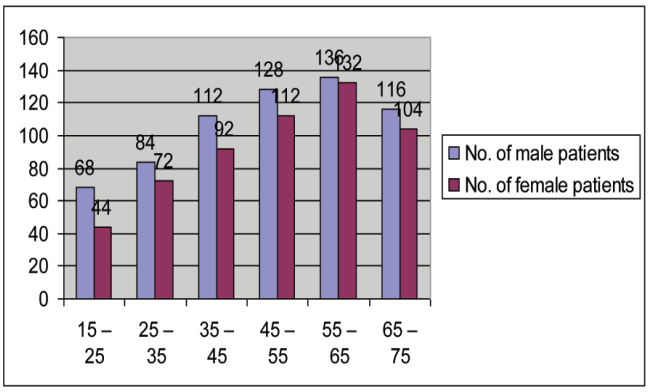

Figure 1 Age and Sex distribution

Diabetic Status: Every patient was a known diabetic; Type 1 or Type 2 diabetes mellitus was diagnosed by the physicians at the Endocrinology department and treated likewise. There were 348 Type 1 and 852 Type 2 DM patients.

Management of DM: 548 patients were on insulin, 388 patients were using Oral hypoglycemic agents (OHA) and 184 were on diet control alone at the time of this study.

IOP Distribution: 156 Patients having IOP >/= 22 mm Hg in any one eye were recorded. Mean IOP among this group of patients: RE=23.77mm Hg, LE= 23.41 mm Hg**.**

DISC Changes: In 32 out of 1200 patients (2.67 %), the disc changes could not be evaluated due to mild to moderate lenticular changes along with pre retinal neovascularization and retinitis proliferans. These patients belonged to the PDR group. (**Figure 2**)

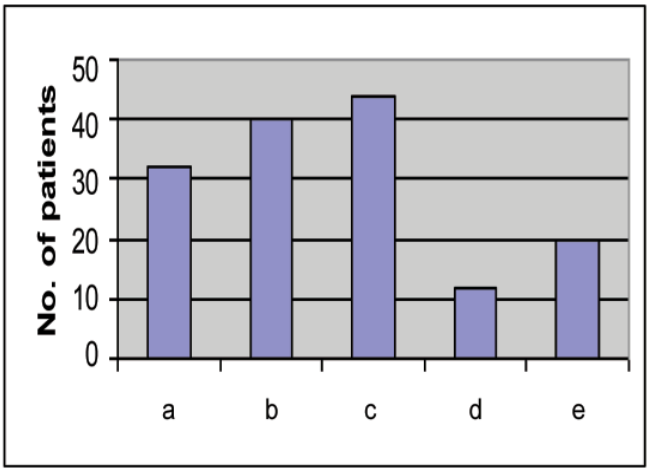

Figure 2 Disc Changes

a = Couldnot be evaluated, b= C:D<0.8,No Assymetry; c= C:D>/=0.8,Assymetry<0.2;

d=C:D<0.8,Assymetry>0.2; e=C:D>0.8,Assymetry>0.2. A large group of other diabetic patients not included.

Table 2 Optic nerve head evaluation

Neuroretinal Rim	No. of patients	Percentage (%)
Temporal Pallor	64	5.33
Saucerization	20	1.67
Peripapillary Atrophy	32	2.67
Splinter Haemorrhage	24	2.00
Cup		
Notching	16	1.33
Lamellar dot sign	68	5.67
Blood Vesels		
Nasal shift	60	5.0
Bayonetting	88	7.33
Baring of CircumlinearVs	52	4.33

Visual Field Changes: Visual field assessment could not be done in 72 patients, 20 of them suffering from retinitis proliferans and 52 from Clinically Significant Macular Edema with visual acuity < 6/60 in either eye. In this study, 1128 patients had their visual field examination done. 124 showed generalized contraction of isopters due to early lenticular changes and media opacities. 12 patients were however found to have depressed retinal sensitivity due to glaucomatous damage. 44 patients were found to have isolated paracentral scotomas, of which 12 were considered significant. 84 patients were found to have glaucomatous field defects represented in **Table 3**.

Table 3 Visual field change distribution

Visual Field Defects	No. of patients (n= 84)	Percentage (%)
A. Generalised contraction of isopters	20	23.81
B. Enlargement of Blind spot	8	9.52
C. Isolated paracentral scotomas	12	14.28
D. Arcuate scotomas-Superior	16	19.05
E. Arcuate scotomas-Inferior	28	33.33
F. Advanced visual field loss	0	0

Ocular Hypertensive: Out of 124 patients with IOP >/=22 mm Hg, 40 patients (3.33%) showed neither any disc changes nor any visual field defects and are thus labeled as ocular hypertensive. Thus primary open angle glaucoma was diagnosed in 84 patients (7.0 %).

