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Original Article

Investigation of Refractive Errors in Congenital Nasolacrimal Duct Obstruction

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Abstract

Objectives: Congenital nasolacrimal duct obstruction (CNLDO) is a condition that can lead to the development of anisometropia and amblyopia. This study aimed to identify refractive errors in children with unilateral and bilateral CNLDO.

Methods: A total of 220 eyes from 110 patients with CNLDO were retrospectively analyzed in this study. All patients underwent at least one surgery, and their most recent refractive errors were compared based on the laterality of the disease. The risk factors for amblyopia were established in accordance with the 2013 and 2021 American Association for Pediatric Ophthalmology and Strabismus guidelines. The investigated risk factors included disease laterality, surgical technique, number of surgeries, age at the time of surgery, and manifest strabismus.

Results: The nasolacrimal duct obstruction was unilateral in 66.4% (n=73) of the patients. The average ages at the last examination and at the time of surgery were 57.3±37.6 months (range: 12–153 months) and 29.6±22.3 months (range: 12–128 months), respectively. Hypermetropia was the most common refractive error, followed by astigmatism. The anisometropia and amblyopia rates were 11.8% (n=13) and 5.4% (n=6), respectively. No significant refractive difference was observed between the eyes in unilateral and bilateral CNLDO ($p>0.05$). After regression analyses, manifest strabismus was the only factor associated with amblyogenic risk factors in children with CNLDO (odds ratio = 0.132, 95% confidence interval = 0.529–17.400, $p<0.001$).

Conclusion: As a result, children diagnosed with CNLDO should be treated at as optimal time as possible, and visual maturation should be monitored for the development of high hypermetropia, anisometropia, and amblyopia. These children should receive a complete ophthalmic examination, including cycloplegic refraction, and orthoptic evaluations.

Keywords: Amblyopia, anisometropia, congenital nasolacrimal duct obstruction, refractive errors

Introduction

The most common cause of persistent epiphora in childhood is congenital nasolacrimal duct obstruction (CNLDO), which in turn is caused by a canalization anomaly of the nasolacrimal duct. Although varying rates are found in the literature, CNLDO symptoms are observed in approximately 6–20% of newborn babies (1). More than 90% of CNLDO spontaneously regresses with conventional treatment in the 1st year of life. However, approximately 4% of patients have symptoms after 1 year (2). Many ophthalmologists have agreed that conservative treatment should be applied before surgery in CNLDO cases. If conventional treatment fails, the

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first recommended surgical intervention is probing. Nasolacrimal tube intubation is an ideal procedure after unsuccessful probing (3).

Previously, CNLDO was perceived as a benign disease that did not affect visual development, but recent studies have demonstrated a relationship between CNLDO and anisometropia and amblyopia (4, 5). Different theories have explained the connection between amblyopia and CNLDO (6). Amblyopia in CNLDO cases may be due to high refractive errors and anisometropia. Abnormal refractive status is attributed to CNLDO and persistent epiphora, which affect visual maturation by causing degeneration (7).

This study aimed to identify refractive errors in children receiving surgical intervention at our institution who underwent a complete ophthalmic examination. The relationships between CNLDO and anisometropia and amblyopia risk were also evaluated.

Methods

This retrospective study was conducted at the Mersin Univesity Ophtalmology Outpatient Clinic. All procedures were performed following the ethical standards of the responsible committee on institutional human experimentation and those of the Helsinki Declaration. Ethics committee approval was granted by the Social and Human Sciences Ethics Committee of Mersin University with protocol number 2015–349, and informed consent was obtained from all participants.

A total of 220 eyes of 110 patients diagnosed with CNLDO aged 1–13 years were included in the study between January 2015 and December 2016. Exclusion criteria were patients with a history of ocular trauma, ophthalmic diseases, such as retinal disease, uveitis, glaucoma, and congenital cataracts, and ocular deformities, such as ptosis or keratopathy, which could affect refractive errors. Cerebral palsy and Down syndrome, premature birth, craniosynostosis, hydrocephalus, and other causes of epiphora and discharge, such as allergies, conjunctivitis, and trichiasis, were also excluded.

