Epidemiology of Glaucoma In South India

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Introduction

Glaucoma is the second leading cause of blindness in the world.1 In chronic diseases such as glaucoma, it is important to estimate the disease burden in the population to plan treatment strategies. This is mainly done by population based prevalence studies that give us an idea of the proportion of people with disease. If they are re-examined a few years later this gives an estimate of the incidence of disease. Incidence studies give a more direct estimate of disease development and are more likely to provide risk factors for disease over time. However, it should be kept in mind that estimates may differ in different population groups or geographical regions and may also be affected by differing methodologies employed in studies. It is noteworthy that four major studies are from South India2-11 and form the bulk of evidence for glaucoma in India. Recently published reports on glaucoma incidence and risk factors from India form an important source of evidence and more reports are likely to follow in near future to better understand the disease in our population.12

Diagnostic definition of glaucoma in population based studies

The major population based studies reported from south India are the Vellore Eye Study (VES),2 Andhra Pradesh Eye Disease Study (APEDS),3-6 Chennai Glaucoma Study (CGS),7-10 Chennai Eye Diseases Incidence Study (CEDIS)12 and the Aravind Comprehensive Eye Survey (ACES).11 Notably, the CGS and CEDIS along with APEDS have used the International Society of Geographical and Epidemiological Ophthalmology (ISGEO) definitions for glaucoma.13 These have standardized the classification for glaucoma in population based studies. Briefly, glaucoma is classified according to three levels of evidence in ISGEO. In category 1 level, both structural and functional evidence are necessary. This requires a cup-disc ratio (CDR) or CDR asymmetry ≥ 97.5th percentile for the normal population or neuroretinal rim width reduced to ≤ 0.1 CDR (between 11 to 1 o’clock or 5 to 7 o’clock) with definite visual field defect consistent with glaucoma. Category 2 needs advanced structural damage (CDR or CDR asymmetry ≥ 99.5th percentile for the normal population) when subject cannot satisfactorily complete visual field test. In Category 3, glaucoma is diagnosed based on IOP≥99.5 percentile for the population in case media haze obscures visualization of optic disc. Being in the same geographical location, APEDS used the CGS normative data for diagnosing glaucoma. Thus while we need to keep in mind the methodology employed to understand study result implications, all studies have given a much needed information in our population.

Methodology of population based studies from south India

The Chennai Glaucoma Study7-10 was a population based prevalence study in subjects 40 years and above and was conducted from 2001-2004. Subjects were enrolled from 5 randomly chosen divisions from Chennai city and 27 contiguous villages from Kancheepuram and Tiruvallur districts. The study used ISGEO criteria to classify subjects with glaucoma and enrolled 3850 subjects from rural and 3934 subjects from urban cohort who were examined at the base hospital. The Chennai Eye Diseases Incidence Study12 was conducted from 2007 to 2010 and re-examined the surviving cohort of subjects after duration of 6 years. A total of 6022 subjects could be contacted/information was available, of whom 590 were not alive. Of the eligible 5432 subjects, 4421 (rural:urban 2510:1911) underwent a similar comprehensive eye examination at the base hospital giving a response rate of 81.3%.

The Vellore Eye Study,2 conducted 140 km away from Chennai, enrolled urban subjects between 30-60 years and was conducted in 1994. A total of 972 subjects were enrolled. A diagnosis of glaucoma required raised IOP with/without typical glaucomatous disc changes and corresponding visual field changes. This was one of first study reports on
glaucoma prevalence from India.

The Andhra Pradesh Eye Disease Study\textsuperscript{6,7} was conducted from 1996-2000. Subjects were enrolled from urban city of Hyderabad and 3 rural districts (Gadavari, Adilabad and Mahabubnagar). Subjects were aged above 40 years and prevalence data was republished for 934 urban and 2790 rural subjects using ISGEO criteria.