Hereditary Role:

Table 4 Relation of Family history with POAG and Diabetes

FAMILY HISTORY	POAG PATIENTS	OTHER PATIENTS
POA Glaucoma	20	16
Diabetes	24	164
Both	12	172

Neovascular Glaucoma: Among 1200 diabetic patients, retinopathy was observed in 344 patients (28.67 %). Non-proliferative diabetic retinopathy was found in 220(63.95%) and proliferative diabetic retinopathy among 124 out of 344 patients (36.05%).

Facts and figures regarding Rubeosis iridis:

- Rubeosis iridis was seen in 76 patients (6.33%) of total study population,
- 22.09% of the retinopathy group of patients had rubeosis iridis.
- All the 76 patients with rubeosis iridis belonged to the PDR group (61.29%).
- 60 out of 76 (78.94%) of patients with rubeosis iridis had angle neovascularization.

Facts and figures about angle neovascularization:

- 5.00 % of the study group had angle neovascularization.
- 17.44 % of the retinopathy group of patients had angle neovascularization (AN),
- 60 out of 124(48.38 %) of the PDR group had AN,
- All the 60 patients with angle neovascularization had rubeosis iridis.

Thus 28 patients having IOP >/= 22 mm Hg with iris /angle neovascularization or both were diagnosed to be suffering from neovascular glaucoma. All of them belonged to the PDR group. It constituted 2.33% of study population, 8.14 % of the NPDR group and 22.58 % among PDR group.

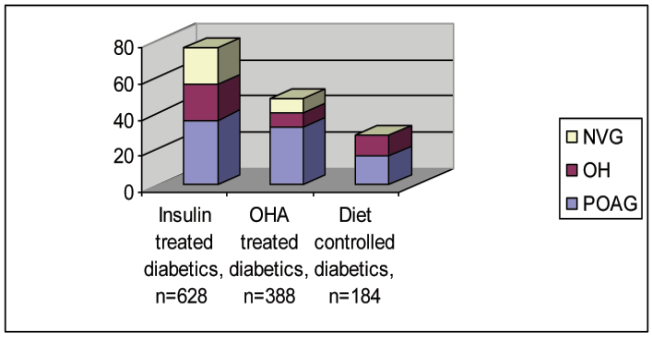

Figure 3 Relationship between the treatment of diabetes and different types of glaucoma

Thus, a total of 156 glaucoma patients were diagnosed in this study. Of which 84 patients had POAG (7.0%), 40 patients had ocular hypertension (3.33%), 28 patients (2.33%) had neovascular glaucoma. 4 patients (0.33%) were incidentally found to have narrow angle glaucoma in one eye. Their opposite eye angle were also narrow, but IOP was normal in all the 4 cases.

DISCUSSION

From the different population based studies, the incidence of POAG ranges between 1 and 2 % over the age of 40 years. The reported incidence of neovascular glaucoma (NVG) in diabetic patients with rubeosis ranges from 13 to 22%.[6]

In the present study, conducted on 1200 diabetic patients, POAG was diagnosed in 84 diabetic patients (7.0%) in the age group of 15-75 years (**Figure 1**), which was more than that as compared to general population (1-2%).[4] This finding was close to the findings of Deepthi S & Gopal B (6.8%)[8], and Neilsen N.V. (6%)[9] but slightly more in comparison to that of Klein BE (4.2%)[5] and less than that of Greco AV et al (9.26%).[10]

Table 5 Various worldwide studies on the relation of diabetes mellitus and POAG

Studies done on Diabetic population	Prevalence of POAG found
Waite&Beetham, 1935	6.0 %
Armstrong et al, 1960	4.1 %
Cristianson J, 1961	4.65%
Derose L et al,1971	20.0%
Greco AV et al, 1974	9.26%
Nielsen NV, 1983	6.0 %
(Falster island,Denmark) Klein BE, 1994	4.2 %
(The Beaver Dam Eye study) Ellis J D et all, 2000	20.0 %
(DARTS, Tayside, Scotland) [11] Shukla A K et all [12], 2009	13.9 %
Deepthi S&Gopal B [8], 2015 (Thiruvananthapuram,Kerela,India)	6.8 %
Present study (Guwahati, Assam,India)	7.0 %

A hereditary preponderance of POAG was reported by Becker et al[13] among 26% of the patients with a positive family history of glaucoma. In this study, it was found to be 23.81% (n=20, **Table 4**).

