Ocular and Cerebral Causes and A New Scoring System to Evaluate Visual Function in Young Children with Visual Impairment

Pinar Bingol Kiziltunc (✉ pinarbingol84@gmail.com)

Ankara Üniversitesi Tıp Fakültesi <https://orcid.org/0000-0003-4394-7926>

Esra Şahli

Ankara Üniversitesi Tıp Fakültesi: Ankara Üniversitesi Tıp Fakültesi

Ömer Bektaş

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Abstract

Purpose:

Childhood blindness is important cause contributing to the burden of blindness. It is necessary to identify the most frequently observed diseases in different populations. We aimed to demonstrate clinical features of low vision children and to evaluate the factors affecting visual function by a new visual function scoring system.

Methods:

249 children between the age of 6 months and 3 years were included. Visual function was scored from 0 to 15 according to; response to threat, light, object, presence of fixation, duration of fixation, following of light and object in horizontal, vertical, oblique, and circular gazes, optokinetic nystagmus. Patients were classified according to neurological diagnosis and cranial magnetic resonance imaging. Correlation between visual function score and ocular and neurologic findings were evaluated.

Results:

While 136 patients (54.6%) had cerebral visual impairment (CVI), 89 (35.7%) had ocular pathology, 24 patients (9.6%) had combined pathology. The most common ocular and cerebral pathologies were oculocutaneous albinism (23.9%) and hypoxic ischemic encephalopathy (HIE) (27.5%), respectively. Patients with CVI had lower visual function than ocular pathologies. Neurological structural disorders and HIE had worse visual function. Widespread involvement of brain had lower visual function score. Seizure negatively affected visual function.

Conclusions:

Cerebral causes were found in approximately half of infants and children with low vision who were referred to our center for visual habilitation. The visual function scoring system we developed in this study will provide an opportunity to be objective in the follow-up of babies and in evaluating the effectiveness of visual habilitation programs.

Introduction:

Childhood blindness is important cause contributing to the burden of blindness. Approximately 1.4 million children suffer from blindness worldwide. Although it accounts a small amount of all blindness, the disability scores are similar or higher than adult blindness. [1] Because of the necessity of a healthy vision for neurological, behavioral, and social development in children, preventable causes of visual impairment in children should be eliminated. In cases where visual impairment cannot be prevented, it should be diagnosed early, and appropriate treatment and/or re/habilitation programs should be initiated as soon as possible. Early initiation of treatment and rehabilitation programs is of

great importance for children since they have a long life expectancy. Hence, World Health Organization has identified childhood blindness as one of the five main topics of the Vision 2020 program.

Causes of childhood visual impairment vary according to the socioeconomic development levels of the countries. Therefore, it is necessary to identify the most frequently observed diseases in different populations to take precautions.

In this study, we aimed to evaluate the causes of visual impairment in children between the age of 6 months and 3 years and to determine the factors affecting the severity of visual dysfunction by a new visual function scoring system.

Materials And Methods:

This study was conducted in line with the dictates of the Declaration of Helsinki and approved by the local ethical committee (IRB Number: 11-746-18) and informed consent was obtained from the parents of participants.

The study was performed between September 2017 and December 2019. All patients between the age of 6 months and 3 years with low vision due to any pathology were included in this cross-sectional study. A detailed medical history was obtained from the families of the patients. Consanguineous marriage and presence of members with low vision in the family and relatives were recorded. Diseases and medications of mothers during their pregnancy were questioned. Birth weights, gestational ages and accompanying systemic diseases of the patients were noted. The families were asked about the eye complaints they noticed, which caused them to admit to the hospital for ophthalmic examination.

All patients were examined by the same ophthalmologist and pediatric neurologist. On ophthalmic examination, response to threat, response to light and object, presence of optokinetic nystagmus and fixation, duration of fixation, horizontal, vertical, oblique, and circular light and object following were examined. All these parameters were scored as 15 points to assess the visual function. (Table-1) Regarding the validity-consistency of the scoring system, no significant difference was found between the scores in the blind pilot evaluation performed on 50 children by two ophthalmologists. Additionally, presence of nystagmus, light reactions, ocular alignments, and anterior segment were examined. Amount of ocular deviation was measured by Krimsky test. After above mentioned examinations, tropicamide 1% one drop was used two times at 5 minute intervals for cycloplegic retinoscopy and fundus examination.

