Prevalence and determinants of age-related macular degeneration in central Sri Lanka: the Kandy Eye Study

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ABSTRACT

Aims To determine the prevalence, associations and risk factors for age-related macular degeneration (ARMD) in central Sri Lanka.

Methods The study was a population-based, cross-sectional survey of residents aged ≥40 years in rural Sri Lanka. ARMD was assessed on dilated fundoscopy using the International Age-Related Maculopathy Epidemiology Study Group classification system.

Results Of the 1721 subjects identified, 1375 participated (79.9%). Of the participants, 1013 were aged ≥50 years (73.6%). The prevalence of any ARMD (adjusted for study design) was 4.72 (95% CI 2.22 to 7.20)% with 3.82 (95% CI 1.60 to 6.04)% early ARMD and 1.70 (95% CI 0.14 to 3.27)% late ARMD. Age ($p<0.001$) and Sinhalese ethnicity ($p=0.016$) were significantly associated with ARMD. Men had a tendency toward a higher prevalence of ARMD than women, although this was not statistically significant ($p=0.081$). Ocular risk factors such as cortical cataract ($p=0.024$) and pseudophakia ($p=0.003$) were associated with ARMD on the univariate but not multivariate analyses. Illiteracy and the identification of social supports were significantly associated with ARMD on univariate analyses. However, only social support was statistically significant after multivariate analysis ($p=0.024$).

Conclusions Although the prevalence of ARMD is slightly lower in Sri Lanka than surrounding regions, it contributes to a higher proportion of visual impairment, including blindness. Risk factors include age and Sinhalese ethnicity.

Age-related macular degeneration (ARMD) is the third leading cause of blindness worldwide, following cataract and glaucoma.[1] Whilst ARMD is the leading cause of visual impairment in industrialised countries,[1] the proportion of vision impairment and blindness in the developing world attributable to ARMD is increasing in the setting of an expanding and ageing population.

WHO has identified Sri Lanka in particular as an area in need of further investigation, in keeping with the aims of the Vision 2020 project. The last population-based study in Sri Lanka was the Kandy Eye Study (KES) of 2006–2007, which showed that the prevalence of ARMD was responsible for 15% of visual impairment (visual acuity (VA) better eye <6/18).[2] However, data relating to retinal disease from this study have not yet been reported.

Risk factors associated with ARMD including hypermetropia, hypertension, smoking, female sex and positive family history have been studied in large well-conducted trials worldwide, although the strength of these associations has been variable.[3 4] Population-based studies conducted in Asia have suggested an association with male sex[5–7] and cigarette smoking,[8] and a reduced prevalence in those with low alcohol intake.[9] Population-specific gene/environment interactions may explain the variability of ARMD risk factors amongst studies.

METHODS

The current study used data from the KES. The principal aims of this study were to determine the prevalence and risk factors of visual impairment. Methods have been described in detail elsewhere.[2]

In brief, the KES was a population-based cross-sectional ophthalmic survey of the inhabitants of rural villages in central Sri Lanka. Subjects were randomly selected using a cluster sampling process. A sampling frame consisting of the list of all villages in the Kandy District with their populations was obtained from the 2001 Sri Lankan Census. The city of Kandy was excluded and one village was randomly selected from the 20 divisions. Households were randomly selected from each village and all inhabitants ≥40 years of age were invited to participate.

Qualified healthcare workers obtained a medical and ophthalmic history from each patient in their own language using a standardised questionnaire. Each participant then received a comprehensive vision and eye examination. If VA was <6/18 in either eye then an experienced ophthalmologist assigned a principal cause of visual impairment. In difficult cases, at least two experienced ophthalmologists reached a consensus on the principal cause of visual impairment.

ARMD was assessed according to the International Age-Related Macular Degeneration Epidemiological Study Group classification system.[10] Following adequate pupillary dilation, fundi were examined using a 78 D lens. Early ARMD was defined as soft drusen ≥63 μm or retinal pigment epithelium (RPE) pigment abnormalities (hyperpigmentation, hypopigmentation, or both) unrelated to any other disease process in participants ≥50 years regardless of VA. Late ARMD was defined as the presence of neovascular (wet) ARMD or geographic atrophy (dry ARMD) in patients of the same age group regardless of VA.

