Clinical Characteristics and Risk Factors of Patients with Pediatric Amblyopia

Pediatrik Ambliyopi Hastalarımızın Klinik Özellikleri ve Risk Faktörleri

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ABSTRACT

Aim: Amblyopia is a common disease characterized by reduced visual acuity in one or both eyes during visual development in early stages of life. Satisfactory outcomes can be achieved with early diagnosis.

Materials and Methods: The study included a total of 341 pediatric patients aged three to 15 years, who presented to our clinic between February 2016 and September 2022 and were diagnosed with amblyopia. Using the follow-up files of all the patients, visual examination findings and data on birth, maternal obstetric history, family history, neurological disease history, chronic systemic disease history, and ocular surgery history were reviewed.

Results: A total of 341 patients, including 171 female and 170 male, were enrolled in the study. The mean age of the patients was 7.81±3.6 years. According to the type of amblyopia, refractive amblyopia was detected in 188 of the 341 patients (55.1%), strabismic+refractive amblyopia in 93 (approximately 27.3%), strabismic amblyopia in 55 (16.1%), and deprivation amblyopia in five (1.5%) patients. It was determined that amblyopia was most common in the age ranges of 3-6 (36.5%) and 7-10 (44.2%) years. Family history was found at a significantly higher rate in the amblyopia types presenting with strabismus compared to the refractive amblyopia type.

Conclusion: The determination of non-ocular risk factors other than the known ocular risk factors of amblyopia will allow for the early treatment of high-risk children and prevent preventable vision loss.

Keywords: Amblyopia, risk factors, refractive errors, strabismus, childhood

ÖZ

Amaç: Ambliyopi, yaşamın erken evrelerinde görme gelişimi sırasında bir veya iki gözde görme keskinliğinde azalma ile karakterize yaygın bir hastalıktır. Erken teşhis ile tedavide tatmin edici sonuçlar alınabilir. Ambliyopinin risk faktörlerinin belirlenmesi, hastalığın erken tanı konulmasını sağlayacak ve dolayısıyla oluşabilecek görme kayıplarını önleyecektir.

Gereç ve Yöntem: Şubat 2016 ile Eylül 2022 tarihleri arasında ambliyopi tanısı konulan 3-15 yaş arası toplam 341 çocuk hasta dahil edildi. Tüm hastaların takip dosyalarından tüm görme muayeneleri ve hastaların doğum, annenin obstetrik öyküsü, aile öyküsü, nörolojik hastalık öyküsü, kronik sistemik hastalık öyküsü ve oküler cerrahi öyküsü hakkındaki dosya bilgileri incelendi.

Bulgular: Bu çalışmamıza hastaların 171'i kadın ve 170'i erkek olmak üzere toplam 341 hasta dahil edildi. Hastaların ortalama yaş aralığı ise 7,81±3,6 idi. Ambliyopi türlerine göre; 341 hastadan 188 kişide refraktif ambliyopi (%55,1), 93 strabismik+refraktif ambliyopi (yaklaşık %27,3), 55 kişide strabismik ambliyopi (%16,1) ve 5 (%1,5) kişide ise deprivasyon ambliyopisi tespit edildi. Bizim çalışmada ambliyopinin en sık 3-6 yaş (%36,5) ve 7-10 yaş (%44,2) aralığında olduğu tespit edildi. Şaşılığın bulunduğu ambliyopi türlerinde aile öyküsünün, refraktif ambliyopi türüne kıyasla daha fazla olduğu görüldü.

Sonuç: Ambliyopinin bilinen oküler risk faktörleri haricindeki, non-oküler risk faktörlerinin belirlenmesi yüksek riskli çocukların erkenden tedavi edilmesini ve önlenebilir görme kayıplarının önüne geçilmesini sağlayacaktır.