The exact mechanism of the association is not known. It could be due to a diabetes related change in the trabecular meshwork causing decreased aqueous outflow.[5] E Marre established a disturbance of mucopolysaccharide metabolism in diabetes leading to raised IOP.[14]

Klein BE et al[5], 1994 in The Beaver Dam Eye Study, Mitchell P et al[15], 1997 in the Blue Mountains Eye Study, Australia and Pasquel L[16], 2006 in the Nurses Health Study, UK all found a significant association between diabetes and glaucoma. The Los Angeles Latino Eye Study (LANES) by Chopra V et al[17], in 2008 reported that OAG was 40% more prevalent in type 2 diabetic Latino subjects, especially those with diseases of long duration.

However, Leske MC et al[18], 2008 in the Barbados Incidence Study of Eye Diseases and Le A et al[19], 2003 of the Melborne Visual Impairment Project failed to conclude that diabetes was a risk factor for the development of POAG. Many other workers

like Bankes20, Tielsch JM et al[21] in the Baltimore Eye Survey did not find any relationship between diabetes and POAG.

In this study, IOP was found to be within the normal limits (<22 mm Hg) by Applanation tonometry in all the 96 patients out of 124 (77.42%) suffering from PDR without secondary neovascular glaucoma. Similar observations were made by many workers.[22,23,24] It could be due to increased interstitial pressure and thereby decreasing transcapillary pressure. Or the condition of POAG might play a protective role in the development of retinopathy.[24]

3.33% patients were diagnosed to have ocular hypertension; i.e., these patients had IOP>/= 22 mm Hg in either eye without any significant disc changes or any visual field defects suggestive of glaucoma. This finding was in agreement with 3% found by Nielsen NV (3%)[9] and 3.6% of Xu L et al[25] in the Beijing Eye Study.

In this study, a splinter haemorrhage was seen in 24 out of 1200 (2.0%) patients at the disc and its 28.57% amongst the POAG group. This finding was higher than that of Poinoosawmy et al[26], 20%.

In 32 patients out of 84 (38.09%) an inferior half visual field defect was noted (Table 4). This was also documented by Zeiter JH, 1991 (64.4%).[27]

Neovascular glaucoma was diagnosed in 28 out of 1200 patients (2.33%) all belonging to the PDR group (n=31). This was close to the report of Nielsen NV (2.1%).[9]

In this study, the incidence of rubeosis iridis was found in 76 out of 1200 patients (6.33%; n=76). This finding was more than that of Armaly MF et al (1%)[28] but less than that of Yanoff (95%).[29] 28 patients were diagnosed to have NVG out of 76 with rubeosis (36.84%). This observation was more than that of Ohrt V (22%).[6]

The incidence of anterior chamber angle neovascularization was 60 out of 1200 patients (5.0%). All had iris neovascularization. Thus, the report of Browning DJ et al[30] that no eye had angle neovascularization without pupillary neovascularization was supported. However, Kevin J Blinder, Tielsch and Walsh[31, 32] found the appearance of angle neovascularization before iris neovascularization.

POAG was seen in 8.25%, 32 out of 388 diabetics getting OHA. Ocular hypertension occurring in all the treatment subgroups almost equally. The same observations were made by Nielsen NV (**Table 5**).[9] Neovascular glaucoma was more prevalent amongst Insulin treated type 1 diabetic 3.18% and same was observed by Ohrt V (3%).[33]

CONCLUSION

The conclusions of this study were drawn as follows: (1) POAG was found to be more prevalent amongst patients suffering from diabetes mellitus (7.0%) as compared to the general population (1 -2%).[4] (2) Neovascular glaucoma was also found in a significant proportion of diabetics (2.33%) with PDR. (3) Ocular hypertension was also diagnosed in 3.33% patients who did not have any visual field defects or cupping of optic disc suggestive of glaucoma. (4) A splinter hemorrhage at the disc was noted in a significant proportion of diabetic patients (2.0%). (5) A predilection for inferior half visual field defect was noted amongst diabetic patients with POAG (38.09%). (6) None of the patients with PDR were found to have POAG.

Conflict of interest: None declared

Ethical clearance: Taken

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