Prevalence of Amblyopia in School-Aged Children and Variations by Age, Gender, and Ethnicity in a Multi-Country Refractive Error Study

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Purpose: To estimate the age-, gender-, and ethnicity-specific prevalence of amblyopia in children aged 5 to 15 years using data from the multi-country Refractive Error Study in Children (RESC).

Design: Population-based, cross-sectional study.

Participants: Among 46 260 children aged 5 to 15 years who were enumerated from 8 sites in the RESC study, 39 551 had a detailed ocular examination and a reliable visual acuity (VA) measurement in 1 or both eyes. Information on ethnicity was available for 39 321 of these participants. This study focused on findings from the 39 321 children.

Methods: The examination included VA measurements, evaluation of ocular alignment and refractive error under cycloplegia, and examination of the external eye, anterior segment, media, and fundus.

Main Outcome Measures: The proportion of children aged 5 to 15 years with amblyopia in different ethnic cohorts. Amblyopia was defined as best-corrected visual acuity (BCVA) of $\leq$20/40 in either eye, with tropia, anisometropia ($\geq$2 spherical equivalent diopters [D]), or hyperopia ($\geq$+6 spherical equivalent D), after excluding children with fundus or anterior segment abnormalities.

Results: The overall prevalence of amblyopia was 0.74% (95% confidence interval, 0.64–0.83) with significant ($P < 0.001$) variation across ethnic groups: 1.43% in Hispanic, 0.93% in Chinese, 0.62% in Indian, 0.52% in Malay, 0.35% in Nepali, and 0.28% in African children. Amblyopia was not associated with age or gender. The most common cause of amblyopia was anisometropia.

Conclusions: In this study, the prevalence of amblyopia varied with ethnicity and was highest in Hispanic children and lowest in African children. Most cases were unilateral and developed before the age of 5 years. The impact of changes of definitions on prevalence estimates is discussed. *Ophthalmology 2015;122:1924-1931 © 2015 by the American Academy of Ophthalmology.*

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Amblyopia is the most common cause of uncorrectable visual impairment in children and in adults up to 60 years of age.[1–3] Amblyopia generally develops in the childhood years up to the age of 7 to 8 years[4] and can be effectively remediated if detected and treated before the age of 9 to 10 years.[2,5] If not treated, amblyopia can produce lifelong uncorrectable visual impairment.[6]

Estimation of the prevalence of amblyopia is important for both clinicians and health policy decision-makers for an understanding of the need for screening, detection, and intervention in the community. The prevalence of amblyopia has been reported in several studies,[7–18] ranging from 0.2% in a school-based study of children aged 7 to 19 years in Tanzania,[18] 1.8% in a school-based study of Australian children aged 6 years,[13] to 3.6% in British children aged 7 years in the Avon Longitudinal Study of Parents and Children (ALSPAC).[16] Higher rates have been reported in

clinical samples,[19] but they clearly do not provide valid estimates of population prevalence. Many of the previous studies lack power and are difficult to compare with each other because of the generally low prevalence of amblyopia, different definitions of disease, and differences in the recruitment of the study samples.

The Multi-Ethnic Pediatric Eye Disease Study; the Baltimore Pediatric Eye Disease Study; the Strabismus, Amblyopia, and Refractive Error in Singapore study; and the Sydney Pediatric Eye Disease Study recently have used standardized methods and definitions to report the prevalence of amblyopia in preschool children aged 30 to 72 months.[8,10,11,20–22] However, visual acuity (VA) testing in younger children of preschool age is problematic because cognitive function is still developing and it is difficult to distinguish poor acuity due to amblyopia from poor performance on this cognitive task.

Setting VA cutoffs for the definition of amblyopia is somewhat easier in older children. The multi-country Refractive Error Study in Children (RESC) is a large-scale population-based, cross-sectional survey of refractive error and visual impairment in school-aged children, which used standard methodology and common definitions, including a standard definition of amblyopia.[23–31] By using RESC data, we report on the age- and gender-specific prevalence of amblyopia in children 5 to 15 years of age in 6 ethnic groups from 8 sites in 6 countries.

Methods

Population

The RESC surveys were conducted in populations with different ethnic origins and environments using a standardized protocol for sampling of the targeted study population and examination of participants. The RESC data used were obtained from 2 sites in China (urban Liwan District in Guangzhou[28] and semi-rural Shunyi District near Beijing[23]), 2 sites in India (urban Trilokupi segment in New Delhi[24] and rural Mahabubnagar District near Hyderabad in Southern India[27]), 1 site in Chile (the urban La Florida area of Santiago[30]), 1 site in Malaysia (urban Gombak District near Kuala Lumpur[26]), 1 site in Nepal (rural Jhapa District in Eastern Nepal[25]), and 1 site in South Africa (a semi-urban area within the South and West Regions of Durban[29]). Children aged 5 and 6 years were not included in the surveys in Kuala Lumpur and Hyderabad.

