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Title: Incidence of primary open angle glaucoma in the Andhra Pradesh Eye Disease Study (APEDS)

Running Head: 15-year incident POAG in APEDS

Authors:

Nikhil S. Choudhari, DNB,[1,2]
Rohit C Khanna MD,[2-5]
Srinivas Marmamula Ph.D.,[2,3,6]
Asha Latha Mettla MSc,[2,3]
Pyda Giridhar Ph.D.,[2,3]
Seema Banerjee B.Opt,[2,3]
Konegari Shekhar DOA,[2,3]
Subhabrata Chakrabarti Ph.D.,[3]
Gudlavalleti VS Murthy MD,[7,8]
Clare Gilbert FRCOphth,[8]
Gullapalli N Rao MD[2,3] and
Andhra Pradesh Eye Disease Study Group*

Institute Affiliation:

1. VST Glaucoma Centre, Dr. Kallam Anji Reddy Campus, L V Prasad Eye Institute, Banjara Hills, Hyderabad, India.
2. Allen Foster Community Eye Health Research Centre, Gullapalli Pratibha Rao International Centre for Advancement of Rural Eye care, L V Prasad Eye Institute, Kismatpur Road, Himayathsagar, Telangana State, India
3. Brien Holden Eye Research Centre, L V Prasad Eye Institute, Banjara Hills
4. School of Optometry and Vision Science, University of New South Wales, Sydney, Australia
5. University of Rochester, School of Medicine and Dentistry, Rochester, NY, USA
6. Wellcome Trust / Department of Biotechnology India Alliance, L V Prasad Eye Institute, Hyderabad, India
7. Indian Institute of Public Health, Madhapur, Hyderabad, India,

8. International Centre for Eye Health, Department of Clinical Research, London School of Hygiene & Tropical Medicine, London, United Kingdom

*Andhra Pradesh Eye Disease Study Group: Maneck Nicholson MD,[2] Raghava JV MD,[2] Sahitya T MD,[2] Lavanya EY MD,[2] Hira B Pant PGDBDM,[4] Ritu Dixit, MS,[3] Goutham Pyatla,[3] Alice Arati Anthony[3], Syed Hameed[3], Samir Bera[3], Sneha Kumari[3] and Inderjeet Kaur PhD[3]

Corresponding Author:

Rohit C Khanna,

Full Postal Address: L V Prasad Eye Institute, Dr. Kallam Anji Reddy Campus, L V Prasad Marg, Banjara Hills, Hyderabad 500 034 Andhra Pradesh, India

Phone: 91-40-3061 2646 (Office), Fax: 91-40-2354 8271

E-Mail: rohit@lvpei.org

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ABSTRACT

Background: To report 15-year incidence rate of primary open angle glaucoma (POAG) in the Andhra Pradesh Eye Disease Study (APEDS)

Methods: A population-based longitudinal study was carried out at three rural study sites. Phakic participants aged ≥ 40 years who participated at baseline (APEDS I) and the mean 15-year follow-up visit (APEDS III) were included. A comprehensive ophthalmic examination was performed on all participants. Mean intraocular pressure (IOP) was average of IOPs of right and left eyes. The definition of glaucoma was based on the International Society of Geographical and Epidemiological Ophthalmology (ISGEO) classification. The main outcome measure was incidence of POAG during the follow-up period in participants without glaucoma or suspicion of glaucoma at baseline.

Results: Data from the available and eligible participants from the original cohort (1241/2790; 44.4%) were analyzed. The mean age (standard deviation) of participants at baseline was 50.2 (8.1) years; 580 (46.7%) were men. Thirty-six participants developed POAG [bilateral in 17 (47.2%)] over 15 years. The incidence rate of POAG per 100-person years (95% confidence interval) was 2.83 (2.6, 3.08). Compared to baseline, the reduction in mean IOP [median (range) mm Hg] was -0.75 (-7.5, 9) in participants with incident POAG and -2.5 (-14.5, 14.5) in those without. The inter-visit difference in mean IOP was a significant risk factor on logistic regression analysis.

Conclusion: We report the long-term incidence of POAG in rural India. A longitudinal change in IOP, specifically a less pronounced reduction in IOP with increasing age, was a novel risk factor.

