British Journal of
Ophthalmology

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Journal:	*British Journal of Ophthalmology*
Manuscript ID	bjophthalmol-2020-316359.R1
Article Type:	Clinical science
Date Submitted by the Author:	n/a
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Keywords:	Epidemiology, Cornea

Fifteen-Year Incidence rate and Risk Factors of Pterygium in the Southern Indian State of Andhra Pradesh

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Running title: 15-year Incidence of Pterygium from APEDS

Word count: 2,927

Funding support: Financial Support for this study is provided by Hyderabad Eye Research Foundation, India, Lions Clubs International Foundation, SightFirst Research grant, USA and Dept. of Biotechnology, Centre of Excellence (CoE) grant, India.

Competing interests: None

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ABSTRACT

Purpose: To report 15-year incidence rate and associated risk factors of pterygium among people aged 30 years and above at baseline in the rural clusters of longitudinal Andhra Pradesh Eye Disease Study(APEDS III).

Methods: The baseline Andhra Pradesh Eye Disease Study I(APEDS I) included 7,771 participants of which, 6,447(83%) were traced and 5,395(83.7%) were re-examined in APEDS III. To estimate the incidence of pterygium, we selected participants who were 30 years and above at baseline(4,188), of which 2,976 were traced and 2,627(88.3%) were examined and based on inclusion criteria, 2,290 participants were included in the study. The incidence rate of pterygium was defined as the proportion of people free of pterygium at baseline who had developed the condition at 15-year follow-up(range 13-17 years). Univariate and multivariable analyses for risk factors were undertaken.

Results: The sex-adjusted incidence rate of pterygium was 25.2 per 100 person-years(95% CI: 24.8-25.7) which was significantly higher for males than females((26.3 per 100 person-years (95% CI: 25.6-27.0) and 24.7(95% CI: 24.1-25.3) respectively). At the multivariable analysis, male gender(RR: 1.35, 95% CI: 1.0-1.83), no formal education(RR: 2.46, 95% CI:1.22-4.93), outdoor occupation(RR: 1.47, 95% CI: 1.14-1.9) and lower body mass index(BMI)(<18.5)(RR: 1.25, 95% CI:1.02-1.55) were associated with increased risk of pterygium.

Conclusions: The overall incidence rate of pterygium was high in this rural population, especially in males and those engaged in outdoor activities, lack of formal education, and with lower BMI. It is likely that greater exposure to UV light is a major contributing factor, thus warranting preventive strategies.

Precis:

The 15-year incidence rate of pterygium among people aged 30 years and above in the longitudinal Andhra Pradesh Eye Disease Study (APEDS III) rural cohort was 25.2 per 100 person-years. Risk factors were likely associated with exposure to UV light warranting preventive strategies.

INTRODUCTION

Pterygium is an elevated, superficial, fibro-vascular proliferation which typically extends from the nasal perilimbal conjunctiva, which can extend onto the corneal surface.[1 2] In advanced cases, pterygium can distort the corneal topography and obscure the optical axis, leading to significant irregular astigmatism and visual impairment.[3 4] Several studies have reported the prevalence and risk factors for pterygium.[2 5-23] According to a recent meta-analysis, the global prevalence of pterygium was 12% which ranged from 3% in those aged 10-20 years to 19.5% in those aged 80 years and above.[23] The lowest prevalence was reported in Saudi Arabia (0.07%, age range: 17-82 years), while the highest was from China (53%, age range: 40-87 years).[23] Risk factors include demographic, environmental and lifestyle factors, with increasing age and outdoor occupation (a surrogate for UV light exposure) being more common across multiple studies.[2 5 7-10 15 16 18-23] Outdoor occupation leads to increased exposure to ultraviolet (UV) light, resulting in cellular changes at the medial limbus.[24] Other factors, such as sex, education, smoking, diabetes and hypertension have given inconsistent findings.[2 5-7 9-12 14 16 18-21 23] However, as all these studies were cross sectional, causality cannot be as implied as readily as in longitudinal, cohort studies. To the best of our knowledge, only four cohort studies have been reported from African, Chinese and South Korean populations with incidence data ranging from 4.9% to 11.6%, depending on the number of years of follow-up.[25-28]

