



AMBLYOPIA AND REFRACTIVE ERRORS IN BULGARIAN PEDIATRIC POPULATION - PROPHYLAXIS AND PREVALENCE

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ABSTRACT

Purpose: To assess the prevalence and prophylaxis of amblyopia and refractive errors in the Bulgarian population according to the existing literature.

Methods: A systematic literature review on the topic was accomplished by searching for articles in PubMed, Google Scholar, and Science.gov databases.

Results: The reviewed articles suggest that refractive errors are the most common cause of decrease in visual acuity among children in Bulgaria, followed by amblyopia. Anisometropia accounts for the major proportion of amblyopia occurrence. As for refractive errors, hypermetropia and astigmatism represent the most frequent refractive status in the childhood population. In addition, the prevalence of amblyopia in Bulgaria differs from worldwide data. Despite the great impact that a lifelong decreased vision, resulting from treatable causes during childhood, can have on an individual, there is no national screening program for preschool children.

Conclusion: The fact that the majority of cases with decreased vision can be managed successfully in the childhood period signifies the importance of timely measures such as prophylaxis and appropriate treatment, which should be adopted as a national healthcare strategy.

Keywords: amblyopia, refractive errors, childhood, prophylaxis,

BACKGROUND

Amblyopia is a decrease in best-corrected visual acuity, which is more commonly unilateral and less frequently bilateral. It develops in childhood and is generally characterized by the lack of organic ocular disease, or if there is one, the decrease in vision is disproportionate and cannot be attributed solely to it [1]. The main amblyogenic factors for the occurrence of amblyopia are the presence of uncorrected refractive error (anisometropia, isoametropia), strabismus (misalignment of the eyes) and visual deprivation (conditions leading to occlusion of the visual axis). These act as a stimulus for inadequate processing of visual information, leading to abnormal functional connectivity between the primary visual cortex and other regions in the brain [2]. Furthermore, disruption of the visual input to the brain during the “sensitive period”, when maximal neuroplasticity is observed, also leads to structural neural changes [3]. Hence, amblyopia could be defined as a neurodevelopmental disorder of the brain’s visual cortex [4].

An important feature, emphasizing the significance of the condition, is that even in unilateral cases, an alteration in the visual functions of the better eye, as well as in binocular visual parameters, has been observed. A study on the topic of binocular function deficits occurring in unilateral amblyopia suggested the presence of oculomotor and visual deterioration in the other eye, which was considered unaffected [5, 6]. These deficits consist mainly of slower reading speed and worsening eye-hand coordination, which is the basis for development of fine motor skills and is related to overall cognitive development. This, in turn, leads to reduced physical activity, with all the ensuing health risks, difficulties in communication, and a decrease in the self-confidence and self-evaluation of a child with amblyopia [7, 8]. In addition to decreased visual acuity, people with amblyopia experience impaired stereovision as well, which affects their career choice to some extent, given the high requirements for these two parameters in certain professions [9]. Another negative aspect of the condition is the almost doubled risk of significant bilateral visual impairment later in life [10].

A recent study suggested there are several critical periods for different visual functions, and individual variability in these time frames definitely plays a role in the

formation of visual acuity [11]. Unfortunately, determining the exact timing of a critical period from the timing of normal development is not possible on an individual basis at the moment [12]. This indicates that promising amblyopia treatment results could be obtained beyond 7 years, an age which is traditionally believed to be the limit for achieving successful therapy. Nevertheless, the treatment until the age of 7 is still considered the most effective in the majority of amblyopia cases [11].

