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Original article

CONGENITAL NASOLACRIMAL DUCT OBSTRUCTION: EPIDEMIOLOGY AND RISK FACTORS

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SUMMARY

Purpose: To discuss the various epidemiological aspects and the impact risk factors for developing CNLDO in children.

Material/Methods: An analytical observational case-control study.

Îne hundred and thirteen children diagnosed and probed for CNLDO in Eye clinic-Pleven were included in a case group. A control group consist of 121 children without CNLDO. All of the parents answered questions from specially designed questionnaires related to the pregnancy of the mother, antenatal risk factors and child's health in the neonatal period.

Results: The demographic profile of the evaluated children in the case group was: 49.6% males and 50.4% females; 33% cases were with affected right eye, 37% left eye, and 30% individuals with bilateral CNLDO after birth. Median gestational age of the children with CNLDO was 40.0. Risk factors for CNLDO development are antibiotics intake and consuming alcohol during the pregnancy.

Conclusion: Congenital nasolacrimal duct obstruction affects full-term born children. Detection of the risk factors for developing CNLDO will improve methods for the prevention of this disease.

Keywords: CNLDO, epidemiology, risk factors,

INTRODUCTION

Congenital nasolacrimal duct obstruction (CNLDO) with a persisting Hasner's membrane is the most common cause of epiphora and ocular discharge in infants [1]. The frequency of this condition in children is around 11% [2, 3]. Congenital blockage of the nasolacrimal duct which may be complete or partial is bilateral in 1/3 of cases without gender predisposition [3].

The first-line therapy for CNLDO is a massage of the lacrimal sac. In case of failure, probing and irrigation of the nasolacrimal drainage system are applied [4]. Persisting CNLDO is associated with the risk of chronic dacryocystitis [5] and amblyopia in children [6, 7].

Although there exist numerous publications on the management of CNLDO, published reports on the epidemiology of this disorder are uncommon. Little is known about the risk factors for this condition. The role of genetics has not been thoroughly investigated in CNLDO. Risk factors for congenital anomalies at all may include maternal infections during pregnancy, exposure to radiation, consuming medications, and some occupational hazards [8]. These are similarly implicated in CNLDO. Several studies have documented the possible association between the incidence of CNLDO and delivery by Cesarean section compared with vaginal delivery [9,10].

The aim of this study was to determine the various epidemiological aspects and the risk factors for developing CNLDO in children.

MATERIALS AND METHODS

An analytical observational case-control study was undertaken in the Eye Clinic at University Hospital - Pleven, Bulgaria. The Commission of the Ethics of Research Activities in the Medical University of Pleven reviewed and approved the protocol for the study. The statistical data for the population of live birth children in the Pleven district are taken by the National Statistical Institute of the Republic of Bulgaria.

A retrospective review of the medical records between 2006 and 2016 identified 224 children with CNLDO who had undergone probing and irrigation of the nasolacrimal duct for tearing and discharge since early infancy. The parents of these children were invited with letters in the Eye clinic. Samples consisted of 113 consecutive patients with CNLDO in the past which were included in the case group.

One hundred and twenty-one consecutive volunteer children without CNLDO were included in the study as a control group. The age of these children was consistent with the age of the patients with CNLDO during their probing. The absence of congenital obstruction was established by anamnestic evidence of lack of tearing and secretion from the eyes. The data for the children in the control group

were collected in the Eye clinic from April to September 2018.

All of the parents signed informed consent for the participation of their child in the study. The mothers of children in the case and control group answered questions in the form of an interview by the same researcher. Epidemiological data on studied children were collected. There were specially designed questionnaires about potential risk factors for CNLDO divided into two sections. The first section of the questionnaire targeted the mother of the child. It explored the maternal factors: way of becoming pregnant, sequence of pregnancy, maternal infection, consuming medications, fetus retention events, pre-eclapsia/eclampsia, hemorrhage, smoking, alcohol, birth mechanism and heredity. The second division was concerned with the childhood factors: gestational age, birth weight, apnea, oxygen therapy, anemia, neonatal jaundice, neonatal infections and birth trauma.