The eyes of patients with a history of epiphora and recurrent discharge were examined in the outpatient clinic. To diagnose CNDLO, the tear meniscus and regurgitation on pressure over the lacrimal sac were examined, and a fluorescein dye disappearance test was performed. Each patient underwent a complete ophthalmologic examination, including slit-lamp biomicroscopy, dilated fundus examination, and cycloplegic refraction. Before the measurement of refractive errors, a cyclopentolate hydrochloride 1% drop was instilled into the lower fornix of both eyes 3 times at 5-min intervals, and measurements were taken 30–40 min after the last drop. For verbal patients, the best corrected visual acuity (BCVA) was measured using the Snellen chart. A diagnosis of strabismus was performed with a cover–uncover test and an alternate cover test. Prism cover tests undertaken at a distance and near in a primary position were used to measure the angle of deviation. This routine ophthalmic examination was performed during diagnosis and an annual follow-up examination.

All patients in our study group had undergone at least one or more surgeries under general anesthesia. Probing was performed as the first procedure for children aged 1–5 years according to our institutional protocol. In bilateral cases, probing or nasolacrimal tube intubation procedures were performed on both eyes in the same session. For some of the children, silicone tube intubation was preferred as a second procedure in the case of one failed probing. However, dacryocystorhinostomy (DCR) was the main technique used in available cases. An external approach without inserting a silicone tube was preferred for the DCR. Patients were examined 1–2 weeks and 1–3 months after the surgery. Preoperative complaints were assessed, and a fluorescein dye disappearance test was performed for each control. All patients cured after surgery were recommended for an annual ophthalmic examination.

Data were collected on demographics and clinical characteristics, including gender, age at last surgery, age at last examination, type of surgery, and the number of surgeries performed. Medical records from available cases were studied for ocular alignment and motility, final cycloplegic refractive errors, anterior and posterior segment findings, and BCVA. The final refractive errors were defined as the latest cycloplegic refraction at the last control for cured patients. Refractive errors were based on the spherical equivalent (sphere plus 1/2 cylinder), sphere, and cylinder. Myopia was classified as a spherical equivalent of −0.50 D or less, hyperopia as a spherical equivalent of +0.50 D or more, and emmetropia as a spherical equivalent between −0.50 D and +0.50 D. Astigmatism was defined as a cylinder of at least 1 D, whether it occurred alone or in association with myopia or hyperopia (8).

According to amblyopia risk factors (ARFs) noted in the 2013 guidelines of the American Association for Pediatric Ophthalmology and Strabismus (AAPOS) as referral criteria, the recommended target refractive magnitudes for detection are as follows: astigmatism >2.0 D, hyperopia >4.5 D, and anisometropia >2.5 D in toddlers (age group: 12–30 months); astigmatism >2.0 D, hyperopia >4.0 D, and anisometropia >2.0 D in early preschool children aged 31–48 months; astigmatism >1.5 D, hyperopia >3.5 D, and anisometropia >1.5 D in late preschool children and kindergarten children aged 49–72 months. The detection of myopia begins to become significant at 49–72 months of age, and myopia >1.5

D should be detectable. For all ages, the manifest strabismus >8 PD in the primary position, and any media opacity greater than 1 mm in size is potentially amblyogenic (9).

The AAPOS guidelines have been updated to have a lower threshold for detecting amblyopia than the 2013 guidelines. According to the 2021 AAPOS guidelines, anisometropia >1.25 D is considered amblyogenic for all age levels. However, the threshold for astigmatism was raised to 3 D for children under 4 years of age due to its relatively high occurrence and lower risk of causing amblyopia. After age four, the thresholds for visually significant refractive errors, such as astigmatism and treatable progressive myopia, were similar to those of the 2013 guidelines (10). For this study, the presence of ARFs was investigated based on the 2013 and 2021 AAPOS guidelines (9,10). Anisometropia was an interocular difference in the spherical equivalent or cylinder of ≥1 D (11). Amblyopia was diagnosed if the interocular BCVA was ≥2 lines of Snellen equivalent in verbal patients.

