
Research Article**Clinical Profile and subtypes of Glaucoma in Northern India**Sharma S¹, Gupta K^{2*}, Kaur P¹, Kaur I¹, Kulshrestha MR³, Aggarwal A¹¹Regional Institute of Regional Institute of Ophthalmology, Amritsar, Punjab, India²BPS GMC for Women, Khanpur Kalan, Sonapat, Haryana, India³Modern Institute of Medical sciences, Indore, Madhya Pradesh, India***Corresponding author**

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Abstract: The aim of this study was to determine and investigate the clinical profile and subtypes of glaucoma in northern India in a prospective study. The study of clinical profile and subtypes of the various glaucomas also aims to help in the screening and early detection of the disease in the at-risk age groups. The study aims to make observations that reflect the pattern and demographic distribution of glaucoma in North India on which current data is lacking, and provide useful background information and knowhow to plan epidemiological surveys on glaucoma. The study was designed as a prospective study of randomly selected patients with a suspicion of glaucoma attending the Outpatient Department of Ophthalmology, Government Medical College, Amritsar. 250 cases of both sexes and all ages, diagnosed with glaucoma were enrolled in the study. Patients were subjected to a comprehensive eye examination to diagnose and classify glaucoma. Compared to the Western world studies, glaucoma patients in north India seem to present earlier. The PACG subtype is the most commonly encountered glaucoma. CACG is the most commonly encountered subtype of PACG with a male predominance. Glaucoma suspects are the second most prevalent entity with POAG a close third. Male predominance is seen in POAG. Acute ACG has a female dominance. Lens-induced glaucoma and PXE glaucoma are the common secondary glaucomas. NTG and Ocular Hypertension are relatively rare. Population-based epidemiologic studies and surveys are needed to validate or disapprove of the data collected in hospital based studies such as ours.

Keywords: glaucoma, demography, PACG, POAG, CACG, ACG

INTRODUCTION

Glaucoma can be defined as a multifactorial optic neuropathy with a characteristic accelerated degeneration of retinal ganglion cells presenting as classical optic nerve head features and correlating visual field changes, which may or may not be associated with angle abnormality in the presence or absence of any cause for the disease [1-3]. Glaucoma is the second leading cause of blindness worldwide, with preponderance in females, Blacks and Asians [4-7]. Various studies have reported different prevalence depending on the population samples, the ages of the individuals studied, the techniques of examination, and the definitions of glaucoma used. The disease varies in different regions of the world. Of the many types of glaucoma, primary open angle glaucoma is probably the most common type in the Western countries [8-10]. Closed angle glaucoma accounts for lesser than 10% of glaucoma cases in the United States and Europe, but as much as half of glaucoma cases in other nations (particularly Asian countries) [11].

The regional burden of blindness (RBB) is the highest for India (23.5% of global blindness), with at

least 5.8 million blind due to glaucoma. India accounts for a minimum of 12.9% of primary open angle glaucoma blindness and 12.7% of primary angle closure glaucoma blindness in world [12, 13]. An estimated 8 million Indians have glaucoma with a 1:1 ratio of primary open angle glaucoma (POAG) to primary angle closure glaucoma (PACG) [4].

There have been five population based studies, three from the state of Tamil Nadu, one from Andhra Pradesh and one from Bengal [14-18]. There is a wide variation in the prevalence data of the five studies because the diagnostic criterion used by each study was different. Data from North India is currently lacking. The World Health Organization (WHO) recommended its member countries to combat the public health problem of glaucoma through a program approach. To plan the strategies, it is of utmost significance that the prevalence, distribution, the various subtypes in a region and risk factors of glaucoma are identified. Such a study has been a challenge so far due to variation in the definitions and diagnostic criteria for glaucoma [19]. The current study is not a prevalence study but rather a study that aims to investigate the variegated

profiles, presentations and diagnoses of glaucoma. Therefore, the aim of this study was to determine and investigate the clinical profile and subtypes of glaucoma in northern India in a prospective study. The study of clinical profile and subtypes of the various glaucomas also aims to help in the screening and early detection of the disease in the at-risk age groups. Another motive behind such studies is to find out the demographic distribution of the glaucomas. The study aims to make observations that reflect the pattern of glaucoma in North India, and provide useful background information and knowhow to plan epidemiological surveys on glaucoma.