As uncorrected refractive errors are the leading cause of visual impairment, leaving them untreated could result in improper development of visual functions and permanent visual deficit, such as amblyopia. Despite the significance that refractive errors and amblyopia have on preventable visual impairment, the prophylaxis of children's vision is dependent on general practitioners and parents' awareness, as there are no mandatory examinations by an ophthalmologist. Currently, eye health evaluation of children, provided by the National Healthcare Insurance fund via the program "Childhood healthcare", consists of a general assessment of vision at 6 and 12 months of age, and annual testing of visual acuity and color vision between 7 and 18 years. There is only one compulsory examination of visual acuity in the interval between 1 and 7 years, which is performed at the age of 5, and all these check-ups are performed by the general practitioner (GP) of the child or a pediatrician [13]. As a result, many children have different eye conditions undiagnosed, reflecting in a high percentage of uncorrected refractive errors and amblyopia among them. Given that even subtle differences in the refraction between two eyes can be amblyogenic, timely prophylaxis and early commencement of treatment in children is of great importance and emphasizes the need for a nationwide screening program.

Even so, there are not that many studies on the prevalence of refractive errors and amblyopia among Bulgaria's child population; however, the existing ones are substantial and provide a good overview of the country's situation.

REVIEW RESULTS

The study included 13 research papers from 1995 to 2020, with eleven being cross-sectional studies and one prospective study.

In one of those cross-sectional studies, conducted among preschool children aged 3-6 years, Slaveykov and Trifonova reported that out of 596 children screened in Kazanlak, 526 had a refractive error (ametropia). The majority of children with deviation from normal refraction had hypermetropia (470 or 89,3%), while the remainder had astigmatism (50 or 9,5%) and myopia (46 or 8,7%). In addition, anisometropia was found in 8 (1,5%) of them, strabismus – in 12 (2,3%) and 8 (1,5%) children were diagnosed with amblyopia. Only 10,49% of children could be categorized as having normal refraction (emmetropia), and just half of the amblyopic cases were previously diagnosed. This is an interesting discovery, provided that Kazanlak is a town with a well-developed economy. Its

proximity to the regional center, Stara Zagora, makes health care coverage easier and more convenient. As the authors stated themselves, the main limitation of their study was the lack of cycloplegia. Due to the strong accommodation in young children, the possibility of a false myopic shift exists, which might be a source of bias and can lead to underestimation of hypermetropia. In this context, the finding that 89,3% of the examined preschool children had hypermetropia is even more impressive [14].

In another cross-sectional epidemiological study aimed to evaluate the prevalence of amblyopia in Bulgaria, Dikova examined 3540 children between 4 and 10 years of age and diagnosed amblyopia in 4,94% of them. Classifying the types of amblyopia was as follows: 2,66% of the children had anisometric amblyopia, 1,81% had isoametropic amblyopia, 0,14% had strabismic amblyopia, and deprivation amblyopia was found in only 0,22%. These statistics support the findings of other Bulgarian authors that uncorrected refractive errors, and anisometropia in particular, are the most common cause for amblyopia development in the country. More precisely, anisometropia accounted for almost all of the cases with amblyopia (90,5%) in her study. Additionally, amblyopia was unilateral in 58,9%, while bilaterality was observed in the remaining 41,1%. As the author pointed out, this data distribution differed from similar research worldwide, where unilateral amblyopia prevalence is in the range between 80% and 100%. One of the few studies reporting figures close to those of Dikova was conducted by Wu and Wang, where only 57,85% of the children were found to have unilateral amblyopia [15,16]. The findings of the Chinese authors should be interpreted with caution, though, because their study cohort was 4 times smaller, which increases the risk of bias. Another important finding of Dikova is that 100 of 2501 children screened (4%) in the group between 7 and 10 years of age had amblyopia, and in most of them it was as a consequence of anisometropia and high bilateral refractive errors (isoametropia) [15]. Due to the later age of diagnosis, these children were at a disadvantage regarding expected maximum benefits from treatment, because they missed most of the neuroplasticity critical period, where the best post-treatment results are observed. It should be emphasized that because amblyopia was related to refractive errors, the visual deficits in all of them were easily avoidable with the prescription of glasses (or with the addition of occlusion in cases of amblyopia), given that there was timely prophylaxis.

