Original Article

Frequency of Normal-Tension Glaucoma in Suspected Cases of Primary Open Angle Glaucoma

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Purpose: To study the frequency of normal-tension glaucoma (NTG) in suspected cases of primary open angle glaucoma (POAG).

Materials and Methods: A descriptive cross-sectional study was done of 150 patients who attended the glaucoma clinic during one year from January 2005 to January 2006. A detailed history was obtained and a thorough ophthalmic examination was performed, including gonioscopy, ophthalmoscopy, applanation tonometery and automated perimetery.

Results: Out of 150 patients of POAG 33 patients (22%) were found to have NTG with mean age 56 ±9.21 years. Mean age of POAG group was 52.5% (±8.7). Of the 33 cases of normal-tension glaucoma 22 patients (66.6%) were male and 11 cases (33.4%) were female, while in POAG 82(70%) were male and 35 (30%) were female. Family history of glaucoma was positive in 42% of NTG cases and 32% of POAG. 82% of NTG and 79.4% of HTPOAG population were ametropic, with mean cup-to-disc ratio 0.5 ±0.24 and mean IOP was 15.13 ± 3.60 mmHg in NTG and 28 mmHg (±6.5), 0.46 (±0.22) in POAG. Maximum IOP in NTG group was 21 mmHg and minimum IOP was observed as 08 mmHg, while these values observed as 50 mmHg and 10 mmHg respectively in POAG. Decreased vision was main complaint of NTG patients, headache was observed in maximum number of POAG patients.

Conclusion: NTG remains a difficult diagnosis for ophthalmologist who favors the argument that raised IOP is essential for the diagnosis of POAG. NTG changes the definition of glaucoma and our concept of IOP as a sole etiological factor is now out dated. The overall frequency of NTG in the current study was 22% among suspected cases of POAG.

Glaucoma is the second leading cause of blindness world wide[1]. Glaucoma cases are expected to hit 80 million by 2020; of these 74% will have primary open angle glaucoma[2] (POAG). POAG is an asymptomatic, progressive optic neuropathy characterized by enlarging optic disc cupping and visual field loss[3]. It has been proven by many studies[3,4] that POAG exhibits two patterns of visual field defects: a relatively diffuse and putatively more intra ocular pressure (IOP) dependant type and a localized and putatively less IOP dependent type.

Normal-Tension Glaucoma (NTG) is a variety of POAG clinically defined[5] as "a condition in which IOP is less than 21mmHg associated with typical glaucomatous optic neuropathy and corresponding visual field changes". In glaucoma IOP is a major risk factor in the development and progression of disease, however, in NTG other risk factors are considered more important, as IOP, by definition, remains within statistically normal limits[6,7]. We can say that, NTG is simply a form of POAG in which one of the sign (IOP) is absent[3]. NTG comprises a significant proportion of the generic grouping of POAG, although this proportion varies between samples and possibly between different populations[8]. Many studies have been done regarding NTG. According to those studies frequency of NTG is not low accounting for one third of POAG in west[9, 11] and two third among Japanese at the time of screening[12]. However, in our country we still lack epidemiologically valid data on NTG. Purpose of this study is to find out the frequency of NTG among suspected cases of POAG.

MATERIAL AND METHODS

This was a cross-sectional study of descriptive type, conducted in the department of Physiology, Dow University of Medical and Health Sciences Karachi, Civil Hospital Karachi in collaboration with glaucoma clinic at Al-Ibrahim Eye Hospital Karachi. Out of all glaucoma patients who visited glaucoma clinic from January 2005 to January 2006, those who satisfied the following criteria were included in this study.

- Open angles of drainage.
- Glaucomatous cupping of optic nerve head and loss of neuroretinal rim.
- Visual field defects compatible with glaucomatous cupping.
- Absence of any secondary cause for glaucomatous optic neuropathy.
- Patients of NTG having IOP less than 21mmHg without any treatment, after confirmation by visual field analysis with Humphrey Field Analyzer.