INTRODUCTION

Glaucoma may be defined as an intraocular pressure-dependent optic neuropathy with progressive loss of neural tissue and consequent visual field defects. It is one of the leading causes of blindness. The global, age-standardized prevalence of glaucoma in populations aged ≥40 years was estimated to be 3·5% in 2013,[1] affecting 64 million people aged 40-80 years. Nearly 70% of those affected have primary open angle glaucoma (POAG). With increasing longevity, the number with glaucoma is projected to increase to over 110 million by 2040.[2] The prevalence of POAG is highest in Africa and lowest in Asia.[2] The pathogenesis of POAG is not fully elucidated and is likely to entail genetic factors, and mitochondrial dysfunction is also being explored as a pathogenic mechanism.[1] Currently the only modifiable risk factor for POAG is intraocular pressure (IOP). Other risk factors include ethnic group, a positive family history of glaucoma, older age and high myopia.[1] In addition, some non-communicable diseases are associated with POAG.[3]

Prevalence and incidence studies provide complementary information about the epidemiology of a disease. While the former estimates the burden of a disease, the latter can provide information about the etiology of a disease and its outcome. However, there are only a few population-based studies on the incidence of POAG,[4-12] including studies in India[4] or of populations of Indian origin.[5]

The Andhra Pradesh Eye Disease Study (APEDS) is a large population-based cohort study in southern India. The baseline study, APEDS I (1996-2000) assessed the prevalence of eye diseases, the magnitude of vision impairment and its effect on quality of life, and barriers to accessing eye health care services.[13] The study had urban and rural sites. The next phase, APEDS II (2009-2010) estimated migration and mortality rates by tracing participants examined in APEDS I. It also identified participants willing to be re-examined.[14] APEDS III (2012-2016) re-examined rural participants about 15 (range 13-17) years after the baseline. We

could not identify the urban site because of development.[14] In this publication, we report the incidence of POAG and its risk factors.

MATERIALS AND METHODS

The study adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of the Hyderabad Eye Research Foundation, L V Prasad Eye Institute (LVPEI), Hyderabad, India and the London School of Hygiene & Tropical Medicine (LSHTM), London. Written informed consent was obtained from all participants.

Methodology of APEDS has already been published in detail,[13,14] and relevant information is summarised here. At baseline, 10,293 participants were examined (7,771 in three rural clusters and 2,522 in one urban cluster in the then undivided Andhra Pradesh state).[14] The second phase of feasibility (APEDS II), traced 5,447 (70.1%) of the original participants in the three rural areas. In APEDS III, the rural areas were revisited after a mean of 15 years from baseline to determine the incidence of eye diseases when 5395 participants (69.4% of the original rural cohort) were re-examined using the same methodology.[14] The study locations were visited as follows: 2012/2013, Thoodukurthy village, Mahbubnagar district; 2013/2014, Mudhole village, Adilabad district; and 2015/2016 Tanuku village, West Godavari district.

We collected socio-demographic, behavioral and past medical history data at baseline (APEDS I) and follow-up (APEDS III).[13,14] Comprehensive eye examinations were performed at each site in eye health care facilities established by LVPEI as a part of its multi-tiered eye health care network in India. The team was trained on the study protocol. There were four clinical investigators in the study but only one was present at any given time. All clinical investigators underwent inter-observer agreement assessment with the principal investigator (PI, an experienced glaucoma specialist) for lens grading, gonioscopy and optic disc evaluation before joining the study. The vertical cup-to-disc ratio (CDR) was assessed subjectively in units of 0.05, with a kappa coefficient ranging between 0.69 and 0.81.[15]

Visual acuity (VA) testing was followed by streak retinoscopy and subjective refraction by a trained optometrist or a vision technician when the presenting distance or near VA exceeded 0.0 on Logarithm of minimum angle of resolution chart. We measured IOP using slit-lamp mounted Goldmann applanation tonometer (Carl Zeiss Meditec, Inc). Tonometry was repeated when the initial reading exceeded 21 mm Hg. Dark room gonioscopy was performed with a short and narrow light beam (1-2 mm) to avoid pupil constriction. We used NMR-K 2-mirror lens (Ocular Instruments, Bellevue, WA) analogous to baseline examination followed by a Sussman 4 mirror lens (Volk, OH, USA) in APEDS III. The angle was defined as open when the pigmented posterior trabecular meshwork was visible in >180° of the angle circumference in the primary position without manipulation under dark room condition. Eyes with an occludable angle underwent laser iridotomy prior to pupil dilation. We examined the optic disc by slit-lamp biomicroscopy using a 78-D (Volk, OH, USA) lens. Indirect ophthalmoscopy was performed to examine the entire fundus using a 20-D (Volk, OH, USA) lens. Participants who were unable to visit the study site were examined at home using similar methods.[14]

