Incidence, Incident Causes, and Risk Factors of Visual Impairment and Blindness in a Rural Population in India: 15-Year Follow-up of the Andhra Pradesh Eye Disease Study

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• PURPOSE: To report 15-year incidence rate of visual loss (blindness and visual impairment [VI]), causes, and risk factors for participants in Andhra Pradesh Eye Disease Study III (APEDS III).

• DESIGN: Population-based cohort study.

• METHODS: From 2012 to 2016, all rural participants were interviewed and underwent a comprehensive eye examination, including dilated fundus examination and imaging. Presenting visual acuity (PVA) and best-corrected visual acuity (BCVA) were measured using a standard logarithm of Minimum Angle of Resolution chart at 3 meters. World Health Organization (WHO) and United States of America (USA) categories of VI and blindness were used. Incident visual loss was defined as the development of or worsening of visual loss of one or more categories.

• RESULTS: In APEDS I, 7,771 rural participants were examined using stratified, random-cluster systematic sampling; in APEDS III, 5,395 participants (69.4% of rural or 52.4% of total participants) were re-examined. Using WHO categories, the crude incidence rate of any visual loss based on PVA and BCVA were 14.6 (95% confidence interval [CI]:13.6-15.7) and 6.3 (95% CI: 6.1-6.4) per 100 person-years, respectively. Using USA criteria, the values were 22.6 (95% CI: 22.3-23.0) and 10.6 (95% CI: 10.3-10.8) per 100 person-years, respectively. More than 90% of visual loss was attributable to cataract and uncorrected refractive error. Using WHO categories, significant independent risk factors for the incident visual loss were increasing age, female gender, illiteracy, past or current smoker, and current use of alcohol. Using the USA definition, an additional risk factor was lower level of education.

• CONCLUSIONS: The high incidence likely reflects poor access to eye care in this population, which needs to be taken into account when planning eye care programs. (Am J Ophthalmol 2021;223:322–332. © 2020 Elsevier Inc. All rights reserved.)

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BLINDNESS AND VISUAL IMPAIRMENT (VI) ARE MAJOR public health problems with a significant impact on quality of life,[1-4] economic productivity, mental health,[5,6] safety[7-10] and mortality.[11] According to recent global data, 36 million people are blind, and 217 million have moderate to severe VI.[12] Although the overall prevalence of blindness fell between 1990 and 2015, the number of people who are blind increased by 17.6%, and the number with moderate-to-severe VI increased by 35.4%. This increase is attributed to population growth and aging and increasing urbanization.[12]

Data on the magnitude and causes of blindness and VI are derived from cross-sectional prevalence surveys, which provide useful information for planning services and resource allocation to address current gaps. However, for long-term planning, the longitudinal incidence data are required. These longitudinal studies can also provide more robust data on risk factors for eye diseases from which causality can be inferred more reliably, and can be used to describe the natural history of the disease. However, there are only a limited number of incidence studies, as they entail complex logistics, require more complex data analysis, and are expensive. Most studies have been undertaken in high-income countries,[13-18] with fewer from India[19] and other regions[20-25]—all focused on adults—and had relatively short follow-up; only a few had a follow-up period

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of 10 or more years,[16-18,26] with only 2 studies with 15 years follow-up.[16,17] The studies also differ in relation to inclusion criteria, age group, and the definitions of risk factors and of endpoints. We have previously reported the prevalence and causes of blindness and VI from our baseline survey, the Andhra Pradesh Eye Disease Study I (APEDS I).[27,28] The aim of Andhra Pradesh Eye Disease Study IIII (APEDS III) was to estimate the incidence and risk factors for blindness and VI, including cataract, diabetic retinopathy, uncorrected refractive error, and glaucoma in participants who did not manifest these conditions at baseline. In this paper, we report on the incidence of blindness and VI over a mean follow-up period of 15 years, stratified by age group and sex, along with causes and risk factors for incident blindness and VI (APEDS III).

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, Hyderabad, India; and the London School of Hygiene & Tropical Medicine, London. Written informed consent was obtained from all participants and legal guardians gave consent for minors (<18 years of age). APEDS III is a follow-up cohort of participants from initial APEDS I. Details of the methods for APEDS I and APEDS III have already been published.[29,30] In brief, APEDS I was conducted between 1996 and 2000, and recruited individuals from 3 rural and 1 urban cluster in undivided Andhra Pradesh state (ie, before it was divided into 2 states) in southern India.[30] In APEDS I, 10,293 participants were examined (2,552 urban and 7,771 rural) using stratified, random cluster systematic sampling. Sociodemographic data and systemic risk factors were recorded for each individual and all underwent a detailed, comprehensive eye examination. Before planning the follow-up study, in 2009-10 a feasibility study (APEDS II) was carried out, to trace participants examined in APEDS I. However, owing to rapid urbanization over the past decade, it was not possible to trace the urban cohort in Hyderabad.[11] Hence, only the 3 rural areas in APEDS I were revisited—Tanuku (West Godavari district), Mudhol (Adilabad district), and Thoodukurthy (Mahabubnagar district). The result of APEDS II showed that 5,447 (70.1%) participants were available for follow-up, 1,453 (18.7%) had migrated, and 871 (11.2%) had died.[11] APEDS III was carried out between 2012 and 2016 when participants from these 3 rural areas were re-examined using the same methodology as in APEDS I.[30]

Sociodemographic data were collected from participants at their residence, as described earlier.[29] For participants aged 30 years and above, demographic data, history of ocular and systemic conditions such as hypertension and diabetes, risk factors, visual function, information related to barriers to the uptake of eye care services, and knowledge about a range of eye diseases were recorded.[29] For those below 30 years of age, personal details, parents education and occupation, spectacle use, reading habits, previous eye examination, consanguinity between parents, and their economic status were recorded.[29] After the interview participants underwent a detailed eye examination at the base hospital.

