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Socio-demographic disparities in amblyopia prevalence among 1.5 million adolescents

Itay Nitzan [1,2], Maxim Bez [2], Jacob Megreli[1,2], Dana Bez[1,2], Adiel Barak[3], Claudia Yahalom[4], Hagai Levine [1]

1 Hebrew University-Hadassah Braun School of Public Health and Community Medicine, Jerusalem, Israel
2 Medical Corps, Israel Defense Forces, Israel
3 Department of Ophthalmology, Tel Aviv Sourasky Medical Center and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
4 Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel

Correspondence: Hagai Levine, Braun School of Public Health and Community Medicine, Hebrew University-Hadassah Faculty of Medicine, P.O Box 12272, Kiryat Hadassah, Ein Kerem, Jerusalem 9112002, Israel, Tel: +972 2 6777452, Fax: +972 2 6431086, e-mail: hlevine@hadassah.org.il
Itay Nitzan and Maxim Bex contributed equally to this work as first authors.
Claudia Yahalom and Hagai Levine contributed equally to this work as last authors.

Background: Amblyopia, when not diagnosed at appropriate age, leads to uncorrectable visual impairment with considerable social and financial implications. The aim of this study was to assess socio-demographic disparities in amblyopia prevalence among Israeli adolescents, in order to identify susceptible groups in the population. **Methods:** A nationwide, population-based, cross-sectional study of Israeli adolescents examined between 1993 and 2017. All study participants underwent visual acuity examination with socio-demographic data and previous medical history documented. Associations were analyzed using univariable and multivariable logistic regression models. **Results:** Among 1 334 650 Israeli-born candidates aged 17.15±0.26 years, amblyopia was diagnosed in 1.07%. The overall prevalence of amblyopia has declined from 1.59% in 1993 to 0.87% in 2017. Being in the lowest socioeconomic status and below average cognitive function scores increased the odds of amblyopia in both males [odds ratio (OR) 1.64, 95% confidence interval (CI) 1.45–1.87; OR 1.27, 95% CI 1.19–1.35, respectively] and females (OR 1.61, 95% CI 1.30–1.98; OR 1.27, 95% CI 1.18–1.36, respectively). Among males, Orthodox and ultra-Orthodox educational systems were associated with increased odds of amblyopia (OR 1.16, 95% CI 1.09–1.25; OR 1.90, 95% CI 1.73–2.09). A significantly higher prevalence of amblyopia was recorded among 219 983 immigrants (1.51%, $P<0.001$). **Conclusions:** Although the overall prevalence of amblyopia has decreased during the observed years, we found substantial evidence of socio-demographic disparities in amblyopia prevalence among adolescents, suggesting disparities in the prevention of the disease and its treatment. Demonstration of inequities at a national level could aid future guidance of health policy and augment current vision screening programs.

Introduction

Amblyopia is a significant cause of visual deficit in childhood and one of the most common causes of persistent unilateral visual impairment in adulthood.[1] The prevalence of amblyopia among children is estimated between 1% and 5%,[2] depending on population of study. The existence of a 'sensitive' period in the development of normal vision is a proven concept, during which amblyopia can develop. Amblyopia is responsive to treatment if diagnosed early enough, predominantly before 6–8 years of age.[3] When treated, older children and even adults may show improvement as well, though to a lesser degree,[4,5] and treatment results are stable in long-term follow-up.[6]

In Israel, visual screening is performed several times during the first years of life. At first, screening is performed postnatally by checking for the presence of the red-light reflex. Later, public health clinics under governmental supervision offer additional screening tests. Every infant undergoes a basic visual function examination either by an optometrist or a nurse, between the age of 9–12 months. At 3–5 years of age, a verbal visual acuity examination is performed by a nurse. Another examination using Snellen charts is performed at 6–7 and 13–14 years of age at school.[7] Every child who fails the evaluation is referred to an ophthalmologist for a comprehensive eye examination. All Israeli citizens have state-mandated medical insurance, thus follow-up is available to all at minimal cost.[8] However, the integrity of the offered visual screening tests has been criticized, as no governmental quality control system assure a homogenous practice across the country.[9]

Previous works have addressed the adverse effects inflicted by amblyopia, including an array of visual disturbances affecting daily activities and superimposed medical costs.[1,10,11] As amblyopia holds both social and financial impacts, the aim of this nationwide, population-based, long-term repeated cross-sectional study was to evaluate socio-demographic disparities in amblyopia prevalence among Israeli adolescents, in order to identify susceptible populations and direct health policy.