The Aravind Comprehensive Eye Survey\textsuperscript{11} was conducted from 1995-1997 and enrolled subjects from 3 rural districts. For glaucoma prevalence, a subset of 5150 subjects aged 40 years and above was included. Primary Open Angle Glaucoma (POAG) was defined as optic disc changes (VCDR>0.8 or narrowest NRR<0.2 or asymmetry >0.2 between eyes) with visual field damage; in those without visual fields, glaucomatous disc damage was considered sufficient for diagnosis.\textsuperscript{11}

### Prevalence of Glaucoma and Ocular Hypertension

#### Primary Open Angle Glaucoma (POAG)

The VES was one of the first studies to report prevalence of POAG as 0.41\% (95\% CI: 0.01-0.81), although it used a different criterion for diagnosis as described.\textsuperscript{1} Both the CGS and APEDS showed an increased prevalence in the urban residence as compared to rural one. The CGS had an urban prevalence of 3.51\% (95\% CI: 3.04-4.0) as compared to 4\% (95\% CI: 2.74-5.25) in APEDS.\textsuperscript{6,8} Similar rates for rural cohort were 1.62\% (95\% CI: 1.42-1.82) and 1.6\% (95\% CI: 1.13-2.06) respectively.\textsuperscript{6,7} The prevalence rates were nearly double in urban cohort at CGS. There were more diabetics and hypertensives in the urban population of CGS,\textsuperscript{8} however no association of these to POAG was noted. The reported prevalence in ACES was 1.7\% (95\% CI: 1.3-2.1).\textsuperscript{11} The lower prevalence in VES may be inherent to the study sample as only 48.5\% of eligible subjects underwent visual fields and the upper age limit of 60 years. Diagnosis of POAG was based on IOP criteria in VES, although glaucomatous visual field defect was mandatory for diagnosis of POAG. Most population based studies have highlighted the fact that a majority of patients with POAG have IOP ≤21 mm Hg. Forty five (52.3\%) of 86 subjects with POAG in ACES had IOP < 21 mm Hg.\textsuperscript{11} On similar lines, majority (67.19\%) of patients in rural cohort of CGS had IOP ≤ 21 mm Hg, although increased prevalence of POAG was noted if IOP> 21 mm Hg.\textsuperscript{6} In APEDS 70.3\% POAG patients had IOP < 22 mm Hg.\textsuperscript{6} The mean IOP in rural cohort of CGS was significantly greater in POAG (17.93± 5.35 mm Hg) as compared to normals (14.29± 3.32 mm Hg).\textsuperscript{7,8}

There is a reported increase in prevalence with age across studies as shown in Table 1. The prevalence of POAG increased from 0.63\% at 40-49 years to 3.25\% to 70 years and above in rural and from 2.25\% to 6.42\% in urban cohort. The Odds for POAG increased exponentially with age and was maximum in over 70 years age group (Table 2).

No gender differences were noted at CGS.\textsuperscript{7,8} ACES noted an increased association with male gender (Odds Ratio [OR] 2.2, 95\% CI: 1.3-3.8), though no other prevalence study notes the same.\textsuperscript{11} No association to gender and myopia were noted in both CGS and APEDS, although ACES reported a significant association with myopia (OR 1.9, 95\% CI: 1.2- 3.9).\textsuperscript{6,8,12} No association of POAG to hypertension or diabetes was noted at CGS and APEDS.\textsuperscript{6,8} Lifestyle changes and/or higher rates of diabetes/hypertension and genetic causes could possibly account for rural urban differences.

Common to all studies was a lack of awareness of their own disease in the population. More than 90\% subjects in most studies were unaware of their disease.\textsuperscript{6,8,11} All except one subject in rural cohort (98.5\%, n=63/64) and 94.1\% subjects (n=127/135) in the urban cohort (n=127) of CGS were diagnosed to have glaucoma in the study.\textsuperscript{7,8} In APEDS, 95.1\% (n=78/82) of the combined cohorts were diagnosed to have POAG in the study.\textsuperscript{6}