In another study, Valcheva et al. examined 2332 children aged 3 to 6 years across 23 childcare facilities and preschools in the city of Pleven and its suburbs. The authors found 236 children (10,1%) with deviation from the predetermined values for normal visual acuity ($e''0.8$ per eye). Unilateral decrease was observed in 67 of them (28,4%), while 96 (40,7%) suffered bilateral reduction in vision [17]. Unlike the previously mentioned Bulgarian researchers, those children who were found to have visual impairment were reevaluated, for the purpose of the study, with the induction of cycloplegia. This objective refrac-

tion allowed more precise categorization of the causes for decreased visual acuity, as well as the type and degree of refractive errors in the examined population, becoming a major strength in the research. Out of the 44 children who showed up for a more comprehensive eye examination, 32 (72.7%) had post-cycloplegic astigmatism, 11 (25%) had hypermetropia, and only 1 had myopia (2.3%). These readings substantially differ from those reported by K. Slaveykov and K. Trifonova (89,3% hypermetropia, 9.5% astigmatism and 8.7% myopia), although the tested group consisted of children of the same age (3-6 years). This example shows the distribution of refractive errors in an identical age cohort is not equal throughout the country. However, a principal difference between the two studies, which might influence the results, is that in the case of Slaveykov and Trifonova, the number of children with different ametropias was calculated from the whole screened group, whereas in the research of Valcheva et al, it was related only to the children who showed for a secondary examination with cycloplegia. More exhaustive breakdown of the findings by Valcheva et al. showed the group of children with astigmatism to be constructed of the following subgroups: 22 children (68.8%) with hypermetropic astigmatism, 6 children (18.7%) with myopic astigmatism and 4 (12.5%) with mixed astigmatism. Additionally, low level hypermetropia (under +2.0 dsph) was observed in 7 (63.6%) children, midlevel (between +2.0 dsph and +5 dsph) in 4 (36.4%) children, while high level (above +5.0 dsph) was not observed. Regarding myopia, low level myopia (under -3.0 dsph) was found in one child, mid-level (between -3.0 dsph and -6.0 dsph) and high level (above -6.0 dsph) was not observed in the examined population. It is worth noting that the majority of ametropia cases consisted of low levels of hypermetropia and myopia. This fact is essential because low level refractive errors have a higher risk of being neglected, unlike their high-level counterparts and strabismus. The latter two are more likely to raise the attention of parents either because of observation of altered visual behavior or simple detection of obvious ocular misalignment. Another finding by Valcheva et al. is that 12 children from the whole examined group had amblyopia, and this prevalence is notably less than the previous two studies. Another interesting constation was that 4 (33.3%) of the amblyopia cases were unilateral and 8 (66.7%) were bilateral. As mentioned above, the ratio of amblyopia bilaterality prevalence is usually reversed (amblyopia in one eye is around two times more frequent than in both eyes). However, the discrepancy in this proportion with the one reported in worldwide literature and from other Bulgarian authors could be contributed to the small sample size, consisting of only 12 children with amblyopia [14,17,18].

Important information about the refraction of children in Bulgaria could be gathered from the dissertation of A. Simeonova. The author examined 324 children in total with the aim of tracking the dynamics in their refractive status change in the age interval between 6-36 months. For research purposes, the children's refractive data were allocated to 4 different age groups (6-12 months,

12-18 months, 18-24 months, 24-36 months). Summarized, the change in refraction in children between 6 months to 3 years is as follows: hypermetropia (86.73% in first age group, 84.75% in second, 82.9% in third and 81.22% in fourth), astigmatism (68.52% in first, 64.43% in second, 31.13% in third and 34.04% in fourth) and myopia (1.7% in first, 1.64% in second, 2.1% in third and 3.99% in fourth). Hypermetropia, being the most prevalent refractive error during the first years of life, is not surprising. Although its gradual decrease thereafter (the process of emmetropization) is well known and documented, there was no significant change in its values until the age of 3. However, the significant dynamics of observed astigmatism, halving during the tested period, is quite interesting and worth noting. This finding has clinical implications for whether to correct astigmatism or not. As the author concluded, "astigmatism should not be corrected before the age of two, except in cases where amblyogenic factors are present!". It is important to note that the great reduction in astigmatism (especially between 1 and 2 years of age) is also documented in other foreign researches [19, 20, 21].