Methods

Study setting and population

All Israeli-Jewish residents, who reach 17 years of age are obligated to serve in the army and undergo processing and evaluation by a draft board, during which their intellectual, medical and social eligibility for military service is evaluated.[12] A total of 1 939 508 Israeli candidates for military service were examined by the military draft board and underwent visual acuity examination by a qualified technician between 1993 and 2017 (Supplementary figure S1). Prior to 1993, visual acuity was not systematically documented and full-year data are currently available until 2017. We included only candidates

who were aged 16.5 through 18 years old at the day of examination, representing 86% of all candidates undergoing evaluation through research years. As candidate appearance in front of a draft board is mandatory predominantly at 17 years of age,[12] candidates who are below 16.5 or above 18 years of age represent a selective population with distinctive characteristics, which mostly embodies a delay in board evaluation that we could not account for. We excluded subjects from non-Jewish populations, as they were not representative of the overall minority group, in which residents are mostly exempt from military service and are not routinely summoned to take a mandatory examination, as in previous studies.[12–14] Candidates with a history of the following ophthalmologic conditions were excluded: keratoconus, uveitis, glaucoma, retinal disorders or degenerative diseases, optic nerve pathologies and subjects recovering from refractive surgery. Candidates who lacked visual acuity or refractive data were also removed. Candidates who were not born in Israel were removed from the main analysis and analyzed separately. Overall, 1 334 650 subjects were included in the assessment of amblyopia prevalence. We further excluded subjects with any missing socio-demographic information, yielding 1 219 464 subjects included in the final analysis of associations. The study was approved by the Israeli Army Institutional Review Board (Approval No. 1669-2016) and adhered to the tenets of the Declaration of Helsinki. Subject anonymity was strictly kept using a unique identification serial number for each subject. Patient consent was waived as the raw data were de-identified.

Visual acuity examination

Best-corrected visual acuity (BCVA) was determined for each candidate, distinctly for each eye. The examination was performed by a qualified technician, using a standard Snellen chart at 6m distance. All candidates with unaided visual acuity lower than 6/6 in either eye underwent non-cycloplegic refraction by using an Autorefractometer (Speedy K; Nikon Corp., Tokyo, Japan; KR-8000, KR7000S and earlier models, Topcon, Tokyo, Japan), followed by a complement subjective refraction validation with a Snellen chart. In cases BCVA of 6/6 is not attained despite these measures, the candidate is referred to a certified ophthalmologist examination.[8,13–16]

Amblyopia definition

Unilateral amblyopia was defined as BCVA worse than 6/9 in the amblyopic eye or as an interocular difference of two lines or more. Bilateral amblyopia was defined as BCVA worse than 6/9 in both eyes.[16] Amblyopia was categorized into six main groups, by way of the underlying mechanism, as defined in Supplementary table S1.[8,16–19]