Anahtar Kelimeler: Ambliyopi, risk faktörleri, kırma kusurları, şaşılık, çocukluk

INTRODUCTION

Amblyopia (lazy eye) can be defined as a decrease in visual acuity that occurs often in one eye and sometimes in both eyes without any visible abnormalities in the visual pathway[1,2]. The prevalence of amblyopia has been reported to range from 1 to 5% in studies conducted in various populations and age groups across the world and 0.6 to 3.5% in those conducted in Turkey[3-6].

Amblyopia results from disturbances in visual development early in life and is classified according to the underlying cause of visual impairment. Refractive amblyopia, strabismic+refractive amblyopia, and strabismic amblyopia constitute most amblyopia cases. In addition, deprivation amblyopia is another rare cause of amblyopia associated with pathologies that can prevent vision, e.g., cataracts, corneal opacity, and ptosis[7-9].

In studies conducted to evaluate perinatal, demographic, and socio-economic risks related to amblyopia, factors such as prematurity, neonatal intensive care requirement, cesarean delivery, and familial predisposition have been defined and associated as non-ocular factors[10,11]. Amblyopia starts from risky delivery and gradually progresses until the period when visual development is completed[12]. Amblyopia has many negative effects on the patient's life, such as decreased quality of life, limited occupational choices, and increased risk of vision loss in the other eye[13]. The treatment options of amblyopia include patch, atropine eye drops, and optical punishment of the non-amblyopic eye. Although children younger than seven years constitute the age group that most benefits from treatment, there are also studies suggesting that visual acuity can be improved in amblyopic children of up to 15 years of age. However, the success rate of treatment decreases with increasing age[14-16].

Amblyopia is a disease with a high rate of treatment response, especially when detected at an early age. Therefore, the identification of risk factors that may affect the development of amblyopia can significantly contribute to the success of treatment. In this study, we aimed to determine the relationship between demographic characteristics, clinical characteristics, and risk factors (such as family history, age of onset, cesarean delivery, and prematurity) in patients diagnosed with amblyopia and followed up in our clinic.

MATERIALS AND METHODS

This study was planned retrospectively and conducted after receiving approval from the Adıyaman University Local Institutional Ethics Review Board (date: 15.11.2022, decision no: 2022/8-1). Because the study was designed retrospectively, no written informed consent form was obtained from patients.

A total of 341 pediatric patients aged three to 15 years, who were diagnosed with amblyopia between February 2016 and September 2022, were included in the study. The follow-up files of all the patients were reviewed in terms of data on birth, maternal obstetric history, family history, neurological disease history, chronic systemic disease history, and ocular surgery history. Refractive error measurement, visual acuity measurement, anterior segment examination findings, and dilated fundus examination findings, including detailed ophthalmological findings, were also recorded. In addition, the presence and degree of shifts in nine cardinal positions of gaze, primary position, and other gaze positions, as well as limitation and weakness in gaze directions were noted. The results of the cover test, prism test, Krimsky test, and head position measurements of the patients were recorded. The cases with strabismus were classified according to the direction of tropia as esotropic, exotropic, and vertical.

Both uncorrected and corrected visual acuity examinations were performed using the Lea symbols in children aged three to five years, the "E" chart in preschool and illiterate children, and the Snellen chart in school-age children.

To measure refractive error, 1% cyclopentolate was applied three times at 5-minute intervals. After 45 minutes, measurements were made using a table-mounted Topcon Autorefractor KR-800 (USA) or hand-held Pediatric Autorefractor plusoptiX A09 (Germany) if possible. In cases where these procedures could not be performed, measurements were undertaken using the Keeler Professional retinoscopy (USA).

Amblyopia was defined as the presence of at least one of the factors of unilateral amblyopia, anisometropia [hypermetropia, 1 diopter (D); ≥1.5 D astigmatism; and ≥3 D myopia), strabismus, history of strabismus surgery, and conditions that obstructed the visual axis (e.g., ptosis and congenital cataract), accompanied by a best-corrected visual acuity (BCVA) of lower than 0.63 (Snellen 20/32) or a two-line difference between eyes, without any pathologies in the eye structure or visual pathway. Bilateral amblyopia was defined as high ametropia with ≥6 D myopia, ≥4 D hyperopia, or ≥2.5 D astigmatism, or conditions obstructing the bilateral visual axis with a BCVA of lower than 0.5 (Snellen 20/32) for children aged three or four years and lower than 0.4 (Snellen 20/32) for those older than four years[17,18].