The Andhra Pradesh Eye Disease Study I (APEDS I) was a cross-sectional survey conducted between 1996 and 2000 in three rural (West Godavari, Adilabad, and Mahbubnagar districts, n=7,771) and one urban area (Hyderabad, n=2,522) in Andhra Pradesh state in Southern India.[29 30] The follow up, APEDS III, was conducted from 2012 to 2016 in rural areas of APEDS I, to estimate the long-term incidence and progression of visual loss from the major eye diseases in this region. The urban area was excluded, as due to rapid urbanization in the past decade, it was not possible to trace the urban population in Hyderabad.[31]

The prevalence of pterygium is high in the ‘pterygium belt’, which lies between 30 degrees north and 30 degrees south of the equator.[32] Andhra Pradesh region also lies in ‘pterygium belt’ and has very high UV exposure and thus the prevalence of diseases related to UV can be high.[33] A large part of the population is engaged in agriculture and several other outdoor occupations. Data from APEDS I reported a prevalence of 11% and risk factors for pterygium.[34] This high prevalence is reflected by the fact that between 2010 and 2019, almost 10% of the 1.6 million outpatients who attended eye care services in our institution had pterygium,[35] and removal was the second commonest surgical procedure after cataract surgery. We now report the 15-year incidence rate of pterygium and its risk factors among people who were ≥30 years at baseline (1996-2000).

METHODS

The study adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of the 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. Detail of the methods for APEDS III, which was carried out between 2012 and 2016 are provided elsewhere.[30] The two earlier studies, APEDS I and II[29 31] have also been described earlier and all the participants in APEDS III were re-examined using the same methodology as APEDS I.

Data were collected during APEDS I on a range of socio-demographic factors, including systemic risk factors, age, occupation, education, residence, history of smoking, hypertension and diabetes, and use of spectacles for distance correction.[34] Occupation was classified using 18 different categories, and participants were asked whether during regular working hours (9 am to 5 pm) their occupation demanded more than 4 hours of outdoor work. If so, it was classified as outdoor; if not, their occupation was classified as indoor. All underwent a comprehensive eye examination and their anthropometric measurements (weight and height) were recorded.

Details of the ophthalmic examination procedure have already been reported.[29] In brief, the clinical team comprised of an ophthalmologist, an optometrist, and a vision technician trained to assess visual acuity, perform refraction and examine the anterior and posterior segment. Presenting distance visual acuity (VA) was measured using a standard, illuminated (at least 200 lux) logarithm of minimum angle of resolution (logMAR) chart at 3 meters, with the participant's current refractive correction, if any. Undilated slit lamp examination (SL 120 Carl Zeiss Meditec, Inc, Dublin, CA) was performed by the clinician, including intraocular pressure measurement by Goldman applanation tonometry (Carl Zeiss Meditec, Inc, Dublin, CA), before and after pupil dilatation. Gonioscopy was performed in all participants using NMR-K two-mirror lens (Ocular Instrument Inc., Bellevue, WA, USA) and graded as previously described.[36] In addition, a four-mirror gonioscopy was performed by the optometrist with an indirect gonioscopic lens (Volk Opticals Inc., Mentor, OH, USA) and any abnormality in the angle was documented. Following gonioscopy, pupils were dilated with tropicamide 1% and phenylephrine hydrochloride 2.5% for lens grading and posterior segment examination, unless contraindicated (i.e. risk of angle-closure acute glaucoma or active infection).

Pterygium was defined as a raised conjunctival fibro-vascular growth crossing the limbus invading onto the clear cornea, which was classified as present or absent by the examining ophthalmologist. Variables at baseline were defined as follows: age (30-39 years, 40-49 years, 50-59 years, 60 years or above); sex (male, female); education (no formal education, class 1-5, class 6-10, and class 11 and above), occupation (indoor, outdoor); history of smoking (non-smoker, past smoker, current smoker); body mass index (BMI) (<18.5; 18.5-24.99; 25-29.99; ≥30); systemic hypertension (defined as a systolic blood pressure of 140 mm Hg and above and/or diastolic blood pressure of 90 mm Hg and above and/or those on anti-hypertensive medication regardless of their blood pressure readings); history of diabetes mellitus and use of spectacles (for near or distance correction, or sunglasses). A positive history of diabetes mellitus was based on the self-report or the detection of diabetic retinopathy at baseline.

Participants in whom the presence of pterygium could not be assessed (due to corneal scarring for example) at APEDS I or APEDS III were excluded from further analysis. The incidence of pterygium was defined as the proportion of people free from pterygium at baseline at baseline who had developed the condition by the 15-year follow-up.

