

Angle closure glaucoma in rural and urban populations in eastern India—The Hooghly River Glaucoma Study

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Purpose: To estimate the prevalence, features, and associations of primary angle closure disease (PACD) in rural and urban populations from West Bengal in eastern India. **Methods:** This was a population-based cross-sectional study with two arms, rural and urban. The rural study area consisted of 28 contiguous villages from 13 gram panchayats in Balagarh Police Station, with rural base hospital at Dhobapara, Balagarh Police Station, in the village Kuliapara of Hooghly district. A tertiary eye hospital in central Kolkata was the urban study center. Individuals residing in the study area aged 40 years and above were included in this study using multistage random cluster sampling. All subjects underwent a detailed ophthalmic examination at our base hospitals including applanation tonometry, ultrasound pachymetry, gonioscopy, and frequency doubling technology perimetry. Data collected were analyzed using SPSS 13. Multiple logistic regressions were used to analyze risk factors for PACD. **Results:** A total of 7,408 and 7,248 subjects aged 40 years or older were enumerated from Hooghly district and Kolkata city, respectively. PACD was detected in 1.9% subjects in rural arm and 1.54% subjects in the urban arm ($P < 0.001$). In rural arm, 0.3% had PACS, 0.56% had PAC, and 1.03% had PACG. In urban arm, 0.22% had PACS, 0.35% had PAC, and 0.97% had PACG. **Conclusion:** The study concludes that higher age, higher CCT, and shorter axial length/presence of hyperopia are important independent predictors of ACD. ACD is more common in eastern India than previous estimates.

Key words: Frequency doubling perimetry, hyperopia, primary angle closure disease, primary angle closure glaucoma

Glaucoma is the leading cause of global irreversible blindness^[1] and an important public health issue.^[2] Population-based studies are important for assessment of disease burden, health-care policy planning, and appropriate resource allocation.^[2] The Hooghly river glaucoma study (HRGS) is a population-based cross-sectional study from rural and urban populations in eastern India, which spanned from April 2011 to January 2014.^[1] In the HRGS, primary angle closure disease (PACD), and primary angle closure glaucoma (PACG) were defined as per ISGEO guidelines.^[3] There is a wide variation in the reported prevalence of angle closure glaucoma (ACG) within India. The prevalence of PACG in southern India ranges from 0.5% to 4.3%^[4] whereas the reported prevalence of PACG in eastern India was only 0.23%.^[5]

In the present paper, we report the prevalence, features, and associations of angle closure disease (ACD) in rural and urban populations from eastern India.

Methods

The methodology of HRGS has been discussed in details elsewhere.^[1] This cross-sectional study was approved by the Institutional Ethics Committee and adheres to the tenets of the Declaration of Helsinki. Kolkata city, our urban study area, is divided into 15 boroughs and 141 wards.^[6-8] Subjects

were enumerated from eight randomly selected divisions from each of these 15 boroughs. The rural study area consisted of 28 contiguous villages from 13 gram panchayats in Balagarh Police Station of Hooghly district in West Bengal.

After enumeration of subjects at field visits, residents of Kolkata were transported to our urban examination center, a tertiary eye hospital in Kolkata and those from Hooghly district were transported to our rural examination center in Kuliapara village, Balagarh Police Station for hospital-based examination. After consenting, the subjects proceeded through various ophthalmic examinations and diagnostic procedures, which have been discussed in details elsewhere.^[1] The current paper deals with ACD. The following definitions, based on the ISGEO guidelines,^[3] were used for the current work:

- (1) Primary angle closure suspect (PACS): An eye in which appositional contact was present on gonioscopy between the peripheral iris and posterior trabecular meshwork and more than 270° of posterior trabecular meshwork could not be visualized.^[9]
- (2) Primary angle closure (PAC): An eye with an occludable drainage angle on gonioscopy (posterior trabecular

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meshwork seen for less than 90°) and features indicating that trabecular obstruction by the peripheral iris had occurred, such as peripheral anterior synechiae, elevated intraocular pressure, iris whorling (distortion of the radially orientated iris fibers), "glaucomflecken" lens opacities, or excessive pigment deposition on the trabecular surface. The optic disc did not have glaucomatous damage.