After neurological examination, motor developmental steps, electroencephalography, and cranio-orbital magnetic resonance imaging (MRI) findings were evaluated by pediatric neurologist. Presence of seizure was evaluated according to International League Against Epilepsy (ILAE) diagnosis criteria.[2] Patients were classified into 7 groups according to their respective clinical diagnosis as follows: prematurity, hypoxic ischemic encephalopathy (HIE), neurological structural disorders, neuromotor developmental retardation due to unknown etiology, chromosome abnormalities, metabolic diseases, and intrauterine

cytomegalovirus infection. Finally, cranial MRI findings were evaluated and classified according to the previous reports. [3–5]

Low vision etiopathogenesis were divided into three periods as prenatal, natal, and postnatal periods, according to the duration in which the injury developed. After the neurological and ophthalmological examinations of the patients were completed, the etiologies were classified into three groups as an ocular pathology, cerebral visual impairment (CVI) and combined group with ocular pathology and CVI together.

SPSS 22 was used for statistical analyses. Descriptive statistics were given for the variables. Continuous variables were presented as means or medians with minimum – maximum values. Categorical variables were presented as numbers and percentages. Visual function score exhibited an abnormal distribution pattern therefore comparison of this score in different study variables which have more than two groups (etiology of visual impairment, MRI finding categories, seizure status) was performed by Kruskal Wallis Test. Bonferroni adjustment was applied to overcome the potential disadvantages of multiple comparisons.

Results:

A total of 249 children with visual impairment were included in the study. Mean age was 16.9 (6–36) months. Of 249 patients, 135 (54.2%) were male and 114 (45.8%) were female. Mean gestational age was 36.5 (23–41) weeks and mean gestational birth weight was 2851 (570–4310) grams. Consanguineous marriage was present in 37.3% of the patients. In 16.9% of the patients, there was family history of similar eye disease.

In 173 (69.8%) patients, the damage developed during the prenatal period. The numbers of patients who developed damage in the natal and postnatal periods were 51 (20.6%) and 25 (9.7%), respectively. The mothers of 202 patients (81.9%) did not have any pathology during pregnancy. The most common pathologies during pregnancy were hypertension (4%), diabetes mellitus (3.2%), hypothyroidism (2.4%) and upper respiratory system infection (2.4%).

Eighty-three patients (33.3%) had seizure. Of these, 50 (60.2%) were under control with treatment. However, remaining 33 (39.8%) had seizure attacks despite intensive treatment. When presence of seizure was evaluated in CVI patients, this rate was 61%. Mild hearing loss was present in 4.4% (11 patients) of all patients, and severe hearing loss in 5.2% (13 patients).

Nineteen patients (17.6%) had invasive ophthalmic procedures. Seven (2.8%) had cataract surgery. Seven (2.8%) had laser photocoagulation or intravitreal anti-VEGF injection for retinopathy of prematurity (ROP). The remaining 5 patients (2%) had vitreoretinal surgery for ROP (1.2%), persistent fetal vasculature (0.4%) and toxoplasma chorioretinitis (0.4%).

The complaints of families at the time of admission are shown in Table-2. Of 249 patients, 124 (49.8%) had nystagmus. This ratio was 75.3% and 32.4% in the ocular pathology and CVI group, respectively.

Forty-eight (19.3%) patients had roving eye movements. Oculodigital reflex was observed in 21 (8.4%) patients. Strabismus was present in 121 (48.6%) patients. The most common strabismus pattern was exotropia with 30.1%, followed by esotropia (18.1%) and hypertropia (0.4%). One hundred thirty (52.2%) patients had refractive error. Rates of hyperopia, myopia, and astigmatism were 26.9%, 7.2% and 16.5%, respectively. In the fundus examination, 91 patients (36.5%) had no abnormality. The most common findings were optic disc pallor (20.1%), albinoid alterations (10.4%) and peripheral pigmentary changes (7.6%).

While 136 patients (54.6%) had cerebral visual impairment (CVI) and 89 (35.7%) had ocular pathology, the remaining 24 patients (9.6%) had combined pathology. Ocular diagnoses of patients in ocular pathology group and combined group are seen in Table-3. Neurological etiologies of patients in CVI group and combined group are shown in Table-4. Additionally, the classification of patients according to the cranio-orbital MRI findings are seen in Table-5.