Definitions

Presenting blindness was defined as presenting VA <3/60 in the better eye; best corrected blindness

was defined as corrected VA <3/60 in the better eye. Presenting low vision was defined as presenting VA <6/18 but ≥3/60 in the better eye. Best corrected low vision was defined as corrected VA <6/18 but ≥3/60 in the better eye. Presenting visual impairment was defined as the combined set of presenting low vision and presenting blindness, and best corrected visual impairment was defined as the combined set of best corrected low vision and best corrected blindness. Field defects were not taken into consideration.

Statistics

Prevalence was calculated as an estimate using appropriate weights and consideration of the design effect using Stata Version 10 (Stata Corp., College Station, Texas, USA), and was calculated on an individual rather than a per eye basis.

The aim of the logistic analyses was to identify risk factors that placed an individual at risk of ARMD in one or both eyes. Early and late ARMD was pooled as the dependent variable. For ocular rather than systemic risk factors only right eye data was used in the univariate analyses and a separate multivariate analysis was performed.

ORs and 95% CIs were calculated using logistic regression with variance calculations allowing for the study design.

A multivariate logistic regression model with any ARMD as the dependent variable was constructed using a pre-determined algorithm for the inclusion of predictors. At least 15 subjects positive for the dependent variable were required per independent variable. Independent variables were selected if the p value, as determined by the Wald chi-squared test, in the univariate analyses was <0.2, and they had a plausible association with but not necessarily causation of ARMD. The a priori strategy for dealing with multicollinearity issues was as follows: predictors would be removed in a hierarchical manner (highest p value from the univariate analysis removed first) if the variance inflation factor (VIF) was >2 or the condition number was >25. If the removal of this predictor did not reduce the condition number to ≤25 then this predictor was retained and the next predictor was removed and the process repeated. All regression analyses were undertaken using Stata 10 for Windows (Stata Corp.). All p values were two-sided and were considered statistically significant when the values were <0.05.

RESULTS

There were 1721 eligible subjects and 1375 participated (79.9% participation rate). Of the participants, 1013 were aged ≥50 years (73.6%), and this number was used as the denominator in analyses. The average age of the participants was 57.0 (SD 10.6) years. There was a significant under-representation of male participants (p<0.001): 39.9% of participants were men compared with 53.2% of non-participants. The average age of the male participants (57.9 (SD 10.6) years) was significantly greater (p<0.001) than the average age of the male non-participants (54.6 (SD 10.4) years). The average age of the female participants (56.4 (SD 10.5) years) was not significantly different (p = 0.31) from the average age of the female non-participants (55.5 (SD 11.1) years).

The overall prevalence any ARMD (early or late) was 4.72% (95% CI 2.22 to 7.20%, 76 participants) adjusted for study design. Early ARMD had an overall prevalence of 3.82 (95% CI 1.60 to 6.04)% and late ARMD of 1.70 (95% CI 0.14 to 3.27)% adjusted for study design (tables 1 and 2).

DISCUSSION

This study represents the first population-based assessment of the prevalence and associations of ARMD in Sri Lanka. Whilst the contribution of ARMD to low vision and blindness in Sri Lanka (figure 1) was higher than in neighbouring countries (figure 2), the overall prevalence of ARMD in Sri Lanka was generally lower than the reported prevalence in neighbouring India (figure 3). This may reflect higher cataract surgery coverage rates in the Kandy region compared with regions in neighbouring countries. Differences in the method of assessment of ARMD amongst studies mean that direct comparisons of data need to be made cautiously.

Age was significantly associated with ARMD in the current study, consistent with all major population-based study results.

