

EXTENDED REPORT

Glaucoma in aphakia and pseudophakia in the Chennai Glaucoma Study

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Aim: To determine the prevalence of glaucoma among aphakes and pseudophakes in a rural population of southern India.

Methods: 3924 subjects aged 40 years or above underwent complete ophthalmic examination. Glaucoma in aphakia/pseudophakia was diagnosed using International Society of Geographical and Epidemiological Ophthalmology criteria in aphakic/pseudophakic people.

Results: 54 subjects (37 aphakes, 17 pseudophakes) (1.38% of 3924 subjects, 11.2% of 482 aphakes/pseudophakes) had glaucoma in aphakia/pseudophakia. Aphakia, age, intraocular pressure (IOP), pseudoexfoliation, and peripheral anterior synechiae greater than or equal to 180 degrees of the angle were risk factors for glaucoma on univariate analysis. On multivariate analysis, IOP and aphakia were independent risk factors for glaucoma. 39 people (72.22%) with glaucoma had normal IOP at presentation. None of the people with glaucoma were aware of the disease. Blindness in one or both eyes was seen in 12 subjects (10 unilateral and two bilateral)—that is, 22.22% of people with glaucoma in aphakia/pseudophakia.

Conclusions: Glaucoma is an important cause of ocular morbidity among aphakes and pseudophakes in this rural population of south India. This glaucoma, responsible for unilateral or bilateral blindness in 22.2% of those affected, was entirely undetected in this study population.

The reported prevalence of glaucoma in aphakic and pseudophakic eyes has shown wide variations over the years.¹ One of the major reasons for this is that microsurgical techniques have evolved over the years, resulting in, on the one hand, decreasing incidence of postoperative leaks and consequent peripheral anterior synechiae (PAS), and on the other hand, tighter wound closure increasing the risk of early and late postoperative intraocular pressure (IOP) elevation.¹

While several hospital based estimates of the incidence of glaucoma in aphakic and pseudophakic eyes are available,^{1–4} only some population based studies report the prevalence of post-surgical glaucoma. These have varied from no cases in some studies^{5–7} to 0.4%⁸ in Zulul of South Africa. Data regarding the prevalence of glaucoma from India are not available. India is a developing country with a large burden of cataract related blindness,⁹ where several cataract eradication programmes are active.¹⁰ It is therefore important to know the prevalence of surgery related glaucoma in this population.

METHODS

This study was part of the Chennai Glaucoma Study, a population based study of glaucoma in rural and urban populations in and around Chennai in southern India. The study design and methods have been discussed in detail elsewhere.¹¹ This paper deals with the rural arm of the study, a brief description of which follows.

In all, 4800 permanent residents aged 40 years or above were enumerated from 27 contiguous villages in Thiruvallur and Kancheepuram districts of Tamil Nadu. Trained social workers performed enumeration by door to door survey and collected demographic information. Eligible subjects were allotted an identification number and invited to the base hospital for detailed ophthalmic examination. The institutional review board approved the study and informed consent was obtained from all participants. All subjects underwent complete ophthalmic examination including history of ocular

problems, trauma or surgery, systemic illness, medications, family and personal history. Best corrected visual acuity testing using the modified ETDRS chart and frequency doubling perimetry (FDP screening C-20-1 and threshold N-30 tests) were administered by one of two optometrists. IOP was recorded with the Goldmann applanation tonometer (Zeiss AT 030 applanation tonometer, Carl Zeiss, Jena, Germany). Gonioscopy was performed in dim ambient illumination with a Sussmann-type 4 mirror hand held gonioscope (Volk Optical Inc, Mentor, OH, USA). Dilated optic disc examination with a +78 D lens and fundus examination with an indirect ophthalmoscope were performed. The above tests were performed by one of two ophthalmologists. Interobserver agreement was high—kappa 0.87 for gonioscopy and vertical cup-disc ratio (VCDR), weighted kappa 0.709 for IOP.

