

Intraocular pressure and gonioscopic findings in primary angle-closure disease in India—a big data study

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Abstract

• **AIM:** To describe the gonioscopic profile and intraocular pressure (IOP) in primary angle-closure (PAC) disease in patients presenting to a tertiary eye care network in India.

• **METHODS:** A cross-sectional hospital-based study that included 31 484 new patients presenting between 2011 and 2021. Patients with a clinical diagnosis of PAC/suspect/glaucoma were included. The data was collected from an electronic medical record system.

• **RESULTS:** PAC glaucoma (PACG) (47.55%) was the most common diagnosis followed by PAC (39.49%) and PAC suspect (PACS; 12.96%). Female preponderance (54.6%) was noted with higher mean age at presentation among males ($P < 0.0001$). PACS and PAC showed the highest prevalence in 6th decade but PACG was higher at 7th decade. The probability of angle opening was 95.93%, 90.32% and 63.36% in PACS, PAC and PACG eyes respectively post peripheral iridotomy (PI). Plateau iris syndrome (PIS) was noted in 252 eyes and all showed post dilated rise of IOP. A post dilated IOP rise was also noted with 8.86%, 33.95% and 57.19% eyes with PACS, PAC and PACG respectively with IOP rise between 6-8 mm Hg across the disease spectrum.

• **CONCLUSION:** The superior quadrant is the narrowest angle and difficult to open with indentation and post PI. The probability of angle opening is less in PIS especially the complete variety along with post dilated IOP rise. The post dilated IOP rise in angle closure eyes warrants a careful dilatation, especially with PIS.

• **KEYWORDS:** angle closure disease; peripheral iridectomy; gonioscopy; post dilated intraocular pressure rise; plateau iris syndrome

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INTRODUCTION

Primary angle-closure glaucoma (PACG) constitutes asymptomatic to intermittently symptomatic and chronic stage with increased propensity of blindness. Asia accounts for the highest number of cases of PACG cases worldwide^[1]. The current estimate is 17.14 million people above 40 years of age worldwide, of which 12.3 million are from Asia. This is estimated to increase to 18.47 million with PACG by 2040 in Asia alone^[1-2]. Accepted classification for primary angle closure is primary acute-closure suspect (PACS), primary angle closure (PAC) and PACG^[3]. Primary angle-closure disease (PACD) includes PAC and PACG. The risk factors for angle-closure disease includes female gender, increasing age, shallow anterior chamber, hyperopic refractive error and genetic factors^[1]. Pupillary and non-pupillary block mechanisms have been described for angle closure. The diagnosis of PACD is mainly clinical with assessment of intraocular pressure (IOP), gonioscopy and optic disc evaluation. The risk of visual disability and blindness is higher in PACG compared to primary open angle glaucoma (POAG) owing to increased severity of disease in PACG^[4]. Andhra Pradesh Eye Disease study (APEDS) showed the blindness in PACG was 20% versus 11.1% (rural) and 2.7% (urban) in POAG subjects^[5]. Vellore eye survey (VES) was the first population based study in India that reported significant proportion of glaucoma in our country to be PACG^[6]. Subsequently, APEDS^[7] and Chennai Glaucoma study (CGS)^[8-9] showed similar results. In angle-closure disease, careful gonioscopy, IOP and disc evaluation helps to identify the stage of the disease. To evaluate occludability of the angle by indentation gonioscopy is critical to diagnosing angle closure and plateau iris syndrome (PIS).

Patients with narrow angles on gonioscopy is an important risk factor for IOP spike post dilatation irrespective of presence or absence of acute angle closure^[10]. Cases with PIS show tendency towards post dilated IOP rise in most of the cases due to closure of posterior trabecular meshwork with IOP rise (complete variety) while some do not show rise in IOP for some time (incomplete variety)^[11].

According to study by Harris^[12] about 1%-2% of normal population show post dilated IOP rise up to 6 mm Hg after treatment with cyclopentolate. It is seen that 32% of POAG patients showed rise in IOP after treatment with 1% tropicamide and 2.5% phenylephrine^[13]. Awareness of post dilated IOP spike is important in patients with advanced disc damage and visual field loss who cannot tolerate high IOP rises. Siam *et al*^[14] have noted that the amount of IOP spike during pharmacological dilatation is an indicator of glaucoma progression. For every 1 mm Hg rise in IOP the likelihood of glaucoma progression increased by 24% ($P=0.008$). Most of the studies in past have looked into IOP fluctuations in undilated state and seen spike in IOP more in PACG and POAG however this was not looked at in eyes with PACS and PAC^[1,15-17].