Data were analysed using STATA (version 13) software (Stata Corp, College Station, TX). The incidence rate was assessed and presented with 95% confidence intervals (CI). Baseline descriptive statistics included a comparison of the socio demographics and clinical findings of those who did and did not participate, and between participants with and without incident pterygium using χ^2 tests. Multiple logistic regression models, including stepwise methods, were used to calculate the odds ratio (OR) and 95% CI for each risk factor, using incident pterygium as the outcome measure. Variance inflation factors (VIF) were used to test for collinearity between the covariates after fitting a multiple regression model. The Hosmer-

Lemeshow test for goodness of fit was used to assess the model fitness. The statistical significance was determined at $p<0.05$ (two-tailed).

RESULTS

The baseline APEDS I included 7,771 people in three rural areas in the Andhra Pradesh state in Southern India. At APEDS III (2012-16), 6,447 (83%) of the 7,771 rural participants originally included in APEDS I were traced and available for examination and remaining 1,324 (17%) had died. Of these, 5,395 (83.7%) were re-examined after a mean of 15 years (range 13-17).

Among the 4,188 participants aged ≥30 years at baseline, 1,212 (28.9%) had died and 2,976 (71.1%) were available for follow up; 2,627 (88.3%) were examined (Figure 1). For those not examined, the reasons were migration (n =168, 5.7%), declined examination (n=98, 3.3%), and could not be traced (83, 2.8%). Excluded were 337 (12.8%) as they either had pterygium at baseline or could not be assessed for pterygium. Finally, 2,290 participants were included in the study (Figure 1).

Figure 1: Flow chart showing the number of participants included in analysis

Those who had died between APEDS I and APEDS III were significantly older than those examined (Table 1). Mortality was also significantly higher in men, those with lower levels of formal education or who stayed indoors, spectacle users and smokers, and people with hypertension, diabetes and a lower BMI. Non-participants were significantly older ($p=0.001$), better educated ($p=0.003$), hypertensive ($p=0.040$), and were less likely to perform outdoor activities ($p<0.001$). There were no differences by sex, smoking or diabetes status, use of spectacles or BMI.

Table 1. Baseline characteristics of participants in the Andhra Pradesh Eye Disease Study III (n=4,188)

	Available and examined (n=2,627)		Available not examined (n=349)		Died before examination (n=1,212)		P value
	n	%	n	%	n	%	
Age group (years)							<0.0001
30-39	1157	44	135	38.7	106	8.7	
40-49	774	29.5	94	26.9	161	13.3	
50-59	454	17.3	64	18.3	269	22.2	
60 and above	242	9.2	56	16.1	676	55.8	
Sex							<0.0001
Male	1179	44.9	147	42.1	638	52.6	
Female	1448	55.1	202	57.9	574	47.4	
Education							<0.0001
Class 11 or above	84	3.2	25	7.2	22	1.8	
Class 6-10	362	13.8	45	12.9	89	7.3	
Class 1-5	539	20.5	66	18.9	275	22.7	
No formal education	1642	62.5	213	61	826	68.2	
Smoking status							<0.0001
Non-smoker	1735	66	244	69.9	621	51.2	
Past smoker	137	5.3	13	3.7	119	9.8	
Current smoker	755	28.7	92	26.4	472	40	
Systemic hypertension[§]							<0.0001
No	1759	67	217	62.2	604	49.8	
Yes	829	31.6	130	37.2	584	48.2	
History of diabetes mellitus							<0.0001
No	2605	99.2	344	98.6	1162	95.9	
Yes	22	0.8	5	1.4	50	4.1	
Occupation[†]							<0.0001
Indoor	701	26.7	144	41.2	593	48.9	
Outdoor	1919	73	205	58.8	616	50.8	
Spectacles							<0.0001
No	2315	88.1	298	85.4	1003	82.8	
Yes	312	11.9	51	14.6	209	17.2	
BMI[‡]							0.001
18.5-24.9	1288	49	174	50	478	39.4	
<18.5	1063	40.5	137	39.3	558	46	
25-29.9	185	7	24	6.9	82	6.8	
≥30	40	1.5	5	1.4	20	1.7	

BMI= body mass index
*= statistically significant value at χ^2 test; †= data not available for 7 (0.3%) available and examined and 3 (0.3%) died before examination.
‡=data not available for 51 (2%) available and examined, 74 (6.1%) died before examination, and 9 (2.6%) available but not examined; §= data not available for 39 (1.4%) available and examined, 24 (2%) died before examination, and 2 (0.6%) available but not examined.