#### Primary Angle Closure Glaucoma (PACG)

Varied classification systems especially in angle closure disease have been used in most population based studies. Primary angle closure as defined by ISGEO\textsuperscript{13} is classified as: (1) primary angle closure suspect (PACS): eye where >180 degree of posterior trabecular meshwork is not visible on gonioscopy; (2) primary angle closure (PAC): PACS with peripheral anterior synechiae (PAS); (3) primary angle closure glaucoma (PACG): PACS with glaucoma as defined above. VES defined PACG as acute or chronic.\textsuperscript{5} The latter was appositional (with raised IOP) or synechial (with PAS). Glaucomatous disc or visual fields were not mandatory for diagnosis of angle closure glaucoma. The prevalence of PACG was 4.32\% (95\% CI: 3.01-5.61) in VES and all were of chronic form.\textsuperscript{2} This prevalence was several times that of POAG and highlighted the high rates of angle closure, though the rates will be different for the currently used ISGEO system.

The rural cohort in CGS had prevalence of 0.87\% for PACG (95\% CI: 0.58-1.16), 0.71\% for PAC (95\% CI: 0.45-0.98) and 6.27\% for PACS (95\% CI: 5.51-7.03).\textsuperscript{9} The urban cohort had 0.88\% prevalence of PACG (95\% CI: 0.60-1.16), 2.75\% PAC (95\% CI: 2.01-3.49) and 7.24\% of PACS (95\% CI: 6.58-
The rural cohort in APEDS showed a prevalence of 0.7% for PACG (95% CI: 0.4-1.1), 0.2% for PAC (95% CI: 0.02-0.35) and 1.5% for PACS (95% CI: 1.1-2.0). The urban cohort had 1.8% prevalence of PACG (95% CI: 0.88-2.70), 0.8% PAC (95% CI: 0.2-1.4) and 3.5% for PACS (95% CI: 2.3-4.5).6 (Table 3-4)

ACES reported a low prevalence of angle closure glaucoma.11 However, their definition of ‘occludability’ was not defined. There may be differences in gonioscopic interpretation by an optometrist and a trained ophthalmologist. This may partly account for the differences noted.

The rural cohort had a female preponderance (3 times) of PACG whereas no differences were noted in urban cohort of CGS. The authors note that though females have a higher risk of angle closure glaucoma, the observed difference in urban cohort may be due to a small sample size (n=34).10 The higher rates for PAC in the urban cohort were attributed to the older age (54.8 vs. 53.8 years).10 Thus the rural population were masked from the effects of PAC due to earlier age at cataract surgery. Diabetes as a risk factor was noted in the urban cohort only. No association to hypertension was noted in both cohorts.8,10

All patients in rural cohort of CGS (n=34) were unaware that they had glaucoma.9 One (2.94%) was bilaterally blind, with none unilaterally blind. In the urban cohort, 14.7% (n=5) were previously diagnosed; of these 2 were diagnosed as POAG elsewhere.10 Two (5.9%) were bilaterally and 3 (8.8%) were unilaterally blind due to PACG.10 Only 2 of the 6 PACG urban cohort patients in APEDS had undergone PI prior to their participation in the study, the others were managed as open angle glaucoma.6 Nearly 82.8% subjects with PACG were undetected at the time of the study.6

There were differences in prevalence rates for PACS and PAC in APEDS as compared to CGS. The differences may have resulted due to different gonioscopic lenses used and/or subjective interpretation of same or an actual difference (APEDS used NMR-K two-mirror lens, CGS used 4 mirror Sussmann lens. Difference in skill sets of examiners could account for this difference. Gonisocopy in the CGS was performed by trained glaucoma specialists and could explain the higher detection rates for angle closure disease. Of the 5 subjects previously diagnosed to have PACG in CGS, 2 were diagnosed as POAG elsewhere.10 Of the 34 subjects diagnosed to have PACG, one was bilaterally blind in rural and 2 subjects (5.9%) were bilaterally and 3 (8.8%) were unilaterally blind in urban cohort. All patients in rural cohort of CGS (n=34) were unaware that they had glaucoma.9

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Ocular Hypertension (OHT)