Statistical Analysis

Statistical analysis was performed using the IBM Statistical Package for the Social Science (SPSS) 20.0 (SPSS Inc., Chicago, IL, USA) package program. The normality test for normal distribution was evaluated using the Kolmogorov-Smirnov test. Normally distributed numerical variables were given as mean ± standard deviation, non-normally distributed numerical variables were presented as median (Q1–Q3), and categorical variables were given as frequency (percentages). When the number of groups was two, the difference between the groups was evaluated using the Mann-Whitney U test for numerical variables lacking normal distribution. Logistic regression analysis was used to determine the risk factors affecting the dependent variable. A $p<0.05$ was considered statistically significant.

Results

In this study, 220 eyes of 110 patients between 1 and 13 years of age who underwent treatment were examined. A total of 54 (49.1%) of the patients were female, and 56 (50.9%) were male. The average ages at the last examination and at the time of surgery were 57.3±37.6 months (range: 12–53), and 29.6±22.3 months (range: 12–128), respectively. Of the patients, 73 (66.4%) had unilateral CNLDO. Probing was performed in 91 (82.7%) patients one or more times, nasolacrimal tube intubation was performed in 17 (15.5%) patients, and DCR was performed in 2 (1.8%) patients. Thirty patients who underwent probing and seven patients who underwent nasolacrimal tube intubation had bilateral obstructions. All patients in the DCR group had unilateral CNLDOs. The baseline clinical characteristics of the study group are shown in Table 1.

Table 1. Baseline clinical characteristics of the study population

Variables	n (%) or Mean±SD
Gender	
Female	54 (49.1)
Male	56 (50.9)
Laterality of CLNDO	
Unilateral	73 (66.4)
Bilateral	37 (33.6)
Affected Eye	
Right	35 (31.8)
Left	38 (34.5)
Bilateral	37 (33.7)
Surgery type	
Probing	91 (82.7)
Silicone Tube Intubation	17 (15.5)
DCR	2 (1.8)
Age at surgery (month)	29.6±22.3
Age at final examination (month)	57.3±37.6
Number of surgery	
Single surgery	88 (80.0)
Multiple surgeries	22 (20.0)

CNLDO: Congenital nasolacrimal duct obstruction; DCR: Dacryocystorhinostomy; n: Numbers; SD: Standard deviation.

In the unilateral CNLDO cases, hypermetropia (n=47, 64.3%) was the most common refractive error in the affected eye, followed by astigmatism (n=15, 20.6%) and emmetropia (n=10, 13.7%). Myopia was found in only 1.4% (n=1) of these patients. For the fellow eyes of unilateral CNLDO and the right-left eyes with bilateral CNLDO, the types of refractive error distribution were similar to those of the affected eyes with unilateral CNLDO (Table 2). Since the patients' age distribution was wide, we divided the study group by age (group 1: 12–30 months, group 2: 31–48 months, group 3: >48 months). There were no significant associations between CNLDO and refractive errors in each age subgroup ($p>0.05$). The rate of anisometropia was 11.8% (hyperopic anisometropia: n=8; astigmatic anisometropia: n=4; and both types: n=1) for all patients. Of these 13 patients, 9 (69.2%) had unilateral CNLDO. High refractive errors were found in the affected eyes in 55.5% (n=5) of the cases, and the affected eyes were mostly (80%) hyperopic. Interestingly, the fellow eyes of patients with anisometropia were highly astigmatic (75%). Four children (75%) with bilateral CLNDO cases had hyperopic anisometropia. In patients with unilateral and bilateral CNLDO, no statistically significant differences were found between the eyes for sphere

Table 2. Distribution of refractive errors in patients with CNLDO

Unilateral CNLDO	**Effected Eyes n (%)**	**Fellow Eyes n (%)**
Emmetropia	10 (13.7)	12 (16.4)
Myopia	1 (1.4)	1 (1.4)
Hypermetropia	47 (64.3)	45 (61.7)
Simple myopic astigmatism	1 (1.4)	1 (1.4)
Compound myopic astigmatism	1 (1.4)	1 (1.4)
Simple hyperopic astigmatism	0 (0.0)	2 (2.7)
Compound hyperopic astigmatism	10 (13.7)	9 (12.3)
Mixed astigmatism	3 (4.1)	2 (2.7)
Bilateral CNLDO	**Right Eye n (%)**	**Left Eye n (%)**
Emmetropia	6 (16.2)	6 (16.2)
Myopia	1 (2.7)	0 (0.0)
Hypermetropia	17 (46.0)	18 (48.7)
Simple myopic astigmatism	0 (0.0)	0 (0.0)
Compound myopic astigmatism	0 (0.0)	1 (2.7)
Simple hyperopic astigmatism	5 (13.5)	5 (13.5)
Compound hyperopic astigmatism	7 (18.9)	7 (18.9)
Mixed astigmatism	1 (2.7)	0 (0.0)

CLNDO: Congenital nasolacrimal duct obstruction.