In this particular study, we are analyzing the gonioscopic profile of all patients with angle-closure disease, their behavior post laser iridotomy and post dilated IOP spike in this cohort.

SUBJECTS AND METHODS

Ethical Approval A standard consent form for electronic data privacy was taken from patients or their attenders at the time of registration. The study adhered to Declaration of Helsinki and approved by local institutional ethical committee board.

This is a cross sectional observational hospital-based study of all new patients presenting from 2011 till date across a network of tertiary eye care covering 4 states of south India. Every patient underwent comprehensive eye examination and data entered to digital medical record system called eyeSmart EMR by uniformly trained optometrists and ophthalmologists in a standardized template^[18].

Cases All patients with diagnosis of PAC were considered in this study. The definition of primary angle closure is by International Society of Geographic and Epidemiologic Ophthalmology (ISGEO) classification^[3]. 1) PACS: Eyes in which appositional angle closure is noted between peripheral iris and posterior trabecular meshwork opening on indentation with no elevated IOP. 2) PAC: Eyes with occludable angle along with any of the features like peripheral anterior synechiae, blotchy pigments on posterior trabecular meshwork, lens opacities like glaucoma flecken, iris whorling, raised IOP but no glaucomatous optic nerve damage. 3) PACG: Eyes with characteristics of PAC and evident glaucomatous optic nerve head and visual field changes. We have considered 180 degrees of angle closure as significant.

Each of these patients were worked up by experienced and trained optometrist in the glaucoma service. Clinical diagnosis of each of these patients were confirmed by glaucoma fellowship trained ophthalmologists. All patients who had peripheral iridotomy (PI) earlier were dilated after careful dark room static gonioscopy after IOP measurement by Goldmann applanation tonometry. Minimum illumination of slit lamp and care was taken to not allow light to fall on pupil border while examination. Gonioscopy was performed using Susmann 4 mirror Gonioscope (Volk Optical Inc., Mentor, OH, USA). Posterior most structure that was visible in all four quadrants before and after indentation was documented. Any presence of blotchy pigments, synechiae was documented in gonioscopic record. Post dilated IOP was measured for all dilated patients. Any IOP>6 mm Hg was considered significant post dilated IOP spike compared to pre dilatation IOP approximately one hour post dilatation. Fundus examination was done for all the patients and visual field assessment was done when appropriate^[12,14].

The eyeSmart EMR data was screened for patients with final diagnoses of PACS/PAC/PACG. We had a total of 59 278 eyes of 31 484 patients with these diagnoses.

Statistical Analysis Baseline demographic details of the subjects were expressed as mean±standard deviation (SD) and median with interquartile range wherever applicable. Significant differences between groups were analyzed using Chi-square test using Stata software (Stata Corp.2019. College station, TX: Statacorp LP, USA).

RESULTS

Of the total of 59 278 eyes, PACS was diagnosed in 7414 (12.5%) eyes, PAC in 23 422 (39.5%) eyes and PACG in 28 185 (47.55%) eyes.

Age The mean age at presentation was 59.13±10.72y, while the median age was 60y (IQR 52-66). We noted that most of PACS (34.73%) and PAC (32.94%) patients presented to clinic at 6th decade and PACG (33.24%) patients at 7th decade. The mean age of presentation was higher among male across the disease spectra (males 59.9±10.9y, females 57.58±10.4y, $P<0.0001$). Table 1 shows the age distribution among our cohort.

Gender Female subjects predominated in all spectra of disease in our cohort (54.6%). We had 2667 (65.32%) females and 1416 (34.68%) male patients under PACS category, 7174 (58.06%) females and 5183 (41.94%) male patients under PAC category and 7340 (48.79%) females and 7704 (51.21%) male patients under PACG group. Table 2 showed the gender distribution among our cohort in different subclass.

We noticed that majority of our cohort presented from higher socio-economic strata (85.62%) overall. About 17.69% of PACG patients belonged to low socio-economic class. Table 3 shows the socio-economic distribution among our cohort.

Table 1 Age distribution of subjects mean±SD

Subtype of glaucoma	Males (y)	Females (y)	P
PACS	57±10.2	55.3±9.9	<0.0001
PAC	59±10.6	56.7±10	<0.0001
PACG	61±11	59.3±10.7	<0.0001

PACS: Primary angle-closure suspect; PAC: Primary angle closure; PACG: Primary angle-closure glaucoma; SD: Standard deviation.

