ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Investigation of Possible Antenatal and Perinatal Risk Factors in Patients with Congenital Epiphora

Konjenital Epiforalı Hastalarda Olası Antenatal ve Perinatal Risk Faktörlerinin Araştırılması

Elif Sedanur Utlu[1], Bahadir Utlu[2], Mustafa Bayraktar[3]

[1]Family Medicine Clinic; [2]Ophthalmology Clinic, Erzurum Regional Training and Research Hospital, Health Sciences University; [3]Family Medicine Department, Ataturk University Faculty of Medicine, Erzurum, Türkiye

ABSTRACT

Aim: *We aimed to investigate the effective factors to increase treatment options in patients with congenital nasolacrimal duct obstruction (LDO).*

Materyal and Methods: *Our study was planned retrospectively. The patients admitted to Erzurum Regional Training and Research Hospital Family Medicine Outpatient Clinic with symptoms such as watering, burring, swelling in the sac area, chronic conjunctivitis < In 200 children under 4 years of age, information on maternal age, mode of conception, gender, birth weight, mode of delivery, presence of multiple pregnancies, sibling history, duration of hospitalization, need for invasive mechanical ventilation, maternal pre-eclampsia, gestational DM, and bilateral or unilateral occlusion, need for surgery, number of surgeries, presence of anisometropia, when epiphora started and when it ended were collected and evaluated.*

Results: *Of the children included in the study, 52% (n=103) were male and 48% (n=95) were female. It was shown that complaints such as watering, redness, and burring due to congenital nasolacrimal duct obstruction mostly started in the first weeks (7.1%), and most of these complaints were relieved by massaging the sac area and topical drops (90.3%) without surgical intervention. There were no significant statistical differences between children with and without congenital epiphora in terms of gender, multiple pregnancies, mode of delivery, delivery week, need for postnatal intensive care, mother's mode of conception, maternal age and chronic diseases (p>0.05). Significant differences were found in birth weight and the presence of positive sibling history (p<0.05).*

Conclusion: *This study was conducted to evaluate the association of congenital epiphora with possible antenatal and perinatal risk factors. It was concluded that low birth weight and positive sibling history may be involved in the etiopathogenesis of epiphora, but it was concluded that studies on this subject should be conducted by reaching large populations.*

Key words: *Epiphora, Caesarean section, Hasner's valve, Lacrimal Duct Embryology*

ÖZET

Amaç: *Konjenital nazolakrimal kanal tıkanıklığı (LDO) olan hastalarda tedavi seçeneklerinin artırılması için etkili faktörlerin araştırılması amaçlanmıştır.*

Materyal ve Metot: *Çalışmamız retrospektif olarak planlanmıştır. Erzurum Bölge Eğitim ve Araştırma Hastanesi Aile Hekimliği Polikliniğine başvuran daha önce sulanma, çapaklanma, kese bölgesinde şişlik, kronik konjonktivit gibi bulguları olan < 4 yaş altı 200 çocuğun anne yaşı, gebe kalma şekli, cinsiyet, doğum ağırlığı, doğum şekli, çoğul gebelik varlığı, kardeş öyküsü, hastanede yatış süresi, invaziv mekanik ventilatör ihtiyacı, annede preeklampsi, gestasyonel DM gibi faktörler ve tıkanıklığın her iki taraflı yada tek taraflı olması, cerrahi gereksinimi, cerrahi sayısı, anizometropi varlığı, epiforanın ne zaman başlayıp hangi zamanda sonlandığı gibi bilgileri toplanıp değerlendirilmiştir.*

Bulgular: *Çalışmaya alınan çocukların %52'si (n=103) erkek, %48'i (n=95) kadın idi. Konjenital nazolakrimal kanal tıkanıklığına bağlı sulanma, kızarıklık, çapaklanma gibi şikayetlerin çoğunlukla ilk haftalarda (%7,1) başladığı, bu şikayetlerin çoğunun da cerrahi müdahale olmaksızın, kese bölgesine masaj ve topikal damlalarla (%90,3) giderildiği gösterildi. Konjenital epiforası mevcut olan ve olmayan çocuklar arasında cinsiyet, çoğul gebelik, doğum şekli, doğum haftası, doğum sonrası yoğun bakım ihtiyacı, annenin gebe kalış şekli, anne yaşı ve kronik hastalıkları açısından önemli istatistiksel farklılıklar bulunmadı (p>0,05). Doğum kilosu ve pozitif kardeş öyküsü varlığı konusunda ise anlamlı farklılık saptandı (p<0,05).*