Although male sex was not statistically significantly related to ARMD in the current study, the trend toward this (p = 0.081) is consistent with other studies from this region. The India Eye (INDEYE) study in North India found that men were more likely to have ARMD (p = 0.03),[6] and the Hisayama study also showed that men had a higher prevalence of late ARMD.[5] Similarly, the Singapore Malay Eye Study found that men were more likely to be affected by early ARMD, with a non-significant trend in late ARMD.[7] These studies contrast with findings from large Western studies such as the National Health and Nutrition Examination Survey (NHANES) III[20] and the Beaver Dam Eye Study[21] which found that women showed significantly more ARMD than men.

The finding that Sinhalese ethnicity is strongly associated with ARMD in a Sri Lankan population is an important one, and may be related to the genetic basis of ARMD. A complex interplay between genetics, ethnicity and environment may contribute to the variable prevalence of the disease.[22]

Participants with ARMD in the current study were significantly more likely to be identified as having social supports. This could reflect a greater need for assistance with daily functioning, and be an indirect marker that ARMD has a wider impact on the community than the single patient affected.

Table 1 Descriptive statistics based on per-participant analysis

Age (years)	Total ARMD (%)	Early ARMD (%)	Late ARMD (%)	Male (%)	Female (%)
50–59	0.82	0.67	0.15	0.44	0.37
60–69	1.85	1.63	0.37	0.67	1.19
≥70	2.97	2.30	1.11	1.70	1.26

ARMD, age-related macular degeneration.
Early ARMD and late ARMD proportions may add to > total ARMD if both eyes from the same patient are variably affected.

Table 2 Univariate analysis of systemic and ocular risk factors and associations of age-related macular degeneration

Variable	OR (95% CI)	p Value
Age	1.13 (1.10 to 1.16)	<0.001*
Sex	1.53 (0.95 to 2.46)	0.081
Ethnicity	7.21 (1.76 to 29.63)	0.006*
Social supports	2.67 (1.54 to 4.60)	<0.001*
Illiteracy	2.22 (1.18 to 4.18)	0.013*
BMI	1 (0.98 to 1.02)	0.75
Smoking	0.73 (0.36 to 1.50)	0.4
Nuclear cataract	1.24 (0.92 to 1.66)	0.157
Cortical cataract	1.31 (1.04 to 1.65)	0.024*
Axial length	1.09 (0.86 to 1.37)	0.49
Pseudophakia	3.91 (1.57 to 9.76)	0.003*
Myopia	1.51 (0.91 to 2.51)	0.112
Hypermetropia	0.73 (0.44 to 1.20)	0.21

ARMD, age-related macular degeneration.
*p<0.05.

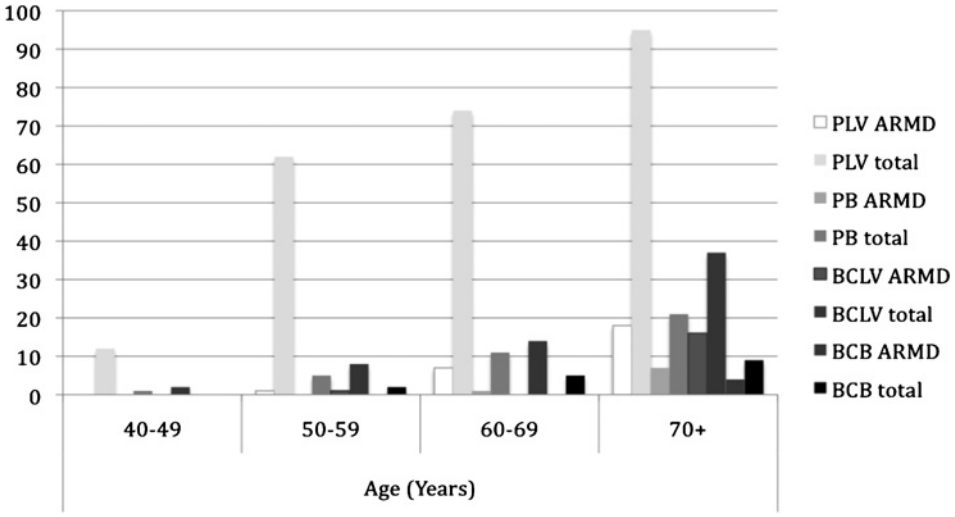

Figure 1 Presenting and best corrected visual impairment and blindness in participants with age-related macular degeneration (ARMD) compared with the total number of participants. BCB, best corrected blindness; BCLV, best corrected low vision; PB, presenting blindness; PLV, presenting low vision.