We performed automated perimetry using the threshold central 24-2 strategy (stimulus size III) on a Humphrey Visual Field (HVF) analyzer (Humphrey Instruments Inc., San Leandro, CA) on all participants with or suspected to have glaucoma.[14] The additional criteria to perform automated perimetry were IOP ≥22 mm Hg in one or both eyes and IOP difference between the two eyes being ≥6 mm Hg. The test was repeated in case of unreliability. A visual field was called glaucomatous when it correlated with optic disc damage and met ≥2 of Anderson's criteria. Ocular biometry diagnostic procedures were added in APEDS III. Corneal thickness, anterior chamber depth and lens thickness were measured using a portable pachymeter (Tomey SP-100, Tomey Corporation, Noritakeshinmachi, Nagoya, Japan). Axial

length was measured using A Scan Ultrasound Biometry (Bio Medix Echo rule 2 serial no. 211887).[14]

Definition of glaucoma

The definition of glaucoma was based on the International Society of Geographical and Epidemiological Ophthalmology (ISGEO) classification.[16] We used normative data from the Chennai Glaucoma Study (CGS) for the 97.5th and 99.5th percentile cutoffs for IOP and cup-to-disc ratios.[17] The rationale for using CGS data for cutoffs, and the three levels of evidence to make the diagnosis of glaucoma in survey settings were explained earlier.[18]

The incidence of POAG was defined as the development of POAG during follow up in at least one eye among participants who were phakic and who did not have glaucoma or suspicion of glaucoma at baseline (APEDS I). Hyperopia and myopia were defined as spherical equivalent ±0.50 D or greater in a phakic eye. Systemic hypertension (HTN) was considered present if a participant had a history of high blood pressure diagnosed by a physician and/or was currently taking anti-hypertensive medication and/or had a blood pressure of ≥140/90 mm Hg. Diabetes mellitus (DM) was considered to be present if there was a positive history and/or diabetic retinopathy was detected on clinical examination.

Statistical analysis

Shapiro-Wilk test was used to check normality of data distribution. Age at baseline (APEDS I) was divided into 3 terciles (40-49, 50-59 and ≥60 years). Similarly, central corneal thickness (CCT) was divided in to 3 terciles (<482, 482-528 and >528 microns). Mean IOP for the person was calculated by averaging IOP measurements in right and left eyes. Intraocular pressure difference was mean IOP measured in APEDS III minus that in APEDS I. The association of POAG with baseline risk factors, such as age, IOP and systemic hypertension as well as difference in right and left eye mean IOP between two follow up times and CCT was evaluated first using univariate analysis, followed by multivariate analysis with logistic regression.

Variables which achieved statistical significance in the univariate analysis at the P <0.05 level, or were considered important on the basis of published literature or our clinical insight, were included in the multivariate analysis. Model selection was performed using the Akaike Information Criterion (AIC). The goodness of fit for logistic regression models was checked using the Hosmer–Lemeshow test, and multi-collinearity was checked by calculating the variance inflation factor (VIF). Statistical analyses were performed using Stata 12.1 (StataCorp, College Station, TX). A two-sided P value of <0.05 was considered statistically significant.

RESULTS

A total of 2,790 participants aged ≥40 years were examined in APEDS I. After a mean follow up of 15 years, 1,470 (52.6%) were re-examined, 1241 (84.4%) of whom met the inclusion criteria for the current study **(Figure 1)**. Baseline demographic characteristics of participants, non-participants and non-responders (participants who migrated, could not be traced or refused to participate) have been published.[15] Non-participants included non-responders and those who had died since APEDS I.

Overall, 36 participants developed POAG over 15 years (**Table 1**). The 15-year cumulative incidence of POAG (95% confidence interval) was 2.9% (2.03, 3.99) or about 0.2% per year, assuming a linear incidence. Incident POAG was bilateral in 17 (47.2%) participants and unilateral in 19 (52.8%). The diagnosis of POAG was based on ISGEO classification level 1 evidence (i.e., structural and functional evidence) in 21 (58.3%) participants and level 2 evidence (i.e., advanced structural damage with unproved visual field loss) in 15 (41.6%) participants.