Sonuçlar: *Bu çalışma konjenital epiforanın olası antenatal ve perinatal risk faktörleriyle ilişkisinin değerlendirilmesi için yapılmıştır. Düşük doğum kilosu ve pozitif kardeş öyküsünün epifora etiyopatogenezinde yer alabileceği sonuçlarına ulaşılmıştır ancak bu konudaki çalışmaların geniş kitlelere ulaşılarak yapılması kanaatine varılmıştır.*

Anahtar kelimeler: *Epifora, Sezaryen doğum, Hasner valvi, Lakrimal kanal embriyolojisi*

İletişim/Contact: *Elif Sedanur Utlu, Health Sciences University Erzurum Regional Training and Research Hospital, Family Medicine Clinic, Türkiye* • ***Tel:*** *0535 400 68 59* • ***E-mail:*** *elif_nmtl90@hotmail.com* • ***Geliş/Received:*** *21.12.2023* • ***Kabul/Accepted:*** *09.01.2024*

ORCID: *Elif Sedanur Utlu: 0000-0001-9791-544X • Bahadır Utlu: 0000-0002-7129-2181 • Mustafa Bayraktar: 0000-0001-8486-9915*

Introduction

Epiphora is one of the common ocular disorders found in newborns starting from the first hours of birth. The first symptom is ponding and outflow of tears around the free edge ofthe lower eyelid and in the medial canthal region, and later, with the progression of symptoms,mucoid secretion reflux with pressure on the nasolacrimal sac, recurrent and persistent conjunctivitis attacks, It is an important clinical entity that manifests itself with a mucoid sticky secretion, discharge and burring at the eyelash margins in the morning or after crying attacks and may cause serious ocular morbidity such as acute dacryocystitis, preseptal and orbital cellulitis in case of development of secondary infection, although there is usually no evidence of serious inflammation[1].

Epiphora is more common in the first years of life and is found in one out of every 5 children[1]. In newborns, incomplete canalization at birth is common. Although it may also beassociated with various agenesic conditions, obstruction-related conditions are usually partial and transient[2,3]. In the majority of infants, it resolves spontaneously with fasciocranial growth until the age of one year[4]. The need for surgical operation is approximately 2 to 5% of children with persistent symptomatic epiphora[5].

Lacrimal duct development is complex. First, nasolacrimal duct growth continues throughout all stages of embryo development. At 32 days of embryo development, the maxillaryand frontonasal processes begin to appear. As these processes grow and expand, a groove forms between them. Simultaneously, the epithelial cord invades the upper and lower eyelid margins to form canaliculi, which fuse to form the nasolacrimal drainage system. Canalization of the epithelial cord begins simultaneously along the entire cord at 4 months. Epithelial remnants inthe cord do not show continuity and form valvula-like folds[6].

Understanding the diseases of the nasolacrimal system is only possible by explaining the histopathologic developmental stages of the duct. Punctal membranes are usually completely open at full term. However, it has been observed that Hasner's Valve is not perforated in 70% of newborns[6]. Understanding the diseases of the nasolacrimal system canonly be possible by explaining the histopathologic developmental stages of the duct and the factors affecting them.

The spontaneous improvement of the condition in children with epiphora <1 year of ageor the differences in its presence between children of the same chronologic age is a subject in need of research. The female predominance of congenital epiphora cases and differences in racial preference suggests a potential hereditary predisposition to nasolacrimal system obstruction[7]. There are also studies showing the effect of antenatal factors such as mode of delivery. These cases may be coincidental; therefore, further studies are necessary to confirm whether there is indeed a correlation.

