Epidemiology of primary angle closure disease—the Chennai glaucoma study and the Chennai eye diseases incidence study

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Introduction
Glaucoma is considered to be the leading cause of irreversible blindness worldwide. Primary angle closure disease (PACD) is a subtype of glaucoma that predominantly affects Asian ethnicity more than Caucasians and Africans.¹–³ Estimating the prevalence and identifying the risk factors for glaucoma are the goals of population-based studies. The information from these studies is used to address treatment protocols and health-care policies. The Chennai Glaucoma Study (CGS) was one such population-based cross-sectional survey designed to estimate the prevalence of glaucoma in a rural and an urban population aged 40 years and above from South India. A sample size of 4758 was arrived for an 85% response rate for an assumed 3% population prevalence of glaucoma with a relative precision of 25% and a design effect of 2. The CGS was conducted between June 2001 and May 2004 by enumerating a cohort of 9600 (4800 each from rural and urban arms) individuals. The rural study arm consisted of residents from 32 consecutive neighbouring villages spread over two districts of the state of Tamil Nadu, whereas urban study population consisted of residents from Chennai city using a multistage random cluster sampling procedure and 960 subjects from five divisions were enumerated. During enumeration demographic information was collected by household questionnaire and the eligible subjects were invited to come to the base hospital that was created exclusively for the study of detailed ophthalmic examination.⁴ From this cohort, 7774 subjects (rural:urban=3924:3850) were examined. Incidence studies provide information on the true risk of developing new disease over a period of time. It also helps in exploring associations between preexisting factors at baseline and the development of the disease. The Chennai Eye Disease Incidence Study (CEDIS) was conducted to find the incidence of eye disease in the same cohort, 6 years from the baseline visit (2007–2010). Five thousand four hundred and thirty-two subjects were eligible; out of this 4421 (rural:urban 2510:1911) subjects were examined at the base hospital.

Glaucoma was diagnosed based on structural and functional evidence of glaucomatous damage as per the International Society Geographical and Epidemiologic Ophthalmology (ISGEO).⁵ Glaucoma was classified into three categories based on three levels of evidence. In category 1, diagnosis was based on structural and functional evidence which required a cup disc ratio (CDR) or a CDR asymmetry equal to or greater than the 97.5th percentile for the normal population or a neuroretinal rim width reduced to 0.1 CDR (between 10 and 1 o’clock or 5 and 7 o’clock) with a definite visual field defect consistent with glaucoma. A glaucomatous field defect was diagnosed on threshold visual field examination (STA standard 24–2) of the central 24°, if the glaucoma hemifield test was outside normal limits and three or more abnormal contiguous non-edge points (except the nasal horizontal meridian) were depressed to the P5% level. Reliability criteria were as recommended by the instrument’s algorithm (fixation losses 20%; false positive and false negative, 33%). Category 2 was based on advanced structural damage with unproved field loss. This included those subjects in whom visual fields could not be done or were unreliable, with CDR or CDR asymmetry equal to or greater than the 99.5th percentile for the normal population. Lastly, category 3 consisted of persons with an intraocular pressure (IOP) greater than the 99.5th percentile for the normal population, whose optic discs could not be examined because of media opacities. Angle closure disease was sub-classified into primary angle closure suspect (PACS), primary angle closure (PAC), and primary angle closure glaucoma (PACG) based on structural and functional evidence of glaucomatous damage as per ISGEO. PACS was defined as an eye in which the posterior trabecular meshwork was not visible for >180° on gonioscopy; PAC, an eye with PACS along with peripheral anterior synechiae and/or elevated IOP without optic neuropathy; and PACG, the presence of PACS combined with clinical evidence of glaucoma.

Prevalence of PACD
The prevalence of PACS⁶,⁷ (6.3%, 95%CI, 5.51–7.03 versus 7.24%, 95% CI, 6.38–8.02) and PACG (0.87%, 95%CI 0.58 to 1.16 versus 0.88%, 95%CI, 0.60–1.16) was similar in the rural and urban populations. However, PAC was found to be significantly higher in the urban population (2.75%,...
95% CI, 2.01–3.49 versus 0.71%, 95% CI, 0.45–0.98). One possible reason for this difference could be earlier cataract surgery in the rural population, which either masks PAC or prevents progression from PACS to PAC. The disease was found to be silent and chronic and none had any evidence of acute attack. Age was found to be a significant risk factor for PACD in both populations, with increasing age the prevalence of the disease increased across both populations. Female gender is considered to be a risk factor for PACD, our rural population had female preponderance whereas in our urban study population this trend was seen only in PACS and PACG groups. One possible reason could be due to the small numbers. Diabetes mellitus and hyperopia were associated with PAC and PACG only in our urban population. Association of diabetes in the urban population can be attributable to the higher prevalence of diabetes in our urban population. We found a definite association between nuclear sclerosis and myopia in the rural population; this secondary myopia could have masked a hyperopic refractive error and resulted in lack of association of hyperopia with angle closure in the rural population. PACG-related blindness was more common among urban subjects (5.9%) than rural subjects (2.9%). None of the PACG subjects in the rural population were aware of their disease, whereas in the urban population 14.7% (5 out of 34 subjects) were diagnosed to have glaucoma earlier. Among the five subjects with PACG 2, 40% were diagnosed to have open-angle glaucoma, this possibly can be explained by failure to do gonioscopy as part of glaucoma clinical evaluation. Using the biometry we found that eyes with PACD seem to be associated with shallower anterior chambers, thicker crystalline lenses, and shorter axial lengths.8 In eyes with pseudoexfoliation deposits of PEX material on the zonules results in zonular weakness. This can lead to an anterior shift of the lens and occludable angle. In the CGS we observed 8.3% of eyes with pseudoexfoliation having occludable angles.9