The clinical team was comprised of 4 ophthalmologists, an optometrist and a vision technician. The optometrist and vision technician were trained to examine the anterior and posterior segment, to measure visual acuity (VA), and to do refraction. Height, weight, and blood pressure were each measured 3 times using standard methods, and mean values were used. Presenting distance VA in each eye and then binocularly were measured using a standard, illuminated (at least 200 lux) logarithm of minimum angle of resolution (logMAR) chart at 3 meters distance, using participant's distance correction, if applicable. For participants who were not literate, a logMAR chart with tumbling E optotypes was used. Unaided and pinhole distance VA were also recorded. Near VA was measured at a distance of 40 cm using a logMAR near vision chart with near correction, if applicable, and unaided. Monocular and binocular near vision were assessed. If the individual was using spectacles, the power of the spectacles was measured. Retinoscopy was undertaken for those with a presenting distance or near VA of less than logMAR 0.0 (6/6) and best-corrected VA (BCVA) was measured. Undilated slit-lamp examination (SL 120; Carl Zeiss Meditec, Inc, Dublin, California, USA) was performed by the ophthalmologist, including intraocular pressure measurement using Goldmann applanation tonometry (Carl Zeiss Meditec, Inc), before and after pupil dilatation. For participants examined at home, IOP was measured using a Perkins tonometer. Gonioscopy was performed on all participants and graded by the ophthalmologist following the APEDS I protocol, using NMR-K 2-mirror lens (Ocular Instrument Inc, Bellevue, Washington, USA).[31] Four-mirror gonioscopy was also performed with an indirect gonioscopic lens (Volk Opticals Inc, Mentor, Ohio, USA). After gonioscopy, pupils were dilated with tropicamide 1% and phenylephrine hydrochloride 2.5% for lens examination and grading and posterior segment examination unless contraindicated (ie, risk of angle closure or active infection). In eyes at risk of angle closure (occludable angles), laser iridotomy was performed and the dilated examination was done at a later date. Phenylephrine was not used in participants with hypertension or cardiac disease. Dilated eye examination included grading of changes in the lens, optic disc, and retina (diabetic retinopathy and age-related macular degeneration [ARMD]) using standard grading systems, as described earlier.[29] Following dilated examination, biometry was undertaken and visual fields were assessed using a Humphrey visual field analyzer (model 720E; Carl Zeiss Meditec, Inc). Stereo-photographs

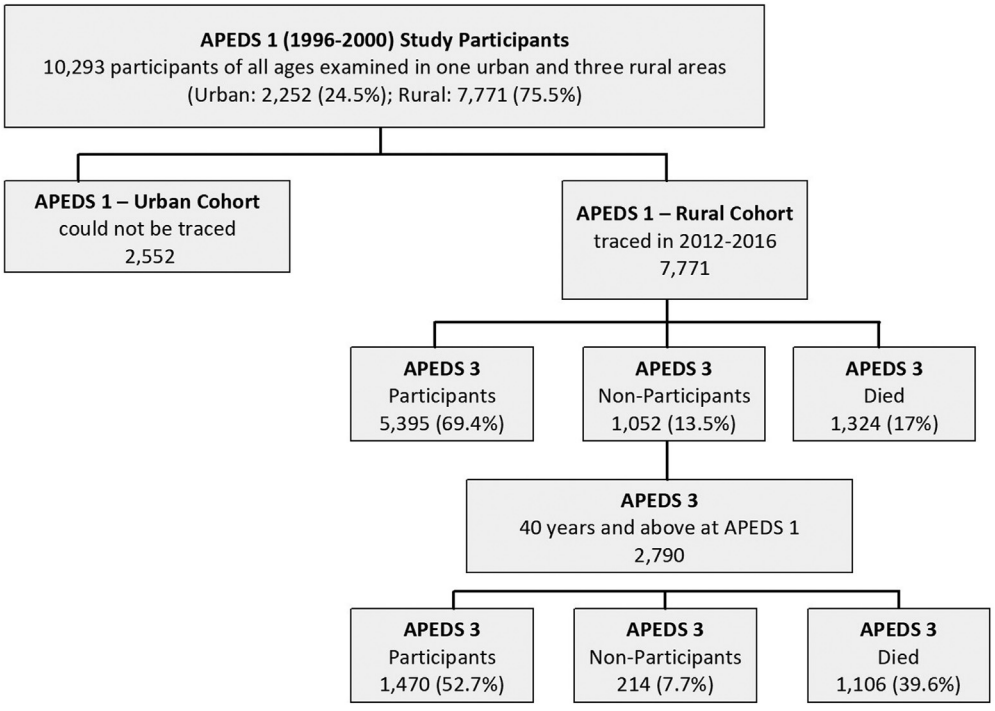

FIGURE 1. Availability of participants at the time of Andhra Pradesh Eye Disease Study III.

of the disc, macula, and retina were taken using a Zeiss FF 450-plus fundus camera with VISUPAC digital image archiving system (Carl Zeiss, Jena, Germany). Corneal, anterior segment, and lens photographs were taken using a Topcon photo-slit lamp camera (Topcon DC 3; Topcon, Oakland, New Jersey, USA). Cirrus high-definition optical coherence tomography (Carl Zeiss Meditec, Jena, Germany) was used to measure retinal nerve fiber layer thickness, optic nerve head, and optic disc cupping.