The overall age and sex adjusted incidence rate of pterygium was 25.2 per 100 person-years (95% CI: 24.8-25.7) (Table 2). Rates were significantly higher in males than females: 26.3

per 100 person-years (95% CI: 25.6-27.0) and 24.7 (95% CI: 24.1-25.3), respectively, but did not increase with age in either sex.

Table 2: Incidence rate of pterygium, by age and sex

	Males			Females			Total		
Age (Years)	**Number at risk***	**Incident cases**	**Incidence rate (95% CI)**	**Number at risk***	**Incident cases**	**Incidence rate (95% CI)**	**Number at risk***	**Incident cases**	**Incidence rate (95% CI)**
30-39	467	116	25.2 (24.2-26.2)	591	130	21.5 (20.7-22.4)	1,058	246	23.1 (22.5-23.8)
40-49	298	84	28.2 (26.9-30.0)	368	100	27.6 (26.4-28.8)	666	184	27.9 (27.0-28.8)
50-59	171	50	29.7 (27.9-31.5)	198	43	21.9 (20.4-23.4)	369	93	25.5 (24.3-26.7)
≥60	84	20	24.2 (21.9-26.7)	113	32	29.1 (26.9-31.3)	197	52	27.0 (25.4-28.7)
Total	1,020	270	26.7 (26.0-27.5)	1270	305	24.0 (23.4-24.6)	2,290	575	25.2 (24.8-25.7)
Adjusted			26.3 (25.6-27.0)			24.7 (24.1-25.3)			25.4 (24.9-25.9)

CI= confidence interval; *=Number of people at risk referred to the number of persons at the start of the observation period who had the potential to get pterygium

Participants with incident pterygium differed from those without in terms of educational status (p<0.001), BMI (p=0.036), and occupation (outdoor versus indoor work; p<0.001) (Table 3).

Table 3. Demographic, environmental, and lifestyle risk factors in incident and non-incident pterygium cases

Variables		Incidence			
		Yes (n= 575) (25.1%)	No (n=1715) (74.9%)	Total (n=2,290)	P value
Age group (years)	30-39	246 (42.8)	812 (47.4)	1,058 (46.2)	0.225
	40-49	184 (32)	482 (28.1)	666 (29.1)	
	50-59	93 (16.2)	276 (16.1)	369 (16.1)	
	>=60	52 (9)	145 (8.5)	197 (8.6)	
Sex	Female	305 (53)	965 (56.3)	1,270 (55.5)	0.178
	Male	270 (47)	750 (43.7)	1,020 (44.5)	
Education	Class 11 and above	11 (1.9)	63 (3.7)	74 (3.2)	<0.001
	Class 6-10	57 (9.9)	276 (16.1)	333 (14.5)	
	Class 1-5	111 (19.3)	379 (22.1)	490 (21.4)	
	No formal education	396 (68.9)	997 (58.1)	1,393 (60.8)	
Smoking	Non-smoker	361 (62.8)	1.152 (67.2)	1,513 (66.1)	0.087
	Past smoker	34 (5.9)	73 (4.3)	107 (4.7)	
	Current smoker	180 (31.3)	490 (28.6)	670 (29.3)	
Systemic hypertension	No	387 (68.6)	1,134 (66.9)	1,521 (67.4)	0.462
	Yes	177 (31.4)	560 (33.1)	737 (32.6)	
History of diabetes	No	569 (99)	1,701 (99.2)	2,270 (99.1)	0.612
	Yes	6 (1)	14 (0.8)	20 (0.9)	
Outdoor work	No	122 (21.3)	535 (31.3)	657 (28.8)	<0.001
	Yes	452 (78.8)	1175 (68.7)	1,627 (71.2)	
spectacles	No	501 (87.1)	1,512 (88.2)	2,013 (87.9)	0.511
	Yes	74 (12.9)	203 (11.8)	277 (12.1)	
BMI	18.5-24.99	259 (46)	866 (51.6)	1,125 (50.2)	0.036
	<18.5	259 (46)	656 (39.1)	915 (40.8)	
	25-29.9	36 (6.4)	129 (7.7)	165 (7.4)	
	>=30	9 (1.6)	29 (1.7)	38 (1.7)	

BMI= body mass index; *= statistically significant value at χ^2 test

In multivariable analysis, male sex (p=0.050), lack of formal education (p=0.011), greater outdoor activities (p=0.003) and lower BMI (<18.5) (p=0.034) and were all associated with incident pterygium (Table 4).