Incidence of PACD

We reported the 6-year incidence of PACD from the CEDIS; the incidence of PACD was defined as the development of PACD during the follow up in subjects without PACD at baseline in a phakic eye.10 Out of 4421 subjects were evaluated in the CEDIS, 134 subjects (M:F 62:72, rural: urban 82:52) were diagnosed to have any form of PACD, incidence of 4.0% (95% CI, 3.3 to 4.7, rural 2.5%, 95% CI, 1.8 to 3.2; urban 1.6%, 95% CI, 0.9 to 2.2). Assuming a linear incidence of PACD the annual incidence was 0.7%. The incidence of the three sub-types of PACD is as follows: PACS—88 subjects (2.6%, 95% CI, 2.1–3.2, M:F 36:52, rural: urban 56:32), PAC—37 subjects (1.1%, 95% CI, 0.7–1.5, M:F 24:13, rural: urban 21:16) and PACG—9 subjects (0.3%, 95% CI, 0.1–0.4, M:F 2:7, rural: urban 5:4). In the nine subjects with PACG, the diagnosis was based on category 1 in five subjects, category 2 in three subjects, and category 3 in one subject. Three subjects had bilateral disease and none were blind.

Higher intraocular pressure, increased lens thickness, shorter axial length, shallow anterior chamber depth, an anteriorly positioned lens and hyperopia were found to be the baseline risk factors for PACD in 6 years. There was an inverse relationship between the incidence of PACD and the cataract surgery rates. The incidence of PACD peaked in the 50–59 years age group and declined after 60 years of age, whereas the cataract surgery rate increased exponentially after the age of 60 years. In the past, a national survey was conducted in 15 states of India that includes the state of Tamil Nadu where our study was carried out, and it was found that the state of Tamil Nadu has a cataract surgery rate of 14.7% and a surgical coverage of 82.8%. In terms of actual number of surgeries Tamil Nadu is listed among the top five states. The decline in PACD incidence after 60 years of age in our study is mainly due to this increase in cataract surgery rates in our study population and due to the successful cataract blindness program.

The incidence of PACD increased in eyes shorter than 21 mm, those with an ACD <2.5 mm and a lens thickness of >5.5 mm. The lens plays an important role in pathogenesis of angle closure disease either because of increased thickness or due to a more anterior position. Both these factors can cause crowding of the anterior chamber angle in eyes with a smaller anterior segment and result in greater predisposition to PACD. But the exact relationship between angle closure disease and lens thickness or lens position is not very clear. Theoretically, the thickness and position of the lens should alter the angle recess width, but the association was found to be equivocal. One possible explanation proposed for this inconsistency is the inability to control the accommodation while measuring the lens thickness. In spite of the limitation we suggest that our biometry data can be used as a risk factors guide for PACD development. We also reported the risk of cataract progression among PACS subjects 6 years after they underwent laser peripheral iridotomy (LPI).11 One hundred ninety subjects who had LPI for PACS at baseline were examined in the CEDIS. We found there was a significant cortical cataract progression in 6 years following LPI for PACS (OR 1.6, 95% CI 1.1–2.3, p = 0.007).

Implications of study findings

There is significant PACD in the population above 40 years of age. Like open angle glaucoma PACD
also is silent and chronic. Majority of it is undiagnosed glaucoma. This suggests that a comprehensive eye exam is essential for diagnosis of glaucoma that includes appropriate application of gonioscopy to diagnose angle closure. Older age and shorter eyes are the risk factors for the disease and needs closer watch for development of angle closure in those eyes. Laser iridotomy for PACS can cause cortical cataract with time, risk, and benefit of the LPI should be discussed in offering LPI for asymptomatic PACS. Cataract surgery seems to have an effect on incidence of PACD, with improvements in cataract surgical techniques and outcomes probably eyes that have PACS and PAC with significant cataract will benefit from cataract surgery.

References

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