The IOP was >21 mm Hg at the follow up visit (APEDS III) in five eyes of three participants with unilateral incident POAG; the fellow eye in two participants had ocular hypertension. Participants with or without incident POAG differed with respect to the

difference in mean of right and left eye IOPs between the two follow up times **(Table 2).** The regression analysis did not reveal any additional risk factor **(Table 3)**. The Hosmer-Lemeshow test indicated a good fit of the regression model (P= 0.2).

DISCUSSION

Our population-based study of a rural cohort of a south Indian population reports a mean 15-year incidence rate (95% CI) of POAG of 2.83 (2.6, 3.08) per 100 person years. Assuming a linear incidence, the cumulative incidence of POAG in our study is about 0.2% per year. A less marked reduction in mean IOP of both eyes between follow up times was a significant risk factor.

Population-based studies show that the highest incidence of POAG is in populations of African descent,[6,7,12] which is consistent with prevalence studies **(Table 4)**. Chronic diseases like glaucoma can have a low incidence in aging populations despite a high prevalence, e.g., POAG incidence study from Australia and the Netherlands.[8] However, comparison of age-standardized data is needed to confirm this observation.

Apart from ancestry, the geographical variation in incidence of POAG could be attributed to methodological differences across studies; the most important being whether participants who were POAG suspects at baseline were included or not. For example, in the Melbourne Visual Impairment Project, the incidence of POAG was five times higher [2.7% (95% CI: 1.8, 3.7)] compared with 0.54% per year, if suspects were included in the analysis.[8] Other methodological differences include how POAG was defined, including the use of relevant normative data, the methods used for clinical examination; such as IOP measurement and visual field analysis, and the steps to achieving consensus on the diagnosis of POAG.

The cumulative incidence of POAG in our study is similar to that reported in the Indian population in Singapore[5] but is lower than in the rural cohort of Chennai Eye Disease Incidence Study (CEDIS).[4] The latter studied the same ethnic group as APEDS. However, the age-

specific incidence rate in our study among those aged 40-49 and 50-59 years is higher than in the same age-groups but was lower amongst those aged 60 years and above in the other two studies.[4,5] The latter likely reflects a shorter life expectancy among rural residents in India compared with Indians living in Singapore. The relatively low number of participants aged 60 years and above in our study may explain why age was not a significant risk factor, unlike all other studies.[4-12,19]

We observed a significant reduction in the mean IOP of right and left eyes between APEDS I and APEDS III, despite adjusting for CCT. Similar findings have been reported in other studies of Asian populations[20-25] but not in Caucasians or populations of African descent.[26-28] In our study, the longitudinal difference in mean IOP of right and left eye was less pronounced amongst participants who developed POAG than those who did not ($P < 0.1$) indicating that longitudinal change in IOP is a risk factor for POAG. The relationship between age and IOP may be explained by a reduction in aqueous humour production and/or a decrease in the resistance to aqueous outflow, but this requires further investigation. Thirty-three (91.6%) participants with incident POAG in our study had an IOP of ≤ 21mm Hg, which is comparable to CEDIS (77%)[4] and the Indian population in Singapore (85%),[5] but is unlike the black population (41.6%).[7] An important caveat is that IOP was only measured once and not throughout the day to identify diurnal variation.

Central corneal thickness can vary across populations. An inverse relationship between odds of incident POAG and CCT was seen in our study. Nevertheless, low statistical power did not allow us to sufficiently explore the role of CCT as a risk factor. Central corneal thickness wasn't a significant risk factor in other studies of Asian populations,[4,5] unlike in Black populations.[12,29] However, whether the relationship between CCT and POAG is due to underestimation of IOP in thin corneas or CCT is an independent risk factor, reflecting altered

biomechanical and structural characteristics of ocular tissues, has not been conclusively determined.