Another vision screening initiative of great importance is "Screening Program for Preserving Childhood Vision" in the region of Varna, first launched in 2013 as a cooperation between the Municipality of Varna and Specialized Eye Hospital - Varna. This large-scale project was conducted as an annual screening of preschool and school-age children (6 and 7 years of age). The first year turned out to be the most successful regarding the number of screened children, totaling 2472 prophylactic examinations. In 942 (38.1%) of them, a visual impairment was found, and a recommendation for more comprehensive examination was made. A total of 259 children showed up for a full visual examination in Specialized Eye Hospital - Varna, with distribution of refractive errors reported as follows: hypermetropia was diagnosed in 49.42% of the children, astigmatism was found in 24.71% and 6.17% had myopia. In addition, 5.02% of the children had established amblyopia, while strabismus was found in 3.47%. Hypermetropia and astigmatism tended to be significantly more common than myopia, a finding which is observed in all the abovementioned research done in Bulgaria. The values for amblyopia (5.02%) are higher than the reported by K. Slaveykov and K. Trifonova (1.5%), Dikova (4.94%) and Valcheva et al (0.51%). This could be due to the fact that the percentage of amblyopia cases is calculated based not on the whole screening group but only on the number of children who went for a second comprehensive eye examination. Nonetheless, it is worth mentioning that in the following years, there was a decrease in the prevalence of amblyopia diagnosed within the screening program in Varna - 2014 (4.16%), 2016 (3.33%), and interestingly, there were no recorded cases in 2015, 2017, 2018 [14, 17, 22].

Kirilova Y, et al published data gathered from several vision screening programs for children throughout the years. In the period 1995-1997, a total of 1863 children aged 0-15 years were examined. In the group from orphan-

ages (consisting of 263 children), a higher frequency of visual impairment was observed, e.g. strabismus (8.74% v. 1.06% in preschool and school children). This, unfortunately, shows the tendency for limited and more difficult access of orphans and other disadvantaged children to health care services. Between 2007-2011, 1437 children were screened, and the authors reported that normal visual acuity was found only in 1120 (78%). Disturbing is the fact that in the age group of 7 years and above, 76 (9.5%) children had amblyopia, meaning that whether newly discovered or not, the treatment success of amblyopia was expected to be poorer because of the age. Additionally, in the school age group (8-14 years), 533 (66.5%) had astigmatism. Another screening initiative took place in Smolyan between 2013-2018, when 860 preschool children (4-5 years of age) were examined. Refractive errors were found in 11% of them, while 17 children (1.9%) had amblyopia. In another study conducted by Kirilova during the period 2010-2012, 1437 children from the "Poduene" district of Sofia, aged 3-14 years, were screened. The results were worrying, showing that 7.07% of the examined children had amblyopia [23, 24].

The study of Chernodrinska (2010), which occurred in 24 kindergartens in Sofia, covered 2060 children from 3 to 7 years. Ocular pathology was found in 11.1% of them, which more precisely consisted of astigmatism (4.7%), hypermetropia more than +1.5 dsph (4.1%), myopia (0.6%) and strabismus – 1.7%. The incidence of amblyopia was 1.97%, significantly lower than the numbers of Kirilova's findings (7.07%). This once again shows the variations of amblyopia frequency even in children