Subjects were advised to have a Humphrey field test (SITA standard 30-2) if they had IOP ≥ 21 mm Hg and/or VCDR ≥ 0.7 or CD asymmetry ≥ 0.2 and/or focal thinning, notching, or splinter haemorrhages. Contact lens correction was used for perimetry in aphakes.

Diagnostic criteria

Glaucoma was defined using the ISGEO classification¹² according to which diagnosis is made using three levels of evidence—level 1 with VCDR or CD asymmetry ≥ 97.5 th percentile of the perimetrically normal population with visual field defects consistent with glaucoma; level 2 with VCDR or CD asymmetry ≥ 99.5 th percentile of normal in the absence of reliable visual fields; and level 3 with IOP ≥ 99.5 th percentile of normal and visual acuity $< 3/60$ if the optic disc could not be assessed. Blindness was defined as best

Abbreviations: ACG, angle closure glaucoma; IOP, intraocular pressure; OAG, open angle glaucoma; PAS, peripheral anterior synechiae; PEX, pseudoexfoliation; VCDR, vertical cup-disc ratio

Table 1 Data of 1810 phakic, perimetrically normal subjects from whom cut-off levels of normal and abnormal were derived

	Mean (SD)	Median	97.5th percentile	99.5th percentile
IOP (mm Hg)	14.29 (3.32)	14	21	25
Vertical cup-disc ratio	0.39 (0.17)	0.4	0.7	0.8
Vertical cup-disc asymmetry	–	–	0.2	0.2

corrected visual acuity of $<2/40$ and /or constriction of the visual field to $<10^\circ$ from fixation.

Statistical analysis

Categorical variables between groups were compared using χ^2 test. The *t* test was used for continuous variables. The eye with higher IOP was considered in bilaterally aphakic/pseudophakic people. Multivariate analysis was performed using logistic regression. The prevalence of aphakia/pseudophakia was age and sex adjusted to the rural Tamil Nadu population.¹³

RESULTS

A total of 3924 eligible subjects responded, a response rate of 81.75%. Data from 1810 subjects with reliable, normal FDP screening C-20-1 tests in both eyes, from whom the distributions of normal VCDR and IOP were obtained, are presented in table 1.

Five hundred and seven subjects (12.92%; age and sex adjusted prevalence 9.16%, 95% CI 8.26% to 10.06%) were aphakic/pseudophakic. Their mean age was 64.85 (8.74) years. There were 212 men and 295 women. Table 2 gives their further details.

Eleven people with unilateral aphakia/pseudophakia had primary glaucoma in contralateral phakic eyes—five angle closure glaucoma (ACG) and six open angle glaucoma (OAG); 12 people with unilateral aphakia/pseudophakia had bilateral OAG. Two people with bilateral pseudophakia had been diagnosed to have primary OAG before surgery at our institute. These 25 people were excluded from further analysis of aphakic/pseudophakic people. Data of the remaining 482 aphakic/pseudophakic people have been considered further. Table 3 compares phakic with aphakic/pseudophakic subjects and table 4 compares aphakic with pseudophakic subjects.

In all, 54 subjects had glaucoma in aphakic/pseudophakic eyes that may be classified as secondary, 11.2% (95% CI 8.38% to 14.02%) of aphakes/pseudophakes, a population prevalence of 1.38% (95% CI 1.01% to 1.75%). Glaucoma was diagnosed in 18.59% of aphakes and 5.99% of pseudophakes. Table 5 presents a comparison of risk factors between those with and without glaucoma, along with a comparison of these risk factors among aphakes and pseudophakes considered separately.

