



Factors Affecting Visual Function in Children with Cerebral Visual Impairment

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Abstract

Objectives: To evaluate the visual functions and their correlation with the neurological status in children with cerebral visual impairment (CVI).

Methods: Case records of children with CVI under 3 years of age at their first visit were reviewed. Children's visual functions were scored between 0 and 15 based on fixation and following skills. The neuromotor assessment was conducted by the Hammersmith Infant Neurological Examination (HINE) tool.

Results: A total of 233 children with CVI (122 male and 111 female) were identified. The median age was 13 months. The etiologies were hypoxic-ischemic encephalopathy (27.5%), prematurity (23.6%), structural abnormalities (24%), metabolic diseases and genetic syndromes (14.2%), and neuromotor retardation (10.7%). There was no difference in visual function score (VFS) among the etiological groups and the magnetic resonance imaging finding groups ($p=0.162$, $p=0.205$, respectively). The VFS values of children without seizures were significantly higher than those with seizures ($p=0.003$). There was a weak correlation between the HINE ratio and VFS ($p<0.001$, $r=0.341$).

Conclusion: The visual functions of children with CVI are usually very poor. The visual functions of these children are related to their neurological and motor retardation levels, seizure states, and the presence of additional ocular problems.

Keywords: Cerebral visual impairment, children, visual function

Introduction

Cerebral visual impairment (CVI) is defined as a verifiable visual dysfunction that cannot be attributed to disorders of the anterior visual pathways or any potentially co-occurring ocular impairment (1). It is the most common cause of visual impairment in children in developed countries. It is thought

that the reason for this is the increase in the survival rates of premature infants and babies with neurological deficits due to the improvements in newborn intensive care services (2). The most common cause of CVI in children is reported to be perinatal or postnatal hypoxic-ischemic encephalopathy (HIE), particularly in premature children (3-7). In premature infants, the periventricular white matter of the brain is more

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susceptible to hypoxia. Hypoxic injury and impaired blood flow autoregulation lead to periventricular leukomalacia (PVL) in these infants (8). The other common etiologies related to CVI are traumatic injury, infections including meningitis and encephalitis, hydrocephalus, seizures, structural abnormalities, and metabolic and genetic disorders (2,9). Although children with CVI often cannot achieve normal visual function, it has been shown that their vision may improve over time (3,4,6,10).

Our study aimed to determine the causes and accompanying features of CVI in children below 3 years of age and to evaluate the correlations between neurological status and visual function in these children.

Methods

Children with CVI under 3 years old who were referred to the Ankara University Vision Research and Low Vision Rehabilitation Center between January 2018 and December 2021 were included in this study. This study was approved by the Ankara University School of Medicine Ethics Committee (Registration Number: 17-454-20) and adhered to the tenets of the Declaration of Helsinki.

A detailed history, including gestational age, birth weight, type of delivery, health problems of the mothers during pregnancy, presence of consanguinity between the parents, and presence of seizures, was obtained from the parents of the children. All children underwent a comprehensive ophthalmological examination, including anterior segment and fundus examination, cycloplegic retinoscopy, and orthoptic examination after functional evaluation, which will be described in detail below.

Since the visual functions of the patients referred to our center are very poor, we could not evaluate the visual acuity using preferential-looking tests in most children. Visual evoked potential (VEP) was also not used in the evaluation because it is difficult to evaluate the VEP in a population under 12 months old. Functional evaluation based on fixation and following examination is preferred instead in all patients. Flashlight in a dark room, an object with black and white lines at 2 cm intervals, and a bright yellow or red colored round object with a diameter of 10 cm were used to evaluate fixation and following function. The objects were shown at a 30 cm distance under normal lighting conditions. Any auditory signals or tactile stimulation were avoided. The object following examination was started by shaking the object since it is easier for some children with CVI to perceive the movement of the stimulus.