Study variables

Documented variables include age, gender, religion, socioeconomic status (SES), cognitive function score (CFS), body-mass index (BMI), height, years of education, educational system, peripherality index, country of birth (including immigration date if born abroad) and country of origin. Candidates underwent cognitive assessment that yields the CSF, which is normally distributed and correlated with the Wechsler Adult Intelligence Scale.[13] CSF was classified into three groups: below average, above average and average, with the latter as reference group. BMI was classified into four groups: underweight (BMI < fifth percentile), normal weight (fifth percentile < BMI < 85th percentile), overweight (85th percentile <BMI < 95th percentile) and obese (BMI > 95th percentile), with normal weight as reference group. Height was classified into three groups: short stature (height < fifth percentile), normal stature (fifth percentile < height < 95th percentile), and tall stature (height > 95th percentile), with normal stature as reference group. This categorization of BMI and height was validated and used previously for Israeli population.[12–14,20] Years of education were classified into three groups: ≤10 years, 11 years and 12 years or more, which also includes higher and academic studies. Educational system was classified into three groups: secular, Orthodox and ultra-Orthodox, determined based on a list provided by the Israeli Ministry of Education.[14,21] SES was determined according to the classification method of the Central Bureau of statistics, based on the site of residence.[22] The Bureau categorizes each municipality to 10 socioeconomic clusters ranked from low to high, considering age distribution, available labor force, level of unemployment, level of education, average per capita income and proportion of income support recipients. SES was categorized into five groups: first–third clusters, fourth cluster, fifth–sixth clusters, seventh cluster and seventh–tenth clusters, with the highest socioeconomic group as reference group. Clusters 4 and 7 were separated due to the large sample size in these groups. Peripherality index was determined according to the classification method of the Central Bureau of statistics, based on residence.[23] Peripherality index was classified into three groups: peripheral (first–fourth clusters), intermediate (fifth–sixth clusters) and central (seventh–10th clusters). Country of origin was determined by the father's or grandfather's country of birth (if the father was Israeli-born). This variable was classified into four groups: Israel, former USSR countries, North Africa and Ethiopia, and other countries [including Asia (non-USSR countries) and western countries (comprised of non-USSR Europe, South and North America, South Africa, Australia and New Zealand)]. Year of examination was classified into five 5-year groups: 1993–97, 1998–2002, 2003–07, 2008–12, 2013–17, with the earliest group as reference. Age at immigration was classified into two groups: immigration before or after 10 years of age, when treatment for amblyopia is not expected to significantly improve visual outcomes.[8]

Statistical analysis

Prevalence of amblyopia was regarded as point prevalence. Among Israeli-born candidates, the associations between amblyopia, as an outcome variable, and each of the independent variables (socio-demographic characteristics), were evaluated using univariable logistic regression models. Then, multivariable logistic regression models, adjusted for all independent variables that were found to be statistically significant in univariable models, were performed. Multivariable models were examined following stratification by gender, in order to highlight gender-based differences in prevalence. Multicollinearity of independent variables was assessed using variance inflation factor (VIF). The results of regression models are reported as odds ratio (OR) with 95% confidence intervals (95% CIs). Sensitivity analysis included partially adjusted multivariable models (excluding education-related variables: CFS, years of education and educational system), and multivariable models in the larger Orthodox and secular educational system groups. The relationship between two qualitative variables was examined using the Chi-squared test. Two-sided P-values <0.05 was considered as statistically significant. All analyses were performed with SPSS statistics for Windows version 23 (IBM, Armonk, NY, USA).

Results

Amblyopia prevalence

A total of 1 334 650 candidates for military service were eligible to be included in assessment of amblyopia prevalence. The majority of subjects were male (744 112, 55.75%) and mean age of subjects was 17.15 ± 0.26. Amblyopia was diagnosed in 14 367 subjects, yielding an overall prevalence of 1.07%. The overall prevalence of amblyopia has declined throughout the years (figure 1). The overall prevalence was 1.59% in 1993 and decreased to 0.87% in 2017, a total change of 54.71%. Unilateral amblyopia was diagnosed in 11 386 subjects (0.85% of the study population, 79.25% of amblyopes),

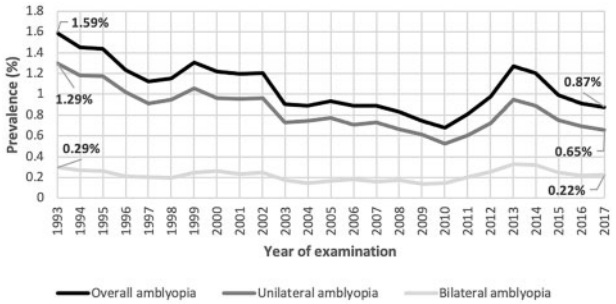

Figure 1 The prevalence of amblyopia; overall, unilateral and bilateral, among Israeli adolescents, 1993–2017

and bilateral amblyopia was diagnosed in 2981 (0.22% of the study population, 20.75% of amblyopes). The most common isolated underlying mechanism of amblyopia was ametropia, found in 2554 amblyopes (17.77% of amblyopes). Amblyopia coexisting with anisometropia, strabismus or deprivation of vision was present in 2264, 750 and 297 of amblyopic subjects, respectively (Supplementary table S2). No evident underlying mechanism of amblyopia was ascertained among remaining amblyopes (7293 subjects, 50.76% of amblyopes).