• **CATEGORIES OF VISUAL IMPAIRMENT:** In order to provide comparable data, the World Health Organization (WHO) categories of VI and blindness were used, as well as the United States of America (USA) criteria. Data are presented using presenting VA (PVA) and BCVA in the better eye.[32] Using WHO criteria, mild VI was defined as VA of less than 6/12 down to 6/18; moderate VI was defined as a VA of less than 6/18 down to 6/60; severe VI as a VA of less than 6/60 down to 3/60; and blindness as a VA of less than 3/60. Using the USA definition, moderate VI was defined as VA of less than 6/12 to better than 6/60; and blindness as a VA of equal to or worse than 6/60.

• **DEFINITIONS OF INCIDENT VISUAL LOSS AND CAUSES:** In this paper we use the term visual loss to encompass all categories of visual impairment and blindness, and used the same definitions of incidence as in other studies.[14,33] The incidence of "any visual loss" was defined as any category of visual loss at APEDS III among those who were not impaired at baseline; that is: (1) incidence of mild VI relates to those who were not impaired at baseline and developed mild VI at follow-up; (2) incidence of moderate VI relates to those who were not impaired or had mild VI at baseline and developed moderate VI at follow-up; (3) incidence of severe VI relates to those who were not impaired or had mild or moderate VI at baseline and developed severe VI at follow-up; and (4) incidence of blindness relates to those who were not impaired or had mild, moderate, or severe VI at baseline and developed blindness at follow-up.

The causes of any VI were documented for each eye and for the person, as in the original APEDS protocol.[27] The causes identified by the examining ophthalmologist were discussed with the principal investigator (R.C.K.) and other co-investigators to reach a consensus. If there was inadequate information to make a decision, the participant was re-examined by the principal investigator. If cataract and ARMD were both present, and in the clinical judgement of the ophthalmologist, cataract surgery would not improve the VA, the cause was recorded as ARMD. Similarly, if index myopia was present and the vision improved with refraction, the cause of VI was recorded as cataract and not uncorrected refractive error.

• **ANALYSIS:** Stata 13 was used for statistical analysis (StataCorp, College Station, Texas, USA). Participants who had VA data recorded at APEDS I and APEDS III were included in the analysis, and the age- and sex-specific incidence rate was calculated using person-time at risk. All participants examined and having VA data at APEDS I and APEDS III were included in analysis, which

TABLE 1. Baseline Characteristics of Participants and Nonparticipants in Andhra Pradesh Eye Disease Study III

Characteristic	Participants	Nonparticipants	
		Alive	Deceased
Age in years, mean (SD)[a]	28.0 (17.5)	23.0 (18.0)	55.2 (16.6)
Age group (years)			
0-29	2,768 (51.3)	703 (66.8)	112 (8.5)
30-39	1,157 (21.5)	135 (12.8)	106 (8.0)
40-49	774 (14.4)	94 (8.9)	161 (12.2)
50-59	454 (8.4)	64 (6.1)	269 (20.3)
60+	242 (4.5)	56 (5.3)	676 (51.1)
Sex[a]			
Women	2,853 (52.9)	610 (58.0)	629 (47.5)
Men	2,542 (47.1)	442 (42.0)	695 (52.5)
Education (grades)[a,b]			
None	2,404 (49.0)	369 (38.9)	873 (66.4)
Primary (1-5)	1,407 (28.7)	314 (33.1)	306 (23.3)
Secondary (6-10)	883 (18.0)	202 (21.3)	110 (8.4)
Higher (11+)	217 (4.4)	63 (4.3)	25 (1.9)
Hypertension[a,c]			
No	2,696 (73.3)	384 (70.9)	657 (52.6)
Yes	984 (26.7)	158 (29.2)	592 (47.4)
Diabetes[a]			
No	5,372 (99.6)	1,047 (99.5)	1,274 (96.2)
Yes	23 (0.4)	5 (0.5)	50 (3.8)
Smoking status[a]			
Never	4,361 (80.8)	918 (87.3)	718 (54.2)
Past	153 (2.8)	15 (1.4)	120 (9.1)
Current	881 (16.3)	119 (11.3)	486 (36.7)
Alcohol status[a]			
Never	4,105 (76.1)	873 (83.0)	744 (56.2)
Past	134 (2.5)	20 (1.9)	141 (10.7)
Current	1,156 (21.4)	159 (15.1)	439 (33.2)

Results are n (%) unless indicated.

[a]*P* value $< .05$.

[b]Data not available for 484 (8.97%) available and examined, 10 (0.76%) died before examination, and 104 (9.89%) available but not examined.

[c]Data not available for 1,715 (31.79%) available and examined, 75 (5.66%) died before examination, and 510 (48.48%) available but not examined.

also included those who had undergone cataract surgery during the follow-up period. Logistic regression modeling was used to assess associations between risk factors and VI and blindness. Model selection was performed using the AIC (Akaike Information Criterion). The choice of risk factors was guided by previous literature and our clinical insight.[34] All data were analyzed for all ages and for participants aged ≥40 years at baseline. For categorical variables in univariable analysis, χ^2 test or Fisher exact test was used. A 2-tailed value of $<.05$ was considered statistically significant. For comparison of continuous variables, *t* tests and 1-way ANOVA were used. Multicollinearity between variables was assessed by looking at the variance inflation factor; and fitness of the model was assessed using the Hosmer-Lemeshow test for goodness of fit.