(p>0.05), cylinder (p>0.05), or spherical equivalent (p>0.05) (Table 3). Concerning the refractive errors, there was no statistical difference between the affected and fellow eyes of patients receiving only probing surgery (p>0.05) (Table 4). Manifest strabismus over eight prism diopters in the primary position was detected in six (5.5%) patients.

Based on the 2013 AAPOS referral criteria, 15 (13.6%) patients exhibited ARFs (12 patients, 16.4% of the unilateral CNLDO; 3 patients, 8.1% of the bilateral CNLDO). High hypermetropia (n=7, 46.6%) was the leading refractive risk factor for ARFs, followed by astigmatism (n=6, 40%), and anisometropia (n=2, 13.3%). In bilateral CNLDO, both eyes had high hyperopia. In unilateral CNLDO with ARFs, six had high astigmatism, four had high hyperopia, two had anisometropia, and two had high myopia. These risk factors were present in eight (53.3%) patients with obstructed eyes. When we assessed the data of patients using the 2021 AAPOS guidelines for ARFs, we found that one patient's refractive error did not meet the revised criteria, and two patients' ARFs were classified as anisometropia (n=4, 28.5%) (Table 5).

The rate of amblyopia was 5.4% (n=6). Five (6.8%) patients had unilateral CNLDO, and one (2.7%) had bilateral CNLDO. Two (33.3%) patients with amblyopia did not exhibit any problems except for refractive errors, while the others (66.6%) had concurrent strabismus (Table 5). The predictors for ARFs according to the 2021 AAPOS guidelines for CNLDO are shown in Table 6. Manifest strabismus was the only factor associated with ARFs in children with CNLDO (Odds ratio = 0.132, 95% confidence interval = 0.529–17.400, p<0.001).

Discussion

CNLDO is a condition that affects 69–86% unilaterally and often has no symptoms (12-15). In this study, most patients (66.4%) had unilateral CNLDO, and the frequency of CNLDO was similar in male and female patients (16). Many studies conducted in the last 20 years have obtained conflicting results concerning the relationship between CNLDO and anisometropia and amblyopia. Thus, we investigated the prevalence of risk factors for amblyopia in children with CNLDO.

Table 3. Distribution of refractive error values in patients with CNLDO

CNLDO	**Median (Q1–Q3)**		**p***
Unilateral	**Affected Eye**	**Fellow Eye**	
Sphere	1.25 (1–2)	1.25 (0.75–2)	0.365*
Spherical equivalent	1.125 (0.75–1.75)	1.125 (0.56–1.68)	0.546*
Cylinder	–0.50 (–0.75–0)	–0.50 (–0.75–0)	0.781*
Bilateral	**Right Eye**	**Left Eye**	
Sphere	1.25 (0.75–1.75)	1.25 (0.75–2)	0.948*
Spherical Equivalent	0.875 (0.437–1.375)	0.875 (0.437–1.625)	0.762*
Cylinder	–0.75 (–1–(–0.25))	–0.75 (–1–(–0.375))	0.978*

CNLDO: Congenital nasolacrimal duct obstruction, Q1–Q3: Interquartile range, *Mann–Whitney U test.

Table 4. Median and interquartile ranges of sphere, cylinder, and spherical equivalent in patients receiving probing surgery

CNLDO	Median (Q1–Q3)		p*
Unilateral (n=61)	**Affected eye**	**Fellow eye**	
Sphere	1.25 (0.875–2)	1.50 (1–2)	0.409*
Spherical equivalent	1.25 (0.75–1.687)	1.125 (0.75–1.75)	0.604*
Cylinder	–0.50 (–0.75–0)	–0.50 (–0.75–0)	0.876*
Bilateral (n=30)	**Right eye**	**Left eye**	
Sphere	1.375 (0.75–1.75)	1.25 (0.75–2.125)	0.888*
Spherical equivalent	1.125 (0.468–1.512)	0.937 (0.375–1.806)	0.842*
Cylinder	–0.75 (–1–(–0.25))	–0.75(–1–(–0.437))	0.976*

CNLDO: Congenital nasolacrimal duct obstruction; *Mann-Whitney U test.