In summary, the issue of a genetic or environmental predisposition to the occurrence ofcongenital epiphora remains an open one. Through ophthalmologic and otolaryngologic collaboration, such familial and non-hereditary assessments could potentially lead to a better understanding and prevention of the potential complications and ultimately economic costs of conditions related to nasolacrimal system development. Studies on this subject may help support and counsel the activities of family physicians. In our study, we aimed to determine theeffect of antenatal and perinatal factors on this condition and to evaluate the results.

Materials and Methods

Study Design, Population, and Clinical Assessment

Our study was planned retrospectively. According to the power analysis performed with the *Power 3.1.9.4* program, the number of participants required for the study was determined as 200 with a type 1 error of 0.05, 80% confidence interval and medium effect size (q=0.3). Thepopulation of our study consisted of 200 children < 4 years of age with symptoms such as watering, burring, swelling in the sac area, and chronic conjunctivitis who applied to Erzurum Regional Training and Research Hospital Family Medicine Polyclinic. Patients who did not agree to participate voluntarily and did not sign the informed consent or whose parents/legal representatives did not agree to participate in the study and patients >4 years of age were excluded from the study. Factors such as maternal age, mode of conception, gender, birth weight, mode of delivery, presence of multiple pregnancies, sibling history, duration of hospitalization, need for invasive mechanical ventilation, maternal pre-eclampsia, gestational DM, and bilateral or unilateral occlusion, need for surgery, number of surgeries, presence of anisometropia when epiphora started and when it ended were collected and evaluated.

Ethical Approval

For this study, permission was obtained from Atatürk University Faculty of Medicine Internal Medicine Sciences Board and Atatürk University Faculty of Medicine Clinical Research Ethics Committee (Ethics committee meeting date and number: 24.06.2021/05-24).

Statistical Analysis

SPSS 20 package program was used for statistics and analysis. Descriptive statistics were presented as frequency and percentage for categorical data and mean and standard deviation for numerical data. The compatibility of numerical variables with normal distribution was examined by the Kolmogorov-Smirnov test. One-way ANOVA was applied for normally distributed variables and the Kruskal-Wallis test was applied for variables that did not show normal distribution. Statistically, the significance limit of $p<0.05$ was accepted.

Results

The data of 198 participants in the study were analyzed. Of the children included in the study, 52% (n=103) were male and 48% (n=95) were female. The mode of delivery was normaldelivery in 37.4% (n=74) and cesarean delivery in 62.6% (n=124), and the rate of spontaneous vaginal delivery without intervention was 81.1%. The mean birth weight was 2562 ± 291.9 g. Spontaneous conception and singleton pregnancy rates of the participating mothers were 97%.The need for intensive care in postpartum children was 84.8% and the need for mechanical ventilation in those who needed intensive care was 23.3%. Among children diagnosed with epiphora by an ophthalmologist or paediatrician, both eyes were involved (n=12). It was shown that complaints such as watering, redness, and burring due to congenital nasolacrimal duct obstruction mostly started in the first weeks (7.1%), and most of these complaints were relievedby massaging the sac area and topical drops (90.3%) without surgical intervention. There wereno significant statistical differences between children with and without congenital epiphora in terms of gender, multiple pregnancies, mode of delivery, delivery week, need for postnatal intensive care, mother's mode of conception, maternal age and chronic diseases ($p>0.05$). Significant differences were found in birth weight and the presence of positive sibling history ($p<0.05$).

Discussion

Epiphora is a common ocular disorder found in newborns starting from the first hours of birth. Congenital epiphora is a common condition, with an incidence ranging from 1.2% to20% in infants. In general, anatomical anomalies in the lacrimal passage should be considered in the approach to infants with epiphora. Tears drain along the lacrimal passage from the level of the punctum canaliculus to the meatus nazi inferior. Absence, stenosis or stenosis may be observed at different levels of the lacrimal passage[8]. Congenital dacryostenosis is the most common cause of watery eyes in childhood. However, although rare, congenital malformationsof the lacrimal drainage system may occur[9-11].