Socio-demographic characteristics and amblyopia

Following exclusion of subjects with missing socio-demographic data (n = 115 186), the association between socio-demographic characteristics and amblyopia was investigated among 1 219 464 candidates (table 1). Gender distribution and mean age of subjects remained unchanged. The prevalence of amblyopia remained 1.07%, with 0.85% unilateral cases. Gender, CFS, SES, BMI, height, years of education, educational system, peripherality index, origin and year of examination were all found to be associated with amblyopia in univariable logistic regression models. Overall, in a univariable analysis, females had higher odds for amblyopia compared with males (OR 1.08, 95% CI 1.04–1.11). Based on these findings, multivariable logistic regression models were performed following stratification by gender (table 2). Multicollinearity of independent variables was ruled out (VIF < 1.5). In relation to average CFS, below average CFS was associated with raised odds for amblyopia for both males (OR 1.27, 95% CI 1.19–1.35) and females (OR 1.27, 95% CI 1.18–1.36), while above average CFS was associated with reduced odds for both genders. The association between SES and amblyopia demonstrated a dose-dependent relationship in both genders, with low, intermediate and high SES having higher odds of having amblyopia compared with the highest SES (OR 1.64, 95% CI 1.45–1.87 and OR 1.61, 95% CI 1.30–1.98 in the lowest SES for males and females, respectively). Overweight, obese and underweight males were associated with elevated odds for amblyopia (OR 1.18, 95% CI 1.09–1.27; OR 1.44, 95% CI 1.32–1.57 and OR 1.28, 95% CI 1.19–1.38, respectively). However, underweight females did not have higher odds of having amblyopia (P = 0.960). Both short and tall statures were associated with raised odds for amblyopia in males (OR 1.27, 95% CI 1.16–1.39 and OR 1.21, 95% CI 1.06–1.38, respectively). However, only short stature was associated with raised odds of amblyopia in females (OR 1.30, 95% CI 1.18–1.43), whereas tall stature was not (P = 0.120). Elevated odds of amblyopia were apparent among female adolescents completing 10 years of education or less, however, the association among females completing 11 years of education was not statistically significant (P = 0.858). The association between years of education and amblyopia among males was not statistically significant. Males and females living in peripheral geographical areas had reduced odds of amblyopia compared with those residing in central areas, while only males living in intermediate-peripheral areas had reduced odds. Males and females originating from USSR or other countries had elevated odds for amblyopia compared with those originating from Israel. Partially adjusted models are presented in Supplementary table S3.

Amblyopia-related risk factors among secular and Orthodox adolescents

Both Orthodox and ultra-Orthodox males presented with elevated odds of amblyopia (OR 1.16, 95% CI 1.09–1.25 and OR 1.90, 95% CI 1.73–2.09, respectively). Following stratification by educational system, the association between SES and amblyopia in the secular educational system accentuated in both genders (Supplementary table S4), while the association among Orthodox adolescents attenuated in both genders (Supplementary table S5).

Amblyopia and immigration

Out of 229 655 immigrants examined between 1993 and 2017, 9672 (4.21%) had missing visual acuity or refractive data, were not aged 16.5–18 years old at examination or had an underlying ophthalmologic condition. Among remaining 219 983 immigrants, 134 946 (61.34%) immigrated from former USSR, 17 265 (7.85%) from North Africa and Ethiopia [North Africa 687 (0.31%), Ethiopia 16 578 (7.54%)] and 67 772 (30.81%) from other countries worldwide. Overall, immigrants exhibited a higher prevalence of amblyopia compared to those born in Israel (1.51% vs. 1.07%, P < 0.001) (Supplementary figure S2). Immigrants from former USSR and North Africa and Ethiopia demonstrated a higher prevalence of amblyopia compared with immigrants from other countries (1.58%, 1.61% and 1.38%, respectively, P < 0.001). Notably, the prevalence of amblyopia among immigrants was higher compared with subjects who were born in Israel and shared the same parental origin (table 3). Gaps were accentuated among immigrants from North Africa, Ethiopia and other countries, who were older than 10 years of age at immigration.