The survey ethnic groups were Hispanic, Chinese, Indian, Malay, Nepali, and African. The study populations in Kuala Lumpur and Durban were of more than 1 ethnicity, with ethnic identification based on self-reporting. The Chinese (East Asian), Indian (South Asian), Malay (South Asian), and African ethnic groups correspond to relatively well-defined population genetic clusters, but the population of Nepal is ethnically heterogeneous, consisting of people with South Asian or East Asian ancestries. Detailed questions about ethnicity were not included in the Nepal study; thus, ethnicity is described only as Nepali. Likewise, the population classified as Hispanic in Chile, as with other populations in the Americas, has mixed and variable ancestry from European, African, and Native American progenitors. This does not correspond to a well-defined population genetic cluster.

Details of the survey enumeration methods and examination procedures have been described.[31] The study adhered to the tenets of the Declaration of Helsinki, and approval for the study protocol was obtained from the World Health Organization Secretariat Committee on Research Involving Human Subjects. Approval to conduct the study at each site was obtained from local health authorities. A guardian of the child was informed of the study details and asked to provide signed, informed consent.

Examinations

Visual Acuity. Uncorrected distance VA was measured with a retro-illuminated logarithm of the minimum angle of resolution chart (Precision Vision, La Salle, IL) with 5 tumbling "E" optotypes on each line in a monocular fashion with the right eye followed by the left eye. If uncorrected VA in either eye was ≤20/40, best-corrected visual acuity (BCVA) was measured using a trial frame under dilation in a monocular fashion.

Ocular Motility. Ocular alignment was assessed using the cover and uncover test. Cover testing was performed using fixation targets at near (0.5 m) and distance (4.0 m). Manifest strabismus

was categorized as esotropia, exotropia, or vertical at 0.5 m and 4.0 m fixation. The degree of tropia was measured using the Hirschberg corneal light reflex.

Cycloplegic Refraction. Refraction measurements were attempted on all children after adequate cycloplegia, achieved using 2 drops of 1% cyclopentolate administered 5 minutes apart to each eye. A third drop was administered if a pupillary light reflex was still present after 20 minutes. At least 15 minutes after the last cycloplegic eye drops, cycloplegic refraction was performed with a streak retinoscope followed by measurement with a handheld autorefractor. The cycloplegic retinoscopy data were used as the outcome for refractive status of the participants.

Definitions

The definition of amblyopia was determined by a panel of experts in an expert consultation meeting sponsored by the World Health Organization and US National Eye Institute. Amblyopia was defined as BCVA ≤20/40 in at least 1 eye associated with ≥1 of the following potential causes: (1) esotropia, exotropia, or vertical tropia at 4 m fixation, or esotropia or vertical tropia at 0.5 m (strabismic amblyopia); (2) anisometropia of ≥2 spherical equivalent diopters (D) (anisometropic amblyopia); or (3) hyperopia of ≥6 spherical equivalent D. Children with fundus or anterior segment abnormalities precluding normal vision were not counted as amblyopic.[31]

If only 1 eye met the criteria, the child was diagnosed with unilateral amblyopia. If both eyes met the criteria separately, the child was diagnosed with bilateral amblyopia.

Although an inter-ocular difference (IOD) of ≥2 lines has become a new standard in the definition of amblyopia, this was not available when we developed the RESC protocol in the year 2000. The possible impact on the prevalence estimation due to the changes of definition is clarified in the "Discussion" section.

Statistical Analysis

Stata Version 11.0 (StataCorp LP, College Station, TX) was used for all statistical analyses. Confidence intervals (CIs) and *P* values (significant at the <0.05 level) for prevalence estimates and regression models were calculated with adjustment for cluster effects associated with the sampling design. Prevalence was calculated as the ratio of the number of individuals with amblyopia to the total number examined with stratification by age, gender, and ethnicity. Multivariate logistic regression was used to investigate the association of age, gender, and ethnicity with amblyopia. Nonparametric analysis (Kruskal–Wallis rank test) was used to investigate differences in the distribution of BCVA in the unilateral amblyopic eyes by the underlying causes.

Results

Study Cohort

Among the 46 260 children enumerated, 39 551 (85.5%) had a detailed ocular examination (external eye, anterior segment, media, and fundus) with a reliable VA measurement in 1 or both eyes. Information on ethnicity was not available for 230 children in Durban and Kuala Lumpur, leaving a total of 39 321 children in the present analysis.

Table 1 shows the demographic characteristics of the study sample by ethnicity. The Chinese children were from Shunyi District (53.5%), Guangzhou (39.6%), and Kuala Lumpur (6.92%). The Indian children were from New Delhi (55.2%), rural Hyderabad (37.1%), Durban (3.85%), and Kuala Lumpur (3.82%). The African, Nepali, Malay, and Hispanic children