Understanding the diseases of the nasolacrimal system is only possible by explaining the histopathologic developmental stages of the duct. Punctal membranes are usually completely open at full term. Lacrimal stenosis can be defined as a congenital defect of any component of the nasolacrimal drainage system. Failure of normal development at any point inthis embryologic process due to genetic or intrauterine factors can cause pathologies in the lacrimal drainage system.

An imaging study showed that the distal part of the lacrimal duct junction was an anthropometric site of obstruction in all patients. In these studies, it was reported that lacrimal duct obstructions are mainly caused by thickening of the bony wall distal to the NLD that narrows the lumen, pathologic persistence of a membrane distal to the NLD, and narrowing ofthe distal duct by abnormal proliferation and apposition of the nasal mucosa. All of these mechanisms are thought to represent different stages in the developmental process that are necessary for continuity between the lacrimal duct and the meatus nasi inferior[12].

Vertical epithelialization and proliferation of the distal portion and its interactions with surrounding mesenchymal tissues determine the shape of the distal lacrimal duct. The presenceof membranous bone tissue or bone canal stenosis distal to the lacrimal duct may be evidence of abnormal inductive interactions.

Another issue is the presence of a nasal mucosa-derived membrane that is in harmony with the LD epithelium, which is detected even in histologic examinations performed in healthy newborns[13]. This membrane causes especially the distal parts of the LD to become more resistant to dilation and is balanced by the hydrostatic pressure, which is highest in the

Table 1. *Demographic characteristics of the participants, various risk situations and statistical comparisons of children with and without LDO diagnosis*

	Frequency %		Sign
	LDO – (n: 105)	LDO + (n: 93)**	P
Gender			
Male	63 (31%, 8)	48 (24%, 2)	0.129*
Woman	42 (21%.21)	45 (22%, 7)	
Multiple pregnancy			
Yes	4 (2%, 02)	2 (1%, 01)	0.238†
No	101 (51%, 01)	91 (45%, 95)	
Mother's mode of conception			
Natural	96 (48%, 5)	87 (43%, 9)	0.238†
IVF – Embryo transfer	9 (4%, 54)	6 (3%, 03)	
Presence of chronic disease in the mother			
There is	14 (7%, 07)	6 (3%, 03)	0.745†
No	91 (45%, 95)	87 (43%, 93)	
Birth week			
Miad 36–40 weeks	88 (44%, 4)	69 (34%, 84)	
Postmature >40 weeks	6 (3%, 03)	6 (3%, 03)	0.724†
Prematurity <36 weeks	11 (5%, 6)	18 (9%, 09)	
Mode of birth			
Normal birth	53 (26%, 8)	21 (10%, 6)	0.064*
Cesarean section (C/S)	52 (26%, 3)	72 (36%, 4)	
Intervention in normal birth			
No intervention	45 (60%, 9)	15 (20%, 3)	0.130†
Intervention/ forceps	8 (10%, 8)	6 (8%, 1)	
The need for intensive care for the child after birth			
Yes	12 (6%, 06)	18 (9%, 1)	0.584†
No.	93 (46%, 9)	75(37%, 9)	
Need for mechanical ventilator if in the intensive care unit.			
Yes	4 (13%, 4)	3 (10%, 0)	0.646†
No.	17 (56%, 7)	6 (20%, 0)	
If you have siblings or multiple pregnancies (twins, triplets. . .), did they have the same complaints?			
Yes	≠	19 (67%, 8)	**<0.001†**
No.	≠	9 (32%, 2)	
Birth weight, gr, mean ± sd	3259.1±628.6	3023.4±479.1	**0.049‡**
Age of mother, years, mean ± sd	31.1±4.6	32±4.3	0.307‡

* Pearson Chi-Square test, † Fisher's Exact test, ‡ Student's t-test
* *LDO: Participants diagnosed with lacrimal duct obstruction by an ophthalmologist

distal part and increases with postnatal lengthening of the LD[14]. It is thought to cause spontaneous perforations when the tensile strength of the membrane is exceeded by hydrostatic pressure, which increases with the accumulation of tears with the mechanical effect of the lids and the pressure created by the opening and closing of the eyelids. The persistence of the obstruction can be explained by the fact that the hydrostatic pressure effect is less or the mucosal membrane is more fibrotic with developmental anomalies. It has been observed that Hasner's Valve is not perforated in 70% of newborns and this explains the more frequent occurrence of epiphora in premature babies compared to term babies[6].