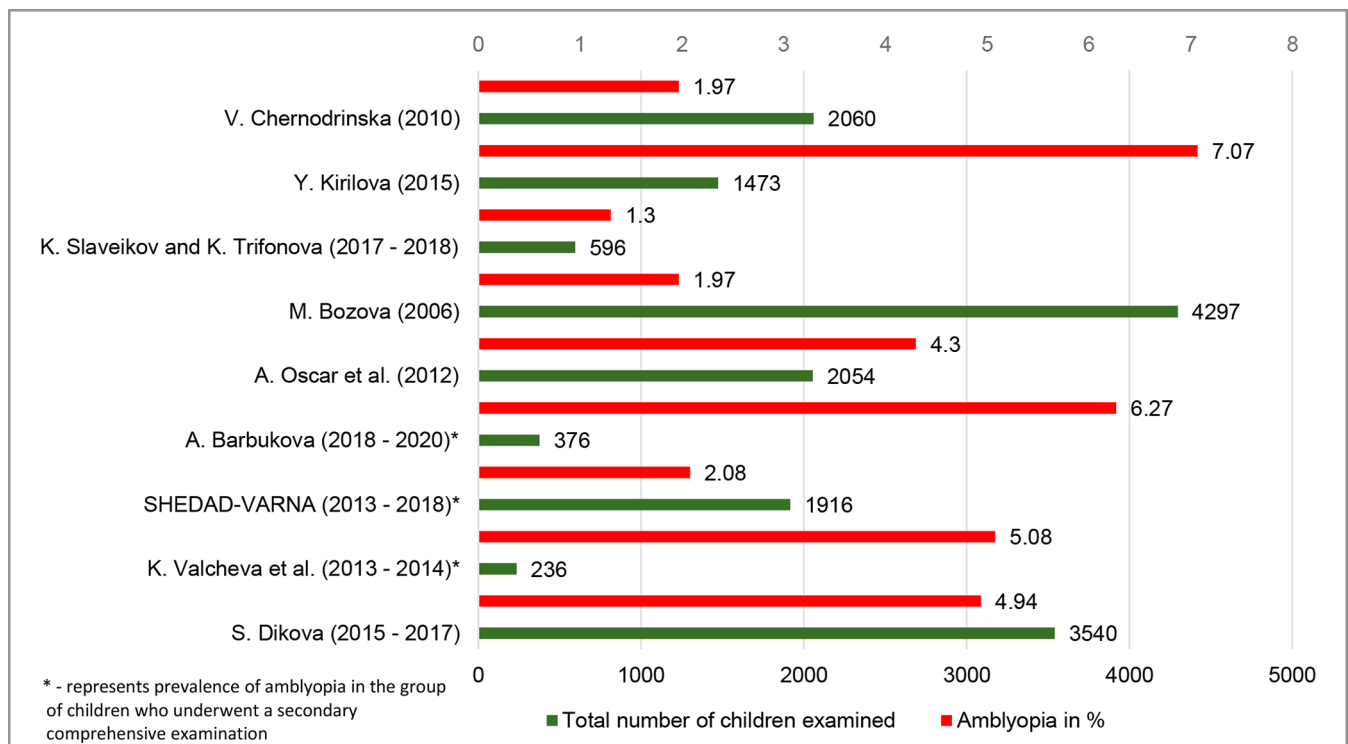
populations living in the same city. However, it should be considered that in the research of Kirilova, children up to 14 years were included, increasing the chance for encountering cases that were already diagnosed and thus raising the overall amblyopia frequency [25].

In 2012, Oscar A, et al screened 2054 children aged 4-10 years across different towns in Bulgaria, as part of the "Do Good" initiative. The results showed that 19.7% had refractive errors, 1.2% had strabismus, and in 4.3% amblyopia was found. In another large-scale study in Stara Zagora, covering 4297 children aged 4-18 years, Bozova M. reported amblyopia frequency of 1.97% [26, 27].

As it became evident from the mentioned researches by Bulgarian authors, hypermetropia and astigmatism constitute the most common refractive errors, while myopia represents the least common refraction, especially in younger children. The fairly low relevance of myopia to amblyopia occurrence does not mean this type of refraction is inconsequential with respect to eye health in children. Just the opposite, high myopia may lead to sight threatening conditions, most notably retinal detachment and open angle glaucoma, among the many others. In this matter, Dragomirova et al evaluated the prevalence and risk factors for myopia in school children aged 6-15 in three Bulgarian towns. The cross-sectional study found that out of the 1041 children examined, 236 (16.85%) had myopic refraction ≤ -0.75 D and decimal visual acuity ≤ 0.8 on at least one of the eyes [28].