We assessed children's visual function according to the presence of light, object, and threat responses, the presence and duration of fixation, the presence of light and object following in the horizontal, vertical, and oblique axes, and the circular direction. Due to the presence of latency that may be present in some patients, we performed the following examination by giving children the necessary time. By summing the scores assigned to each visual parameter, we obtained a visual function score (VFS) between 0 and 15 for each patient (Table 1).

Grating acuity was measured in children who paid attention to the preferential-looking test with Lea Gratings. The CPCM values obtained with this test were first converted to CPD and then to LogMAR values to be able to compare. The visual acuity of the children who did not respond to Lea

Table 1. Detailed description of the visual function scoring system

Visual function	Score		
Behavioral light response	Yes (1)	No (0)	
Behavioral object response	Yes (1)	No (0)	
Threat response	Yes (1)	No (0)	
Fixation	Yes (1)	No (0)	
Length of fixation time	No fixation (0)	Below age requirement (1)	Meets age requirement (2)
Horizontal light following	Yes (1)	No (0)	
Vertical light following	Yes (1)	No (0)	
Oblique light following	Yes (1)	No (0)	
Circular light following	Yes (1)	No (0)	
Horizontal object following	Yes (1)	No (0)	
Vertical object following	Yes (1)	No (0)	
Oblique object following	Yes (1)	No (0)	
Circular object following	Yes (1)	No (0)	
Optokinetic nystagmus	Yes (1)	No (0)	

Gratings was recorded as 3.1 logMAR, which is considered the lowest value in LogMAR. All patients were examined by the same ophthalmologist (E.S.).

Patients' data included gender, age at the first visit (month), gestational age, birth weight, presence of additional non-ocular pathology, presence of seizures, hearing loss, parental consanguinity, and family history of similar diseases also considered in the study.

All patients were also examined by pediatric neurologists (OAG, OB). First, patients were classified into five groups according to their respective clinical diagnoses as follows: Prematurity, HIE, structural abnormalities, metabolic diseases, genetic syndromes, and neuromotor developmental retardation due to unknown etiology. Then, neurological examinations, motor developmental steps, cranial magnetic resonance imaging (MRI), and electroencephalography findings were evaluated for each patient.

A neuromotor assessment was conducted following the World Health Organization's neuromotor development milestones (11). The Hammersmith Infant Neurological Examination (HINE) tool, which was objective, simple, and reliable, was used to standardize all assessments. We used the motor development milestones part of the HINE scale to illustrate our patients' gross motor functions which include head control, sitting, standing, and walking. According to HINE motor developmental scoring module; the part of "head control" was scored as follows; (0) unable to maintain head upright, (1) wobbles, and (2) maintain upright all time; the part of "sitting" was scored as follows; (0) cannot sit, (1) sits with support at hips, (2) props self-up, (3) stable sitting, and (4) pivots (rotates); the part of "standing" was scored as follows; (0) does not support weight, (1) supports weight, (2) stands with support, and (3) stands unaided; the part of "walking" was scored as follows; (1) bouncing, (2) cruising, and (3) walking independently. The sum of the four scores yielded HINE scores for the patients. As the age range of patients was wide, statistical evaluation was made calculating their percentile according to the HINE score expected in a healthy child at that age.

MRI findings were classified according to previous reports (12-16). The cranial MRI findings were classified into six groups as follows: Optic nerve and optic tract involvement, optic radiation and occipital cortex involvement, basal ganglia and brain stem involvement, widespread white matter involvement, brain widespread involvement (including cystic encephalomalacia, cortical malformations, etc.) and normal MRI finding. The patients were divided into epilepsy diagnosed and epilepsy-non-diagnosed according to the International League Against Epilepsy diagnosis criterion (17).

We previously evaluated the response to visual habilitation in visually impaired children under the age of 3 using the

visual function scoring system like the one in this study, and we found an increase in the VFS in children who received regular visual stimulation (18). Of the 233 patients with CVI included in this study, 70 were in common with the patients in the previous study.