Discussion

In this nationwide population-based study, conducted on over one million Israeli adolescents, we found that the overall prevalence of amblyopia decreased throughout the years, starting at 1.59% in 1993 and reaching 0.87% in 2017. Up to 50% of amblyopic subjects were found to have a history of underlying mechanism that might lead to amblyopia. To the best of our knowledge, this report presents the largest population-based study evaluating the prevalence of amblyopia among adolescents. We identified considerable socio-demographic disparities, fundamentally suggesting that females, adolescents belonging to lower SES, adolescents with lower CFS, Orthodox, ultra-Orthodox and immigrants suffer from an increased prevalence of amblyopia.

Amblyopia prevalence estimations in non-pediatric populations collected worldwide are diverse. The overall prevalence we report is among the lowest described. A study from China assessed a prevalence of 2.8% among rural Chinese population aged 30–80 years old.[19] Additional studies from Sydney and Victoria, Australia, found a prevalence of 3.2% and 3.06% among adults, respectively.[17,24] A lower prevalence compared with ours was described in a work by Rosman et al.[18] This study was conducted on male conscripts in Singapore aged 18–19 years old and found an overall prevalence of 0.35%. However, comparison of results across studies is problematic due to differences in study methodologies, population characteristics and diagnostic criteria for amblyopia.

In 2018, Shapira et al.[16] analyzed trends in amblyopia prevalence among a northern Israeli population aged 16–19 years old. Several methodological differences between the studies merit consideration. As Shapira et al. divulge, their data could not be generalized on a national scale since participants were from a particular geographical area. We present similar results using the same definition for amblyopia, with the advantage of whole population-based data,

Table 1 Association of socio-demographic characteristics with amblyopia in total, in univariable model

Variable		Prevalence No./total No. (%)	OR (95% CI)	*P*-value for category	*P*-value for variable
Gender	Female	6091/544 425 (1.12)	1.08 (1.04, 1.11)	<0.001	<0.001
	Male	6992/675 039 (1.04)	1.00		
CFS	Below average	2866/202 790 (1.41)	1.32 (1.26, 1.38)	<0.001	<0.001
	Average	7350/686 668 (1.07)	1.00		
	Above average	2867/330 006 (0.87)	0.81 (0.77, 0.84)	<0.001	
Socioeconomic status	Lowest	524/28 346 (1.85)	2.10 (1.91, 2.31)	<0.001	<0.001
	Low	2937/254 259 (1.16)	1.30 (1.24, 1.38)	<0.001	
	Intermediate	3945/343 909 (1.15)	1.29 (1.23, 1.36)	<0.001	
	High	3159/308 547 (1.02)	1.15 (1.09, 1.22)	<0.001	
	Highest	2518/284 403 (0.89)	1.00		
BMI[a]	Underweight	1351/111 346 (1.21)	1.19 (1.12, 1.26)	<0.001	<0.001
	Normal weight	9451/929 708 (1.02)	1.00		
	Overweight	1327/112 149 (1.18)	1.16 (1.10, 1.23)	<0.001	
	Obese	954/66 261 (1.44)	1.42 (1.33, 1.52)	<0.001	
Height[a]	Short	946/65 317 (1.45)	1.38 (1.29, 1.48)	<0.001	<0.001
	Normal	11 678/1 114 979 (1.05)	1.00		
	Tall	459/39 168 (1.17)	1.12 (1.02, 1.23)	0.018	
Years of education	≤10	538/37 456 (1.44)	1.38 (1.26, 1.50)	<0.001	<0.001
	11	532/32 496 (1.64)	1.57 (1.44, 1.72)	<0.001	
	≥12	12 013/1 149 512 (1.05)	1.00		
Educational system	Secular	10 746/1 048 405 (1.02)	1.00		<0.001
	Orthodox	1631/139 779 (1.17)	1.14 (1.08, 1.20)	<0.001	
	Ultra-Orthodox	706/31 280 (2.26)	2.23 (2.06, 2.40)	<0.001	
Peripherality index	Peripheral	1980/201 267 (0.98)	0.89 (0.85, 0.94)	<0.001	<0.001
	Intermediate	4105/379 172 (1.08)	0.98 (0.95, 1.02)	0.558	
	Central	6998/639 025 (1.10)	1.00		
Origin	USSR	1241/99 858 (1.24)	1.35 (1.26, 1.45)	<0.001	<0.001
	North Africa and Ethiopia	3251/296 099 (1.10)	1.19 (1.13, 1.26)	<0.001	
	Other countries	6350/579 842 (1.10)	1.19 (1.13, 1.25)	<0.001	
	Israel	2241/243 665 (0.92)	1.00		
Year of examination	1993–97	3318/242 732 (1.37)	1.00		<0.001
	1998–2002	3025/249 044 (1.21)	0.88 (0.84, 0.93)	<0.001	
	2003–07	2155/237 822 (0.91)	0.66 (0.62, 0.69)	<0.001	
	2008–12	1936/243 283 (0.80)	0.57 (0.54, 0.61)	<0.001	
	2013–17	2649/246 583 (1.07)	0.78 (0.74, 0.82)	<0.001	