RESULTS

AT BASELINE (APEDS I), 7,771 PARTICIPANTS FROM THE 3 RURAL clusters aged 0-95 years were examined. At follow-up (mean 15 years, range 13-17 years), 5,395 (69.4%) rural participants were re-examined, constituting 69.4% of rural participants at baseline (52.4% of total urban and rural participants) (Figure 1). Reasons for non-response at APEDS III were death (1,324, 17.0%), migration (778, 10.0%), declined examination (165, 2.1%), and not traceable (109, 1.4%). Among 2,790 participants aged ≥40 years at baseline, 1,470 (52.7%) were examined. Reasons for non-response were death (1,106, 39.6%), migration (92, 3.3%), declined examination (71, 2.5%), and not traceable (51, 1.8%).

TABLE 2. 15-Year Incidence Rate of Any Visual Impairment in Andhra Pradesh Eye Disease Study III According to World Health Organization and United States Criteria

		Incidence in Men				Incidence in Women				Total Incidence			
Visual Impairment	Age at Baseline (Years)	N	n	%	95% CI	N	n	%	95% CI	N	n	%	95% CI
Presenting	0-29	1,011	14	1.3	1.2-1.5	1,083	38	3.4	3.1-3.7	2,094	52	2.5	2.2-2.6
(WHO)	30-39	496	53	10.4	9.8-11.2	623	104	16.7	15.9-17.4	1,119	157	13.9	13.4-14.5
	40-49	309	94	30.3	28.9-31.6	366	126	34.6	33.3-35.9	675	220	32.6	31.7-33.5
	50-59	154	66	42.9	40.9-45.0	149	71	47.9	45.7-49.9	303	137	45.4	43.9-46.8
	60+	51	31	42.6	39.1-46.3	52	32	61.1	57.5-64.5	103	63	60.5	58.0-62.9
	Crude overall[a]	2,021	258	12.6	12.3-13.0	2,273	371	16.3	15.9-16.7	4,294	629	14.6	13.6-15.7
	Age & sex adjusted[a]			15.4	13.8-17.0			18.5	16.9-20.2			17.0	15.9-18.2
Best-corrected	<30	1,027	3	0.3	0.2-0.4	1,103	3	0.3	0.2-0.4	2,130	6	0.3	0.2-0.3
(WHO)	30-39	500	5	0.9	0.7-1.1	640	25	4.1	3.7-4.5	1,140	30	2.5	2.2-2.7
	40-49	336	23	6.4	5.8-7.1	412	50	12.0	11.2-12.9	748	73	9.6	9.1-10.2
	50-59	194	47	24.1	22.6-25.7	213	66	30.4	28.8-32.0	407	113	28.0	26.9-29.2
	60+	84	28	33.1	30.6-35.9	93	42	45.3	42.6-47.9	177	70	39.4	37.6-41.3
	Crude overall[a]	2,141	106	4.8	4.6-5.1	2,461	186	7.6	7.3-7.9	4,602	292	6.3	6.1-6.4
	Age & sex adjusted[a]			6.3	5.3-7.4			9.1	7.8-10.3			7.8	7.0-8.6
Presenting	0-29	998	29	2.8	2.6-3.1	1,068	91	8.5	8.1-8.9	2,066	120	5.8	5.1-5.6
(USA)	30-39	479	115	24.2	23.2-25.2	593	178	30.7	29.8-31.7	1,072	293	27.8	27.1-28.5
	40-49	283	125	44.9	43.4-46.4	313	165	53.1	51.7-54.6	596	290	49.1	48.1-50.2
	50-59	123	76	62.2	60.0-64.5	119	78	65.5	63.2-67.7	242	154	63.8	62.2-65.4
	60+	39	29	73.6	69.8-77.1	28	24	85.2	81.5-88.6	67	53	78.4	75.7-81.0
	Crude overall[a]	1,922	374	19.6	19.2-20.1	2,121	536	25.4	24.9-25.9	4,043	910	22.6	22.3-23.0
	Age & sex adjusted[a]			22.4	20.5-24.3			29.8	27.8-31.7			26.1	24.7-27.5
Best-corrected	0-29	1,026	6	0.6	0.4-0.7	1,099	7	0.6	0.5-0.7	2,125	13	0.6	0.5-0.7
(USA)	30-39	499	21	4.2	3.7-4.6	637	40	6.1	5.6-6.5	1,136	61	5.2	4.9-5.6
	40-49	331	59	17.8	16.7-18.9	402	98	24.5	23.5-25.7	733	157	21.5	20.7-22.3
	50-59	182	69	38.3	36.5-40.2	189	90	48.3	46.4-50.2	371	159	43.4	42.1-44.8
	60+	67	43	63.6	60.5-66.6	70	44	62.8	59.8-65.8	137	87	63.2	61.1-65.3
	Crude overall[a]	2,105	198	9.4	9.1-9.7	2,397	279	11.6	11.3-11.9	4,502	477	10.6	10.3-10.8
	Age & sex adjusted[a]			12.0	10.7-13.5			14.6	13.2-16.1			13.4	12.4-14.4

BCVA = best-corrected visual acuity; N = number at risk at baseline; n = incident cases; PVA = presenting visual acuity; USA = United States criteria; VI = visual impairment; WHO = World Health Organization criteria.

United States criteria: Incidence of any presenting VI is measured as PVA at baseline of 20/40 or better with follow-up PVA worse than 20/40. Incidence of best-corrected VI is measured as baseline BCVA of 20/40 or better with follow-up BCVA worse than 20/40.