All statistical analyses were performed using IBM Statistical Packages for the Social Sciences (SPSS) for Windows version 15.0 (SPSS, Chicago, IL, USA). Kolmogorov-Smirnov test was used to assess the assumption of normality. Comparisons for non-normally distributed continuous variables, differences within groups were tested using the Wilcoxon test, and differences between groups were tested using the Mann-Whitney U-test and the Kruskal-Wallis test. Associations between continuous variables were determined by the Spearman rho correlation coefficient. Associations between categorical variables were determined by Chi-square analysis and the Fisher Exact test. Logistic regression analysis was performed to determine the independent predictors affecting VFS. A $p < 0.05$ was considered significant.

Results

A total of 233 patients with CVI (122 males [52.4%] and 111 females [47.6%]) under 3 years old at the initial evaluation were included in the study. The median age at the first eye examination was 13 months (range: 3-36 months). The injury period was the prenatal period in 131 patients (56.2%), the natal period in 68 (29.2%), and the postnatal period in 34 patients (14.6%). The median gestational age was 38 weeks (ranges between 24 and 43 weeks), and the median birth weight was 2700 g (range: 570-4250 g). One hundred and three patients (44.2%) were born preterm (before 37 weeks of gestational age). 33% of the patients' parents had consanguineous marriages, 61% of which were 1st consanguineous. A positive family history of the same disease was present in 9% of the study population. 3% of the patients had a 1st relative who had a similar disease. There was no history of a health problem or drug intake in 81.1% of the mothers of the patients during pregnancy. Twelve had hypertension, seven had diabetes, six had hypothyroidism, six had urinary tract infections, and four had cytomegalovirus infections during pregnancy. 137 out of 233 patients (58.8%) had seizures and were treated with at least one anti-epilepsy drug. Seventy-nine of them (57.6%) had seizures controlled with medication, and 58 of them (42.3%) had seizures not controlled with medication. 33 out of 233 patients (14.1%) had hearing loss, 17 of which were severe.

The most common eye complaint that the families of the children noticed was the lack of eye contact (46%) and not being able to follow objects (36.1%). Other complaints can be listed as abnormal eye movements, squints, and being unable to recognize small objects. 21% of the patients had

nystagmus. Strabismus with variable angle was present in 154 out of 233 patients (66%). The most frequent squint was exotropia which was seen in 34.8% of the cases. 15.9% of the patients had esotropia, and 13.7% of the patients had roving eye movements. 111 out of 233 children had a refractive error that needed to be corrected with spectacles. The most frequent refractive error was hypermetropia (17.6%). The others were astigmatism (15%), compound hyperopic astigmatism (6%), myopia (4.3%), compound myopic astigmatism (3%), and mixed astigmatism (1.3%).

The median VFS at the first examination was 4 with a range of 0–15. Forty-seven (20.1%) children had only light responses but had no light fixation, whereas 40 (17.1%) children did not even have a light response at the initial evaluation. There was no response to objects in 130 patients (55.8%). The reflex blink-to-threat response was absent in 142 out of 233 patients (60.9%). There was no light fixation in 98 out of 233 patients (42.1%). Optokinetic nystagmus was seen only in 24.9% of the patients. Only 50 of the patients (21.4%) paid attention to the Lea Gratings test. When grating acuity converts to logMAR value, the median was 3.1 logMAR with a range of 3.1–0.9 logMAR. There was no difference in VFS between the genders ($p=0.436$). There was a weak correlation between age at first examination and VFS ($p<0.001$, $r=0.273$). The VFSs were similar among the prenatal, natal, and postnatal injury period groups ($p=496$). There were no correlations between VFS and gestational age and birth weight ($p=0.875$ and $p=0.730$, respectively). VFS values were found to be similar in the presence or absence of prematurity ($p=0.390$). The VFS values of children without seizures were significantly higher than those without seizures ($p=0.003$). When patients with seizures were evaluated according to whether their seizures could be controlled with medication, the difference between the VFS value of children with seizures that could not be controlled with medication and the VFS value of children without seizures was statistically significant ($p=0.005$).