MATERIAL AND METHODS

The study was designed as a prospective study of randomly selected patients with a suspicion of glaucoma attending the Outpatient Department of Ophthalmology, Government Medical College, Amritsar. Clearance was taken from the institutional ethical committee. 250 cases of both sexes and all ages, diagnosed with glaucoma were enrolled in the study. After obtaining an informed consent, each selected case was subjected to a comprehensive eye examination and included in the study. The diagnosis of glaucoma was made on the basis of clinical manifestations using following methods:

- Careful ocular examination including slit lamp bio-microscopy, visual acuity and best corrected visual acuity. Refraction was done where it was indicated.
- Tonometry: Goldmann Applanation tonometry for measuring intraocular pressure. IOP > 21 mm of Hg on two or more separate occasions was considered raised IOP. In glaucoma suspects i.e., those with symptoms suggestive of glaucoma but with intraocular pressure within the statistical 'normal' range of the Gaussian distribution curve, diurnal variation of intraocular pressure measurement was performed. An absolute value of more than 30 mm Hg or a difference of > 8 mm Hg between maximum and minimum values of IOP was taken as significant.
- Direct Ophthalmoscopy and Slit-lamp biomicroscopy with 90 D lens for optic disc changes suggestive of glaucoma.
- Indirect Gonioscopy with a three mirror/four mirror gonioscope for detecting narrow occludable angle. Van Herick's method was used as the screening method for patients requiring gonioscopy, with the cut-off being Peripheral Anterior Chamber Depth \geq 1/4th Corneal Thickness. Any patient with peripheral anterior chamber depth \leq 1/4th corneal thickness was subjected to gonioscopy. The anterior chamber angle was classified using Shaffer's grading. Grade 2 or less was considered occludable, and grade 3 or more as open. Eyes with occludable angles and no

glaucoma were classified as latent Angle closure glaucoma. Prone provocation tests were done in asymptomatic patients with occludable angles.

- Perimetry on the Humphrey Visual Field Analyser (Static Perimeter) for visual field changes suggestive of glaucoma. SITA STANDARD and 24-2 field was the protocol for visual field analysis. Hodapp-Parrish-Anderson's criteria were used as the benchmark to define a glaucomatous visual field defect, in clinical correlation with the optic disc and (Retinal Nerve Fibre Layer) RNFL findings.
- Optical Coherence Tomography was also performed in some suspect patients with normal appearing discs and normal appearing retinal nerve fibre layers (on slit-lamp biomicroscopy) as a new modality for corroborating the retinal nerve fibre thickness.

Patients previously diagnosed with glaucoma, those on anti-glaucoma medication and those with ocular surface disorders were excluded.

Patients were classified under the following subtypes based on the above clinical and investigation parameters:

- Congenital/Developmental glaucoma
- Primary Open Angle Glaucoma (POAG)
- Juvenile glaucoma (JOAG)– when patient presents clinically as primary open angle glaucoma but before 40 years
- Primary Angle Closure Glaucoma (PACG): Primary angle closure was further classified into acute, intermittent and chronic types
- Ocular Hypertension (OHT) – subset of patients with open angle and elevated IOP but with neither optic disc changes nor visual field defects.
- Normal Tension Glaucoma (NTG)
- Glaucoma suspects included (a) ocular hypertensive; (b) latent angle closure glaucoma; (c) subset of patients with open angles, intraocular pressure less than 22 mm of Hg, absent field changes but with optic nerve head changes; and (d) patients with strong family history of glaucoma in absence of optic nerve head changes or high intraocular pressure. POAG suspects, JOAG suspects, ocular hypertensives (OHT) and latent ACG cases were grouped under a common heading as glaucoma suspects.
- Secondary glaucoma: increased intraocular pressure or changes suggestive of glaucomatous optic neuropathy in a patient with any ocular or systemic conditions (steroid use) predisposing to glaucoma.

Criteria for blindness was best corrected visual acuity less than 3/60 in the better eye in patients with bilateral blindness and in the worse eye for unilateral blindness. The data was compiled and statistically analyzed.