Table 4. Multiple logistic regression analysis for association between pterygium and demographic, environmental and lifestyle risk factors

	RR†	95% CI	P value
Age (years)			
30-39	(base)		
40-49	1.24	0.99-1.57	0.063
50-59	1.04	0.78-1.39	0.795
>=60	1.07	0.74-1.56	0.706
Sex			
Female	(base)		
Male	1.35	1.0-1.83	0.050*
Education			
Class 11 and above	(base)		
Class 6-10	1.27	0.62-2.6	0.517
Class 1-5	1.83	0.91-3.69	0.090
No formal education	2.46	1.22-4.93	0.011*
Smoking status			
Non-smoker	(base)		
Past smoker	1.26	0.77-2.0	0.353
Current smoker	0.91	0.67-1.23	0.539
Systemic hypertension			
No	(base)		
Yes	1.0	0.8-1.27	0.899
History of diabetes mellitus			
No	(base)		
Yes	1.68	0.62-4.58	0.311
Occupation			
Indoor	(base)		
Outdoor	1.47	1.14-1.9	0.003*
spectacles			
No	(base)		
Yes	1.27	0.93-1.71	0.129
Body mass index			
18.5-24.9	(base)		
<18.5	1.25	1.02-1.55	0.034*
25-29.9	1.19	0.78-1.81	0.416
≥30	1.36	0.62-2.98	0.436

OR= odd ratio; CI= confidence interval; BMI= body mass index
†= Based on multiple logistic regression with incident pterygium as the outcome and all the predictors entered at the same time
*= statistically significant value at multiple logistic regression
Hosmer-Lemeshow test for goodness for fit for the regression model, P=0.8
Variance Inflation factor for the multiple logistic regression model=2.3

DISCUSSION

In this study we assessed the mean 15-year incidence of pterygium in three rural areas of undivided Andhra Pradesh. To the best of our knowledge, this is the first large-scale study to report the incidence of pterygium in India.

The overall incidence was 25.4 per 100 person-years which was slightly higher in males than females. This is one of the highest incidences reported.[25-28] Among the four previous longitudinal studies, two were undertaken in countries in the "pterygium belt"; the Barbados Incidence Study of Eye Diseases (BISED) and the Yunnan Minority Eye Studies (YMES)",[25 26] and two were outside the pterygium belt; the Beijing Eye Incidence Study (BEIS) and the Korean cohort study (KCS).[27 28] (Table 5). As three of these studies reported cumulative incidence, the annual incidence has been estimated for each study, by dividing the cumulative incidence percentage by the mean follow-up in years (Table 5). This gave values of 1.3% per year for the BISED[26] and 1.4% per year for the YMES[25], the two countries in the pterygium belt, and 0.5% per year for the BES which is outside the pterygium belt.[28] The fourth study, KCS, which was again outside the pterygium belt, reported incidence rate as 2.1 per 1000 person-years.[27] In our study the crude annual incidence was higher than these earlier studies i.e., 1.7% per year in those 30 years and above and 2.4% per year in those 40 years and above (data not shown), being comparable to BISED and YEMS. The higher incidence rate in our analysis indicates pterygium to be a public health issue in Southern India, mostly due to high UV exposure. Hence, appropriate preventive strategies are warranted.

Table 5: Cumulative and annual incidence of pterygium in different countries

Authors	Year	Region (country)	Follow-up (years)	Sample size	Age (years), mean±SD#	Number of cases	Cumulative incidence (%, 95% CI@)	Annual Incidence
Nemesure B, et al.[26]	2008	Barbados (North America)	9	1888	56.7±10.8	218	11.6 (10.1–13.1)	1.3
Zhao L, et al.[28]	2013	Greater Beijing (China)	10	2628	54.6 ± 9.8	129	4.9 (N/A)	0.5
Li L, et al.[25]	2015	Yunnan province (China)	5	941	63.5±8.3	64	6.8 (5.2-8.4)	1.4
Rim T, et al.[27]	2017	South Korea	12	10,060,383	N/A	21,465	N/A	N/A
Our study	2012-16	India	15	2,290	42.7±10	575	25.2 (24.8-25.7)	1.7