A summary about the prevalence of amblyopia among children, gathered from the most recent and influential studies in Bulgaria, can be seen in Figure 1.

Fig. 1. Prevalence of amblyopia among children in Bulgaria



According to different authors, the worldwide prevalence of amblyopia differs widely in the range between 1% and 6% [29,30]. However, in a systematic review by Budan et al., information from 4,645,274 children and 7,706 patients with amblyopia was analyzed, and the authors concluded that the overall worldwide pooled prevalence of amblyopia was 1.36%. Europe (data included from the UK, Bulgaria, Denmark, Netherlands, Sweden, Spain, Iceland, Finland, Norway) had the highest rate of amblyopia prevalence (2.66%) among the other continents and regions in the world [31]. Despite that, this estimate is still lower than the average prevalence of amblyopia among children in Bulgaria, derived from the data in fig. 1 (3.89%). This could be contributed to the lack of a national screening program, as well as the limited number of pediatric ophthalmologists in Bulgaria and insufficient knowledge on the topic among parents.

Several studies on the topic of prophylaxis and the effectiveness of vision screening programs for children were carried out in Bulgaria. In 2010, Marinov examined 171 children as part of a screening study in "Osmi Mart" kindergarten in Plovdiv and found abnormal ocular status in 46 (26.9%) of them. Regardless of the high number of children with ocular problems, only 10 of them were examined by an ophthalmologist before the screening took place [32]. Even more disturbing information about the lack of previous eye examinations could be obtained from a study by Oscar et al, covering over 5000 children of preschool and early school age (6-10 years old), where over 90% of the children had not been consulted by an ophthalmologist, with an average age of amblyopia diagnosis establishment being 8 years and 2 months [26]. Similarly, in another research from 2013, Oscar et al analyzed the average age of diagnosis of children with amblyopia, who visited the pediatric eye clinic of the University Hospital "Aleksandrovska" for a period of one year. During that time, 92 children were examined, with the average age of amblyopia diagnosis being 6 years and 9 months. It was also found that the major cause for amblyopia development in those children was uncorrected refractive error. Thus, the late average age at which amblyopia was diagnosed in the mentioned cases and the presence of a large number of children with uncorrected refractive errors are alarming symptoms that there are significant gaps in the Bulgarian healthcare system, regarding vision screening of children [33].

In her dissertation, Dikova reported that more than half (54.9%) of the 3540 children screened from all statistical regions in Bulgaria had not been examined by an ophthalmologist previously, and amblyopia was diagnosed in 55.4% of them for the first time. Some differences were noted, with a lower percentage of children who had never visited an eye specialist in the regions where screening programs were often conducted and vice versa. As mentioned previously, the author observed the same relation with regard to the frequency of amblyopia in different regions of Bulgaria [15].

Valcheva et al announced an even higher percentage of children (77.2%) who never visited an ophthalmologist for a comprehensive eye examination. It is worth

noting that the majority (53.4%) of those who visited an eye specialist did so at their parents' discretion [17]. This fact shows that because of the lack of a national vision screening program, parents have a significant role in preserving their children's vision by scheduling prophylactic examinations with a specialist.

The lowest number of children who never had a previous ophthalmic examination before the screening in which they participated was published by Dragomirova et al – 28.4% [28]. A possible explanation is that the study cohort consisted only of myopic children. Myopia, compared to the same degree of hypermetropia and astigmatism, tends to decrease visual acuity more profoundly, thus increasing the chance of parents noticing a problem and seeking medical attention.

In 2015, Kirilova reported that 95% of the children attending state kindergartens in the "Poduene" district of Sofia had their first eye examination in the screening, conducted as a part of her dissertation [24]. One of the main factors that could explain the differences between studies regarding the percentage of children not having a previous ophthalmological check-up is the parents' level of awareness about the importance of such examination. In this matter, Dimitrova et al surveyed 328 parents of children up to 7 years from Varna, and found that 96% answered "yes" to the question "Should prophylactic eye examinations be performed in childhood?". This clearly showed what parents thought about the significance of their children's eye health status. However, worrying was the fact that 14.33% of the same parents answered they took their kids to a specialist only when there was a problem, while 21.65% never did so [34].