USSR, Union of Soviet Socialist Republics; BMI, body-mass index; CFS, cognitive function score.

a: Sex and age (by months) adjusted percentiles of BMI and height according to the United States Center for Disease Control and Prevention 2000 growth charts. BMI classification: underweight (BMI<fifth percentile), normal weight (fifth percentile<BMI<85th), overweight (85th percentile<BMI<95th) and obese (BMI>95th percentile). Height classification: short (height<fifth percentile), normal (fifth percentile<height <95th) and tall (height >95th percentile).

allowing for a broader understanding of the epidemiologic profile of the disease. Of note, our study included more recent years eligible for investigation, indicating a peak in prevalence around 2013 for males and 2014 for females. As amblyopia screening policies in Israel have not significantly changed since early 1990s, and military vision test practice has remained consistent, this finding is intriguing. One possible explanation is the law alternation in Israel in 2012, resulting in military draft board assessment of a sizable portion of ultra-Orthodox male candidates, who as our results further suggest, suffer from an increased morbidity.[14]

Amblyopia was more common among females compared with males, representing a modest gender effect. This is consistent with some previous studies in children and adults.[25,26] However, the majority of previous works reported an equal distribution between genders.[17,24,27,28] Still, arguments exist to support our findings. Differences in prevalence could be related to variation in screening program participation rates at an earlier stage in life, resulting in an increased prevalence among under-screened groups. Furthermore, as some studies suggest, there is an increased prevalence of mechanisms leading to amblyopia, such as hyperopia and anisometropia among females.[29,30] Finally, our sample might not be entirely representative of Jewish women, as up to 30% of this population is not obligated to military service.[12–14] Nevertheless, since we found an increased prevalence among ultra-Orthodox males, assumed to reflect the general trend in the ultra-Orthodox population, such possible selection bias is expected to lead to under-estimation of the prevalence among females.

Analysis of the association between SES and amblyopia revealed a near dose–response relationship across a five-level SES gradient, emphasizing the gap between the lowest and the highest groups. This association has several possible explanations. First of all, factors related to low SES, such as alcohol and drugs consumption and maternal smoking during pregnancy, have been associated with strabismus and other vision problems among children, that might result in amblyopia.[31,32] Moreover, this association might also exemplify a failure on the timeline arraying from vision screening to timely and adequate treatment for amblyopia, resulting in selectively increased morbidity during adolescence.[33] Further studies were able to elucidate this association by indicating underutilization of medical services in lower SES, resulting in worse vision-related outcomes.[34,35] In addition, even when a positive vision screening test is obtained, factors associated with low SES might negatively influence treatment compliance[36] and the desired vision correction.[37] These behaviors might also explain the association between below average CFS, religiosity level, and higher prevalence of amblyopia, as these factors are all affiliated with low SES.[38] The ORs for amblyopia by SES levels were higher in partially adjusted models compared with fully adjusted models. Though attenuated when adjusting for further education-related variables (CFS, years of education and educational system), the association between SES and amblyopia remained independently evident. Following stratification to educational system, the association accentuated among seculars, but attenuated among Orthodox. Of note, multicollinearity of independent variables was not observed in our multivariable regressions, and therefore unlikely

Table 2 Association of socio-demographic characteristics with amblyopia, stratified by gender, in multivariable models