World Health Organization Criteria: Incidence of any presenting VI is measured as PVA at baseline of 20/60 or better with follow up PVA worse than 20/60. Incidence of best-corrected VI is measured as baseline BCVA of 20/60 or better with follow-up BCVA worse than 20/60.

Age and sex standardized to the undivided Andhra Pradesh state population as per 2010-11 census.

[a]*P* value < .05.

Table 1 shows the baseline characteristics difference among participants and nonparticipants in APEDS III. The mean age of participants at baseline (APEDS I) was 28 (SD ± 17.5) years (Table 1); 52.9% were female and 49.0% had not received any formal education. The majority of participants did not have diabetes (99.6%) or hypertension (73.3%), and did not smoke (80.8%) or consume alcohol (76.1%).

• **INCIDENCE RATE OF ANY VISUAL LOSS FOR ALL AGES:** Using WHO categories, the crude incidence rate of any visual loss based on PVA and BCVA were 14.6 (95% confidence interval [CI]: 13.6-15.7) and 6.3 (95% CI: 6.1-6.4) per 100 person-years, respectively. Using USA criteria, the values were 22.6 (95% CI: 22.3-23.0) and 10.6 (95% CI: 10.3-10.8) per 100 person-years, respectively. The crude and age- and sex-adjusted incidence of any visual loss was significantly higher in women than in men ($P < .05$) for WHO and USA criteria. The incidence increased with age at baseline (Table 2). Figure 2, A and B show the incidence of any visual loss for men and women for different age groups, using WHO and USA criteria, respectively.

• **INCIDENCE OF SUBCATEGORIES OF INCIDENCE FOR ALL AGES:** Using the sub-categories of incidence, WHO definitions, and PVA, the crude rates were as follows: mild VI 11.8 (95% CI: 11.5-12.0), moderate VI 13.4 (95% CI: 13.1-13.6), severe VI 2.1 (95% CI:2-2.2), and blindness

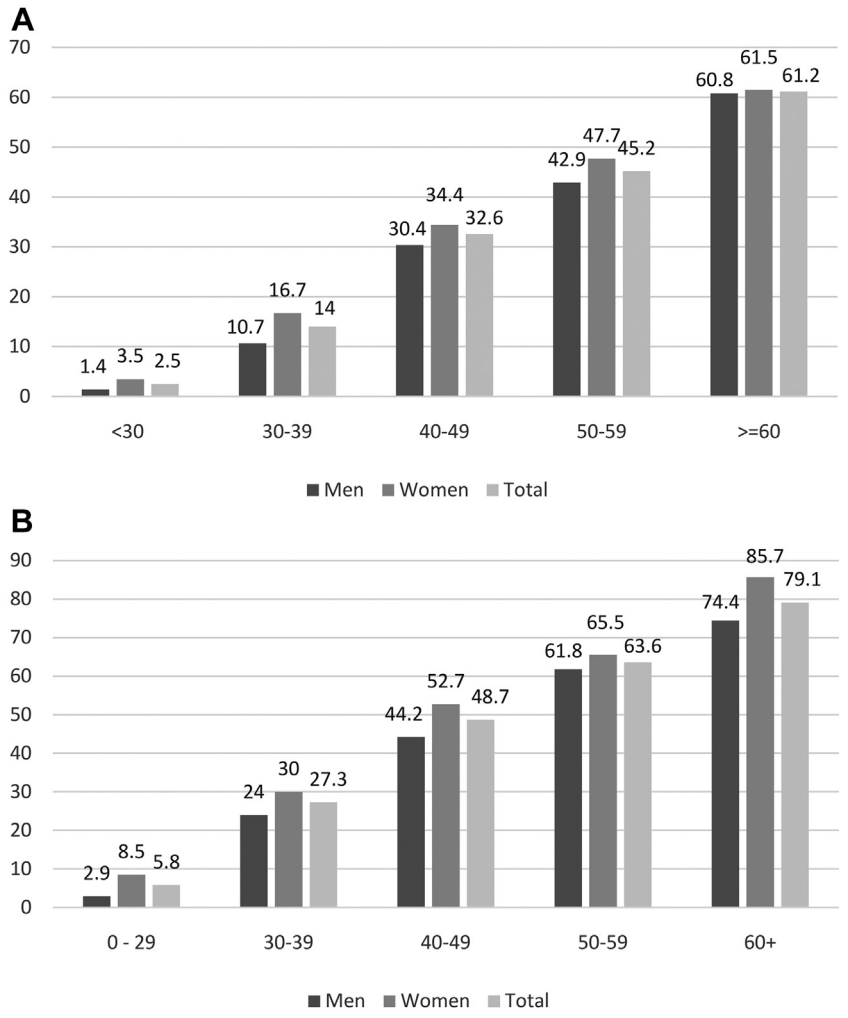

FIGURE 2. Incidence rate of any visual loss per 100 person-years among participants without visual impairment at baseline, using presenting visual acuity in the better eye. A. Using World Health Organization categories of visual impairment. B. Using United States of America categories of visual impairment

0.9 per 100 person-years (95% CI: 0.9-1.0) (Supplemental Tables 1, available at AJO.com). Women had significantly higher crude incidence of mild VI ($P = .005$), moderate VI ($P = .02$), and severe VI ($P = .001$) than men, but for blindness there was no significant difference by sex ($P = .5$). Using BCVA, the crude incidence rates were as follows: mild VI 7.9 (95% CI: 7.1-8.8), moderate VI 5.5 (95% CI: 5.3-5.7), severe VI 0.5 (95% CI: 0.4-0.6), and blindness 1.0 per 100 person-years (95% CI: 0.9-1.1) (Supplemental Tables 2, available at AJO.com). Women had a significantly higher incidence of moderate VI ($P = .02$) and severe VI ($P = .01$) than men, but for blindness there was no significant difference by sex ($P = .7$).