On multivariate analysis including the whole group (aphakes + pseudophakes), IOP (OR 1.15; 95% CI 1.09 to 1.21) and aphakia (OR 2.54; 95% CI 1.28 to 5.03) were

significantly associated with the development of glaucoma. On similarly analysing aphakic and pseudophakic groups separately, IOP (OR 1.13; 95% CI 1.05 to 1.21) was significantly associated with glaucoma among aphakes, while among pseudophakes, higher age (OR 1.11; 95% CI 1.03 to 1.21) and IOP (OR 1.21; 95% CI 1.10 to 1.32) were significant. However, the mean age of aphakes with glaucoma was not significantly different from the mean age of pseudophakes with glaucoma ($p = 0.68$). When IOP was removed from risk factor analysis, aphakia (OR 2.69; 95% CI 1.43 to 5.07) and the presence of PAS (OR 3.10; 95% CI 1.11 to 8.60) were significantly associated with glaucoma. Among aphakes alone, PAS was significant (OR 4.19; 95% CI 1.14 to 15.43) while among pseudophakes, only age was still significant (OR 1.07; 95% CI 1.004 to 1.15). Thirty nine people (72.22%) with glaucoma had normal IOP at presentation. None of the subjects with glaucoma were aware of the disease.

Table 6 presents the classification of glaucoma patients as described by the ISGEO, and the blindness data (see also fig 1). Unilateral or bilateral blindness was seen in 12 subjects—that is, 22.22% of people with glaucoma and 2.49% of aphakes/pseudophakes. Monocular blindness was seen in 18.52% and binocular blindness was seen in 3.7% of subjects with glaucoma. Among all aphakes/pseudophakes, the rates of unilateral and bilateral blindness due to glaucoma were 2.07% and 0.41% respectively. All subjects with blindness were diagnosed using visual acuity criteria.

DISCUSSION

We found a 9.16% (age-sex adjusted) prevalence of aphakia/pseudophakia in this population. Previous studies in predominantly white populations have reported much lower prevalence rates of 5.1% in the United States, 4.7% in Australia, and 5.3% in Western Europe.¹⁴ The Andhra Pradesh Eye Diseases Study (APEDS)¹⁵ conducted in the urban Indian city of Hyderabad reported a prevalence of 14.6% in their population, which is higher than our estimate. Several factors like race,¹⁶ environment (sunlight and ultraviolet-B exposure),¹⁷ diet, nutrition,^{14 18} and smoking^{14 19} may influence the cataract burden of a community. In addition, visual needs of people, which depend on their occupation, awareness, education, and access to health care, determine the number of patients who avail themselves of cataract surgery in a community. The fact that the APEDS studied an urban population, with possibly lower thresholds for cataract surgery, while we studied a rural one, where access to health care and awareness are likely to be lower, may account for

Table 2 Details of aphakia and pseudophakia (n = 507)

	Aphakia	Pseudophakia	1 Eye aphakia + 1 eye pseudophakia
Unilateral *	97	171	–
Bilateral	111	112	–
Total	208	283	16†

*Other eye phakic.

†Considered as aphakic/pseudophakic for further analysis depending on status of the right eye.

Table 3 Comparison of phakic with aphakic/pseudophakic subjects

	Phakic* (n = 3440)†	Aphakic/ pseudophakic (n = 482)†	p Value	OR (95% CI)
Mean age (SD) (years)	52.46 (10.09)	64.69 (8.72)	<0.0001	–
Females	1880 (54.65%)	282 (58.51%)	0.1224	1.17 (0.96 to 1.42)
Mean IOP (SD) (mm Hg)	14.35 (3.78)	14.01 (5.57)	0.08	–
Glaucoma	110 (3.20%)	54 (11.2%)	<0.0001	3.82 (2.72 to 5.37)
PEX	117 (3.40%)	68 (14.11%)	<0.0001	4.67 (3.40 to 6.40)

*Includes 23 people with unilateral aphakia/pseudophakia and glaucoma in phakic eyes as surgery was not instrumental in their developing glaucoma.

†Includes people with and without glaucoma.

OR, odds ratio; CI, confidence interval; PEX, pseudoexfoliation.

the difference observed in the prevalence of aphakia/pseudophakia between these two communities which are ethnically, geographically, and culturally much closer to each other than the white population.