Our study has a few limitations. We did not have information on family history of POAG. It is attributable to a limited access to healthcare in rural India. Intraocular pressure is known to vary during the 24-hour cycle and between visits. Multiple IOP readings over the day of examination can provide a better IOP profile.[30] Even so, it would have been resource intensive for a population-based study. This factor is unlikely to have had a significant impact on the incidence rate as the diagnosis of POAG was largely based on evidence of structural damage to the optic disc. We did not perform ocular biometry at baseline but added it in APEDS III. Yet, considering the low rate of change in CCT over time,[31] not having CCT data at baseline is unlikely to affect the outcome of our study. The number of participants with diabetes was low in our study as we relied on self-reporting of diabetes and performed blood sugar testing only on selected participants.[14] This limited our ability to explore diabetes as a risk factor for POAG. The risk factors were fixed at baseline, but in real life, these factors can vary over time. The size of the at-risk population was least in our study compared to the other incidence studies on POAG,[4-11] with an exception.[12] However, ours is the longest-ever study on the incidence of POAG, and the fundamental reason for non-participation was mortality (figure 1). We have published the incidence of mortality in APEDS.[32] We compared mean IOP of right and left eye instead of IOP in the worse or affected eye or a randomly selected eye. This is because the fellow eye in participants with unilateral incident POAG may not be normal since adaptive optics has shown damaged RNFL at subclinical stage of glaucoma.[33]

Conclusion

This long-term population-based study reports the incidence rate of POAG in the rural population of southern India. The results indicate longitudinal change in IOP, possibly due to altered aqueous humour dynamics with advancing age as a novel risk factor. The rate of

incident glaucoma was relatively low, such that the power to analyze risk factors with more modest effect sizes is decreased. Nevertheless, studies on the incidence of POAG are limited and ours might be a valuable addition to the literature. We recommend that a standardized methodology be used for future studies to enable comparisons.

Supplementary information is available at Eye Journal's website.

Author Contribution Statement:

NSC was responsible for data analysis, drafted the manuscript, approved the final version and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. RCK conceived and designed the work that led to the submission, acquired data, and played an important role in interpreting the results, revised the manuscript, approved the final version and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. CG played an important role in interpreting the results, revised the manuscript, approved the final version and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All the remaining authors acquired data, played a role in interpreting the results, revised the manuscript, approved the final version and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data availability statement:

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

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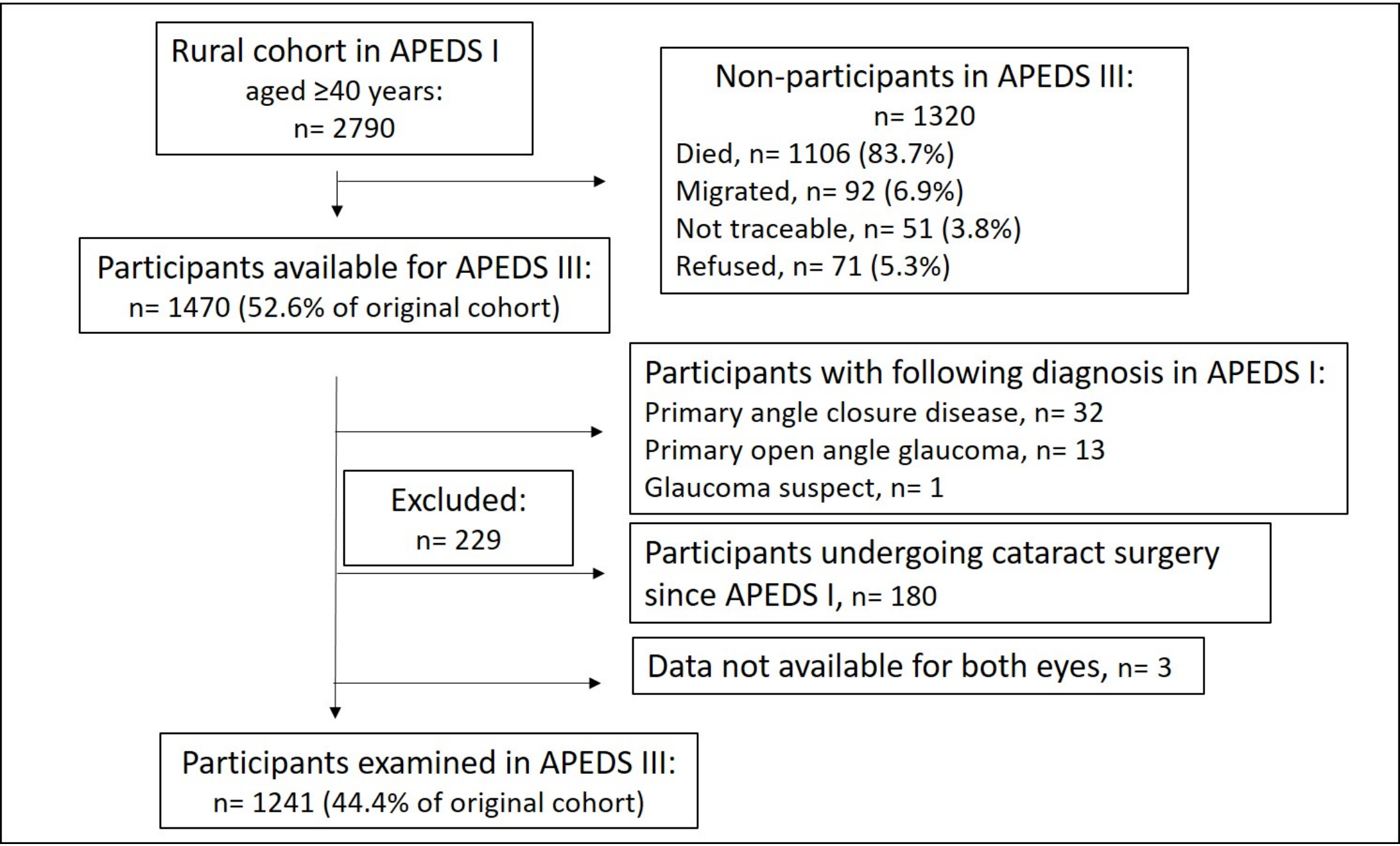
Rural cohort in APEDS I
aged ≥40 years:
n= 2790
Non-participants in APEDS III:
n= 1320
Died, n= 1106 (83.7%)
Migrated, n= 92 (6.9%)
Not traceable, n= 51 (3.8%)
Refused, n= 71 (5.3%)
Participants available for APEDS III:
n= 1470 (52.6% of original cohort)
Participants with following diagnosis in APEDS I:
Primary angle closure disease, n= 32
Primary open angle glaucoma, n= 13
Glaucoma suspect, n= 1
Excluded:
n= 229
Participants undergoing cataract surgery since APEDS I, n= 180
Data not available for both eyes, n= 3
Participants examined in APEDS III:
n= 1241 (44.4% of original cohort)