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 25.0 (SPSS Inc., Chicago, IL, USA). The normality of numerical data distribution was evaluated with the Kolmogorov-Smirnov test. Categorical data were analyzed with the chi-square test, and numerical data with the independent-samples t-test and Mann-Whitney

test. A p value of less than 0.05 was considered statistically significant.

RESULTS

This study included a total of 341 patients, of whom 171 were female and 170 were male. The mean age of the patients was 7.81±3.6 years. The gender distribution according to the types of amblyopia was as follows: 93 girls and 95 boys with refractive amblyopia (55.1%), 47 girls and 46 boys with strabismic+refractive amblyopia (27.3%), 28 girls and 27 boys with strabismic amblyopia (16.1%), and 3 girls and 2 boys with deprivation amblyopia (1.5%). In addition, unilateral amblyopia was present in 264 patients (77.4%) and bilateral amblyopia in 77 (22.69%). There was no statistically significant difference between the types of amblyopia in terms of gender (p=0.940). When evaluated according to the strabismus type, the mean age was 7.39±2.8 years in the refractive amblyopia group, 6.94±4.3 years in the strabismic+refractive amblyopia group, 6.94±3.8 years in the strabismic amblyopia group, and 4.00±1.0 in the deprivation amblyopia group. Table 1 presents the distribution of patients according to the amblyopia type and age range (3-6 years, 7-10 years, 11-14 years, and 15-18 years).

The mean BCVA was 0.62±0.44-0.61±0.43 in the patients with refractive amblyopia, 0.66±0.27-0.67±0.28 in those with strabismic+refractive amblyopia, 0.61±0.29-0.61±0.30 in those with strabismic amblyopia, and 0.64±0.33-0.61±0.34 in those with deprivation amblyopia (right, left respectively).

When the relationship between refractive error and amblyopia types was examined, the mean spherical values (1.76±3.6) - (1.92±3.6) and cylindrical values were (-0.85±1.7) - (-0.92±1.3) in refractive amblyopia; the mean spherical values (1.34±2.4) - (1.29±2.8) and cylindrical values were (-0.49±1.5) - (-0.55±1.4) in strabismic+refractive amblyopia; the mean spherical values (0.31±0.95) - (0.28±0.90) and cylindrical values were (-0.45±0.40) - (-0.50±0.42) in strabismic amblyopia; and the mean spherical values (1.40±1.3) - (1.35±1.3), and cylindrical values were (-0.25±0.3) - (-0.20±0.2) in deprivation amblyopia. (right, left respectively). The distribution of refractive errors according to the amblyopia type is shown in Table 2.

The anisometropia values were as follows: mean spherical, 1.65±2.2 and mean cylindrical, -0.95±0.92 in unilateral amblyopia and mean spherical, 0.18±0.60 and mean cylindrical, -0.15±0.24 in bilateral amblyopia. Table 3 presents the detailed anisometropia values in unilateral and bilateral amblyopia.

We detected esotropia in 68 (73%) and exotropia in 25 (27%) of the 93 patients with strabismic+refractive amblyopia. Of the 55 patients with strabismic amblyopia, 30 (54.5%) had esotropia and 25 (45.5%) had exotropia. When all the 148 patients with strabismus were evaluated together, there were 98 (66.2%) cases of esotropia and 50 (33.8%) cases of exotropia. We determined that esotropia was more likely to cause amblyopia than exotropia (p=0.015). Figure 1 shows the distribution of amblyopia cases affected by strabismus.