Those with cataract or any other eye disease producing optic neuropathy, congenital eye diseases, or previous medical, surgical or laser treated eyes were excluded from this study.

In all the patients presenting with history of glaucoma in glaucoma clinic visual acuity was checked using Snellen's chart, after that eyes were examined using slit lamp to visualize anterior chamber of eye as well as interior of the eye either by using contact lenses or direct ophthalmoscope. Although contact lenses provide good view of chamber angles[8], but to confirm the diagnosis a separate gonio lens was used. Later in all those patients with open angles and glaucomatous optic disc changes IOP was measured using Goldmann Applanation Tonometer. Visual field were analyzed by the help of Humphrey Visual Field Analyzer using 30-2 program, after calibration and standardizations according to manual of manufacturer. Consent of all patients was taken and confidentiality maintained. A detailed questionnaire of all patients was filled, this individual record sheet of the patients were than processed for data analysis. The data collected for present study was entered and verified by using the SPSS version 10.0 software packages. Descriptive statistics were computed. Relative frequencies (percentages) of groups were shown, result expressed as mean ± SD/SEM.

RESULTS

A total of 150 patients of all ages and both sexes were selected by convenient sampling. Out of these patients one hundred and four were male (69.4%) and forty six were female (30.6%). In NTG group 22 (66.6%) were male and 11 (33.4%) were female, while in POAG 82(70%) were male and 35 (30%) were female. From these, NTG was found to be present in 33 cases (22%) of POAG cases, while rest of the population of non-NTG group is from high tension primary open angle glaucoma (HTPOAG) 117 cases (78%) (Table 1).

Age ranges from 35-75 years in study population and mean age was found to be 56 years (±9.21) in the group of NTG and 52.5% (±8.7) in HTPOAG group. Comparison of frequencies of various age groups among NTG and HTPOAG was described in Table 2. Family history of glaucoma was positive in 42% of NTG patients and 32.4% in HTPOAG groups (Table 2).

Ocular examination revealed that 82% of NTG and 79.4% of HTPOAG population were ametropic. Mean cup-to-disc ratio was 0.5 (±0.24) in NTG and 0.46 (±0.22) in HTPOAG group. Cup-to- disc ratio more than 0.5 was observed in about 64% eyes with NTG and 34% with HTPOAG (Table 3). Mean IOP in NTG group was 15.13 mmHg (±3.60) while it was 28mmHg (±6.5) in HTPOAG group. Maximum IOP level in NTG was 21mmHg and in HTPOAG it was found as high as 50 mmHg, minimum IOP level was as low as 8 mmHg

and 10 mmHg in NTG and in HTPOAG respectively (Table 3).

Maximum number of patients with NTG presented with decreaseed vision (42%), while headache was the main complaint (25%) among HTPOAG group (Fig. 1).

DISCUSSION

The type of POAG with normal IOP levels was first observed in 1875 by a great ophthalmologist Von Grafes[12]. Since the introduction of term NTG for such type of low-pressure glaucoma, it was subject of debate among many ophthalmologists who favors the argument that raised IOP is essential for diagnosis of POAG[13].

Table 1:. Demographics of study population

	NTG* Group N= 33	**HTPOAG** Group N= 117**
Age (Years) Mean	56	52.5
SD	±9.21	±8.7
Minimum	37	35
Maximum	75	75
Male	22(66.6)	82(70)
Female	11(33.4)	35(30)
Positive family history of glaucoma	14(42.4)	38(32.4)

Table 2: Comparative analysis of frequency of NTG and HTPOAG in various age groups

Age(Years)	NTG * Group n (%)	HTPOAG ** Group n (%)
≤40	3(9)	20(17)
40.1-50	5(15)	30(25)
50.1-60	15(46)	57(49)
>60	10(30)	10(9)

In our study out of total 150 patients of POAG 33 patients (22%) have IOP less than 21mm Hg and 117(78%) patients had IOP more than 21mm Hg. So the prevalence of NTG was about 22% in our study. According to another study carried out in Japan the incidence of glaucoma was much higher than the rest of the world. It has been reported that prevalence of NTG among Japanese at the time of screening was accounting for two third of cases, i.e. 2% of Japanese total population[14]. According to Tajimi a study carried out in Japan by Iwase et al included randomly selected subjects of more than 40 years[13]. Among these 3021 participants prevalence of POAG is 3.9% out of which 92% of patients had IOP less than 21 mmHg which is about 3.6% of total population examined. This incidence is much higher than our results but this shows that prevalence of NTG is highest in Japan probably because of their tendency for IOP to fall with increasing age[15] instead of lowering down like rest of the world.