Table 1: Incidence of POAG by age at baseline in males and females

Age group (years)	Male		Female		Total		Incidence rate/100 person years (95% CI*)
	At risk	n (%) (95% CI*)	At risk	n (%) (95% CI*)	At risk	n (%) (95% CI*)	
40 - 49	325	8 (2.46) (1.06, 4.79)	379	11 (2.9, 1.45, 5.13)	704	19 (2.69) (1.63, 4.18)	2.73 (2.42, 3.06)
50 - 59	175	8 (4.57) (1.99, 8.8)	187	5 (2.67) (0.87, 6.12)	362	13 (3.59) (1.92, 6.06)	3.4 (2.93, 3.93)
≥ 60	80	2 (2.5) (0.3, 8.74)	95	2 (2.1) (0.25, 7.39)	175	4 (2.28) (0.62, 5.74)	2.1 (1.58, 2.73)
Total	580	18 (3.1) (1.84, 4.86)	661	18 (2.72) (1.62, 4.26)	1241	36 (2.9) (2.03, 3.99)	2.83 (2.6, 3.08)

*CI: Confidence Interval

Table 2: Comparison of participants with or without incident POAG

Variable	**Participants** 1241 n (% or Range)	**Without POAG** 1205 (97.1%) n (% or Range)	**With POAG** 36 (2.9%) n (% or Range)	**P value**
Study center, n (%)				
Mahbubnagar	488 (39.3)	471 (96.5)	17 (3.4)	
Adilabad	379 (30.5)	368 (97.1)	11 (2.9)	0.5
West Godavari	374 (30.1)	366 (97.8)	8 (2.1)	
Age Group (years), n (%)				
40- 49	704 (56.7)	685 (97.3)	19 (2.7)	
50- 59	362 (29.1)	349 (96.4)	13 (3.5)	0.62
≥60	175 (14.1)	171 (97.7)	4 (2.2)	
Male sex, n (%)	580 (46.7)	562 (96.9)	18 (3.1)	0.69
Myopia > ±0.50 D spherical equivalent, n (%)	305 (24.5)	296 (97)	9 (2.9)	0.95
Hyperopia > ±0.50 D spherical equivalent, n (%)	206 (16.6)	197 (95.6)	9 (4.3)	0.16
Baseline Mean IOP in mm Hg Median (Range)	Missing 16[1] 15.5 (8, 20)	15.5 (8, 20)	15.5 (11, 19.5)	0.85 (MW)
Difference in mean IOP between APEDS III and APEDS I (mmHg) Median (Range)	Missing 74[1] -2.5 (-14.5, 14.5)	-2.5 (-14.5, 14.5)	-0.75 (-7.5, 9)	**<0.01** (MW)
Central corneal thickness, APEDS III, right eye (µm), n (%)	Missing 62[1]			
>528	291 (24.6)	283 (97.2)	8 (2.7)	0.44
482 - 528	600 (50.8)	584 (97.3)	16 (2.6)	
<482	288 (24.4)	276 (95.8)	12 (4.1)	
Axial length, APEDS III, right eye (mm) Median (Range)	Missing 188[1] 22.5 (18.5, 28.6)	22.5 (18.5, 28.6)	22.7 (20.18, 24.92)	0.31
Body mass index (kg/m^2), n (%)	Missing 27[2]			
18.5 – 24.99	599 (49.3)	583 (97.3)	16 (2.6)	
<18.5	502 (41.3)	485 (96.6)	17 (3.3)	
25 – 29.9	91 (7.5)	90 (98.9)	1 (1.1)	0.61
≥30	22 (1.8)	21 (95.4)	1 (4.5)	
Systemic hypertension, n (%)	Missing 21[2] 451 (36.9)	442 (98)	9 (2)	0.16