Using the USA definitions, the findings were similar for the incidence rates of moderate VI and blindness using PVA and BCVA, with similar differences between men and women (Supplemental Tables 3 and 4, available at AJO.com).

• **INCIDENCE RATE OF VISUAL IMPAIRMENT FOR PARTICIPANTS AGED ≥40 AT BASELINE:** Using WHO definitions and PVA and BCVA, the incidence rate of any visual loss was 38.9 (95% CI: 35.9-41.8) and 19.2 (95% CI: 17.1-21.4) per 100 person-years, respectively. The incidence of blindness (VA <20/400) using PVA and BCVA was 2.6 (95% CI: 1.8-3.5) and 2.7 per 100 person-years (95% CI: 1.9-3.6), respectively. Using the USA definition along with PVA and BCVA, the incidence of any visual loss was 54.9 (95% CI: 51.6-58.2) and 32.5 per 100 person-years (95% CI: 29.9-35.2), respectively. The incidence of blindness (VA ≤20/200) using PVA and BCVA was 8.4 (95% CI: 7.0-10.0) and 4.1 per 100 person-years (95% CI: 3.1-5.2), respectively.

• **CAUSES:** Using WHO and USA categories of visual loss, cataract and uncorrected refractive error were the commonest causes of incident VI and blindness for all

TABLE 3. Causes of Incident Visual Impairment and Blindness by Age and Category of Visual Loss

	WHO Categories of VI		USA Categories of VI	
	Visual Impairment, N (%)	Blindness, N (%)	Visual Impairment, N (%)	Blindness, N (%)
All age groups at baseline				
Cataract	392 (62.3)	27 (62.8)	394 (43.3)	108 (76.1)
Uncorrected refractive error	187 (29.7)	0 (0)	473 (52.0)	2 (1.4)
Corneal pathology	8 (1.3)	3 (7)	6 (0.7)	8 (5.6)
Glaucoma	4 (0.6)	2 (4.7)	2 (0.2)	3 (2.1)
Age related macular degeneration	4 (0.6)	2 (4.7)	2 (0.2)	3 (2.1)
Diabetic retinopathy	1 (0.2)	0 (0)	2 (0.2)	0 (0)
Retinitis pigmentosa	1 (0.2)	5 (11.6)	1 (0.1)	3 (2.1)
Other retinal diseases	8 (1.3)	2 (4.7)	8 (0.9)	5 (3.5)
Optic atrophy	8 (1.3)	0 (0)	0 (0)	1 (0.7)
Amblyopia	1 (0.2)	0 (0)	0 (0)	1 (0.7)
Others	14 (2.2)	2 (4.7)	12 (1.3)	6 (4.2)
Cannot be determined	1 (0.2)	0 (0)	2 (0.2)	2 (1.4)
Total	629 (100)	43 (100)	910 (100)	142 (100)
Aged ≥40 years at baseline				
Cataract	308 (73.3)	26 (70.3)	299 (60.2)	92 (76.7)
Uncorrected refractive error	77 (18.3)	0 (0)	171 (34.4)	1 (0.8)
Corneal pathology	5 (1.2)	2 (5.4)	2 (0.4)	7 (5.8)
Glaucoma	4 (1)	2 (5.4)	2 (0.4)	3 (2.5)
Age-related macular degeneration	4 (1)	2 (5.4)	2 (0.4)	3 (2.5)
Diabetic retinopathy	1 (0.2)	0 (0)	2 (0.4)	0 (0)
Retinitis pigmentosa	1 (0.2)	2 (5.4)	1 (0.2)	1 (0.8)
Other retinal diseases	7 (1.7)	2 (5.4)	7(1.4)	5 (4.2)
Optic atrophy	2 (0.5)	0 (0)	2 (0.4)	2 (1.7)
Amblyopia	0 (0)	0 (0)	0 (0)	1 (0.8)
Others	11 (2.6)	1 (2.7)	9 (1.8)	0 (0)
Cannot be determined	0 (0)	0 (0)	0 (0)	5 (4.2)
Total	420 (100)	37 (100)	497 (100)	120 (100)

USA = United States of America; WHO = World Health Organization.

ages and for those aged ≥40 years at baseline (Table 3), accounting for more than 90% of all causes. Cataract was the leading cause of blindness in each group, accounting for more than 70% of the blindness. Other, less important causes of blindness were retinitis pigmentosa, corneal pathology, glaucoma, ARMD, and other retinal conditions.

• **RISK FACTORS:** Using WHO categories, significant independent risk factors for the incidence of any visual loss of any degree comparing 15 years follow-up to baseline data were increasing age and being female, not literate, a past or current smoker, and a current user of alcohol (Table 4). Increasing age was also an independent risk factor for blindness, as were hypertension, diabetes, and a low body mass index (less than 18.5) but not sex, smoking, or alcohol use. The risk factors for any visual loss were similar using the USA definition, with lower level of education as an additional risk factor. Current use of alcohol was not significant. For blindness, significant risk factors were increasing age, female sex, and current use of alcohol.