Table 2 Gender distribution of subjects n (%)

Subtype of glaucoma	Males	Females	P
PACS	1416 (34.68)	2667 (65.32)	0.00001
PAC	5183 (41.94)	7174 (41.94)	0.00001
PACG	7704 (51.21)	7340 (48.79)	0.015

PACS: Primary angle-closure suspect; PAC: Primary angle closure; PACG: Primary angle-closure glaucoma.

Geographic Distribution We noticed that PACS was diagnosed in urban population (1908, 46.73%) more compared to rural and metropolitan population. PACG was more common in rural population (5504, 36.54%). PAC was almost equally seen in urban and rural population [Urban (5170, 41.84%) and rural (5111, 41.36%)]. Table 4 showed the geographic distribution among our cohort.

Gonioscopy Findings Gonioscopic examination of these patients revealed that 1269 (2.14%) eyes had 1 quadrant, 20 984 eyes (35.40%) had 2 quadrants and 1842 eyes (3.11%) had 3 quadrants and 32 300 (54.49%) eyes with all 4 quadrants closed in primary position without indentation. Totally 2883 eyes (4.86%) had no documentation of gonioscopy. We noted to have 7414 (12.5%) eyes with PACS, 23 422 eyes (39.5%) with diagnoses of PAC, 28 185 (47.55%) eyes with PACG diagnosed at first visit to our centre.

Overall, we noted that inferior (48.63%) quadrant was closed followed by nasal (48.30%), superior (46.90%) and temporal (45.60%) quadrant. On indentation we found opening on angles more in inferior (69.97%) quadrant followed by temporal (61.10%), nasal (60.50%) and superior (58.44%) quadrant. Similar trend was noted in PAC. The PACG eyes behaved almost similarly with inferior followed by temporal, nasal and superior quadrant.

We also analyzed the probability of angles opening in various subtypes of angle closure. We found 95.93% of angles opened in PACS followed by PAC (90.32%) and 63.36% in PACG eyes. Totally 27 162 (45.82%) eyes had YAG PI elsewhere and 19302 (35.56%) at our centre. Totally 12 814 eyes (21.62%) of eyes did not undergo YAG PI. Of those eyes that had PI at first visit, we noticed an average angle opening of 73.5% in PAC and 22.5% in PACG category. Most of these eyes still has occludability and Inferior>temporal>nasal>superior quadrants opened up in most of these eyes especially with indentation.

Table 3 Socio-economic distribution of subjects n (%)

Subtype of glaucoma	Paying	Nonpaying
PACS	3540 (86.70)	543 (13.30)
PAC	11035 (89.30)	1322 (10.70)
PACG	12383 (82.31)	2661 (17.69)

PACS: Primary angle-closure suspect; PAC: Primary angle closure; PACG: Primary angle-closure glaucoma.

Table 4 Geo distribution of subjects n (%)

Subtype of glaucoma	Urban	Rural	Metropolitan
PACS	1908 (46.73)	1241 (30.39)	934 (22.88)
PAC	5170 (41.84)	5111 (41.36)	2076 (16.80)
PACG	7322 (48.67)	5504 (36.59)	2218 (14.74)

PACS: Primary angle-closure suspect, PAC: Primary angle closure; PACG: Primary angle-closure glaucoma.

Table 5 The IOP profile of all patients examined and documented in the eyeSmart EMR at their first visit in the hospital

IOP measured at first visit	n (%)
PACS	7414 (12.5)
1-9 mm Hg	105 (1.37)
10-21 mm Hg	7189 (96.96)
NA	120 (1.61)
PAC	23422 (39.5)
1-9 mm Hg	294 (1.26)
10-21 mm Hg	19963 (85.23)
22-30 mm Hg	2717 (11.6)
>30 mm Hg	448 (1.91)
NA	257 (1.10)
PACG	28185 (47.55)
1-9 mm Hg	593 (2.10)
10-21 mm Hg	17847 (63.32)
22-30 mm Hg	4921 (17.46)
>30 mm Hg	4503 (15.98)
NA	321 (1.14)
Total eyes	59278 (100.00)

PACS: Primary angle-closure suspect; PAC: Primary angle closure; PACG: Primary angle-closure glaucoma; IOP: Intraocular pressure; NA: Data not available.