Varied reported prevalence of OHT in the population occurs largely due to differing definitions for OHT. Prevalence in VES was 3.08 % (95% CI: 1.98-4.19%) which was defined as IOP>21 mm Hg with open angles and no evidence of glaucomatous optic neuropathy or visual field changes.2 Prevalence in APEDS was 0.42% (n=7, 95% CI: 0.11%–1.12%) where OHT was defined as IOP ≥ 22 mm Hg.6 ACES reported prevalence of 1.1% (n=57, 95% CI: 0.84-1.4%).11

Secondary and pseudoexfoliation glaucoma

In ACES the prevalence of secondary glaucoma was 0.3%.11 The age- and gender-adjusted prevalence of secondary open-angle glaucoma in APEDS was 0.11% (95% CI.0.01–0.46) in participants ≥ 30 years age.5 In rural cohort of CGS, the prevalence of glaucoma in aphakia/pseudophakia was 1.38% (37 aphakes, 17 pseudophakes).14 Blindness (defined as best corrected visual acuity (BCVA) <2/40 and/or constriction of visual field to <10° from fixation) was seen in 22.2% subjects with glaucoma (constituting 2.49% of aphakic/pseudophakic subset). Aphakia and IOP were noted as risk factors for glaucoma in multivariate analysis. Aphakes had significantly higher IOP than pseudophakes and had more proportion of subjects with pseudoexfoliation, possibly reflecting a complicated cataract surgery. These rates, the authors concluded, required a need to concentrate on quality of surgery and follow up for patients undergoing cataract surgery.

Pseudoexfoliation (PXF) is a known risk factor for glaucoma and its reported prevalence from India is between 3-6%.6,15-17 The mean age in PXF subjects was higher by a decade in CGS and ACES. Of the 108 (16.7%) subjects with PXF in CGS, 14 (13%) had glaucoma.15 In APEDS, glaucoma was seen in 3.02% subjects with PXF and was predominant with outdoor activities.11 Prevalence of PXF in ACES was 6% and glaucoma was seen in 7.5% of these subjects.17

Incidence of Glaucoma

Till recently, VES was the only study providing some
evidence on the incidence of glaucoma in India. It gave some insight on the rates of conversion of PACS to PAC and PAC to PACG. At 5 years, 11 of the 50 subjects with PACS progressed to PAC (22%, 95% CI: 9.80-34.2). Progression was noted in bilateral PACS. Of the original 37 PAC patients, 28 were re-examined. Eight of these (28.5%, 95% CI: 12-45%) progressed to PACG. There was a greater risk of progression in bilateral PAC. Seven of the 14 bilateral and 1 out of 14 unilateral cases progressed to PACG. Progression was noted in 1 out of 9 (11.1%) who underwent peripheral iridotomy as compared to 7 out of 19 subjects (36.8%) who refused. No case of blindness due to glaucoma or acute angle closure were noted.²⁰

Twenty one of 28 OHT were re-examined at 5 years in VES. Among untreated OHT, 17.4% (95% CI: 1.95-32.75) progressed to POAG. One patient from normal cohort also progressed to POAG. Thus the relative risk (RR) of POAG in untreated OHT was noted as 19.1 (95% CI: 2.2-163.5).²⁰

Recently, the results of six year incidence of primary angle closure disease in Chennai Eye Disease Incidence Study were published. Subjects with angle closure disease at baseline and bilateral aphakia/pseudophakia were excluded. Incident angle closure disease was noted in 134 (4.0%, 95% CI: 3.3-4.7) subjects of the eligible 3350 subjects. Of these 88 (2.6%) were PACS, 37 (1.1%) had PAC and 9 (0.3%) had PACG. Significant risk factors associated were a higher IOP, smaller axial length, shallow anterior chamber depth, increased lens thickness, anteriorly placed lens and hyperopia. Biometric parameters were associated with a higher risk of angle closure disease. A relative higher incidence of primary angle closure disease of 14.2% (95% CI: 9.7-18.5) in subjects with anterior chamber depth less than 2.5mm and of 18.5% (95% CI: 6.3-30.7) in axial length less than 21 mm was noted. In thicker lenses more than 5.5 mm, risk of primary angle closure disease was 10.1% (95% CI: 6.0-14.3). An interesting observation was a decline in angle closure disease in subjects above 60 years in concurrence with higher rates of cataract surgery in this age group.²³