All the patients were scored between 0 and 12 according to the motor development milestones part of the HINE scale by a pediatric neurologist. The median HINE score was 1 (ranges between 0 and 12), and the median ratio of the patient's HINE score to the expected HINE score at that age (HINE ratio) according to her/his age was 0.17 (ranges between 0 and 1). No difference was found among the etiological groups according to the VFS ($p=0.162$). There was no difference in VFS among the MRI finding groups, either ($p=0.205$). The distribution of etiologies according to neurological assessment and MRI findings and VFSs of the subgroups are shown in Table 2. There was a weak correlation between the HINE ratio and VFS ($p<0.001$, $r=0.341$).

Table 2. The distribution of the subgroups according to the neurological assessment and MRI findings and their visual function scores

Etiology	Frequency (%)	Median VFS
Hypoxic-ischemic encephalopathy	64 (27.5)	3
Prematurity	55 (23.6)	3
Structural abnormalities	56 (24)	4
Metabolic diseases	16 (6.9)	7
Genetic syndromes	17 (7.3)	6
Neuromotor developmental retardation	25 (10.7)	7
Classification of MRI findings		
Optic nerve and optic tract involvement	10 (4.3)	5
Optic radiation and occipital cortex involvement	12 (5.2)	4
Basal ganglia and brain stem involvement	19 (8.2)	6
Widespread white matter involvement	74 (31.8)	4
Brain widespread involvement	83 (35.6)	3
Normal MRI	35 (15)	8

MRI: Magnetic resonance imaging; VFS: Visual function score.

Forty-nine of 233 patients were visually impaired due to combined cerebral and ocular pathologies, including optic atrophy (6%), retinopathy of prematurity (4.3%), optic disc hypoplasia (3.9%), chorioretinitis (1.7%), microphthalmia (1.3%), and retinal dystrophy (1.3%). The median VFS of the patients with combined cerebral and ocular pathologies was lower than that of those with CVI ($p=0.040$).

Factors affecting VFS were also evaluated by logistic regression analysis. For this analysis, a VFS value of 10 and above out of 15 was considered good vision. This score corresponds to the presence of all functional parameters except object following and optokinetic nystagmus, as can be seen in Table 1. In the analysis including the variables of age, gender, etiological groups, MRI finding groups, HINE score, gestational age, birth weight, presence of prematurity, and status of seizures; HINE score (95% CI: 1.0152 to 1.338; $p=0.005$) and age (95% CI: 1.012–1.102; $p=0.012$) were found to be independent predictors of better visual outcome. These findings are consistent with the statistical analysis above.

Discussion

CVI is the leading cause of childhood visual impairment in developed countries. Increasing numbers in the survival of children with severe neurological damage may have also led the frequency of CVI to increase. Perinatal hypoxic-ischemic insult is reported as the most common etiology of CVI (19-

21). There is a close relationship between CVI formation and prematurity. Approximately 42% of our patients had a history of premature birth. Prematurity can cause intraventricular hemorrhage and PVL that damage posterior visual pathways (22). Hydrocephalus may also develop secondary to prematurity and ischemia or be associated with central nervous system malformations in most cases (20,23,24). Central nervous system malformations were reported up to 29% in some series (20). Similarly, in our study, CVI resulted from HIE in 27.5%, prematurity in 23.6%, structural abnormalities in 24%, metabolic diseases in 6.9%, and genetic syndromes in 7.3% of the patients, and there was only neuromotor retardation in 10.7% of the cases.

Within our patient group, 58.8% of the patients had superimposed seizures. Our data are consistent with the previous studies that documented seizures as the most common neurological association in children with CVI, accounting for up to 93% (20). We found that the visual functions of children without seizures were better than those with seizures. The functions were worse in patients with seizures that could not be controlled with medication. It has previously been reported that visual function improves with better control of seizures (5). Wong et al. (25) reported a poor prognosis in children who had uncontrolled seizures for 3 months after an initial neurological insult.