- (3) PACG: PAC, along with evidence of glaucoma with characteristic disc and field changes. The diagnostic criteria for glaucoma in the HRGS has been discussed elsewhere.^[1]

Among the subjects diagnosed with glaucoma, patients with history of use of topical steroids in the last 6 months, history of trauma or ocular surgery (excluding squint or oculoplastic surgeries), history of chronic uveitis, evidence of pseudoexfoliation or pigment dispersion on slit lamp examination and those with hypermature or intumescent cataract were grouped under secondary glaucomas.

Statistical analysis

The data collected from both the rural and urban cohorts were analyzed using SPSS Statistics software package version 13 (SPSS Inc., Chicago, IL). $P < 0.05$ was taken to be

statistically significant and $P < 0.001$ was taken to be statistically highly significant. The primary outcome was the prevalence PACG with 95% confidence interval. Age- and gender-specific prevalence estimates of PACG were also calculated. Prevalence of PACD, PACS, and PAC were also calculated. Multiple logistic regressions were used to analyze the risk factors for PACD. The independent risk factors analyzed include age, sex, IOP, CCT, presence of diabetes, hypertension, and hyperopia.

Results

A total of 7,248 subjects aged 40 years or older were enumerated from Kolkata city using multistage random cluster sampling whereas 7,408 subjects were enumerated in the rural phase. Data from 7,128 subjects were analyzed in the urban phase and 6,964 subjects were analyzed in the rural phase of this largest Indian epidemiological study on glaucoma prevalence. A sum of 52.6% of the subjects analyzed were males in the urban group and 51.8% were males in the rural group (no statistically significant difference between the rural and urban sex distribution) [Table 1]. The average age of the subjects in our study was 59.34 (± 12.63) years for the urban group and 59.25 (± 9.28) years for the rural group ($P > 0.05$; no significant difference).

Table 1: Various ocular parameters in the PACD, PACS, and PACG subgroups in both the rural and urban arms of the HRGS

	Rural population	Urban population	P
PACD			
N (%; 95% CI)	132 (1.9; 1.76-2.04)	110 (1.54; 1.46-1.62)	<0.001
Male:female	71:61	60:50	0.17
Mean age (SD)	59.9 (9.8)	59.7 (5.6)	0.48
Mean IOP (SD)	24.56 (5.0)	24.42 (5.6)	0.06
VCDR (SD)	0.66 (0.14)	0.62 (0.18)	0.10
Axial length (SD)	20.9 (0.9)	21.1 (0.6)	0.16
PACS			
N (%; 95% CI)	21 (0.3; 0.27-0.33)	16 (0.22; 0.19-0.25)	0.10
Male:female	10:11	8:8	0.24
Mean age (SD)	58.1 (10.5)	57.6 (9.9)	0.19
Mean IOP (SD)	18.2 (4.4)	19.1 (3.9)	0.11
VCDR (SD)	0.53 (0.14)	0.54 (0.11)	0.6
Axial length (SD)	22.1 (0.7)	21.9 (1.3)	0.13
PAC			
N (%; 95% CI)	39 (0.56; 0.51-0.61)	25 (0.35; 0.31-0.39)	0.32
Male:female	16:23	12:13	0.08
Mean age (SD)	57.8 (8.7)	56.1 (7.9)	0.11
Mean IOP (SD)	22.7 (3.7)	23.2 (4.1)	0.21
VCDR (SD)	0.52 (0.03)	0.54 (0.04)	0.33
Axial length (SD)	21.2 (1.9)	21.4 (1.6)	0.17
PACG			
N (%; 95% CI)	72 (1.03; 0.99-1.07)	69 (0.97; 0.94-1.0)	0.09
Male:female	45:27	40:29	0.19
Mean age (SD)	60.4 (7.7)	61.3 (8.1)	0.62
Mean IOP (SD)	26.7 (2.2)	25.4 (2.9)	0.48
VCDR (SD)	0.68 (0.04)	0.65 (0.03)	0.11
Axial length (SD)	19.2 (1.1)	19.7 (0.99)	0.09