Table 3: Occular Examination Of Study Population

	NTG* Group	HTPOAG** Group
Ametropic	27(82) Patients	93(79.4) Patients
Cup-To-Disc Ratio Mean	0.5	0.46
SD	±0.24	±0.22
≤0.5	42(63.6) Eyes	79(33.7)Eyes
>0.5	24(36.3) Eyes	155(66.2) Eyes
Mean IOP	15.13 mmHg	28mmHg
SD	±3.60	±6.5
Minimum	8 mmHg	10 mmHg
Maximum	21 mmHg	50 mmHg

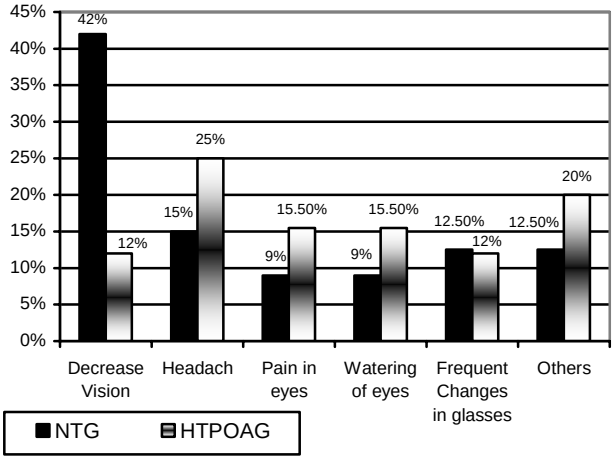

Fig. 1: Frequencies of various presenting occular symtoms in NTG and HTPOAG** Groups
*NTG = Normal-tension glaucoma
**HTPOAG= High tension primary open angle glaucoma

In the west incidence of NTG is not low, accounting for one third to half of POAG cases[16]. Sommer[17] states that 20-25% of glaucomatous neuropathy develops with normal IOP; this incidence is very near to our study.

In Rotterdam Study, which was a population based study carried out in Netherlands, out of 3062 eligible participants of 55 years of age or older, the over all prevalence of POAG was 1.10%. Of these patients about 39% had IOP less than 21 mm Hg[18] with male predominance. The results of this study are comparable to ours, in our study frequency of NTG among individuals between 50 to 60 years is 46% and 30% in patients more than 60 years of age.

The Swedish Dalby study found NTG in 61% of the total POAG cases[19]. In another population based survey carried out in same set up including 760 people 65 to 74 years of age, 18% of individuals of POAG had IOP less than 21 mmHg[20]. In the Barbados eye study[21] including 3427 patients, about half of the newly diagnosed POAG patients had IOP less than 21 mmHg which are about 1.2% of total population. In this study incidence rate of POAG increased from 1.25% at ages 40 to 49 years to 4.2% at ages of 70 years or more, tending to be higher in men than women (2.7% vs 1.9%). This study revealed high risk of low pressure POAG in the population of African origin, especially in older adults. In our present study incidence of both POAG and NTG increased with age as observed in this study, though the incidence of NTG was much higher than our study but in Barbados study participation rate is different though the diagnostic criteria were same.

The incidence of POAG in patients attending glaucoma clinic in a major eye hospital in India[22] is much less than angle closure glaucoma (ACG) (37:63), NTG accounting for 0.62% hospital referral, peak presentation in seventh decade. Mean age for presentation was 60.04 years, with male representing 74% cases. A remarkably low number of NTG cases were noted in this study as compare to rest of the world including ours, may indicate that most of the population were affected by ACG and over all rate of POAG is less. Though there is male predominance like our study but the mean age is bit more than ours indicating delay in diagnosis.