Implications for the population
Quigley et al. estimated an overall worldwide prevalence of glaucoma to be 60.5 million in 2010 and increasing to 79.6 million by 2020. However, glaucoma affects Asians disproportionately to that in Western population with an increased propensity for angle closure disease as compared to Caucasians. It is estimated that 87% of angle closure throughout the world would be contributed by Asians. An estimated 11.2 million people are affected with glaucoma in India.²¹

These facts are especially important for our population as the higher rates for angle closure glaucoma are also associated with a higher risk of blindness in India. Blindness was more due to angle closure (20% for both rural and urban) than for open angle glaucoma in APEDS (11.1% rural, 2.7% urban). CGS also reported a higher blindness for angle closure glaucoma (5.9% vs 1.5%). More than 90% subjects were unaware of their disease in CGS. This is even when we expect the urban population to have better access to medical care and a greater awareness on these disorders.

There are some fundamental questions which we need to answer with the available evidence. This is especially important of glaucoma being a blinding, asymptomatic disease and without a perfect way to screen for glaucoma in the population. Intraocular pressure in itself has a low sensitivity and specificity for diagnosis. Besides, glaucoma remaining undiagnosed despite an ophthalmic consultation done in past or was misdiagnosed was apparent in these studies.

In essence, we need a stepwise approach to effectively diagnose and treat the enormous amount of undiagnosed glaucoma in the population. The focus could start from an effective case detection to pick at least high risk cases or those with moderate to advanced glaucoma and gradually shifting focus to early glaucomas and/or ocular hypertensives. The best way forward initially is to effectively look for glaucoma during planned cataract surgery and to provide reasonable and effective treatment for same. An eye examination during cataract surgery may be the first and probably the last interaction the rural population has with an ophthalmologist and the opportunity needs to be used to its maximum use. Blood relatives of glaucoma subjects should be counselled for a comprehensive eye examination and an increased awareness and knowledge of glaucoma to the population is necessary. The high rate of blindness in subjects with glaucoma clearly undermines the need for same. Nearly 20.9% (n=18) were blind in at least one eye, of these 6 had bilateral blindness in ACES. An overemphasis on using IOP as a diagnostic criterion for glaucoma should be discouraged. All facilities providing cataract surgeries should be encouraged to maintain hospital records for random scrutiny and data so that possible loopholes in system can be plugged.

We also need to have an effective training mechanism. This possibly needs to start at the basic training level for postgraduate courses. Any postgraduate degree in ophthalmology should ensure an individual has the capacity and skills for a comprehensive eye examination. These
can partly be addressed by Continuing Medical Education (CME) and skill transfers in places needing support for same. Fortunately the basic infrastructure required is less and requires a good tonometer (Goldmann’s Applanation), gonioscope (preferably indentation) and stereoscopic disc examination by a 90D or 78D lens. In addition, basic visual field testing is preferable.

Training modules should focus on postgraduate colleges and ensure that the faculty has the necessary skills to impart students. Some amount of basic funding and equipment should be mandatory for all postgraduate colleges. However, it is not essential to have the armamentarium kept under lock and key for as and when use. Training optometrists and vision technicians for basic glaucoma diagnosis is mandatory. In future, technology is expected to play a larger role in medicine. Teleophthalmology and distance learning may help improve the lacunae and may reduce the borders to receiving good medical care at reach.

Conclusions
The burden of glaucoma is huge and undetected according to available evidence and is expected to rise further with the aging population. Training skills are essential to diagnose and treat glaucoma before visual morbidity sets in and a significant impact on quality of life occurs. Otherwise, millions will continue to suffer with this blinding disease.

References