When all patients were evaluated together, the median score of visual function was 6 (0–15). The median score of patients with CVI (3.5) was significantly lower than patients with ocular pathologies (11). ($p = 0.001$) Additionally, patients in combined group had significantly lower score (1.5) than patients with ocular pathologies ($p = 0.003$). When etiologies of patients with CVI were evaluated separately, median scores of neurological structural disorders and HIE were lower than the other etiologies ($p < 0.05$). Additionally, median score of patients with widespread involvement of grey and white matter in cranial MRI was significantly lower ($p < 0.001$). The patients with seizure had significantly lower median score than the patients without seizure. ($p = 0.001$)

Discussion:

In this study, we demonstrated that only 35.7% of the patients under 3 years of age with low vision had isolated ocular pathologies. Remaining 64.3% had CVI alone or CVI and ocular pathologies together. While the most common ocular pathologies were oculocutaneous albinism and Leber congenital amaurosis (LCA), the most common causes of CVI were HIE and prematurity. The patients with CVI had lower visual function score than the patients with ocular pathologies. The patients with neurological structural disorders and HIE had worse visual function than the other etiologies of CVI. When the MRI findings were evaluated, the most common finding was widespread white matter involvement. The patients with widespread involvement of grey and white matter had lower visual function score. Presence of seizure negatively affected the visual function.

Factors causing low vision in children vary according to the development levels of the countries. Cerebral visual impairment was reported as the most common cause of visual impairment in children in developed countries. [6–8] Additionally, avoidable causes including preventable and treatable causes are less in these countries. [9, 10] Although preventable and treatable causes are more common in developing countries, the frequency of CVI is also increasing. [11–13] With advances in perinatal care, survival of babies with low gestational age increased. Therefore, CVI has become one of the main causes of low

vision in children nowadays. In our study, we found CVI as the main cause of visual impairment in children under 3 years, like the results of developed countries.

Although CVI may occur due to different etiologies including hypoxia, seizure, hypoglycemia, trauma, neurodevelopmental and neurodegenerative disorders, HIE was reported as the most common cause.[14] In the presence of hypoxia and accompanying hypercarbia, vascular autoregulation of brain is impaired, and this results in decreased cerebral perfusion and brain damage. [15] Khetpal et al. evaluated 161 children with CVI, and they found that the most common etiology was perinatal hypoxia (36%). [16] Huo et al. reported the ratio of perinatal hypoxia in patients with CVI as 22.3%. [17] Similar to the literature, HIE was the most common cause of CVI (27.5%) in our study. Another important finding of this study in terms of HIE was that patients with HIE had lower visual scores than other causes of CVI, at the time of admission. Due to the proximity of the visual pathways to the periventricular white matter, this region is of great importance for visual function. Hypoxic ischemic encephalopathy often involves periventricular white matter. The poor visual function in HIE patients can be explained by the damage to the visual pathways.

Prematurity is the other common cause of CVI. The incidence of prematurity in CVI patients was 30% in the study of Khetpal et al. [16] Similar to the reported study, the second most common cause of CVI was prematurity (26.9%), in the present study. Periventricular leukomalacia, reduced volume of periventricular white matter and delayed myelination result in CVI in premature babies. As the periventricular leukomalacia is the most common form of cerebral injury in premature infants, these babies have a high risk of developing visual impairment. Additionally, in this study we demonstrated that patients with CVI alone or CVI and ocular pathology together had worse visual scores than patients with ocular pathologies. This finding suggests that effect of brain structures that are responsible for visual physiology, results in worse visual score of low vision patients.

Different types of cerebral injury may be seen in children with low vision. Depending on the cause, optic nerve, optic tract, optic radiation, occipital cortex, brainstem, basal ganglia, gray and white matter may be affected. In addition, the severity and spread of the involvement may differ between patients depending on the etiopathogenesis. Location and severity of the involvement affect the ocular findings and visual function. Association between different types of brain injury and visual function was evaluated in a few studies. Hoyt et al. found that visual functions of patients with periventricular leukomalacia and striate cortex damage were similar in CVI patients. [15] Cioni et al. showed that patients with damage to periventricular white matter involving optic radiations had worse visual function than visual cortex involvement.[18] Either extensive periventricular white matter damage or striate cortex infarcts was correlated with poor visual function in the study of Eken et al. [19] We also evaluated the association between the location of brain damage and visual function. The most common involvements were widespread white matter involvement (24.5%) and widespread involvement of grey and white matter (15.3%). Patients with widespread involvement of grey and white matter had the worst visual function in our study. Different results of these studies may be related to the method for evaluating visual function. While Eken et al. used Teller acuity tests, Hoyt et al. used a 6 point scoring system. Unlike other studies,

we developed a new 15 point scoring system which can evaluate visual function parameters more detailed.