We used Microsoft Exel and Statgraph to analyze our data from the case and control group. The *P* value for Chi square test was calculated in all risk factors potentially associating with CNLDO. A $p<0.05$ was considered significant. The ODDS RATIO was calculated to describe the relative risk.

RESULTS

Of the 26 532 live births in Pleven district, Bulgaria during the period from 2006 to 2016, 224 infants were treated with probing for CNLDO, yielding a probing frequency of 0,8%.

A total of 234 questionnaries have been satisfactorily filled by the mothers of evaluated children in the case and control group. Two of the children with CNLDO have no data on maternal factors because they were adopted. We received the answers from their adoptive parents. There were 56 (49.6%) males and 57 (50.4%) females in the first group and 64 (52.9%) males and 57 (47.1%) females in the second group. Median gestational age of the children with CNLDO was 40.0 (ranging from 34.0 to 41.0 months) and in children without CNLDO: 39.0 (ranging from 25.0 to 41.0 months). *The m*edian age of infants with CNLDO at the time of probing was 11.0 months (ranging from 2.0 to 41.0 months) and of children in the control group was 22.0 months (ranging from 1.0 to 75.0 months). In the case group, 37 (33%) children were with affected right eye and 42 (37%) with affected left eye, and 34 (30%) individuals were with bilateral CNLDO after their birth. Approximately 34% of patients with CNLDO were diagnosed by primary care physicians (paediatricians and general practitioners). The epidemiology characteristics of the study children are summarised in table 1**.**

Table1. Epidemiology characteristics of children in case and control group.

Character		Case group (with CNLDO)	Control group (without CNLDO)
Number of children, %	Total 234(100%)	113 (48%)	121 (52%)
Gender	Males Females	56 (49.6%) 57 (50.4%)	64 (52.9%) 57 (47.1%)
Median gestational age Range		40.0 weeks of gestation from 34.0 to 41.0	39.0 weeks of gestation from 25.0 to 41.0
Median age Range		11.0 months from 2.0 to 41.0	22.0 months from 1.0 to 75.0
Laterality		Right eye: 37 (33%) Left eye: 42 (37%) Bilateral: 34 (30%)	-
Primary diagnosis provider, %	Ophthalmologist Paediatrician General practitioner Other (themother)	52 (46%) 8 (7%) 30 (27%) 23 (20%)	121 (100%)
Primarydiagnosis, %		Congenital nasolacrimal duct obstruction (100%)	Healthy:59(48%) Allergic conjunctivitis: 16(13%) Esotropia: 14(12%) Prematurity: 14(12%) Astigmatism: 6 (5%) Hordeolum: 5 (4%) Other: 7 (6%)

Statistically significant maternal factors were found to be consuming medications (χ^2=22.9, df=1, p=0.0001) and alcohol (χ^2=6.64, df=1, p =0.009) during the pregnancy, fetus retention events (χ^2=5.62, df=1, p =0.01) and birth mechanism (χ^2=13.66, df=1, p =0.001). The answers of the questions explored the maternal factors divided into case and control groups are shown in table 2. The childhood factors are presented in table 3. We found significance in gestational age (χ^2=27.3, df=1, p =0.04), birth weight (χ^2=10.1, df=1, p =0.001), oxygen therapy (χ^2=8.4, df=1, p =0.004), birth trauma (χ^2=3.26, df=1, p =0.07) and neonatal infections (χ^2=5.04, df=1, p =0.02).

Table 2. Evaluated maternal factors in the case and control group.