OBSERVATIONS & RESULTS

The findings are summarized in the tables 1-4 and figure 1. 51.2% patients were male. The majority of patients presenting in the outpatient department enrolled in our study were from rural areas (60.8%). An observation worth mentioning here was the fact that irrespective of the dwelling of the patient, most patients had the awareness about glaucoma. This could be attributed to better socio-economic conditions, even in rural areas. Male dominance was seen in POAG, Chronic CACG, JOAG, Developmental/Childhood glaucomas and Secondary glaucomas. Female dominance was seen in Acute ACG and glaucoma suspects. Equal gender distribution was observed in Intermittent ACG. Normal tension glaucoma subject was a male. The one Ocular Hypertensive patient was a female.

The highest number of patients were seen in the age groups of 51-60 years and >60 years. Incidence increased with age. Decreased vision, headache and eye ache were the three most common symptoms leading to consultation. Family History in a first degree relative was another significant factor in POAG (14 cases),

PACG (10 cases), Glaucoma Suspects (9 cases) and JOAG (one case).

Primary Angle Closure Glaucoma (34.8%) was the most predominant glaucoma subtype. Further, Chronic Angle Closure (CACG) was the most common PACG subtype. Glaucoma suspects (24%) and Primary Open Angle Glaucoma (22%) were the second and third most common subtypes respectively. Ratio of PACG to POAG was 61:39.

The mean age at presentation (in years) was 56.908±8.934 years for PACG and 60.8±9.105 years for POAG.

In the Glaucoma Suspect sub-group, POAG suspects were the predominant group of patients (48.33 %). Secondary glaucoma constituted 15.6 % of all the cases. The three most common secondary glaucomas seen were: lens-induced glaucoma, pseudoexfoliation glaucoma and uveitic-glaucoma. Childhood/developmental glaucomas formed 2% of the patients in the study. These cases were rare. Primary Congenital glaucoma (2 cases) and Aniridia (2 cases) were the predominant cases. Juvenile Open Angle Glaucoma constituted 1.2% of the two hundred and fifty cases. Mean age at presentation was 28.33±8.50 years. All the cases were males. Normal Tension Glaucoma was a relatively rare subtype with only a single case reported in the study that fitted its profile.

Table-1: Distribution of Patients According To Subtypes And Gender

	MALE	FEMALE
PRIMARY ANGLE CLOSURE GLAUCOMA	42	45
PRIMARY OPEN ANGLE GLAUCOMA	32	23
JUVENILE OPEN ANGLE GLAUCOMA	03	00
DEVELOPMENTAL/CHILDHOOD GLAUCOMA	04	01
NORMAL TENSION GLAUCOMA	01	00
SECONDARY GLAUCOMAS	21	18
GLAUCOMA SUSPECTS (includes Ocular hypertensives, POAG suspects, JOAG suspects, latent ACG etc.)	25	35
TOTAL (n= 250)	128	122

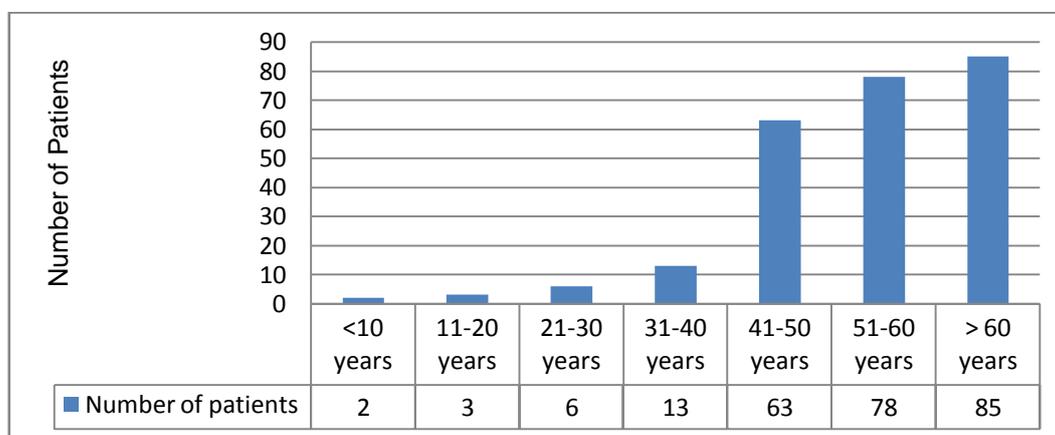


Fig-1: Age distribution of glaucoma in the study

Table-2: Age Distribution of Glaucoma Patients in the Study

AGE (yrs)	POAG	PACG	SECONDARY GLAUCOMA	DEVELOPMENTAL GLAUCOMA	JOAG	GLAUCOMA SUSPECTS	NTG	TOTAL
< 10	-	-	-	2	-	-	-	2
11-20	-	-	-	2	1	-	-	3
21-30	-	-	2	1	1	2	-	6
31-40	-	1	2	-	1	9	-	13
41-50	10	21	9	-	-	23	-	63
51-60	18	28	12	-	-	20	-	78
> 60	27	37	14	-	-	6	1	85