DISCUSSION

THIS IS THE FIRST POPULATION-BASED STUDY TO REPORT the incidence of visual loss (VI and blindness) in a cohort of all ages. Differences between incidence rates estimated using PVA and BCVA indicate that uncorrected refractive error is a major cause of incident VI. However, comparison with other studies is limited as they differ in terms of the age group studied, the level of socioeconomic development of the countries where the studies were undertaken, ethnicity, follow-up time, and different definitions of risk factors and incidence that were used. For example, most used WHO and USA categories of visual impairment,[15,20,22-25] while some used one definition, limiting comparability across studies.[13,17,18,21]

Studies of those aged 40 years or above at baseline that reported the incidence of VI and blindness using PVA are shown in Table 5, where all the incidence data have been converted to an annual percentage incidence.[14,18,20,21,23-25] Using the WHO categories of visual

TABLE 4. Multivariable Analysis of Risk Factors Using World Health Organization and United States Categories for Incident Visual Impairment and Incident Blindness

	Incident Visual Impairment		Incident Blindness	
	WHO Definition	USA Definition	WHO Definition	USA Definition
	Odds Ratio (95% CI)			
Age group[a]				
<40 years	Reference	Reference	Reference	Reference
40-49 years	3 (2.4-3.8)	2.6 (2.1-3.2)	2 (0.6-7.2)	2.4 (1.3-4.4)
50-59 years	5.1 (3.8-6.9)	5.1 (3.7-7.0)	5.4 (1.6-17.6)	7.0 (3.9-12.6)
≥60 years	9.3 (5.9-14.7)	9.4 (5.1-17.4)	22.2 (7.2-68.3)	13.6 (7.4-25)
Sex				
Male	Reference	Reference	Reference	Reference
Female	1.8 (1.2-2.5)[a]	1.5 (1.1-2.0)[a]	1.7 (0.6-4.7)	2.4 (1.2-4.5)[a]
Education				
Class 11 and above	Reference	Reference	Reference	Reference
Class 6 to 10	1.0 (0.4-2.2)	1.9 (0.96-3.8)	0.4 (0.3-5.0)	0.6 (0.3-1.5)
Class 1 to 5	2 (0.9-4.3)	3.2 (1.6-6.3)[a]	1 (0.1-8.4)	1 (0.6-1.7)
None	2.5 (1.2-5.4)[a]	3.8 (1.9-7.4)[a]	0.5 (0.1-4.6)	
Hypertension				
No	Reference	Reference	Reference	Reference
Yes	1.2 (0.95-1.5)	1.1 (0.9-1.4)	2.1 (1.1-4.4)[a]	1.4 (0.9-2.0)
Diabetes				
No	Reference	Reference	Reference	Reference
Yes	0.7 (0.2-2.2)	1.7 (0.5-5.6)	4.7 (1.1-20)[a]	2.5 (0.6-9.5)
Body mass index				
18.5-24.99	Reference	Reference	Reference	Reference
<18.5	1.2 (0.9-1.5)	1.1 (0.9-1.4)	2.3 (1.1-4.8)[a]	1.4 (0.9-2.0)
25-29.9	0.9 (0.6-1.4)	1.0 (0.7-1.6)	0.9 (0.2-3.2)	0.9 (0.4-1.9)
>30	0.6 (0.2-1.5)	0.4 (0.2-1.0)		1.1 (0.3-5.0)
Smoking				
Never smoker	Reference	Reference	Reference	Reference
Past smoker	1.9 (1.1-3.3)[a]	1.8 (1.1-3.1)[a]	1.1 (0.3-4.5)	1.1 (0.4-2.8)
Current smoker	1.5 (1.1-2.3)[a]	1.4 (1.0-1.9)[a]	1.4 (0.5-3.9)	1.1 (0.6-2.2)
Alcohol consumption				
Never	Reference	Reference	Reference	Reference
Past	1.1 (0.6-1.9)	0.8 (0.4-1.3)	1.6 (0.4-6.3)	1.7 (0.8-4.0)
Current	1.5 (1.2-1.9)[a]	1.1 (0.9-1.4)	0.9 (0.4-2.0)	1.7 (1.1-2.6)[a]
Hosmer-Lemeshow test	0.18	0.72	0.37	0.13
Area under the curve	0.73	0.70	0.85	0.78

USA = United States of America; WHO = World Health Organization.
[a]*P* value < .05.

loss, the APEDS III study had the highest annual incidence of VI and the second-highest incidence of blindness. Using the USA categories, APEDS III had the highest incidence of blindness and the second-highest incidence of VI. These findings need to be seen against the relatively lower mean age of our participants at baseline (54.7 years). Apart from this, as compared to studies that reported 15 years incidence, the APEDS III study had the highest annual incidence of VI and blindness.[16,17] As cataract and refractive error were the two most common causes of incident visual loss, the higher incidence in APEDS III might be explained by low access to eye care services; a higher incidence on account of greater exposure to risk factors such as environmental factors (ultraviolet exposure), dietary differences, as well as genetics, cannot be ruled out.

As expected, and as in other studies, the incidence of any visual loss increased substantially with age (Figure 2, A and B).[13-25] More than 50% of those aged 50 years and older at baseline developed some degree of VI, which reinforces the need for eye health program planning to target the older population.