Question	Answer	Case group	Control group	p-value Odds ratio(OR)
Way of becoming pregnant	Natural In vitro	107(96%) 4(4%)	115(95%) 6(5%)	p>0.05
Sequence of pregnancy	First Second Third and more	63(57%) 41(37%) 7(6%)	57(47%) 53(44%) 11(9%)	p>0.05
Maternal infection	No Yes	108(97%) 3(3%)	116(96%) 5(4%)	p>0.05
Consuming medications:	No Yes	83(75%) 28(25%)	53(44%) 68(56%)	P=0.0001
Progesterone	No Yes	105(93%) 8(7%)	80(66%) 41(34%)	OR=0.15
Antibiotics	No Yes	102(90%) 11(10%)	115(95%) 6(5%)	OR=2.07
L-thyroxine	No Yes	109(96%) 4(4%)	112(93%) 9(7%)	OR=0.4
Fetus retention events	No Yes	88(79%) 23(21%)	79(65%) 42(35%)	P=0.01 OR=0.49
Pre-eclapsia/eclampsia	No Yes	104(94%) 7(6%)	108(89%) 13(11%)	p>0.05
Haemorrhage	No Yes	99(89%) 12(11%)	103(85%) 18(15%)	p>0.05
Smoking	No Yes	81(73%) 30(27%)	92(76%) 29(24%)	p>0.05
Alcohol	No Yes	99(89%) 12(11%)	118(97%) 3(2%)	P=0.009 OR=4.77
Birth mechanism *	Natural Cesarean Section Forceps delivery	70(63%) 39(35%) 3(2%)	52(43%) 69(57%) 0(0%)	P=0.001 OR=0.42
Heredity	No Yes	98(88%) 13(12%)	111(92%) 10(8%)	p>0.05

*Values of Natural and Cesarean section were taken in OR calculation of birth mechanism.

Table 3. Evaluated childhood factors in the case and control group.

Question	Answer	Case group	Control group	p-value Odds ratio
Gestationalage	<37 weeks	3(3%)	25(21%)	P=0.04
	>37 weeks	109(97%)	96(79%)	OR=0.11
Birthweight	<2500grams	6(5%)	23(19%)	P=0.001
	>2500grams	107(95%)	98(81%)	OR=0.24
Apnea	No	98(87%)	112(93%)	p>0.05
	Yes	15(13%)	9(7%)	
Oxygen therapy	No	104(92%)	95(79%)	P=0.004
	Yes	9(8%)	26(21%)	OR=0.32
Anemia	No	107(95%)	111(92%)	p>0.05
	Yes	6(5%)	10(8%)	
Neonatal jaundice	No	98(87%)	108(89%)	p>0.05
	Yes	15(13%)	13(10%)	
Neonatal infections	No	107(95%)	104(86%)	P=0.02
	Yes	6(5%)	17(14%)	OR=0.34
Birth trauma	No	110(97%)	121(100%)	P=0.07
	Yes	3(3%)	0(0%)	OR=3.30

Calculation of the Odds ratio (OR) associated with these significant factors was made (table 2 and 3). Confidence intervals (CI) and p-value under 0.05 were used to describe the signiûcance of differences. Significant risk factors for developing CNLDO with OR>1 and p<0.05 are: consuming alcohol (OR=4.77, CI 1.31-17.37, p=0.02) and antibiotics (OR=2.07, CI 1.0-4.28,p=0.047) during the pregnancy. Birth trauma is not a significant risk factor (OR=3.30, CI 0.34-32.20, p=0.56).

Consuming Progesterone (OR=0.15, CI 0.08-0.26, P=0.0001) and L-thyroxin (OR=0.4, CI 0,14-1.53, p>0.05), fetus retention events (OR=0.49, CI 0.27-0.89,p=0.026), birth mechanism (OR=0.42, CI 0.25-0.71, p=0.002), gestational age (OR=0.11, CI 0.03-0.36, p=0.0001), birth weight (OR=0.24,CI 0.09-0.61, p=0.003), oxygen therapy (OR=0.32, CI 0.14-0.71, p=0.006) and neonatal infections (OR=0.34, CI 0.34-0.90, p=0.04) have no risk effect on the occurrence of congenital nasolacrimal duct obstruction. Contrariwise, Progesterone intake in relation with fetus retention events, Cesarean section, prematurity, oxygen therapy and neonatal infection significantly reduce the risk of congenital nasolacrimal duct obstruction.

DISCUSSION

There is considerable variability in the reported incidence of CNLDO from 5% to 20% [11-14], but in the literature, the frequency of probing procedure is not usually mentioned. In this study, the prevalence of probing among the population in risk for Pleven region is 0.8%. I.e. about 1 in 100 live births is needed probing due to congenital nasolacrimal duct obstruction.

The current study showed 30% bilateral affection by CNLDO which is similar to the reported results by Paediatric Eye Disease Investigator Group (33%) [15]. Regardless some authors declared lower frequencies of bilateral cases (17%) [16] or higher percentages (43%) with affected both eyes [17].