PACD: Primary angle closure disease, PACS: Primary angle closure suspect, PAC: Primary angle closure, PACG: Primary angle closure glaucoma, IOP: Intraocular pressure, VCDR: Vertical cup disc ratio

One hundred and ten subjects (1.54%) in the urban arm of HRGS had PACD. Of them, 60 were males and the rest 50 females. PACD in both the eyes was detected in 62 subjects and PACG was detected in 69 subjects. A total of 53.4% of those with PACG were males [Table 1]. No cases of secondary angle closure glaucoma were detected in our urban cohort.

One hundred and thirty-two subjects (1.9%) in the rural arm of HRGS had PACD. ACD in both the eyes was detected in 50 subjects. Among the subjects diagnosed with glaucoma in the rural arm, 72 subjects had PACG. Eight subjects (six females and two males) had secondary angle closure glaucoma due to hypermature/intumescent cataract. Out of the 80 subjects with angle closure glaucoma, 47 (59%) were males and the rest 41% females [Table 2]. No cases of acute angle closure glaucoma were detected in either the rural or the urban division of our study cohort. It is clearly evident from Table 3 that subjects in the PACG group had a statistically significantly higher IOP.

A further analysis of the ocular axial lengths, anterior chamber depths and crystalline lens thickness of the various subjects in the rural and urban arms of the HRGS is detailed

in Tables 4a and b. Table 5 shows that increasing age, male sex, higher IOP, presence of diabetes or hypertension and hyperopia are risk factors for PACG.

Discussion

Glaucoma has been estimated to affect 60.6 to 79.6 million people during 2010 to 2020.^[10] Among those detected with glaucoma, approximately 26% have angle closure glaucoma, which accounts for half of the cases blinded from glaucoma.^[11] The HRGS is one of the largest population-based glaucoma prevalence cross-sectional studies from Asia and the results have been discussed elsewhere.^[12] In the current paper, we deal with subjects detected with ACD and the various subtypes of the same.

Primary angle-closure glaucoma is a multifactorial disease. Major risk factors include age, female gender, ocular biometric features, and ethnicity (e.g., African and Chinese). Shallow anterior chamber depth, thicker lens with increased anterior curvature, short axial length, small corneal diameter, and short radius of curvature also are known factors related to PACG.^[11] There is also evidence for a genetic basis of

Table 2: The age and sex distribution of subjects detected with PACG in the two divisions of the HRGS

Age groups (years)	Subjects detected with PACG in rural division			Subjects detected with PACG in urban division			P (total [n] urban vs. rural)
	Total	Males	Females	Total	Males	Females	
Total	72 (1.03%, CI: 0.99%-1.07%)	45 (62.5%)	27 (37.5%)	69 (0.97%, CI: 0.94%-1.00%)	40 (53.42%)	29 (46.58%)	0.09
40-49	19	12	7	15	9	6	0.07
50-59	16	11	5	16	9	7	0.11
60-69	24	13	11	26	15	11	0.08
≥70	13	9	4	12	7	5	0.08

PACG: Primary angle closure glaucoma

Table 3: Distribution of IOP in the subjects not detected to have glaucoma and comparison of the same with those detected with PACG in each of the two divisions of the HRGS

	Rural			Urban		
	IOP in "normal subjects"	IOP in PACG group	P (IOP normal PACG)	IOP in "normal subjects"	IOP in PACG group	P (IOP normal PACG)
Total	17.20	26.7	<0.001	17.40	25.4	<0.001
40-49	16.20	25.5	<0.001	16.34	23.8	<0.001
50-59	16.71	25.8	<0.001	16.75	24.4	<0.001
60-69	17.10	26.6	<0.001	17.12	25.1	<0.001
≥70	18.20	27.7	<0.001	18.24	25.9	<0.001