Of the five patients with deprivation amblyopia, four had ptosis and one had a cataract. First-degree familial amblyopia status was detected in 28 (8.2%) of the 341 patients, including 10 (5.3%) of the 188 patients with refractive amblyopia, nine (9.7%) of the 93 patients with strabismic+refractive amblyopia, and nine (16.3%) of the 55 patients with strabismic amblyopia. The rate of family history was higher in amblyopia types presenting with strabismus compared to the refractive amblyopia type (p=0.024).
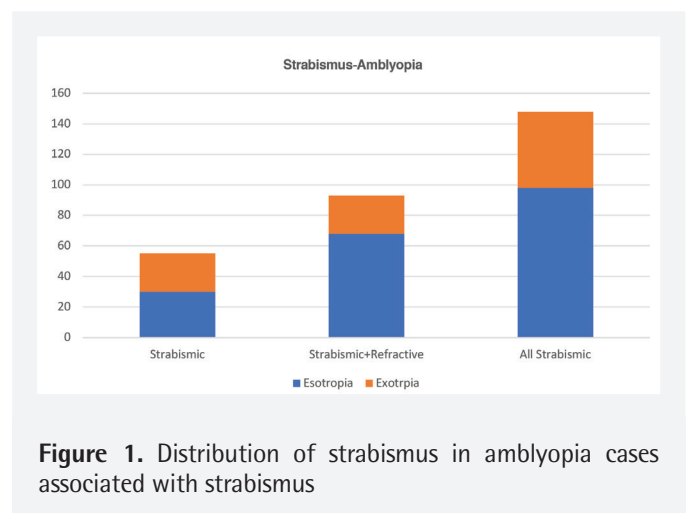
Figure 1. Distribution of strabismus in amblyopia cases associated with strabismus

Table 1. Distribution of age groups according to the amblyopia types			
	Refractive	**Strabismic+refractive**	**Strabismic**	**Deprivation**
	Unilateral–bilateral	**Unilateral–bilateral**		
Age				
3-6 years	55 (16.1%) 26 (7.6%)	20 (5.9%) 12 (3.5%)	7 (2%)	5 (1.4%)
7-10 years	67 (19.7%) 20 (5.9%)	34 (9.9%) 8 (2.4%)	21 (6.3%)	–
11-14 years	20 (5.9%) 8 (2.4%)	8 (2.4%) 4 (1.2%)	18 (5.2%)	–
15-18 years	2 (0.6%) –	7 (2%) –	9 (2.6%)	–
Total	134 (39.3%) 54 (15.9%)	69 (20.2%) 24 (7.1%)	55 (16.1%)	5 (1.4%)

History of preterm delivery was present in 18 patients with refractive amblyopia, 16 patients with strabismic+refractive amblyopia, and six patients with strabismic amblyopia; history of neonatal intensive care stay was detected in 18 patients with refractive amblyopia, 14 patients with strabismic+refractive amblyopia, five patients with strabismic amblyopia, and one patient with deprivation amblyopia; history of cesarean delivery was found in 45 patients with refractive amblyopia, 27 patients with strabismic+refractive amblyopia, 21 patients with strabismic amblyopia, and two patients with deprivation amblyopia; and epilepsy was detected in 10 patients with refractive amblyopia, nine patients with strabismic+refractive amblyopia, and five patients with strabismic amblyopia. The distribution of these non-ocular risk factors according to the amblyopia type is given in Table 4.

DISCUSSION

Although amblyopia is most common in the age group of three to four years, studies have found that this condition is also seen at a high rate in school-age children[19-21]. In a meta-analysis conducted by Hu et al.[22], it was reported that the prevalence of amblyopia varied between boys and girls but did not significantly differ according to geographical area, sample size, and economic status[22]. In contrast, in an amblyopia prevalence study on children, Li et al.[18] detected no significant difference between the genders. In the current study, we found that amblyopia was most common in children aged three to six years (36.5%) and seven to 10 years (44.2%). We observed no statistically significant difference in terms of gender.