The topic about parental opinions on children's prophylactic check-ups was also researched by Boyadzhieva et al, where the question "If your child does not have an eye problem, when would you take them for a prophylactic eye exam?" 46.29% of parents answered "every year" and 39.58% "at 1, 3, 5, 7 years and annually during school years" [22]. A. Barbukova stated in her dissertation that 56.16% of surveyed parents, whose children took part of the "Screening program for preserving childhood vision in the region of Varna", believed "Eye screening program in childhood is useful for early detection of ophthalmic diseases" and 16.44% thought that such a screening program would be beneficial "for timely treatment of ophthalmic diseases" [35].

The surveys included in the table unequivocally show the positive opinion that parents have about prophylaxis of their children's eye health. However, this positive attitude does not necessarily mean that parents are willing to consult their child with an ophthalmologist, especially in cases where obvious problems are absent. (Table 1)

Measures taken for the prevention of avoidable blindness and visual impairment are most successful when initiated as early as possible. A national vision screening program could lower the number, if not eliminate, of cases of visual impairment due to treatable conditions. The

“Rotterdam Amblyopia Screening Effectiveness Study” provides such an argument in favor of national vision screening programs. Its conclusions were that amblyopia detection after vision screening followed positive results in 56 (67.5%) children, out of the 83 cases who were diagnosed before the age of 7, and most of the amblyopia cases were discovered by visual acuity measurement [36]. The effectiveness and benefits from a visual screening program were demonstrated by Dikova in Bulgaria too, as in her dissertation the author stated that in Northwestern region, where many screening programs took part in the re-

cent years, the prevalence of amblyopia among children between 4 and 10 years of age was 3.61%, while in South-eastern and South Central region, due to lack of large-scale and frequent screening programs, the numbers are 5.92% and 7.92%, respectively. Even though good results were demonstrated by the lower prevalence of amblyopia in particular parts of the country, it is important to mention that a national screening program would be even more successful in terms of effectiveness and especially coverage, compared to programs which are part of local campaigns or sponsored by benefactors [15].

Table 1. Children examined in different screening programs, for whom this was their first eye examination

Author of the study	Patient age	Total number of children examined examination	Percentage of children for whom this is the first eye
S. Dikova	4-10 years	3540	54.90%
K. Valcheva et al.	3-6 years	2332	77.20%
A. Barbukova	5-8 years	1387	30.90%
Y. Kirilova	3-14 years	1437	95%
Dragomirova et al	6-15 years	1401	28.40%

CONCLUSION

Uncorrected refractive errors, mainly hypermetropia and astigmatism, are the main cause for decreased vision, as well as the primary factor, chiefly in the form of anisometropia, for developing amblyopia among children in Bulgaria. As amblyopia is most successfully treated until the age of 7-8, it is of high importance that a national vision screening program be developed. Although a screening result is not a definite diagnosis, it can serve as grounds for a more comprehensive eye examination conducted by an ophthalmologist. This will allow early identification

of visual problems during the critical period of visual system development and, as a result, will lead to timely treatment with better outcomes. The lack of a national vision screening program, along with the limited number of pediatric ophthalmologists and insufficient knowledge of parents regarding the importance of children’s eye health prophylaxis, could explain the higher prevalence of amblyopia in Bulgaria compared to other countries. The benefits of implementing such programs can already be seen as a reduction in amblyopia incidence in populations where screenings were performed.

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Please cite this article as: Vrachev P, Trifonova K. Amblyopia and refractive errors in Bulgarian pediatric population - prophylaxis and prevalence. *J of IMAB.* 2025 Oct-Dec;31(3):6560-6566. [Crossref - <https://doi.org/10.5272/jimab.2025314.6560>]

Received: 18/06/2025; Published online: 23/10/2025



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