PACG: Primary angle closure glaucoma, IOP: Intraocular pressure

Table 4a: Ocular axial lengths, anterior chamber depths, and crystalline lens thickness of the various subjects in the rural arm

Diagnosis (Male:female)	Axial length		AC depth		Lens thickness	
	n	Mean (mm) (SD)	n	Mean (mm) (SD)	n	Mean (mm) (SD)
Normal (3,503:3,273)	6,330	23.1 (0.91)	6,142	2.91 (0.41)	5,672	4.3 (0.32)
PACS (10:11)	21	22.1 (0.7)	18	2.62 (0.56)	18	4.3 (0.78)
PAC (16:23)	39	21.2 (1.9)	38	2.55 (0.44)	38	4.5 (0.71)
PACG (45:27)	72	19.2 (1.1)	70	2.42 (0.46)	68	4.4 (0.64)
P		<0.0001		0.082		0.077

Table 4b: Ocular axial lengths, anterior chamber depths and crystalline lens thickness of the various subjects in the urban arm

Diagnosis (Male:female)	Axial length		AC depth		Lens thickness	
	n	Mean (mm) (SD)	n	Mean (mm) (SD)	n	Mean (mm) (SD)
Normal (3,503:3,273)	6,210	23.6 (0.97)	6,010	2.87 (0.44)	5,954	4.3 (0.38)
PACS (8:8)	15	21.9 (1.3)	13	2.57 (0.54)	13	4.3 (0.84)
PAC (12:13)	25	21.4 (1.6)	25	2.49 (0.49)	24	4.4 (0.81)
PACG (40:29)	67	19.7 (0.99)	66	2.38 (0.47)	62	4.5 (0.74)
P		<0.0001		0.101		0.082

PACS: Primary angle closure suspect, PAC: Primary angle closure, PACG: Primary angle closure glaucoma, AC: Anterior chamber

Table 5: Relation between PACD and age, sex, IOP, CCT, presence of diabetes, hypertension, and hyperopia

Number of subjects	No. of subjects		Odds ratio PACD, Rural (95% CI)	Odds ratio PACD, Urban (95% CI)
	Rural	Urban		
	132 (1.9% of rural sample)	110 (1.54% of urban sample)		
Age (yrs) [% of subjects in respective age bracket of rural/urban division]				
40-49	32 [1.37]	25 [1.01]	1.0	1.0
50-59	31 [1.58]	26 [1.34]	2.09 (1.99-2.19)	2.9 (2.832-97)
60-69	39 [2.01]	33 [1.84]	3.57 (3.4-3.74)	4.4 (4.2-4.6)
70-90	30 [4.18]	29 [3.18]	4.12 (4.01-4.23)	3.92 (3.81-4.03)
Gender				
Male	71	60	1.0	1.0
Female	61	50	0.84 (0.49-1.19)	0.93 (0.53-1.33)
IOP	132	110	2.72 (2.62-2.82)	2.66 (2.41-2.91)
CCT	132	110	2.65 (2.44-2.86)	2.82 (2.7-2.94)
Diabetes				
Absent	60	52	1.00	1.00
Present	72	58	1.2 (1.0-1.4)	1.12 (1.0-1.24)
Hypertension				
Absent	57	44	1.00	1.00
Present	75	66	1.3 (0.7-1.9)	1.5 (0.9-2.1)
Hyperopia				
Absent	43	33	1.00	1.00
Present	89	77	2.1 (1.8-2.4)	2.3 (1.9-2.7)
Axial length	132	107	0.6 (0.3-0.9)	0.4 (0.2-0.6)
Anterior chamber depth	126	104	0.25 (0.15-0.35)	0.19 (0.11-0.27)
Lens thickness	124	99	1.87 (1.77-1.97)	1.92 (1.8-2.04)

PACD: Primary angle closure disease, IOP: Intraocular pressure, CCT: Central corneal thickness