In studies from high-income countries, ARMD is one of the leading causes of incident VI,[14,15,17,35] but in our study ARMD was not a common cause. This likely reflects racial,

TABLE 5. Annual Incidence of Visual Impairment and Blindness Using Presenting Visual Acuity in High-, Middle-, and Low-Income Countries

Study, Country	Baseline Data Collection	Age at Baseline (Mean, Min. Years)	Mean Follow-up (Years)	Participants at Baseline (% at Follow-up)	Category of VI Used	Annual Incidence (Presenting Visual Acuity	
						Visual Impairment	Blindness
Ponza Eye Study, Italy[18]	1986-1988	55.5 (40)	12	1,028 (40%)	WHO	0.79	0.1
Melbourne Visual Imp. Project, Australia[14]	1992-1994	59.0 (40)	5	3,271 (79%)	Melbourne	0.84	0.06
Los Angelos Latino Eye Study, USA[23]	2000-2003	54.7 (40)	4	6,357 (73%)	WHO	0.45	0.05
					USA	0.73	0.08
Beijing Eye Study, China[25]	2001	55.3 (40)	5	4,439 (73%)	WHO	0.28	0.02
					USA	0.76	0.04
Liwan Eye Disease Study, China[24]	2003	63.4 (50)	5	1,405 (88%)	WHO	2.48	0.06
					USA	4.12	0.36
Nakuru Eye Disease Study, Kenya[20]	2007-2008	62.5 (50)	6	4,414 (49%)	WHO	1.98	0.25
					USA	NR	0.45
Shahroud Eye Cohort Study, Iran[21]	2009-2010	50.9 (40-64)	5	5,190 (91%)	WHO	0.20	0.02
Andhra Pradesh Eye Disease Study, India[a]	1996-2000	54.7 (40)	15	2,790 (53%)	WHO	2.59	0.17
					USA	3.66	0.56

NR = not reported; USA = United States of America; VI = visual impairment; WHO = World Health Organization.
[a]Current study.

ethnic, and demographic differences between studies, and the high incidence of cataract, which may have masked the presence of ARMD. As in other studies, cataract was an important cause of incident VI,[13,18,25] as was uncorrected refractive error. In our study cataract and uncorrected refractive error were the major causes of any visual loss for all age groups as well as those 40 years and older , and together they accounted for nearly 90% of any incident visual loss. The high incidence of visual loss owing to cataract in our study may reflect that, in rural areas of Andhra Pradesh, individuals either did not access eye care services or only did so when they had considerable loss of vision. The incidence could also be higher in this rural population where agriculture is an important occupation, owing to exposure to ultraviolet light, a poor diet, episodes of severe dehydration, and exposure to biomass cooking fuel.[36]

Some studies, but not all, reported a higher incidence of visual loss in female participants, as we found in our study,[13-16,20,21,23,25,33] but some reported a higher incidence in male participants.[22,26,37] As the major causes of incident blindness in our study were cataract and uncorrected refractive error, the sex difference in incidence likely reflects sex differences in access to optical and cataract surgical services, although there is some evidence that women are at greater risk of cataract than men after taking age into account, but the reasons are not clear.[38]

Lower levels of education was another risk factor in our study, with a clear trend for incident visual loss. Similar association has been reported in cross-sectional studies and in the Beijing Eye Study, another cohort study.[25] Prospective studies provide greater evidence of causality than cross-sectional studies, and in our study, the better-educated were more likely to have occupations with less exposure to known risk factors for cataract, and to be more aware of and able to access services for cataract surgery and spectacle correction. A history of past and current smoking and current alcohol consumption were also associated with incident visual loss. Smoking was one of the major risk factors for cataract in APEDS I,[39] as has been reported in a large number of other studies.[40] Smoking raises the cadmium levels in the blood, which inactivates the superoxide dismutase as well as causes oxidative stress, thus affecting the lens and causing cataract. Although the association between alcohol consumption and cataract is controversial, the alcohol consumed in rural areas in Andhra Pradesh may contain toxins, as it is locally brewed and distilled from molasses, a by-product of sugarcane.

Using the WHO definition, nearly two-thirds of blindness and VI was attributable to cataract (ie, an annual incidence of 1.85%). In Andhra Pradesh there are approximately 190,000 adults per million population who are aged 40 years and above (27%) who live in rural areas (70%). With an adjusted annual incidence of cataract of 1.80% (95% CI: 1.69-1.90), this would translate to 3,400 (95% CI: 3,200-3,600) new cataract blind or VI per million population in rural areas. This is despite a high cataract surgical rate of approximately 6,000 per million population per year.

The strengths of this study include the large sample size, which was representative of all ages at baseline, the long follow-up, and the detailed clinical examination. In addition, quality control measures implemented during the study minimized errors and bias.[29] The response rate among those who survived was 80.5%, which is high. The quality and standards applied were similar to studies conducted in high-income settings.[14,16,17,23]

Limitations of the study included non-response bias, as those who had died were older, those who had migrated were younger, and those who declined not to take part were also younger, and were more likely to be female, better educated, non-smokers, and non-consumers of alcohol. In addition, it was not possible to trace participants in the urban cluster. Given the variability of the non-response it is difficult to say in which non-response bias may have influenced the estimate, but an overestimate cannot be ruled out. In the risk factor analysis, all the factors were fixed at baseline, whereas in real life these factors can vary over time. We assume no clustering effect, whereas the possibility cannot be ruled out. However, we did not find any difference in variance with or without use of robust variance method, suggesting no clustering effect in this population. Another limitation is that the definition of visual loss did not include visual field loss, thus underestimating the incidence, particularly of glaucoma. However, as most population-based studies on the incidence of VI refer only to VA measurements, the data in this study can be compared with previous studies conducted on other ethnic groups.

In conclusion, the incidence of visual loss in this rural population in India was high, with cataract and uncorrected refractive error as the main causes. Increasing age, female sex, lack of education, smoking, and alcohol intake were significant risk factors. The findings highlight the need to increase access to eye care and optical services in rural areas in the State of Andhra Pradesh, particularly for women patients and the less well educated.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

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