Table 5. Refraction and findings of six children with amblyopia, and fifteen children with amblyopia risk factors based on 2013 and 2021 AAPOS ARFs

CNLDO laterality	Age at surgery (month)	Refractive errors				BCVA		Additional pathology
		Right		Left				
		Sphere	Cylinder	Sphere	Cylinder	OD	OS	
OS	128	3.5	–2	5.00	–3	0.7	0.5	OS Esotropia
OS	31	1.25	–0.75	4.25	–4.25	1.0	0.3	OD Exotropia
OD	15	0.75	–2.25	0.50	–1.5	0.8	1.0	OD Exotropia
OS	31	–9.25	–3.25	–9.25	–2.5	0.2	0.2	OU Exotropia
OS	51	4.75	–0.5	4.00	–0.25	0.8	0.8	None
OS	16	3.5	–1.25	4.75	–1.25	1.0	1.0	None
OD	122	–1.5	–0.25	–1.75	0	1.0	1.0	OD Exotropia
OU	18	4.75	–0.75	4.75	–1.25	1.0	1.0	None
OU	12	6	–0.75	5.5	–1.25	-	-	OU Exotropia
OS	14	7.0	–0.75	6.75	–1.5	-	-	None
OD	72	1.25	–2.0	1.25	–1.25	-	-	None
OS	13	3.75	–1.0	5.75	–0.75	-	-	None
OS*	12	3.25	–2.75	2.75	–1.25	-	-	None
OU**	25	5.25	–1.50	3.75	–1.25	0.8	1.0	None
OD**	18	0	–1.0	0	–3.0	-	-	None

CNLDO: Congenital nasolacrimal duct obstruction; BCVA: Best corrected visual acuity; *The data for this patient did not meet the revised criteria in 2021 AAPOS guidelines for ARFs; **The data were classified as anisometropia according to the 2021 AAPOS guidelines.

Ellis et al (6). first introduced the idea that the tear film layer may interfere with visual maturation in CNLDO. The accumulation of mucopurulent discharge, excessive tear production, and antibiotic ointments used in treatment cause deformation in visual images on the corneal refractive surface and prevent proper emmetropization in the affected eye (17). Another theory is that asymmetric orbital anatomic differences contribute to CNLDO and refractive errors (14). Based on these theories, patients with unilateral obstructions may exhibit anisometropia. While some

Table 6. Predictors of amblyogenic refractive errors based on the 2021 AAPOS guidelines for CNLDO

Variables	Univariate Analysis		
	OR	95% CI	p
Age at surgery	1.015	0.994–1.036	0.155
CNLDO laterality	1.11	0.334–3.590	0.860
Surgery type	0.578	0.350–1.096	0.093
Number of surgery	1.105	0.280–4.357	0.886
Manifest strabismus	0.132	0.529–17.400	<0.001

CNLDO: Congenital nasolacrimal duct obstruction; OR: Odds ratio; CI: Confidence interval.