Variable		Males[b] (*n*=675 039)			Females[b] (*n*=544 425)		
		OR	95% CI	*P*-value for category	OR	95% CI	*P*-value for category
CFS	Below average	1.27	(1.19, 1.35)	<0.001	1.27	(1.18, 1.36)	<0.001
	Average	1.00			1.00		
	Above average	0.83	(0.78, 0.88)	<0.001	0.87	(0.81, 0.93)	<0.001
Socioeconomic status	Lowest	1.64	(1.45, 1.87)	<0.001	1.61	(1.30, 1.98)	<0.001
	Low	1.23	(1.13, 1.33)	<0.001	1.21	(1.12, 1.32)	<0.001
	Intermediate	1.30	(1.20, 1.41)	<0.001	1.24	(1.15, 1.34)	<0.001
	High	1.15	(1.06, 1.24)	<0.001	1.11	(1.03, 1.20)	0.015
	Highest	1.00			1.00		
BMI[a]	Underweight	1.28	(1.19, 1.38)	<0.001	1.002	(0.91, 1.09)	0.960
	Normal weight	1.00			1.00		
	Overweight	1.18	(1.09, 1.27)	<0.001	1.17	(1.07, 1.27)	<0.001
	Obesity	1.44	(1.32, 1,57)	<0.001	1.38	(1.23, 1.54)	<0.001
Height[a]	Short	1.27	(1.16, 1.39)	<0.001	1.30	(1.18, 1.43)	<0.001
	Normal	1.00			1.00		
	Tall	1.21	(1.06, 1.38)	0.003	1.11	(0.97, 1.27)	0.120
Years of education	≤10	0.96	(0.86, 1.07)	0.513	1.34	(1.11, 1.61)	0.002
	11	1.10	(0.98, 1.23)	0.090	1.01	(0.85, 1.21)	0.858
	≥12	1.00			1.00		
Educational system	Secular	1.00			1.00		
	Orthodox	1.16	(1.09, 1.25)	<0.001	1.08	(0.99, 1.18)	0.078
	Ultra-Orthodox	1.90	(1.73, 2.09)	<0.001	0.43	(0.16, 1.15)	0.094
Peripherality index	Peripheral	0.79	(0.73, 0.85)	<0.001	0.86	(0.80, 0.93)	<0.001
	Intermediate	0.92	(0.87, 0.97)	0.007	0.96	(0.90, 1.02)	0.188
	Central	1.00			1.00		
Origin	USSR	1.42	(1.28, 1.57)	<0.001	1.41	(1.26, 1.58)	<0.001
	North Africa and Ethiopia	1.02	(0.94, 1.11)	0.572	1.22	(1.11, 1.34)	<0.001
	Other countries	1.11	(1.02, 1.20)	0.008	1.22	(1.12, 1.34)	<0.001
	Israel	1.00			1.00		
Year of examination	1993–97	1.00			1.00		
	1998–2002	0.87	(0.81, 0.93)	<0.001	0.89	(0.83, 0.96)	0.002
	2003–07	0.64	(0.60, 0.69)	<0.001	0.66	(0.61, 0.72)	<0.001
	2008–12	0.56	(0.52, 0.60)	<0.001	0.56	(0.52, 0.61)	<0.001
	2013–17	0.72	(0.67, 0.79)	<0.001	0.86	(0.79, 0.94)	0.002

USSR, Union of Soviet Socialist Republics; BMI, body-mass index; CFS, cognitive function score; OR, odds ratio; 95% CI, 95% confidence interval.

a: Sex and age (by months) adjusted percentiles of BMI and height according to the United States Center for Disease Control and Prevention 2000 growth charts. BMI classification: underweight (BMI<fifth percentile), normal weight (fifth percentile<BMI<85th), overweight (85th percentile<BMI<95th) and obese (BMI>95th percentile). Height classification: short (height <fifth percentile), normal (fifth percentile<height<95th) and tall (height>95th percentile).

b: Adjusted to CFS, SES, BMI, height, years of education, educational system, peripherality index, origin and year of examination.