Cerebral visual impairment is rarely seen alone and is often accompanied by another ophthalmic or neurological disorder. Seizures may be the cause of CVI alone or accompany other causes leading to CVI. Huo et al. reported that the most common neurological abnormality in the CVI patients was seizure. [17] Additionally Handa et al. found the coexistence of seizure with CVI as 93%. [20] We evaluated the effect of seizure on visual function, and we found that patients with seizure had worse visual scores. The negative effect of the seizure on visual function can be explained by the damage of the seizure to optic radiations and visual cortex.[17, 21]

In our study the most common causes of ocular pathologies were albinism and LCA. These diseases are hereditary diseases and the prevalence of hereditary diseases are higher in countries where consanguineous marriage is more common. In the present study, hereditary ocular pathologies were the most common causes since consanguineous marriages were more than one third of the patients. The third most common ocular pathology was ROP. Nowadays, with the development of neonatal intensive care conditions, ROP does not take the first place among ocular pathologies in developed countries. [22] Ocular pathologies responsible for visual impairment were like the results of developed countries in our study.

This study evaluated a broad number of low vision children between the age of 6 months and 3 years. Thereby, etiologies in children with low vision could be studied in a large population. Unlike other studies, we developed a new scoring system to evaluate visual function. Thus, we were able to evaluate the visual function even in children with very low vision. Additionally, we could identify the parameters that affect the visual function.

This scoring system will enable us to make a numerical evaluation in following the visual functions of babies and young children. In addition, it will provide an opportunity to objectively evaluate the effectiveness of visual habilitation programs that we prepare and implement individually depending on whether they are ocular or cerebral.

Declarations

Funding:

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Conflicts of interest/Competing interests:

Not applicable

Availability of data and material:

The authors will share the data in case of a valid request

Code availability:

Not applicable

Authors' contributions:

Data acquisition: PBK, EŞ, ÖB, ÖAG, MFY, Aİ Concept and Design: PBK, EŞ, ÖB, ÖAG, MFY, Aİ Writing: PBK, EŞ, Aİ

Critical Revision: PBK, EŞ, Aİ, ÖB

Ethics approval

Approved by the local ethical committee (IRB Number: 11-746-18)

Consent to participate:

Informed consent to participate in the study was obtained from participants

Consent for publication:

Patients signed informed consent regarding publishing their data.

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Tables

Table-1

Scores of parameters which were used to assess visual function

Parameter	Score
Response to threat	1
Response to light	1
Response to object	1
Presence of optokinetic nystagmus	1
Presence of fixation	1
Duration of fixation	
No fixation	0
0-10 seconds	1
>10 seconds	2
Following of light	
Horizontal	1
Vertical	1
Oblique	1
Circular	1
Following of object	
Horizontal	1
Vertical	1
Oblique	1
Circular	1
Total score	15

Table-2

Complaints of patients at the time of admission

Complaint	Number of Patients (%)
Lack of eye contact	97 (39.0)
Inability to follow objects	72 (28.9)
Nystagmus	36 (14.5)
Ocular deviation	22 (8.8)
Inability to see small objects	9 (3.6)
Small eyes	5 (2.0)
Leukocoria	4 (1.6)
Photophobia	3 (1.2)
Opacity of the eye	1 (0.4)
Total	249 (100)

Table-3

Ocular diagnoses of patients in ocular pathology group and combined group

Ocular Diagnosis	Number of Patients (%)
Ocular and oculocutaneous albinism	27 (23.9)
Leber congenital amaurosis	18 (16)
Retinopathy of prematurity	13 (11.5)
Optic disc hypoplasia	13 (11.5)
Ocular structural disorders (microphthalmia, nanophthalmos, sclerocornea)	9 (8)
Retinal dystrophy	8 (7.2)
Chorioretinal coloboma	7 (6.3)
Congenital cataract	6 (5.4)
Chorioretinal scar	5 (3.9)
Retinal detachment	3 (2.7)
Retinal dysplasia	2 (1.8)
Congenital glaucoma	1 (0.9)
Infantile nystagmus syndrome	1 (0.9)
Total	113 (100)

Table-4

Etiologies of patients with cerebral visual impairment

Etiology	Number of Patients (%)
Hypoxic ischemic encephalopathy	44 (27.5)
Prematurity	43 (26.9)
Neurological structural disorders	33 (20.6)
Chromosome abnormalities	14 (8.7)
Metabolic diseases	13 (8.1)
Neuromotor developmental retardation due to unknown etiology	11 (6.9)
Intrauterine CMV infection	2 (1.3)
Total	160 (100)
CMV: Cytomegalovirus	

Table-5

Cranio-orbital MRI findings of all patients

MRI Findings	Number of Patients (%)
Normal	107 (43)
Widespread white matter involvement	61 (24.5)
Widespread involvement of grey and white matter	38 (15.3)
Basal ganglia and brainstem	17 (6.8)
Optic nerve and tract	13 (5.2)
Optic radiation and occipital cortex	13 (5.2)
Total	249 (100)
MRI: Magnetic resonance imaging	