Illiteracy (defined as no schooling) was significantly associated with the presence of ARMD. Literacy and level of education have been variably related to ARMD in past studies.[4] Asian studies such as the Andhra Pradesh Eye Study[9] found no association between education and ARMD.

The current study showed no relationship between BMI and ARMD. A number of other Asian studies have recorded similar findings,[5 8 9 19] but some Western studies such as the Blue Mountains Eye Study have shown that BMI is significantly associated with ARMD.[23]

Smoking has also been variably linked with ARMD. There was no association between smoking and ARMD in the current study, in keeping with some Asian studies.[18 19] Others have shown an increased prevalence of ARMD in smokers in Indian, Japanese and Singaporean populations,[8 9] and in Western populations.[24]

The ocular risk factors for ARMD seen on univariate analysis in the current study, namely cortical cataract (but not nuclear cataract) and pseudophakia, are supported by a number of other population studies. The Andhra Pradesh Eye Study found a higher incidence of ARMD in participants with cortical cataract.[9] Increased prevalence of ARMD has been found in subjects with lens opacities[25] and in those who have undergone cataract surgery.[9 25] The association of ARMD with both cataract and pseudophakia is confusing, and has several possible interpretations, including the presence of cataract (certain subtypes) or pseudophakia as surrogate biomarkers of ocular ultraviolet (UV) damage, or pseudophakia removing the natural lens UV filters.

Refractive error and axial length are not associated with ARMD in Sri Lanka. Whilst these factors have not been assessed in most Asian population-based studies, a number of large well-conducted population-based studies have shown hypermetropia to be significantly associated with ARMD.[3 4]

The larger representation of older men in the participant group than the non-participants may falsely elevate the prevalence estimates of ARMD in the Kandy region. Despite this, male sex was a risk factor at all ages. Most population-based studies of ARMD in the developed world have assessed ARMD from fundus photos graded by a medical retinal specialist. The level of agreement between the clinical examination methodology used in the current study compared with examination of fundus photographs by a retinal specialist is unclear.

In summary, the current study estimates an overall prevalence of ARMD in Sri Lanka of 4.72%. This is the first study assessing ARMD in Sri Lanka. Significant risk factors include age and Sinhalese ethnicity, and identifying social supports was a significantly associated. A trend toward male predisposition for ARMD