studies have found that the spherical refractive errors and spherical equivalent values were significantly higher in the affected eye than in the fellow eye ($p<0.001$ for both refractive errors) in patients with unilateral CNLDO, we found that the affected and fellow eyes showed similar differences in terms of refractive errors as in Kılıç et al.'s (16) study (7,18,19). Moreover, no significant refractive difference was observed between eyes in bilateral CNLDO cases. The mean prevalence of anisometropia (greater than 1 D) in the general population at various ages is approximately 2% (10, 20). In this study, the incidence of anisometropia and amblyopia were higher than in the general population and consistent with prior studies that have noted that the rates of amblyopia and anisometropia were 3–5% and 5.5–12%, respectively (4, 7, 14, 21). Although the refractive errors between eyes were not statistically different, anisometropia was more prevalent in unilateral cases than in bilateral cases (18, 21). Following Piotrowski et al.'s (14) study, Eshraghi et al. (7) and Saleem et al. (19) established that the affected eyes were mostly hyperopic. In this study, hyperopic anisometropia was determined to be the most common type. Previous studies by Pyi Son et al. (17), Sims et al. (21) , and Kiliç et al. (16) investigating the effect of delayed surgical intervention or symptom relief on spherical and astigmatic defects in obstructed eyes have found no significant differences in rates of amblyopia or anisometropia between early and late treatment groups (16, 17, 21). In our study, the average age of the patients at the time of surgery was relatively high, and we found that ARFs were not associated with age at surgery. These studies have shown that the duration of epiphora does not affect the development of anisometropia or amblyopia (16, 17, 21).

Based on the 2013 AAPOS referral criteria, ARF rates ranged between 5.4% and 35% in previous studies, while the rate of ARFs was 13.6% (5, 7, 12, 13, 15, 16, 22). The rate decreased to 12.7% when we used the 2021 AAPOS guidelines. The 2021 guidelines have made changes to the ones released in 2013. The threshold for anisometropia has been lowered to increase sensitivity in detecting amblyopia. However, the threshold for astigmatism has been increased for children under the age of four. Due to these changes, the revised guidelines increased the number of patients diagnosed with anisometropia in this study group (10). Although various studies have reported that high astigmatism or anisometropia is the leading cause of ARFs, high hypermetropia was identified as the main cause of ARFs in this study and Kim et al.'s (5) study (15,16,18). However, in the former study, early unilateral visual deprivation has been linked with myopia, not hypermetropia (23).

The severity of ARFs can be determined based on the causes. Deprivation, constant strabismus, and anisometropia are likelier to cause dense amblyopia than symmetric hyperopia, astigmatism, and myopia (10). Anisometropia, hyperopia, and astigmatism may also trigger the development of strabismus in susceptible patients, owing to disturbances of fusion (13). Therefore, after regression analyses were established, we observed that neither timing, type, and number of surgeries nor disease laterality resulted in strabismus being the only factor associated with ARFs in children with CNLDO. This finding aligned with that of Yoo et al. (13). In our study, it was unsurprising that most patients with amblyopia had accompanying manifest strabismus and a low rate of amblyopia due to refractive causes alone. In contrast, Matta et al. (24). noted that amblyopia was attributable to strabismus in 36.3% of patients. However, they claimed that refractive errors are likelier to resolve spontaneously than strabismus.

This study is the first in which refractive errors of children with CNLDO were evaluated using the 2013 and 2021 AAPOS guidelines for pediatric vision screening. The patients underwent a long-term follow-up period, and epiphora was successfully treated. Due to the retrospective design, we could not evaluate the severity of discharge and the impact of chronic antibiotic drop usage on refractive status. Biometric values, such as keratometry data and axial length measurements, are crucial for emmetropization. However, one study found that these parameters did not show statistically significant differences between eyes in patients with unilateral CNDLO and those with successful or failed probing. Thus, we did not use biometric measurements (25). The major limitations of our study were the absence of a control group of age-matched normal children and the heterogeneity of the patients in age and type of surgery. Further studies with larger sample sizes and longer follow-up times are required to establish the exact causes of amblyopia and CNLDO.

Conclusion

Although anisometropia was found to be more prevalent in unilateral cases, no significant difference was observed between eyes in terms of refractive errors in patients with unilateral and bilateral CNLDO. ARFs were not associated with clinical parameters, such as disease laterality, the patient's age at the time of surgery, the type of surgery performed, and the number of surgeries. Children who present with CNLDO symptoms require a comprehensive ophthalmic evaluation, including cycloplegic refraction and subsequent follow-up to prevent amblyopia, since the frequency of anisometropia and amblyopia in CNLDO was higher than in the general population. However, amblyopia in CNLDO may not be relevant to refractive errors. Surgical treatment may be delayed in children with mild symptoms and without anisometropia, strabismus, and high refractive errors.

Disclosures

Ethics Committee Approval: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Ethics committee approval has been granted from our institution. As this was a retrospective research, no informed consent was obtained from participants.

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