Studies have shown that the most frequent ocular risk factors of amblyopia are refractive errors, strabismus, or coexistence

Table 2. Distribution of refractive errors according to the amblyopia types				
	Refractive	Strabismic+refractive	Strabismic	Deprivation
Spherical	Unilateral/bilateral n=134/54	Unilateral/bilateral n=70/23	55	5
≤1.00	13 (9.7%) 3 (5.6%)	8 (11.4%) 1 (4.3%)	10 (18.2%)	1 (20%)
>1.00 to <+4.00	21 (15.6%) 7 (13%)	11 (15.9%) 1 (4.3%)	19 (34.6%)	2 (40%)
≥4.00 to <6.00	31 (23.1%) 13 (13.0%)	16 (22.8%) 6 (26.3%)	2 (3.6%)	-
≥6.00	36 (26.8%) 15 (27.8%)	16 (22.8%) 7 (30.5%)	-	-
≤-1.00	9 (6.7%) 1 (1.8%)	4 (5.7%) 1 (4.3%)	12 (21.8%)	2 (40%)
>-1.00 to <-400	10 (7.6%) 1 (1.8%)	5 (7.1%) 1 (4.3%)	10 (18.2%)	-
≥-4.00 to <-6.00	8 (6.0%) 7 (13.0%)	5 (7.1%) 2 (8.6%)	2 (3.6%)	-
≥-6.00	6 (4.5%) 7 (13.0%)	5 (7.1%) 4 (17.4%)	-	-
Astigmatism				
<1.50	44 (32.8%) 10 (18.5%)	24 (34.3%) 6 (26.3%)	36 (65.5%)	4 (80%)
≥1.50 to <2.50	56 (41.8%) 15 (27.8%)	26 (37.1%) 7 (30.4%)	14 (25.4%)	1 (20%)
≥2.50	34 (25.4%) 29 (53.7%)	20 (28.6%) 10 (43.4%)	5 (9.1%)	-

Table 3. Distribution of anisometropia according to the laterality of amblyopia				
	Unilateral (n=264)		Bilateral (n=77)	
Anisometropia	Spherical	Cylindrical	Spherical	Cylindrical
<1.00	66 (25.0%)	86 (32.6%)	44 (57.2%)	51 (66.2%)
1.00 to <1.50	80 (30.3%)	100 (37.9%)	28 (36.3%)	22 (28.6%)
≥1.50	118 (44.7%)	78 (29.5%)	5 (6.5%)	4 (5.2%)

Table 4. Distribution of non-ocular risk factors according to the amblyopia types					
	Refractive	Strabismic+refractive	Strabismic	Deprivation	Total
Family history	10/188 (5.3%)	9/93 (9.7%)	9/55 (16.3%)	-	8/341 (8.2%)
Premature birth	18/188 (9.6%)	16/93 (17.2%)	6/55 (10.9%)	1/5 (20%)	41/341 (12%)
Neonatal intensive care requirement	18/188 (9.6%)	14/93 (15%)	5/55 (9%)	1/5 (20%)	38/341 (11.1%)
Cesarean delivery	45/188 (24%)	27/93 (29%)	21/55 (38.1%)	2/5 (40%)	95/341 (27.8%)
Epilepsy	10/188 (5.3%)	9/93 (9.7%)	5/55 (9%)	-	24/341 (7%)

of both, as well as conditions that affect vision (such as ptosis, congenital cataract, and corneal opacity) to a lesser extent[23,24]. Studies examining the relationship between refractive error and amblyopia have shown that amblyopia is associated with refractive error in approximately 50-70% of cases. Pascual et al.[25] evaluated 3,869 children and found unilateral amblyopia in 296 (7.7%) and bilateral amblyopia in 144 (3.7%). Children with unilateral amblyopia had hyperopia of ≥2 D, astigmatism of ≥1 D, or anisometropia of 0.5 D to ≥1 D, while those with bilateral amblyopia had bilateral hyperopia of ≥3 D or astigmatism of ≥1 D. Pai et al.[26] detected both hyperopia (66.7% of patients) and astigmatism (48.1%) to be major amblyogenic risk factors for anisometropia or isoametropia. Margines et al.[27] found that 568 of 780 pediatric amblyopia cases were unilateral and 212 were bilateral, and the rates of hyperopia, myopia, and astigmatism were 75%, 15%, and 92%, respectively, in the unilateral amblyopia group. In our study, 59% of all the patients had hyperopia of ≥1 D and 64% had astigmatism of ≥1 D. Of the 264 (77.4%) patients with unilateral amblyopia, approximately 35% had hyperopia of ≥4 D, 60% had astigmatism of ≥1.5 D, 10% had myopia of ≥4 D and had anisometropia of greater than 1 D spherical in 74% and cylindrical in 68%. Of the 77 (22.69%) patients with bilateral amblyopia, approximately 59% had hyperopia of ≥4 D, 62% had astigmatism of ≥1,5 D, 25% had myopia of ≥4 D and had anisometropia of ≥1,5 D spherical in 41% and cylindrical in 43%. This is consistent with the findings reported by previous studies.