Table 3 Prevalence of amblyopia by parental origin, country of birth and age at immigration among Israeli adolescents

Region	No. of amblyopic adolescents/total no. (%)			*P*-value
	Parental origin among adolescents born in Israel (*n*=1 334 650)	Birth country of immigrants 10 years old or less (*n*=138 396)	Birth country of immigrants older than 10 years old (*n*=81 587)	
North Africa and Ethiopia	3459/313 766 (1.10)	202/13 470 (1.50)	76/3795 (2.00)	<0.001
USSR	1316/105 505 (1.25)	1501/94 872 (1.58)	628/40 074 (1.57)	<0.001
Other countries	6770/612 867 (1.10)	385/30 054 (1.28)	548/37 718 (1.45)	<0.001

contributed to the observed ORs. Recent research of myopia, which has grown to 'pandemic' size worldwide, supports causal relationships between near work, reading time and higher intelligence, more common for higher SES.[13,14] Amblyopia on the contrary, as our findings suggest, is associated with lower SES and CFS. Still, since we cannot point the direction of this association, there is also the possibility that the association between CFS and amblyopia has reversed contribution; amblyopia might negatively affect CFS, possibly by causing difficulties in reading.[10]

Lastly, the association between country of birth and amblyopia prevalence among Israeli adolescents was investigated by Morad et al.[8] in 2007. This study found that 1.5% of immigrants who lived in former USSR during the first 10 years of life had amblyopia, compared with 0.98% of native-Israelis. Similarly, we found a prevalence of 1.58% compared with 1.07% in non-native- and native-Israelis, respectively. We also found an elevated disease prevalence among immigrants from other countries, compared with native-Israelis. However, the interaction with age at immigration in this study was only apparent in a sub-group of subjects who immigrated from North Africa and Ethiopia. We speculate that differences in prevalence could be partially explained by differences in offered screening programs and treatment options between countries. Vision screening policy in Israel includes several junctions for the detection of visual impairment during the first years of life.

Therefore, alongside other factors that have been found to influence the prevalence of amblyopia, such as ethnicity,[27,39] differences in prevalence might also denote varying screening programs efficacy.

Our study has certain limitations. First, since this is a cross-sectional study, causality cannot be assumed and the ORs are associated with having amblyopia rather than becoming amblyopic. Second, the refractive measurements were collected without cycloplegia, which might have led to misclassification by overestimating the prevalence of myopia.[40] Third, a limited number of variables that might be associated with amblyopia were evaluated, and for several only crude measures were available. For instance, SES and peripherality index were based on residential locality, which lacks refinement in cities. As a result, it is possible that some confounders were not measured (e.g. intra-utero exposures or family history of amblyopia) or were not measured precisely, and hence were not adequately adjusted for. This might also explain why we found reduced OR for amblyopia in subjects from peripheral localities, compared with central localities. Fourth, we used the Central Bureau of statistics classification based on the data of 2006 for SES and 2015 for peripherality index. Though not considering changes in SES cluster classification through the years, changes were relatively rare and not extreme. In addition, we used data reflecting residential locality during adolescence and may have missed important influences from previous periods in life. Furthermore, our findings are limited to the specific age group included in this study. Lastly, as noted, our sample was less representative of Israeli females compared with males, especially of ultra-Orthodox females, and our results should be verified in other diverse populations.

In conclusion, while the overall prevalence of amblyopia in Israel has reduced over the last 25 years, we found evidence of disparities in prevalence by socio-demographic factors. Lower SES and lower CFS were found to increase the ORs of amblyopia, stressing the need for special care in these groups. These findings might enhance re-allocation of resources dedicated to the screening, diagnosis and treatment of amblyopia during childhood, and facilitate directed risk mitigation strategies in high prevalence populations. Further research into the barriers that result in differences in amblyopia prevalence by socio-demographic characteristics, in the setting of a present screening program, is warranted.

Supplementary data

Supplementary data are available at *EURPUB* online.

Conflicts of interest: A.B. reported receiving personal fees from Nanoretina and grants from Cellcure, Byonics, Novarits, and MicroSert outside the submitted work. The rest of the authors declare that they have no competing interests.

Key points

- In a study comprised of 1.5 million Israeli adolescents, we found evidence of an association between socioeconomic status, cognitive function score, immigration and amblyopia.
- Israeli-born adolescents from lower socioeconomic status and those with below average cognitive function scores were found to have increased ORs of amblyopia.
- Over the last 25 years, the overall prevalence of amblyopia among Israeli-born adolescents was 1.07%, while the prevalence among immigrants was 1.51% ($P < 0.001$).
- These findings stress the need for reallocation of resources dedicated to the screening, diagnosis and treatment of amblyopia during childhood among these groups.

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