In our study, no correlation was found between gestational age and visual function, but there was a weak correlation between age at presentation and visual function. This confirms the assumption that vision will improve over time in children with CVI. The subgroups formed according to their etiology and MRI findings did not differ in terms of visual function. However, there was a weak correlation between the neuromotor developmental status of the children and their visual functions.

To our knowledge, there is no other study in the literature evaluating such a large number of young children with CVI. We think that this study with its wide scope will be useful in terms of giving an idea about the etiological distribution, accompanying ocular and neurological findings, and visual functions of children with CVI. In addition, the visual function scoring system we developed seems to be a new method that can be used to evaluate and record the visual functions of children with CVI who have very weak visual functions and to monitor the changes in their functions.

Our study has several limitations. Since our center is a tertiary center, the patients referred to us may have been more severely ill with poorer visual outcomes than those in other clinics. Few of our patients had quantifiable visual acuity by preferential looking tests such as Lea Gratings in their first examination. Preferential-looking tests have limited value in assessing the visual acuity of children with CVI

which is frequently associated with severe neurological disorders and superimposed optic atrophy, nystagmus, strabismus, and features such as fluctuations in visual attention, variable latency in saccades, presence of visual field deficits, and abnormal head position and frequently inadequate visual acuity (3,7,10,21,25,26). Therefore, we developed a scoring system that evaluates the fixation and following skills of children in this patient group, in which visual acuity is difficult to measure even with a preferential-looking test.

Conclusion

Children with CVI may have very limited visual functions. The visual functions of these children are related to their neurological and motor retardation levels, seizure states, and the presence of additional ocular problems.

Disclosures

Ethics Committee Approval: This study was approved by the Ankara University School of Medicine Ethics Committee (Registration Number: 17-454-20) and adhered to the tenets of the Declaration of Helsinki.

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References

1. Sakki HEA, Dale NJ, Sargent J, Perez-Roche T, Bowman R. Is there consensus in defining childhood cerebral visual impairment? A systematic review of terminology and definitions. *Br J Ophthalmol* 2018;102:424–32. [\[CrossRef\]](#)
2. Hoyt CS. Visual function in the brain-damaged child. *Eye* 2003;17:369–84. [\[CrossRef\]](#)
3. Huo R, Burden SK, Hoyt CS, Good WV. Chronic cortical visual impairment in children: Aetiology, prognosis, and associated neurological deficits. *Br J Ophthalmol* 1999;83:670–5. [\[CrossRef\]](#)
4. Matsuba CA, Jan JE. Long-term outcome of children with cortical visual impairment. *Dev Med Child Neurol* 2006;48:508–12. [\[CrossRef\]](#)
5. Good WV, Jan JE, DeSa L, Barkovich AJ, Groeneweld M, Hoyt CS. Cortical visual impairment in children. *Surv Ophthalmol* 1994;38:351–64. [\[CrossRef\]](#)
6. Khetpal V, Donahue SP. Cortical visual impairment: Etiology, associated findings, and prognosis in a tertiary care setting. *J AAPOS* 2007;11:235–9. [\[CrossRef\]](#)
7. Fazzi E, Signorini SG, Bova SM, La Piana R, Ondei P, Bertone C, et al. Spectrum of visual disorders in children with cerebral visual impairment. *J Child Neurol* 2007;22:294–301. [\[CrossRef\]](#)