Aphakes constituted 43.36% of people previously operated upon for cataract. Aphakes were significantly older than the pseudophakes and had significantly higher IOP. Higher IOP may be explained at least partly by the fact that the aphakes had a significantly higher proportion of subjects with PEX that, on one hand is a risk factor for higher IOP²⁰ and on the other hand, is also a risk factor for vitreous loss²¹ and inability to insert an intraocular lens resulting in aphakia. The duration from surgery to current examination, which would have been expected to be longer among aphakes, was however not significantly different between aphakes and pseudophakes. The aphakes in our study therefore possibly represent the complicated surgeries with more trabecular damage, outflow obstruction, and higher IOP, rather than the planned intracapsular extractions that were performed in the previous era. Considering this, the high proportion of aphakia to pseudophakia is disturbing, and may suggest the need for better facilities and/or training with closer monitoring of cataract surgery standards.

Aphakic/pseudophakic subjects had a significantly higher proportion of glaucoma (OR 3.82), compared to phakic subjects, emphasising the fact that previous cataract surgery was a significant risk factor for glaucoma in this population. The prevalence of glaucoma in aphakia/pseudophakia, after excluding clearcut primary glaucoma, in our population was 11.2% of aphakes/pseudophakes, which is a large proportion. Many epidemiological studies of glaucoma report only their prevalence of primary glaucoma. Of those studies that do report their rates of post-surgical glaucoma, the Tanjong Pagar survey of Chinese residents in Singapore⁵ and studies from Thailand⁶ and Mongolia⁷ report no cases of glaucoma attributable to cataract surgery. A study from Ireland

reported a prevalence of 0.05%, while the Melbourne Visual Impairment Project reported two cases in 3265 people, a prevalence of 0.06%. Two reports from South Africa have shown higher prevalence rates of 0.2–0.4%.^{8, 22} However, all of them are lower than our prevalence of 1.38%. The reason for a prevalence higher than even those in African communities could be that India has, for some time, been a focus for several cataract surgical programmes, but the quality of surgery offered has not been standardised. Though urban India now has several hospitals where state of the art surgical facilities are available, several rural areas in India still suffer from lack of adequate surgical facilities. This may partly account for the higher prevalence of glaucoma in our study. We do not, however, have the details regarding the nature (outreach or inreach) of programmes under which the subjects in our study underwent cataract surgery. In addition, if we exclude the 12 patients with bilateral glaucoma and 10 patients with unilateral glaucoma and PEX on the premise that they may represent primary or PEX glaucoma we are left with a population prevalence of 0.82%, which is not very much higher than other estimates.

Increasing age, higher IOP, aphakia (versus pseudophakia), PEX, and PAS were all found to be risk factors for glaucoma on univariate analysis. Among aphakes the risk factors were IOP, PEX, and PAS, while among pseudophakes, IOP and higher age were found to be risk factors for glaucoma on univariate analysis. All the above factors have been known to influence each other. IOP is known to be affected by age,²³ PEX,²⁰ and outflow obstruction caused by PAS. PEX, in addition to being a risk factor for high IOP and glaucoma,²⁰ also has an effect on the development of cataract²⁰ and complications during cataract surgery. On multivariate analysis, IOP and aphakia emerged as independent risk factors that influence the development of glaucoma in the group as a whole after adjusting for all the other variables. On multivariate analysis of the aphakic and

Table 4 Comparison of aphakes and pseudophakes

	Aphakes* (n = 209)	Pseudophakes* (n = 273)	p Value	OR (95% CI)
Mean age (SD)	66.59 (8.76)	63.22 (8.42)	<0.001	–
Females	120 (57.42%)	162 (59.34%)	0.67	1.082 (0.75 to 1.56)
Mean IOP (SD)	14.76 (5.27)	13.43 (5.73)	0.009	–
Glaucoma	37† (17.70%)	17† (6.23%)	<0.0001	3.24 (1.77 to 5.94)
PEX	47 (22.49%)	21 (7.69%)	<0.0001	3.48 (2.0 to 6.04)
PAS ≥180°	11 (5.26%)	12 (4.40%)	0.65	1.20 (0.52 to 2.80)
Mean Sx-Ex (SD) (months)	53.73 (57.44)	46.53 (55.57)	0.167	–

*Includes those with and without glaucoma.