*N/A: Not Available; #SD: Standard Deviation; @CI: Confidence Interval

In present study, the incidence of pterygium was estimated using baseline data from the APEDS I.[34] The baseline APEDS I reported a prevalence of 11.7%. Significant associations in the cross-sectional analysis were older age, low educational level, outdoor occupation, and living in a rural area. Interestingly, the longitudinal studies failed to find an association between age at baseline and the incidence of pterygium, including the APEDS III.[25 26] One possible explanation which could justify the lack of association between older age and pterygium rate in the APEDS III is that individuals at the highest risk of pterygium may have already developed pterygium at baseline, thus being excluded from the present investigation. Another possible explanation is behavioural change, with less outdoor exposure over time.

In our study sex was an independent risk factor for pterygium, with males being at increased risk. This finding might be discordant with a recently published study carried on in our hospital based data, which reported a higher prevalence of pterygium in women.[35] The reason for difference could be explained by the study methodology as well as population included in these studies. The study from Das et al. is a cross-sectional investigation, calculating the prevalence of pterygium in a hospital-based cohort. Our study is a longitudinal sample-based epidemiological observation reporting on the incidence of pterygium. The median age of the former study was 55 years, while only 17% of our sample was aged between 50 and 59 years. Furthermore, nearly 50% of their population belonged to urban or metropolitan districts, while 100% of our cohort included rural areas. This relationship of pterygium and male gender was also not reported in BISED or YMES,[25,26] but has been stated in several cross-sectional analyses.[7,8,10-12,16,18-22,37,38] The fact that nearly 80% of men have outdoor occupations (mainly agriculture) in rural areas, probably accounts for these findings. The role of genetics and sex hormones in pterygium development has also been advocated.[39] In vitro studies on corneal fibroblasts have proven that female sex hormones as 17β-estradiol and progesterone inhibit IL-1β–induced collagen degradation and the expression or activation of matrix metalloproteinases (MMPs), which contribute to the pathogenesis of pterygium.[40] By contrast, in vivo analysis have found that oestrogen replacement therapy was associated with a low prevalence of pterygium in postmenopausal women.[41]

We identified lack of formal education as a risk factor in our cohort, which was not reported in other studies.[25,28,42] The relatively small number of incident cases in other studies this might account for the difference as these studies would have been relatively underpowered to demonstrate this relationship. The way educational categories were classified in (four categories of educational level, as in our study versus binary classification in the studies published previously) might also explain the differences.[25,28,42]

Like the BISED and YMES studies, we confirmed the association between outdoor activities and the risk of developing pterygium.[25,26] This is the most compelling evidence to date, further corroborating the strong association between pterygium and cumulative UV exposure.[2,10,15,19-22,43] Although quantifying ocular exposure to UV radiation is very challenging,[44] it is well-known that high UV exposure leads to chronic cellular changes at the medial limbus.[24] As nearly 70% of the population of Andhra Pradesh (and the rest of India) lives in rural areas and most are engaged in agricultural activities, a high proportion would be at high risk for developing pterygium during their lifetime.[45]

Unlike previous study, we found no protective role of regular use of spectacles.[26] However, only 12% of participants wore spectacles which would have reduce the power the analysis. The BISED study found a negative association between the incidence of pterygium and the use of spectacles,[26] which has been interpreted as a surrogate of office work and decreased UV exposure. In the present study, the usage of spectacles was marked as positive without differentiating refractive correction lenses from sunglasses. It's also likely that there may be a lack of UV filter on the lenses in this cohort. Moreover, adherence to spectacle-wearing was not directly assessed, which might be very low especially in rural districts. Both these factors might have reduced the power of the analysis. As in other studies, we did not find any association between pterygium and hypertension or diabetes after adjusting for other covariates.[25,28]

The adjusted analysis showed an interesting association between pterygium and low BMI. We can speculate an indirect causative relationship between low weight, low socio-economic status and exposure to risk factors for pterygium, although the most likely explanation is residual confounding.

The role of cigarette smoking in pterygium development is under debate, although recent evidence point towards a protective role.[11 12 46] However, this was not confirmed in any of the longitudinal studies[25 42] indicating that the association might be spurious.