The respiratory efforts of the newborn during labour usually cause perforation of this membrane and provide LD patency[15]. The reason why lacrimal duct obstruction is less common in vaginal deliveries compared to cesarean deliveries may be due to possible physiologic effects of normal vaginal delivery. It is known that the pressure in the birth canal increases excessively during normal vaginal delivery. This is thought to increase the hydrostatic pressure, especially in the body cavities, leading to perforation of membranous structures. It is thought that the frequency of LCO due to lower external pressure will increase in children born by cesarean delivery or even after the first delivery due to weakening of the pelvic muscles[16–20]. In addition, it

has been reported that the amount of various enzymes in favour of collagen destruction increases in the amniotic fluid during vaginal delivery and this may lead to the destruction of membranous structures similar to Hasner's valve[16]. For these reasons, the belief that vaginal delivery may prevent epiphora in newborns has gained weight. In our study, no statistical difference was found between the mode of delivery and LDO.

Another risk factor we examined in our study was gestational age. Although the numberof premature babies was low in our study, it was observed that epiphora complaints started earlier and lasted longer in babies with low gestational age and low birth weight among term babies. As known, the incidence of congenital nasolacrimal duct obstruction in premature infants may be affected by lacrimal duct immaturity. Sathiamoorthi et al. suggested that the lacrimal duct shows partial intrauterine development until the 32nd week and the canalization is not completed[21]. The results of our study show that lacrimal duct maturation continues even after birth depending on gestational age.

According to the results of our study, there was a statistical difference between siblingsin terms of the incidence of LDO. As stated in previous studies on lacrimal duct obstruction, female gender and Caucasian race suggest a potential hereditary predisposition to the lacrimal duct system[22]. Another study with varying demographic characteristics reported a familial involvement of approximately 11% in a series of dacryocystitis cases[23]. In another more recent study, familial cases reported belonged to the findings of siblings with craniofacial developmental anomalies[24]. Even though the results of our study suggest that there is a significant difference, the possibility of underreporting familial cases is high, especially because the disease progresses with subclinical findings in some individuals and only severe cases are referred to medical professionals. Therefore, we think that more studies are needed toconfirm whether there is indeed a familial correlation.

According to the results of our study, no significant association was found between lacrimal duct obstruction and maternal age, history of drug use, preeclampsia, presence of maternal infection, gestational diabetes, smoking, educational status and occupation. Although there are limited studies on this subject in the literature, Aldahash et al. reported that maternal infections may be a risk factor for lacrimal duct obstruction[25].

The retrospective design of the study has some limitations as it may lead to incompletedocumentation and misrepresentation. The actual incidence in the population may be overestimated or underestimated as clinical findings may be confounded with other ocular infections and allergic conditions. In addition, some infants with LDO may be asymptomatic in the first months, then improve after some time and ultimately go unnoticed by the patient'scaregiver or physician.

In summary, epiphora, which is frequently observed in the neonatal and early childhood periods, usually occurs due to LDO. The results suggest that the disease may be hereditary and many authors consider it to be due to acquired sporadic embryologic factors. Several factors have been suggested to play a role in the aetiology of LDO, including genetics, maternal infections, radiation exposure, medications or certain occupational hazards during pregnancy. Since LDO carries a risk of acute dacryocystitis and amblyopia even with minimal frequency, screening and vigilance in individuals with risk factors should be performed[26]. Understanding these factors is crucial for developing effective strategies for the prevention andmanagement of CNLDO in infants.

Conclusion

This study was conducted to evaluate the association of congenital epiphora with possible antenatal and perinatal risk factors. It was concluded that low birth weight and positivesibling history may be involved in the etiopathogenesis of epiphora, but it was concluded that studies on this subject should be conducted by reaching large populations.

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