We noticed that 96.96%, 85.23%, and 63.32% of patients had their IOP profile between 10-21 mm Hg in PACS, PAC and PACG category respectively. About 3.3% eyes initially diagnosed as PACS with their IOP between 22-30 mm Hg were classified under PAC and underwent appropriate treatment. We noted that the IOP profile was higher than 21 mm Hg in approximately 33.5% patients in PACG group who needed urgent treatment with PI and antiglaucoma medications. Table 5 showed the IOP profile of patients examined at their first visit.

We noticed that 207 (2.69%) eyes under PACS, 793 (3.39%) eyes under PAC and 1336 (4.74%) eyes under PACG had

Table 6 Distribution of post dilated IOP rise in our subjects

Subtype of glaucoma	6 mm Hg IOP rise	7 mm Hg IOP rise	8 mm Hg IOP rise	Total number of subjects	<i>n</i> (%)
PACS	90 (43.48)	32 (15.46)	40 (19.32)	207	(8.86)
PAC	279 (35.18)	129 (16.27)	121 (15.26)	793	(33.95)
PACG	388 (29.04)	179 (13.40)	194 (14.52)	1336	(57.19)

PACS: Primary angle-closure suspect; PAC: Primary angle closure; PACG: Primary angle-closure glaucoma; IOP: Intraocular pressure.

post dilated IOP rise from their predilated IOP. Those PACS eyes were reclassified under PAC and managed accordingly. We also noted that maximum percentage of patients with IOP rise was between 6-8 mm Hg in each of these categories. Totally 43.48% (90/207) eyes, 35% (279/793) eyes, and 29% (388/1336) eyes in PACS, PAC, and PACG category had post dilated IOP rise that was significant. Table 6 showed the distribution of post dilated IOP rise among the groups.

PIS was diagnosed in 252 of the 59 278 eyes of 31 484 patients (0.004%). There were 96 females (51.89%) and 89 male patients (48.11%) who presented to us. Their average age at presentation was 57.30±12.35y. All of the 252 eyes had post dilated IOP rise of >6 mm Hg. We noted 17 eyes (6.75%) with PACS, 110 eyes (43.65%) with PAC and 125 eyes (49.60%) with PACG diagnoses among these PIS patients. These PACS eyes were later recategorized into PAC group at their subsequent visit. Four quadrants were open in 115 eyes (48.32%) and 2 quadrants were open in 109 eyes (45.80%) post PI in such eyes with indentation. Cataract was present in 107 eyes (42.46%), clear lens was noted in 60 eyes (23.81%) and pseudophakic in 6 eyes (2.38%).

DISCUSSION

Gonioscopy is an essential examination tool in the armamentarium of comprehensive eye examination to diagnose and treat glaucoma cases at the earliest. The current ISGEO^[3] classification describes the angle-closure disease according to gonioscopic damage defined by extent of irido-trabecular contact and optic nerve and visual field damage. It is also noted that gonioscopic damage occurs ahead of optic nerve head damage and correlates with it most of the time. Hence PACD encompasses a wide spectrum of cases at different stages of disease involvement.

Our study analyses the gonioscopic features of large set of population from a big data set driven by electronic medical record system built inhouse to document findings. We found 47.55% of PACG eyes in our study.

This highlights the burden of PACG, particularly in regions with a high prevalence of angle closure^[4,19-20]. We also noted the mean age at presentation was slightly higher in males compared to females, consistent with that in literature^[9,20]. Early presentation among female cohort could be due to inherent anatomical risk factor for disease predisposition. We noted the female preponderance prevailed in our cohort

across the disease spectra of PACS, PAC and PACG in ratio of 54.6:45.4. PACS and PAC were noted to increase in trend from 4th decade onwards in our cohort. We also noted that female preponderance among those diagnosed as PIS in our cohort. These gender specific susceptibility to disease along with demographic patterns can help us in targeted screening and intervention strategies. The age distribution of PACD in our study, with peaks in sixth and seventh decades for PACS/PAC and PACG, respectively underscores the importance of age as important risk factor for development of PACD and emphasizes the need for increased awareness and screening for older individuals.

Approximately 45.82% of patients who presented to our referral centre with prior diagnosis of angle closure disease had PI done elsewhere. On the contrary, a study from north India showed they had 8.34% of patients who had iridectomy prior to referral^[20]. On examination we found that after indentation, inferior>nasal>temporal>superior quadrants opened up with an average angle opening by 90.32% post PI in PAC. In PACG, inferior>temporal>nasal>superior quadrants opened up post PI with an average angle opening of 63.36%. Hence, we noticed that as disease progresses it is evident that angle opening decreases and correlates with disc damage. This highlights the importance of targeted intervention such as PI to address angle closure. Our study also identified the challenges in achieving angle opening post-PI, particularly in PACG cases, which underscores the need of close monitoring and alternative management strategies in these cases.