There is no gender predisposition in patients with CNLDO in our study, such as the findings in the literature [3, 17]. However there is a study by Dareshani et al. reported a slight female preponderance (62.5%) in children with CNLDO [18].

Approximately 90% of patients in the study by Sathiamoorthi in Minnesota, USA were diagnosed by a primary care physician [3]. In our research, this percentage is too small-only 34%. This demonstrates the need for more information and monitoring of newborns about CNLDO by pediatricians and general practitioners in Pleven region.

Scarce reports have looked at the risk factors for congenital nasolacrimal duct obstruction. There is a need to understand both impact and potential risk factors for CNLDO. Aldahash et al. [17] reported in a cross-sectional study the potential risk factors for developing congenital nasolacrimal duct obstruction. They concluded that CNLDO could have a genetic predisposition and maternal infection is a possible risk factor for developing this condition. Barham et al. also argued the inheritance of CNLDO [19] while Yie suggested a sporadic or multiagency mode of inheritance [20]. Comparing the case and control groups in our study, we did not find a hereditary predisposition for congenital nasolacrimal duct obstruction (p>0.05). Maternal infection during pregnancy was not significant according to our data (p>0.05). Aldahash et al. [17] also found that drug intake during first trimester and smoking status were not significant. We report significant results about consuming medication (p=0.0001) during hall of the preg-

nancy. Smoking status is also not significant in our study (p>0.05). Significant risk factors for CNLDO development are antibiotics intake (increases the risk twice) and consuming alcohol (increases the risk about five times) during the pregnancy.

Several studies address the possible association between CNLDO and Cesarean section (CS) delivery and results are conflicting. Kuhli-Hattenbach et al. [9] report that delivery via Cesarean section is associated with a significantly higher prevalence of congenital dacryostenosis. Tavakoli et al. [21] found in a retrospective study, that Caesarean section was an indipendent risk factor for development of CNLDO. However, they did not use a control group in their study. Mansha Palo et al. [22] performed an analysis of 200 consecutive patients with CNLDO and did not find an overall significant association between the disease and the mode of delivery. A study by Spaniol et al. [10] classified patients born via CS as primary (before the onset of labor and rupture of the membranes) or secondary (after the onset of the active phase of the labor) and found no significant association between the overall rates of CS and development of CNLDO. However, the authors found that the relative risk of CNLDO was 1.7-fold higher in children delivered by primary CS than in children delivered vaginally or by secondary CS. According to our results Cesarean section significantly reduces the risk for development of CNLDO (OR=0.42). The limitation to this finding is that we do not divide CS as primary and secondary.

Premature birth has been shown to be associated with the presence of CNLDO. Complete development of the nasolacrimal duct occurs in the eighth month of gestation [23]. First Lorena et al. [24] reported this association in a cohort of 200 premature infants in which 32 had CNLDO. Prematurity in this study was defined by the World Health Organization as birth before 37 weeks of gestation [25]. Their results suggested a predominance of CNLDO bilaterality in premature infants because of the incomplete development of the duct. Prematurity was similarly shown to be associated with the development of CNLDO in the study by Sathiamoorthi [3]. According to our data CNLDO is more frequent in full-term children who correspond to the results by Kendig and Guerry [12]. We found that prematurity (gestational age <37 weeks and birth weight <2500grams) decrease the risk for CNLDO.

To our knowledge, this study is the first in the literature to evaluate the relationship between Progesterone intake in relation with fetus retention events, oxygen therapy and neonatal infection, and CNLDO. These factors reduce the risk of congenital nasolacrimal duct obstruction. However additional studies of larger scale should be performed to better understand risk and protective factors for CNLDO.

CONCLUSION

Congenital nasolacrimal duct obstruction usually affects full-term born children with no gender predisposition and is bilateral in 1/3 of cases. Risk factors for developing congenital nasolacrimal duct obstruction are consuming alcohol and antibiotic taking during pregnancy. There is a need for an educational program to increase the awareness of nature and risk factors of the CNLDO both physicians and parents.

Abbreviation list:

CNLDO - congenital nasolacrimal duct obstruction
CS - Cesarean section
OR - Odds ratio
CI - Conûdence intervals

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