8. Chhablani PP, Kekunnaya R. Neuro-ophthalmic manifestations of prematurity. *Indian J Ophthalmol* 2014;62:992–5. [\[CrossRef\]](#)
9. Chang MY, Borchert MS. Advances in the evaluation and management of cortical/cerebral visual impairment in children. *Surv Ophthalmol* 2020;65:708–24. [\[CrossRef\]](#)
10. Good WV, Jan JE, Burden SK, Skoczinski A, Candy R. Recent advances in cortical visual impairment. *Dev Med Child Neurol* 2001;43:56–60. [\[CrossRef\]](#)
11. WHO Multicentre Growth Reference Study Group. WHO Motor Development Study: Windows of achievement for six gross motor development milestones. *Acta Paediatr Suppl* 2006;450:86–95. [\[CrossRef\]](#)
12. Bathelt J, Dale NJ, de Haan M, Clark CA. Brain structure in children with congenital visual disorders and visual impairment. *Dev Med Child Neurol* 2020;62:125–31. [\[CrossRef\]](#)
13. Shu N, Li J, Li K, Yu C, Jiang T. Abnormal diffusion of cerebral white matter in early blindness. *Hum. Brain Mapp* 2009;30:220–7. [\[CrossRef\]](#)
14. Himmelmann K, Horber V, De La Cruz J, Horridge K, Mejaski-Bosnjak V, Hollody K, et al; SCPE Working Group. MRI classification system (MRICS) for children with cerebral palsy: Development, reliability, and recommendations. *Dev Med Child Neurol* 2017;59:57–64. [\[CrossRef\]](#)
15. Cioni G, Bertuccelli B, Boldrini A, Canapicchi R, Fazzi B, Guzzetta A, et al. Correlation between visual function, neurodevelopmental outcome, and magnetic resonance imaging findings in infants with periventricular leucomalacia. *Arch Dis Child Fetal Neonatal Ed* 2000;82:F134–40. [\[CrossRef\]](#)
16. Ortibus E, Lagae L, Casteels I, Demaerel P, Stiers P. Assessment of cerebral visual impairment with the L94 visual perceptual battery: Clinical value and correlation with MRI findings. *Dev Med Child Neurol* 2009;51:209–17. [\[CrossRef\]](#)
17. Gómez-Alonso J, Bellas-Lamas P. The new International League Against Epilepsy (ILAE) classification of epilepsies: A step in the wrong direction? *Rev Neurol* 2011;52:541–7. [\[CrossRef\]](#)
18. Sahli E, Bingol Kiziltunc P, Idil A. Visual habilitation in young children with visual impairment. *Child Care Health Dev* 2022;48:378–86. [\[CrossRef\]](#)
19. Flodmark O, Jan JE, Wong PK. Computed tomography of the brains of children with cortical visual impairment. *Dev Med Child Neurol* 1990;32:611–20. [\[CrossRef\]](#)
20. Handa S, Saffari SE, Borchert M. Factors associated with lack of vision improvement in children with cortical visual impairment. *J Neuroophthalmol* 2018;38:429–33. [\[CrossRef\]](#)
21. Groeneweld M. Observations on the habilitation of children with cortical visual impairment. *J Vis Impair Blind* 1990;84:11–5. [\[CrossRef\]](#)
22. Alimović S, Jurić N, Bošnjak VM. Functional vision in children with perinatal brain damage. *J Matern Fetal Neonatal Med* 2014;27:1491–4. [\[CrossRef\]](#)
23. Persson EK, Anderson S, Wiklund LM, Uvebrant P. Hydrocephalus in children born in 1999–2002: Epidemiology, outcome and ophthalmological findings. *Childs Nerv Syst* 2007;23:1111–8. [\[CrossRef\]](#)
24. Chen TC, Weinberg MH, Catalano RA, Simon JW, Wagle WA. Development of object vision in infants with permanent cortical visual impairment. *Am J Ophthalmol* 1992;114:575–8. [\[CrossRef\]](#)
25. Wong VC. Cortical blindness in children: A study of etiology and prognosis. *Pediatr Neurol* 1991;7:178–85. [\[CrossRef\]](#)
26. Salt AT, O'Reilly MA, Sakkalou E, Dale NJ. Detection vision development in infants and toddlers with congenital vision disorders and profound-severe visual impairment. *Dev Med Child Neurol* 2020;62:962–8. [\[CrossRef\]](#)