In studies on strabismus, this condition has been detected as a risk factor for amblyopia, with the rate of strabismic amblyopia ranging from 10 to 40% and that of strabismic+refractive amblyopia ranging from 20 to 25% according to various population and ages, and esotropia being determined as a factor causing a higher risk of amblyopia than exotropia[7,11,28]. Malik et al.[29] found that 67.3% of 150 patients with strabismic amblyopia had esotropia and 32.6% had exotropia. In another study, Ryu and Lambert[30] detected esotropia in 71% and exotropia in 21% of 295 patients with strabismic, strabismic+refractory, and strabismic amblyopia types. In our study, we observed that 16.1% of the amblyopia cases were strabismic and 27.3% were strabismic+refractive. Of the patients with amblyopia affected by strabismus, 66.2% had esotropia and 33.8% had exotropia, and we found that the former constituted a higher risk of amblyopia compared to the latter.

Deprivation amblyopia, which is rare (<3%) in amblyopia cases, occurs as a result of the complete or partial obstruction of the visual axis due to conditions such as congenital cataract, ptosis, vitreous hemorrhage, and corneal opacity. In our study, deprivation amblyopia was present in five patients (four with ptosis and one with cataract) (1.5%)[31–33].

Various studies suggest that a history of amblyopia, especially in first-degree relatives, increases the risk of amblyopia development[10,34]. Mocanu and Horhat[10] found that 6% of patients with amblyopia had a family history. Çakır et al.[35] detected a family history of amblyopia in 5.3% of the patients they followed up. Guimaraes et al.[36] reported that strabismus-related amblyopia was more familial than the refractive amblyopia type. In our study, the rate of those with a family history was 5.3% in the refractive amblyopia group, 9.7% in the strabismic+refractive amblyopia group, and 16.3% in the strabismic amblyopia group. We found that a positive family history was higher in the amblyopia types associated with strabismus.

Studies investigating pregnancy- and birth-related risk factors of amblyopia have shown that low birth weight, premature birth, cesarean delivery, and neonatal intensive care requirement increase the risk of amblyopia development[36-38]. In the current study, we found that 41 (12%) cases had a history of preterm delivery, 38 (11.1%) had a history of neonatal care unit admission, and 95 (27.8%) had a history of cesarean delivery.

In a study conducted with 327 patients having amblyopia, Çakır et al.[35] reported that the rate of those with a history of febrile seizures was 9.7%. In our study, epilepsy was present in 34 (7%) patients.

Study Limitations

The relatively low number of patients, retrospective design, and inclusion of the three-year-old subgroup in the sample can be considered as factors limiting this study.

CONCLUSION

Amblyopia is an eye disease that is commonly seen in childhood and responds well to treatment. In addition to known risk factors affecting refractive error, strabismus, and visual axis of amblyopia, it is very important to determine other risk factors related to family history, pregnancy, and birth. The identification of these risk factors will facilitate the early diagnosis of the disease in high-risk children, and the initiation of early treatment in these children can prevent vision loss.

Ethics

Ethics Committee Approval: The study was approved by the Adıyaman University Local Institutional Ethics Review Board (date: 15.11.2022, decision no: 2022/8-1).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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