†11 people with bilateral and 26 people with unilateral glaucoma.

‡Includes 16 subjects with unilateral glaucoma and one person with bilateral glaucoma with pseudophakia in the right eye and aphakia in the left.

OR, odds ratio; CI, confidence interval; PEX, pseudoexfoliation; PAS, peripheral anterior synechiae; Sx-Ex, time from surgery to current examination.

Table 5 Comparison of aphakic/pseudophakic subjects with and without glaucoma

	No glaucoma (n=428)	Glaucoma (n=54)	p Value	OR (95% CI)
Aphakes:pseudophakes*	172:256	37:17	0.0001	3.24 (1.78 to 5.94)
Mean age (SD) (years)	64.38 (8.73)*	67.13 (8.36) *	0.03	–
Aphakes	66.55 (8.76)	66.81 (8.85)	0.86	–
Pseudophakes	62.92 (8.4)	67.82 (7.38)	0.02	–
Sex (M: F)	178:250*	22:32*	0.9	0.96 (0.54 to 1.72)
Aphakes	76:96	13:24	0.41	0.68 (0.33 to 1.43)
Pseudophakes	102:154	9:8	0.32	1.70 (0.63 to 4.55)
Mean IOP (SD) (mm Hg)	13.32 (4) *	19.43 (10.09)*	<0.0001	–
Aphakes	14.07 (4.27)	17.97 (7.80)	<0.0001	–
Pseudophakes	12.82 (3.73)	22.58 (15.52)	<0.0001	–
PEX	55 (12.85%)*	13(24.07%)*	0.026	2.15 (1.08 to 4.27)
Aphakes	34	13	0.04	2.19 (1.02 to 4.76)
Pseudophakes	21	0	–	–
PAS \geq 180°	17 (3.97%)*	6 (11.11%)*	0.033	3.02 (1.14 to 8.03)
Aphakes	6	5	0.028	4.3 (1.24 to 15.02)
Pseudophakes	11	1	0.545	1.39 (0.17 to 11.47)
Mean Sx-Ex (SD) (months)	48.85 (57.43) *	56.22 (48) *	0.30	–
Aphakes	50.70 (58.13)	67.83 (52.54)	0.1	–
Pseudophakes	47.58 (57.03)	30.94 (20.65)	0.23	–

*Values pertain to the whole group consisting of aphakes and pseudophakes.
OR, odds ratio; CI, confidence interval; PEX, pseudoexfoliation; PAS, peripheral anterior synechiae; Sx-Ex, time from surgery to current examination.

pseudophakic groups separately, IOP was an independent risk factor in both groups. Among pseudophakes, higher age was an additional independent risk factor. However, the mean age of people with glaucoma was similar in aphakic and pseudophakic groups. Age being a risk factor in the pseudophakic group alone may be explained by the fact that the pseudophakic group was, as a whole, significantly younger than the aphakes and among them, the older people tended to develop glaucoma.

A majority of people with glaucoma presented with normal IOP (72.22%) and were detected based on optic disc examination. None of our patients was aware of the presence of glaucoma. This emphasises the fact that glaucoma is largely underdiagnosed even in a group of people who have, at some time, had ophthalmic care services in the form of cataract surgery. This presumably indicates inadequate follow up care either because of lack of awareness or accessibility to follow up examinations. In addition, the general ophthalmologist who looks for raised IOP as an indicator or diagnostic parameter for glaucoma is likely to miss more than 70% of patients with glaucoma. Stereoscopic disc examination is extremely important to suspect glaucoma and its importance cannot be overemphasised.