We also analyzed those 207 (8.86%) eyes under PACS, 793 (33.95%) eyes under PAC and 1336 (57.19%) eyes under PACG had post dilated IOP rise mostly fluctuating between 6 mm Hg to 8 mm Hg. Majority in them had IOP rise with a difference of 6 mm Hg in all three groups: PACS (43.48%), PAC (35.18%) and PACG (29.04%). We noted that overall PAC and PACG eyes showed increased tendency for post-dilated IOP rise (Table 6). Interestingly we found that PACS eyes showing greater tendency of post dilated IOP rise. This can be explained possibly due to PIS or pigment release following dilation which could be the cause for IOP spike. Post dilated IOP spikes are well known facts in PIS, pigment dispersion syndrome and pseudoexfoliation eyes but less known in PACS eyes that are known to have occludable angles without other significant damage^[11,21].

PIS is most common non-pupil block angle closure glaucoma that presents with gonioscopically closed/occludable angles despite a patent PI^[22-23]. Seen mostly in females <50y similar to that in our cohort^[24]. Majority of PIS patients in our study population were either PAC or PACG. We also noticed few PACS (6.75%) presenting as PIS post PI compared to a cross sectional study that showed prevalence of PIS in PACS eyes using ultrasound biomicroscopy in 54/167 (32.3%) eyes after PI mostly in superior and inferior quadrant^[25]. A small cohort of PACS post PI showed significant post dilated IOP rise in our study. We assume that these eyes could be having narrow angles with plateau iris configuration before PI and these eyes were relabelled as PAC in later visits. There are no definitive criteria to diagnose PIS on gonioscopy as it is very subjective and it may underestimate the condition. It warrants the use of ultrasound biomicroscopy (UBM) in both light and dark condition along with pre and post PI which can clearly delineate the anatomy and mechanism of PIS. However, even with UBM, the diagnostic criteria are not standardized, it is expensive and not widely available. A combination of clinical acumen and diagnostic aid might help in diagnosis of PIS. Our study thereby shows PIS in a small but notable proportion of patients which highlights the importance of thorough evaluation and consideration of adjunctive diagnostic modalities to help us understand the disease characteristics when in doubt and in cases where a targeted approach helps to achieve optimized outcomes in such challenging cases.

Strengths and Limitations We have analyzed the gonioscopy of all patients at their first visit only here in our cross-sectional study. To the best of our knowledge, we were reporting the gonioscopic features of angle closure patients quadrant wise before and after indentation, probability of angle opening following PI in suitable eyes for the first time in a large data set from a hospital setting similar to a study that showed gonioscopic features in chronic angle-closure disease^[26]. We have not presented the correlation between gonioscopy, optic nerve head and visual field changes which is beyond the scope of this paper. The course following PI and risk of progression in those eyes with post dilated IOP rise need to be looked into which is beyond the scope of this paper. Also we have not presented the anterior chamber depth (ACD) and lens thickness for all patients as we do not follow doing biometry routinely for all patients unless advised with cataract surgery at our centre. UBM examination in these cases would have given clearly defined the anatomy better.

In conclusion, our study sheds light on gonioscopic features in a large cohort of PACD patients in a tertiary eye care network in India. We found PACG was most frequently diagnosed subtype and observed a higher mean age at presentation among males and consistent female preponderance across all spectra

of PACD. Furthermore, we found that the superior quadrant is the narrowest angle and difficult to open with indentation and post PI. The probability of angle opening post PI reduces as disease progresses to PACG. Importantly, we found a subset of patients, particularly in PACS category who exhibited a significant post dilated IOP rise. Those patients diagnosed as PACS in their first visit, but had post dilated IOP rise and gonioscopic picture showed plateau iris configuration were labelled as PAC in their subsequent visits. Patients with narrow angle on gonioscopy and raised IOP recurrently especially on dilatation need to be suspected for PIS. Our study highlighted the importance of PIS in a small but notable proportion of patients diagnosed as PAC/PACG. This highlights the need more frequent follow up, must be individually evaluated with repeated gonioscopy to understand sequential angle narrowing and appropriate case based targeted treatment supported by adjunctive diagnostic modalities like UBM. Future research aimed at elucidating the impact of IOP post dilatation and the risk of progression of glaucoma both structurally and functionally help us understand the dilatation protocols for any subtype of glaucoma and thereby efficiently manage this sight threatening condition.

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