Table-3: Presenting Symptoms of Glaucoma Subtypes (N=250)

Symptom	Primary Angle Closure Glaucoma	Primary Open Angle Glaucoma	Primary Open angle glaucoma suspect	Juvenile Open angle glaucoma suspect	Latent Angle Closure Suspect	Ocular Hypertension	Juvenile Open Angle Glaucoma	Normal Tension Glaucoma
Asymptomatic	32	14	07	02	09	-	01	-
Decreased Vision	39	32	07	03	07	-	-	01
Headache	31	20	19	03	10	01	02	01
Eye ache	37	17	17	05	11	01	02	-
Halos	21	06	03	01	07	-	01	-
Blurring attack	17	05	02	-	-	-	-	-
Frequent change of glasses	04	11	04	-	04	-	01	-
Redness	27	04	04	-	04	-	-	-
Scotoma	-	04	-	-	-	-	-	-

Table-4: Relevant risk factors associated history in patients

Relevant Factors in Patients	Primary Angle Closure Glaucoma	Primary Open Angle Glaucoma	Primary Open Angle Glaucoma suspect	Juvenile Open Angle Glaucoma suspect	Latent Angle Closure suspect	Ocular Hypertension	Juvenile Open Angle Glaucoma	Normal Tension Glaucoma
Family History	10	14	4	2	3	-	1	-
Hypertension	8	15	3	-	2	-	-	-
Diabetes Mellitus	7	10	3	-	4	-	-	-

DISCUSSION

Reduced vision, headache and ocular ache or eye ache were the three most prevalent symptoms warranting an ophthalmological consultation. Of the 58 cases of chronic angle closure glaucoma, 35 patients (60.344%) presented without a past history of an acute or sub-acute attack. A shallow anterior chamber depth by oblique flashlight illumination and van Herick's method was noted in 58 patients (66.667%), the others had an anterior chamber depth deemed normal. A family history of glaucoma in the first degree relatives was seen in 14 cases (25.45%) of Primary Open Angle Glaucoma, 10 cases out of 87 (11.49%) of Primary Angle Closure Glaucoma, 4 cases out of 29 (13.79%) in Primary Open Angle Glaucoma suspect, 3 cases out of 22 (13.63%) in Latent Angle Closure suspect, 2 cases out of 8 (25%) in Juvenile Open Angle Glaucoma

suspect and one case amongst the diagnosed Juvenile Open Angle Glaucomas.

In separate studies conducted by Wilson and Cronemberger, glaucoma was observed to be a disease with few symptoms in the initial stages, with late presentation being common. They also noted that when visual field loss threatens central vision in glaucoma, it is an important risk factor for blindness [20, 21]. In a study conducted by Gogate, painless diminution of vision was the most common symptom in the patients (82.5%). Most patients presented with more than one symptom. Glaucoma was an incidental finding in the majority of cases in the study. This proves the importance of comprehensive eye examination in every patient who attends an eye clinic [22]. Das observed similar presenting symptomatology of patients referred to the glaucoma clinic. Decreased vision, eye ache and

headache were the three major symptoms. Family history in first degree relatives was reported in 21.80% cases of Primary Open Angle Glaucoma, 2.70% cases of Primary Angle Closure Glaucoma, 29.27% cases of Juvenile Open Angle Glaucoma, 12.07% cases of Ocular Hypertension and 10.71% cases of Primary Congenital Glaucoma [23]. In a hospital based study by Rashid *et al.*, 96.5% of patients presented with decreased visual acuity which was the commonest presentation. 63% patients presented with pain ranging from severe in angle closure glaucoma to moderate/mild in other glaucomas. 30% patients complained of headache. Results of our study are comparable [24].