Strengths of our study include its population-based longitudinal design, long-term follow-up, high participation, and standardized protocols. Reporting on education status, systemic disease, and BMI is also a novelty in comparison with previous studies. Limitations include loss to follow-up during the 15-year study period (due to death and non-participation), which may have led to selection or survival bias.[47] In the risk factor analysis, all the factors were fixed at baseline, whereas in real life these factors can vary over time. In addition, we only used a binary measure of presence or absence of pterygium at baseline or during follow-up, without accounting for a clinical grading of the disease. In addition, we only used a binary measure of outdoor / indoor activity as a proxy for UV exposure, which may have led to misclassification. This may have been more applicable for women, most of whom described themselves as housewives which was classified as an indoor activity. Similarly, history of smoking was assessed as a categorical variable (i.e., non-smoker, past smoker, current smoker), rather thein being expressed as pack-years, which would provide a better measure of long-term smoking habits. Another limitation is that inter-observer agreement studies were not undertaken for pterygium, but all assessments were made by qualified ophthalmologists after rigorous training. As data were not available on the time of onset of pterygium, the hazard ratio would not be calculated. Finally, the urban cluster in APEDS I could not be included in APEDS III due to urbanization with out-migration of the population, which limits generalizability.[31]

In conclusion, this is the first study to report the incidence of pterygium in India. Our results indicate that the incidence is relatively high in this rural population which lies within the "pterygium belt". The study confirmed that there is an increased risk in males, the uneducated, those with outdoors activities and those with lower BMI. Knowledge of these associations may be useful in the long-term planning of eye care services and public health preventive measures in these regions.

ACKNOWLEDGMENTS

None

CONTRIBUTORSHIP STATEMENT

Rohit C Khanna (RCK): Contributions to the conception and design of the work, acquisition, analysis and interpretation of data. Drafting the work and revising it critically and final approval of the version published.

Srinivas Marmamula (SM): Contributions to the design of the work, acquisition, analysis and interpretation of data analysis. Revising it critically and final approval of the version published

Maria Vittoria Cicinelli (MVC): Contributions to analysis and interpretation of data. Drafting the work and revising it critically and final approval of the version published.

Asha Latha Mettla (ALM): Contributions to the acquisition and interpretation of data analysis. Revising it critically and final approval of the version published

Pyda Giridhar (PG): Contributions to acquisition of data. Revising it critically and final approval of the version published.

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Gudlavalleti V S Murthy (GVSM): Contributions to the conception and design of the work and interpretation of data. Revising it critically and final approval of the version published.

Clare Gilbert (CG): Contributions to the conception and design of the work and interpretation of data. Revising it critically and final approval of the version published.

Gullapalli N Rao (GNR): Contributions to the conception and design of the work and interpretation of data. Revising it critically and final approval of the version published.

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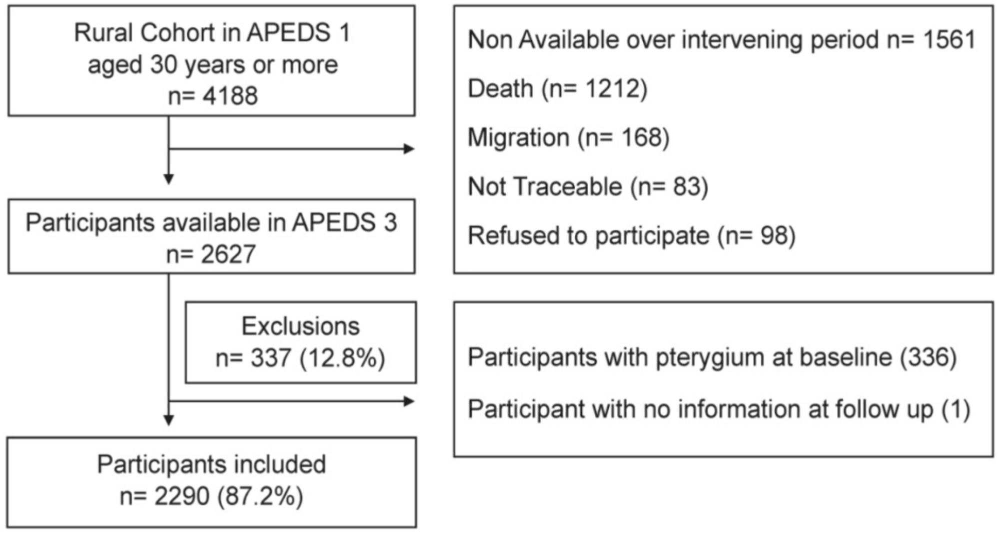

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