According to another study[23] carried out at Al-Shifa Eye Hospital Islamabad, among total hospital admissions NTG was responsible for 3.0% of total hospital visit. This study did not explain frequency of NTG among POAG cases and demographics of study population, so lacking much valuable knowledge in this respect.

It is believed that NTG occurs more commonly and severely in women, Levene review of the relevant studies found an over all higher female prevalence ranging from 6% to 75%[6]. The Beaver Dam Eye Study[24] found equal prevalence among both genders. There is a preponderance of females in Moorfield normal-tension glaucoma group with a ratio of 2:1 in all age groups[13], while in Low-pressure Glaucoma Treatment Study[25] out of 190 patients with NTG 60% were females. In another study carried out in Moorfield eye hospital by Noureddin et al[26], out of 84 patients with low-tension glaucoma 69% were females. Fontana et al[27], also found the same in their clinical study on 54 patients out of which 34 (63%) patients were females. These studies show that prevalence of NTG is more among females than male glaucoma patients, which is not seen in our study. Although one study indicated that in younger samples, newly diagnosed males with normal-tension glaucoma may show more severe field loss than in similar age females[28]. In our study there are more (22, 64%) males with normal-tension glaucoma than females (11, 26%). This may be because of our socio-economic setup and lack of visits to hospitals by females.

The incidence of normal-tension glaucoma increases with age[13]. In our study mean age for normal-tension glaucoma was 56 years (range 37-75 years).

While Fontana et al[27], reported mean age around 59 years, Lake et al[29], reported 70 years, Plange et al[30], considered 51 years, Noureddin et al[26], found 66 years, Krupin et al[25], found mean age around 65 years.

NTG is considered as a disease of elderly[8], in our study only 9% of the patients were below the age of 40 years, 15% between 41 to 50 years, while maximum incidence of disease 46% were between 51 to 60 years and 30% were more than 60 years of age. In the Beaver Dam Eye Study[24] the prevalence of NTG increases from 0.2% in 43 to 54 years of age group to 1.6% in those over 75 years of age. However, there is significant minority of the patients who are below the age of 50 years. While in Japan, Shiose et al[14], observe that four times as many patients in the over 40 year age group have NTG as having HTG, accounting for 2% of the total Japanese population. This theory was also supported by Beaver Dam Eye Study[24] but its frequency is less than that in Japan. Aung T et al[31] found in their study carried on 108 normal-tension glaucoma patients that 66 patients were more than 60 years of age while only 42 were less than 60 years category. In an Italian study 40 years of age found a prevalence of 0.6%, showing that 33% had NTG out of POAG[10].

Like many other diseases glaucoma runs in families, several cases of both NTG and HTPOAG may occur in the same family[12]. The presence of a positive family history of glaucoma has been reported in 5% to 40%[11]. There appear to be a genetic component related to the development of NTG[31,32]. The molecular mechanism underlying NTG is still unknown. A study carried out to find out the phenotype of NTG patients with and without OPA1 polymorphism suggested that, out of 108 patients with NTG positive family history was present in (35 cases) 32.4%[31]. In another study carried out by Anderson et al[33], out of 136 patients with NTG positive family history of glaucoma was present in 53 cases (39%). In our study family history of glaucoma was positive in 42% of the cases with NTG while in HTPOAG family history was positive in 32.4% of the cases. This may prove that NTG runs in families with history of glaucoma.

Though numerous data presented regarding frequency of POAG throughout the world, thorough investigation regarding NTG is still required. Follow up of these patients is very important to observe the pattern of progression of disease and differentiate NTG from other forms of glaucoma at different stages of disease. Public awareness on normal-tension glaucoma should be increased to address the challenges of disease and similar studies should be conducted in other areas to establish frequency of NTG in various cities of our country.

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