Diabetes mellitus, n (%)	12 (0.9)	12 (100)	0	0.54
Smoking status, n (%)				
Never	777 (62.6)	758 (97.5)	19 (2.4)	
Past	80 (6.4)	78 (97.5)	2 (2.5)	0.36
Current	384 (30.9)	369 (96)	15 (3.9)	

Alcohol consumption, n (%)				
Never	711 (57.2)	689 (96.9)	22 (3)	0.69
Past	74 (5.9)	73 (98.6)	1 (1.3)	
Current	456 (36.7)	443 (97.1)	13 (2.8)	
Education level (years), n (%)				
No education	801 (64.5)	774 (96.6)	27 (3.3)	0.18
Education (school or higher)	440 (35.4)	431 (97.9)	9 (2)	

POAG: Primary open angle glaucoma, M. Nagar: Mahabubnagar, IOP: Intra-ocular pressure; MW: Mann Whitney

All the risk factors were assessed at the baseline unless stated otherwise.

1: Not missing from any participant with incident POAG

2: Missing in one participant with incident POAG

Table 3: Logistic regression to assess the association between incident Primary Open Angle Glaucoma and risk factors

Variable	**Sub-Variable**	**Univariate Regression**		**Multivariate Regression**	
		Odds Ratio (95% CI)	P value	Odds Ratio (95% CI)	P value
Study Center	Mahbubnagar				
	Adilabad	0.82 (0.38, 1.78)	0.63		
	West Godavari	0.6 (0.25, 1.41)	0.24		
Age group	40 - 49	1.0			
	50 - 59	1.34 (0.65, 2.75)	0.42	1.29 (0.6, 2.78)	0.51
	60 and above	0.84 (0.28, 2.51)	0.76	0.82 (0.22, 2.99)	0.77
Male sex		1.14 (0.58, 2.22)	0.69	1.23 (0.6, 2.52)	0.55
Myopia, n (%)		1.02 (0.47, 2.2)	0.95	0.83 (0.34, 1.99)	0.68
Hyperopia, n (%)		1.7 (0.78, 3.68)	0.17		
Mean IOP (APEDS I)		0.96 (0.81, 1.14)	0.72		
IOP difference (Difference in mean IOP, APEDS III minus APEDS I)		1.17 (1.07, 1.28)	**<0.01**	1.15 (1.05, 1.27)	**<0.01**
Central corneal thickness (Microns) of Right Eye (APEDS III)	>528	1.0			
	482 - 528	0.96 (0.4, 2.29)	0.94	1.45 (0.54, 3.86)	0.45
	<482	1.53 (0.61, 3.82)	0.35	2.57 (0.91, 7.25)	0.07
Axial Length of Right eye (APEDS III)		1.19 (0.83, 1.72)	0.33		
BMI	18.5 – 24.99	1.0			
	<18.5	1.2 (0.59, 2.42)	0.6	1.12 (0.53, 2.34)	0.75
	25 – 29.9	0.39 (0.05, 3)	0.36	0.42 (0.05, 3.32)	0.41
	≥30	1.8 (0.22, 14.3)	0.57	2.32 (0.26, 20.11)	0.44
Systemic Hypertension		0.58 (0.27, 1.25)	0.16	0.62 (0.27, 1.41)	0.25
Diabetes Mellitus		1.0			
Smoking Status	Never smoker	1.0			
	Past smoker	1.02 (0.23, 4.47)	0.97		