PACG. First, reported prevalence of PACG varied among different ethnicities, such as 0.4% in white subjects,^[12] 1.4% in Chinese,^[13,14] and 2% to 8% in Eskimos;^[15,16] second, PACG is more prevalent in first-degree relatives of patients;^[17] and third, the heritabilities for a shallow anterior chamber and narrow angle (both are key features of PACG) are approximately 93%^[18] and 49%,^[19] respectively. However, majority of PACG cases are silent and chronic with the majority remaining undiagnosed.^[20]

In a recent systematic review and meta-analysis conducted by Tham *et al.*, the prevalence of PACG was found to be highest in Asians.^[21] This finding provides evidence consistent with previous PACG reviews,^[10,22] indicating that greater emphasis on the development of methods to identify and

treat PACG would be particularly needed in Asia.^[21] One of the highest prevalence of PACG ever reported in the previous population-based studies in which diagnosis was based on gonioscopic findings and the presence of glaucomatous optic neuropathy was 2.7% in northwest Alaskan Inuits, followed by 2.5% in Myanmar.^[23] The prevalence of PACG in a rural population of Kumejima in Japan was 2.2% that was 3.7 times higher than that in the Takmi Study carried out in an urban center in Japan.^[23] The prevalence of PACG in southern India ranges from 0.5% to 4.3%.^[20] It is worth mentioning that the South Indian study that reported a prevalence of 4.3% did not include the VF findings for diagnosing PACG.^[4] The WBSG, which included 1,324 subjects from rural West Bengal found a crude PACG prevalence of 0.23% in people aged 50 years

or more.^[5] The prevalence of PACG in the current study from Eastern India, in which gonioscopic findings along with glaucomatous optic neuropathy, VF test results, or both were considered in diagnosing PACG, was 1.03% in the rural population and 0.97% in the urban population (no statistically significant difference between the two groups). There was however no significant difference between the two groups with respect to age distribution, as is seen in Table 3. The average IOP among those detected with PACG was very significantly higher than the IOP in those not detected with glaucoma in both the rural and urban groups, as is seen in Table 3. The prevalence of PACD was also found to be higher in the rural group (1.9%) as compared to the urban group (1.54%) and the difference was found to be statistically highly significant, which can possibly be attributed to the ethnic variation between the two groups.

From Tables 4a and b, it is evident that the AC depth in subjects diagnosed with PACD is lesser than normal subjects in both the rural and urban groups, though the results are not statistically significant. The lens thickness also showed no statistically significant difference between subjects diagnosed with PACD and normal subjects. However, we did observe a statistically significant association between PACD and hyperopia [Table 5]. There was however no significant difference between the rural and urban arms with respect to this association. Most studies have reported a significant association between hyperopia and PACD^[24] whereas some studies have found no such association.^[2,25] From Table 5, it is also evident that axial length and anterior chamber depth are inversely related to PACD. We are aware that hyperopia is inversely related to ocular axial length and anterior chamber depth. It is also established that anterior chamber depth is affected by race, ethnicity, age, and gender that suggests a potential role for genetic influences, which is consistent with a recent report of a genetic variant within the *ABCC5* gene that influences anterior chamber depth and the risk of PACG among Asians.^[25]

Conclusion

In conclusion, the current epidemiological cross-sectional study carried in rural and urban eastern Indian populations found the prevalence of PACD to be 1.9% in the rural population and 1.54% in the urban population ($P < 0.0001$). Among those detected with PACG, 94% of the respondents were unaware of the disease. Similar findings have also been found in the CGS,^[23] which further states that even among those diagnosed with PACG, a significant proportion were being treated as POAG. The study also concludes that higher age, higher CCT, and shorter axial length/presence of hyperopia are important independent predictors of ACD. No significant relationship could however be established between ACD and female sex, presence of diabetes or hypertension, and smaller anterior chamber depth. The findings of this study establishes the fact that ACD is more common in eastern India than previous estimates have shown, hence adequate changes in health-care policies should be introduced to address this issue. As a first step, the authors recommend that a simple and inexpensive procedure like gonioscopy should be made mandatory in basic eye check-up protocols.

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Conflicts of interest

There are no conflicts of interest.

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