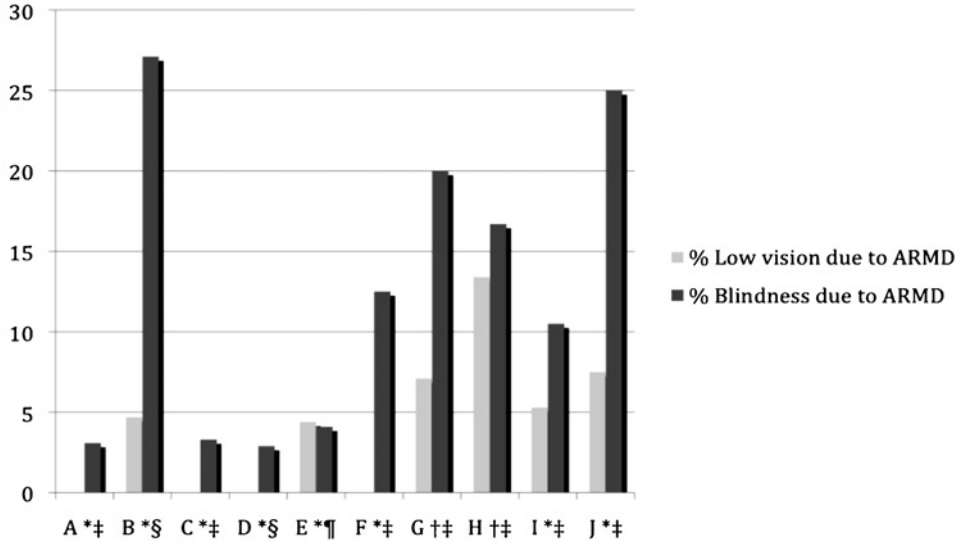

Figure 2 Age-related macular degeneration (ARMD) as a cause of visual impairment and blindness in Asia. A, Bangladesh;[11] B, Hong Kong;[12] C, India (Rajasthan);[13] D India (Thirunelveli);[14] E, India (Andhra Pradesh);[9] F, Indonesia;[15] G, Singapore;[16] H, Sri Lanka; I, Sri Lanka; J, Taiwan.[17] *Presenting visual acuity (VA). †Best corrected VA. ‡Definition of low vision: <6/18—≥3/60; blindness <3/60. §Definition of low vision: <6/18—≥6/60; blindness <6/60. ¶Definition of low vision: <6/12—≥6/60; blindness <6/60.

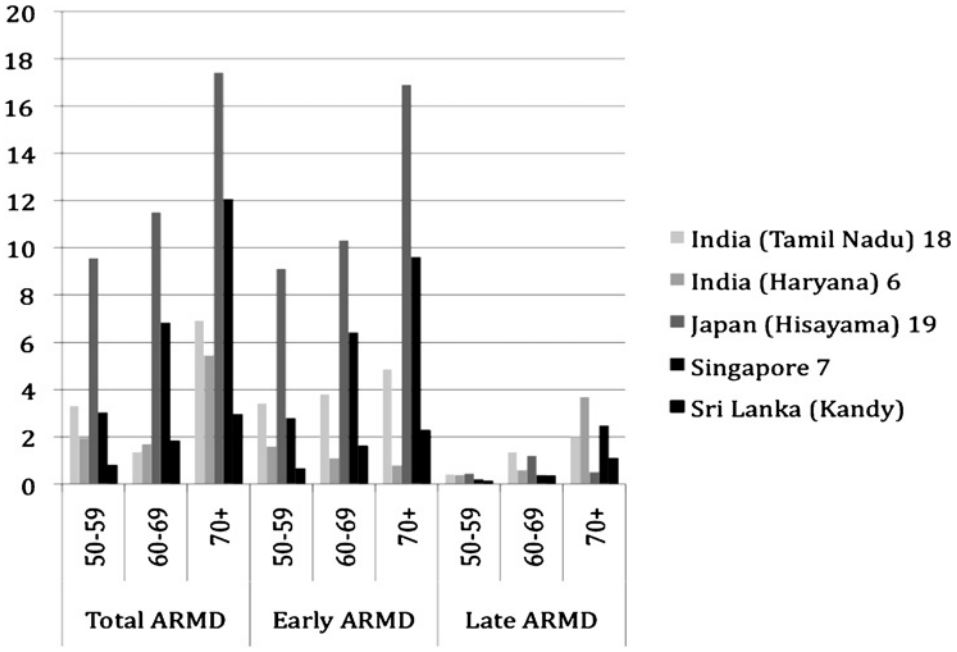

Figure 3 Prevalence of age-related macular degeneration (ARMD) in Asia.

was seen, which is consistent with other population-based studies from Asia, and contrary to the female predominance seen in Western studies. Further studies into the genetic variants predisposing to ARMD in Sinhalese participants may be useful in investigation of a basis for the apparent discrepancy between the prevalence and risk factors for ARMD in Asian and Western populations.

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Competing interests None declared.

Ethics approval The Kandy Eye Study had ethical approval from the Royal Adelaide Hospital Ethics Committee. The study was conducted in accordance with the Declaration of Helsinki.

Patient consent Consent for participation was obtained from the head of each village prior to commencement of the survey. Informed consent, in the participant's own language, was obtained from all participants.

Provenance and peer review Not commissioned; externally peer reviewed.

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