	Current smoker	1.62 (0.81, 3.22)	0.16		
Alcohol consumption	Never alcohol	1.0			
	Past alcohol	0.42 (0.05, 3.22)	0.41		
	Current alcohol	0.91 (0.45, 1.84)	0.81		
Education level (years)	No Education	1.0			
	Education (School or Higher)	0.59 (0.27, 1.28)	0.18		

All the risk factors were assessed at the baseline unless stated otherwise.

CI: Confidence interval, APEDS: Andhra Pradesh Eye Disease Study, IOP: Intra-ocular pressure, BMI: Body mass index

Table 4. Comparison with previous population-based studies on incidence of primary open angle glaucoma (POAG)

Study/population/ year	**Ethnic group**	**No. at risk**	**Age** (years), Minimum (mean ± SD)	**Follow up** (years)	**Incident cases, n**	**Incidence rate /** 1000 person years)	**Cumulative incidence** % (95% CI)	**Annual cumulative incidence** %	**Risk Factors**
Melbourne Visual Impairment Project,[8] 2002	Mainly white	2427	40 (58.7±11.4)	5	12		0.5 (0.3-0.7)	0.1	Age, higher IOP, H/O α blocker, presence of PXF, CDR >0.7
Rotterdam Eye Study,[10] 2017	Multi-ethnic	3939	55	12	48	1.0 (0.7-1.3)	1.2 (0.9-1.5)	0.1	Age, baseline IOP, IOP lowering Rx, family history, body mass index
Rotterdam Eye Study,[9] 2005	Multi-ethnic	3842	55, 65.7±6.9	5	29	1.2 (0.8-1.7)	0.6	0.12	Age, ocular HTN at baseline, fellow eye of unilateral POAG at baseline
Singapore Indian Eye Study,[5] 2021	Indian	2158	40 (56.5±9.2)	6	37		1.37[&] (0.94-1.96)	0.22	Older age, higher IOP, raised CDR
*CEDIS,[4] 2014	South Indian, rural	2469	40	6	59		1.9 (1.4-2.4)	0.31	
Barbados Eye Study,[7] 2007	Black	3222	40 (56.9±11.3)	9	125		4.4 (3.7-5.2)	0.48	Older age, family history, low ocular MPP, thinner CCT, higher IOP at baseline (HTN protective)
*CEDIS,[4] 2014	South Indian	4316	40 (58.4±9.7)	6	129		2.9 (2.4-3.4)	0.48	Older age, urban, higher IOP, myopia, higher AXL (HTN protective)
Barbados Eye Study,[6] 2001	Black	2989	40 (57.5±11.5)	4	67		2.2 (1.7-2.8)	0.55	Older age, men, higher IOP, (OHT) or suspect at baseline
Los Angeles Latino Eye Study,[11] 2012	Latin American	3772	40 (54.6±10.3)	4	87		2.3 (1.8-2.8)	0.57	Older age, fellow eye of POAG

Tema Eye Survey,[12] 2018	West African, urban	1101	40	8	51		4.7 (4.5-4.8)	0.59 (0.5-0.6)	Male gender, older age, higher IOP, larger CDR, thinner central cornea
**APEDS. Current study	South Indian, rural	1241	40 (49.4±7.8)	15	36	0.2 (0.2-0.3)	2.9 (2.0-3.9)	0.19	IOP difference at two time points

&: Age-standardized incidence; *CEDIS: Chennai Eye Disease Incidence Study; **APEDS: Andhra Pradesh Eye Disease Study

AXL: Axial length; BMI: Body mass index; CCT: Central corneal thickness; CDR: Vertical cup-to-disc ratio; CI: Confidence interval; HTN: Systemic hypertension; IOP: Intra-ocular pressure; MPP: Mean perfusion pressure; OAG: Open angle glaucoma; OHT: Ocular hypertension; PXF: Pseudo-exfoliation; SD: Standard Deviation