In all, 22.22% of people with glaucoma in aphakia/pseudophakia were blind in one (18.52%) or both (3.70%) eyes as a result of glaucoma. The APEDS reported one case of surgery related (aphakic) glaucoma with visual acuity <20/200 among 91 aphakes/pseudophakes a prevalence of 1.1%,

compared to 2.49% in our study. Though the difference is not large, it may be accounted for by the fact that the APEDS studied an urban population where surgical facilities are likely to be better than the rural areas that we studied, and by the fact that the population we studied was almost three times larger.

To the best of our knowledge, this is the first descriptive report of glaucoma in aphakia and pseudophakia in a population based study. We report data using the ISGEO criteria from rural India, where the majority of the Indian population resides.¹³ These criteria, which were introduced primarily to minimise variability between studies and ensure comparability between studies done in different parts of the world, provide a framework by which glaucoma can be diagnosed even in the absence of a reliable threshold visual field. Many of our patients were diagnosed based on level 2—that is, optic disc criteria alone. The population studied was a rural, predominantly illiterate one, which accounted for their unwillingness to return for a field examination. Among those who came, many could not perform a reliable threshold test (in spite of using contact lens correction for aphakic patients for perimetry). Jacob *et al*²⁴ reported a similar problem in a population based prevalence study of glaucoma from a different population in south India. This study also does not distinguish between patients who have had immediate postoperative IOP elevations in the past for short periods, giving rise to one time damage to the optic disc, from those who continue to have spikes of IOP with periods of normal

Table 6 Categories of glaucoma diagnosis according to ISGEO and blindness among patients with glaucoma in aphakia and pseudophakia

	Level 1*	Level 2*	Level 3*	Unilateral blindness	Bilateral blindness
Aphakes	1	35	1	7	2
Pseudophakes	1	13†	3	3	0
Total	2	48†	4	10	2

*Classified according to the three levels of evidence described by the ISGEO.¹²
Level 1: Vertical cup-disc ratio (VCDR) or cup-disc asymmetry \geq 97.5th percentile of perimetrically normal population with visual field defect consistent with glaucoma.
Level 2: Vertical cup-disc ratio (VCDR) or cup-disc asymmetry \geq 99.5th percentile of perimetrically normal population.
Level 3: IOP \geq 99.5th percentile of normal population with visual acuity <2/40.
†Includes 1 person who had bilateral glaucoma with aphakia in one eye and pseudophakia in the other.

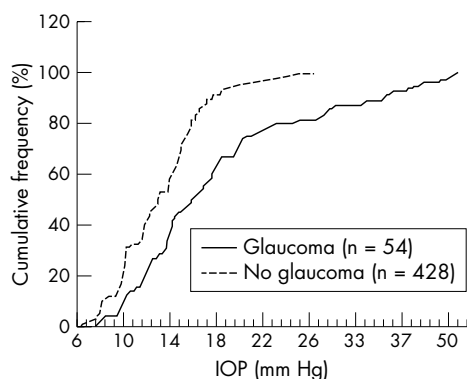


Figure 1 Intraocular pressure (IOP) of aphakic/pseudophakic subjects stratified by glaucoma status.

IOP, and require antiglaucomatous treatment to retard progression of the disease.

In conclusion, glaucoma is an important cause of ocular morbidity among aphakes/pseudophakes in this rural population of south India. This glaucoma, responsible for unilateral or bilateral blindness in 22.2% of those affected, was entirely undetected in this study population. With India's older population expected to expand dramatically over the next few years, and several cataract eradication programmes being put into force, one can reasonably expect the burden of cataract surgery related glaucoma to increase, as with all other diseases of ageing. In order to tackle this silent and potentially blinding disease on a long term basis, cataract surgical programmes need to concentrate on quality of surgery as well as providing extended follow up of operated people.

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