A study conducted by Congdon reported that in Caucasian races, Primary Open Angle Glaucoma accounted for 75-95% of the primary glaucomas, the disease presents later and is less severe at presentation [25]. Quigley also corroborated that Primary Open Angle Glaucoma was the most common form of glaucoma in many countries and accounted for 60-70% of the cases in the United States [26]. Scharioth noted that closed angle glaucoma accounted for less than 10% of glaucoma cases in the United States and Europe, but as much as half of glaucoma cases in other nations (particularly Asian countries) [11]. In Africa, the predominant form of glaucoma was Primary Open Angle Glaucoma. Glaucoma has been shown to affect a higher proportion of people of African ancestry, has a younger age of onset and results in greater visual morbidity as compared to most other populations [14]. A study conducted in North India by Das showed the Primary Angle Closure Glaucoma (PACG) sub-group to be the most common glaucoma subtype (36.62%). The Primary Open Angle Glaucoma (POAG) to PACG ratio was 37:63 [23]. In our study, Primary Angle Closure glaucoma (34.80%) was the most common subtype of the disease, followed by the entity of Glaucoma Suspects (24 %). Primary Open Angle Glaucoma was the third most common subtype (22 %) in contrast to the studies in the western world, where it is the most widespread subtype of glaucoma. The POAG to PACG ratio was 39:61 in our study. In fact, most studies done in India depict the PACG group to constitute the largest subtype. These results therefore seem to match with our study.

In a study conducted by Martin, the average age of presentation of POAG in Caucasians was 69.1 years [27]. In the present study, the mean age in years at presentation was 56.908±8.934 years for PACG and the mean age at presentation of Primary Open Angle Glaucoma (POAG) was 60.8±9.105 years. This could indicate that glaucoma probably occurs almost a decade earlier in Indians as compared to Caucasians. The decreased life expectancy of an average Indian could also reflect such results. In a study in north India, Das observed a mean age of presentation for POAG (60.54

years) and a mean age of presentation for PACG (55.13 years) similar to the present study [23].

Male to female ratio was 1.049:1. Rural to urban patient ratio in the present study was 1.55:1. Gupta reported a significantly high incidence of angle closure glaucoma (ACG) in India, which formed almost half of all adult primary glaucomas seen [28, 29].

Sihota reported that angle closure glaucoma constituted 45.9% of all primary adult glaucomas in a study. Chronic Angle Closure Glaucoma (CACG) was the most common PACG subtype (44%). 31.2 % of the cases were Sub-acute/Intermittent and acute PACG accounted for 24.8% of the cases. Angle closure glaucoma occurred maximally in the sixth decade (50-59 age groups) and females constituted 51.4% of those affected [30]. Das similarly reported CACG to be the most prevalent subtype of PACG. The majority of the cases of CACG were male and asymptomatic. Females showed predominance in the acute and intermittent subtypes of ACG.²³ Results of our study are comparable.

Various studies have put the incidence of POAG between 27%, 29%, 37%, and 41% [23, 15, 31]. POAG (55 patients) was the third largest sub-category of patients in our study (22%). The peak age distribution was in the > 60 years age group (49.09% of all cases). The incidence increased with age. In all the prevalence studies from South India and West Bengal, namely the Andhra Pradesh Eye Diseases Study (APEDS), the Aravind Comprehensive Eye Survey (ACES), the Chennai Glaucoma Study (CGS), the Vellore Eye Study (VES) and the West Bengal Glaucoma Study (WBGs), the distribution of POAG increased with age. Increasing age and higher IOP was a consistent risk factor for glaucoma in all the prevalence studies [15, 18, 35]. Studies by Leske and Mitchell noted variable gender dominance for POAG. Das found a male predominance for POAG (male to female ratio of 1.35:1) [32-34]. In the present study, the male to female ratio was 1.39:1.

Glaucoma Suspects formed the second most frequent number of patients in our study (60 cases, 24%). POAG suspects were the most common subtype of Glaucoma suspects (48.33%) with a male dominance (male to female ratio 1.42:1). Latent ACG (36.67%) was the second most common subtype and had a female dominance with double the number of cases in comparison to the male gender. Juvenile Open Angle Glaucoma (JOAG) suspects (13.33%) had a male dominance. The lone ocular hypertensive patient was a female. Das also reported Glaucoma suspects as being the second most predominant category of glaucomas (29.94%) with POAG suspects forming the major subtype. The JOAG suspects however, formed the second largest group of the Glaucoma Suspects. This was in contrast to our results, probably due to the

smaller size of the study sample [23]. In a study of the PXE syndrome in south India by Aravind *et al.* the prevalence of pseudoexfoliation glaucoma was reported as 13% [36]. Lindblom and Thorburn, observed an incidence as high as 50% of glaucoma patients in Sweden [37]. Therefore pseudoexfoliation glaucoma (PXE glaucoma) seems to have a regional and genetic influence on its prevalence and distribution.

The population-based Aravind comprehensive eye survey from south India reported a 0.7% incidence of secondary glaucomas where the total prevalence of glaucoma was 2.6%, i.e. a third of all glaucoma cases [38]. A study on secondary glaucomas by Krishnadas in a large tertiary eye care centre in south India, lens induced glaucoma was the most common entity and it formed 2.50% of the total glaucoma in the year [39]. In a retrospective 10-year study on secondary glaucoma cases by Agarwal, aphakic glaucoma and glaucoma secondary to senile cataract accounted for nearly 50 percent of all causes of secondary glaucoma [40]. In the present study, secondary glaucomas formed 15.6 % of the total number of diagnoses. The three most common secondary glaucomas were lens-induced (23.07%), pseudoexfoliation (17.94%) and uveitic glaucomas (15.38%). The ethnic and racial diversity might be the reason for marked differences in the frequency of various glaucoma subtypes, even amongst Asians. This could explain the variation in incidence of pseudoexfoliation glaucoma.

Developmental/Childhood glaucomas constituted 2% (5 cases) with primary congenital glaucoma (PCG) being the predominant. It is difficult to form an opinion on the incidence of congenital glaucomas on the basis of such a low number of cases. Aniridia and Sturge Weber syndrome were the other causes reported. The British Infantile and Childhood Glaucoma (BIG) Eye Study reported primary congenital glaucoma to be the major subtype of congenital glaucoma (45.45%). South Asian children were at major risk of PCG. This finding reflected a higher incidence of monogenic disease in consanguineous families and highlighted the importance of screening siblings and offering genetic counselling in these cases. Parental concern was the main reason leading to the diagnosis of PCG [41]. In a study by Genicek the incidence of PCG increased when "founder effect" or a high rate of consanguinity were found in a population. The "founder effect" is a gene mutation observed in high frequency in a specific population due to the presence of that gene mutation in a single ancestor or small number of ancestors. The incidence was 1 in 1250 in the Slovakian Roms (Gypsies) [42], 1 in 2500 in the Middle East [43], and 1 in 3300 in Andhra Pradesh, India [44]. In Andhra Pradesh, the disease accounts for 4.2% of all childhood blindness [44].

In our study, Juvenile Open Angle Glaucoma formed 1.2% of all cases with all three cases being

males and a mean age at presentation of 28.33±8.50 years. Das described a male predominance and a mean age at presentation of 29.16 [23]. Komolafe studied JOAG in Nigeria and the mean age of presentation was 25.1 ± SD 6.0 years [45].

Ocular hypertension and Normal Tension glaucoma both contributed one patient each to the study (0.4%). 0.5 to 1% of cases of ocular hypertension per year develop visual field loss as detected by kinetic perimetry. The findings of ocular hypertension are found in upto 4-10% of cases above the age of 40 years. Thinner corneas, raised intraocular pressure, increasing age and female gender are the putative risk factors [1]. Our patient was a 38 year old female. Normal tension glaucoma (NTG) is a rare diagnosis of exclusion in which the optic nerve head is proposed to be susceptible to statistically 'normal' intraocular pressures. The Tajima Study, in Japan, described a greater prevalence of glaucoma in Japan as compared to other Asian and Caucasian societies, with 3.9% of those over 40 years having primary open angle glaucoma, and the vast majority had intraocular pressures below 21 mm of Hg [46]. In India, Das reported NTG to be relatively rare [23].

CONCLUSIONS

Thus it is concluded that compared to the Western world studies, glaucoma patients in north India seem to present earlier. The PACG subtype is the most commonly encountered glaucoma. CACG is the most commonly encountered subtype of PACG with a male predominance. Glaucoma suspects are the second most prevalent entity with POAG a close third. Male predominance is seen in POAG. Acute ACG has a female dominance. Lens-induced glaucoma and PXE glaucoma are the common secondary glaucomas. NTG and Ocular Hypertension are relatively rare. Population-based epidemiologic studies and surveys are needed to validate or disapprove of the data collected in hospital based studies such as ours.

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