fortune Journals

Research Article

JOURNAL OF OPHTHALMOLOGY AND RESEARCH

ISSN: 2644-0024

Simple Congenital Ptosis and Maternal Immune Factors

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Abstract

Introduction: Congenital ptosis, characterized by eyelid drooping, poses significant risks to visual development, emphasizing the need for early diagnosis and intervention. While several risk factors are known, many cases remain idiopathic. This pilot study aims to explore additional obstetric risk factors associated with simple congenital ptosis (SCP).

Methods: A retrospective cohort study was conducted at the Shaare Zedek Medical Center, analyzing electronic records of mothers and newborns from 2002 to 2022. Inclusion criteria encompassed SCP diagnosed before 3 months without established ptosis etiologies or known risk factors.

Results: 51 SCP cases were identified, showing distinctions in gestational age (38.5±2.6 weeks), birth weight (2998±506 gr), and a higher incidence of preterm births (15.7%) compared to the general population. Intrapartum fever incidence was notably elevated (5.9%) in SCP cases, whereas GBS carrier status and CMV infection rates were similar to the general population.

Conclusion: This study highlights intriguing associations between SCP and obstetric factors, particularly intrapartum fever and younger gestational age. The findings suggest a potential link between immune compromise and SCP pathophysiology, warranting further investigation. Despite limitations, these insights could enhance early detection and management of congenital ptosis, potentially averting vision-related complications.

Keywords: Simple congenital ptosis; Intrapartum fever; Group B Streptococcus.

Introuduction

Ptosis, a deviation from a normal margin-reflex distance height [1], is a common eyelid malposition found in both children and adults. Congenital ptosis refers to eyelid drooping occurring within the first years of life. In most instances, congenital ptosis stands as an isolated condition, unrelated to any other systemic issue (i.e., simple congenital ptosis; SCP) [2]. This condition might lead to amblyopia due to visual deprivation or induced astigmatism, particularly if it is unilateral or asymmetric. Hence, early diagnosis and proper management become crucial for maximizing potential visual development [3].

Several risk factors associated with congenital ptosis have been identified through population-based [4-5] and tertiary center-based [6] studies, including male sex, family history, obesity, and eyelid trauma. Obstetric complications such as forceps delivery, vacuum extraction, and shoulder dystocia are also recognized as contributing factors. Despite this, the underlying cause in most cases of SCP remains unknown [2]. In this pilot study, our aim is to uncover additional obstetric risk factors for SCP.

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Citation: Konstantin Gushansky, Simple Congenital Ptosis. Journal of Ophthalmology and Research. 7 (2024): 01-04.

Received: December 28, 2023
Accepted: January 06, 2024
Published: January 09, 2024

Gushansky K, et al., J Opthalmol Res 2024
DOI:10.26502/fjor.2644-00240087

Methods

This population-based retrospective cohort study encompassed mothers and newborns at the Shaare Zedek Medical Center in Jerusalem, Israel. We conducted a comprehensive review of electronic medical records belonging to women who delivered newborns diagnosed with SCP between January 1, 2002, and December 31, 2022. Within our study cohort, the Shaare Zedek Medical Center served as the exclusive provider of all medical care for both mothers and infants, overseeing pregnancy follow-up, labor, pediatric check-ups, and ophthalmologic diagnoses.

Study population The study's inclusion criteria necessitated a diagnosis of SCP before the age of 3 months. Exclusions comprised patients with potential ptosis origins such as birth trauma, neoplasia, or neurological conditions (e.g. myasthenia gravis, Horner syndrome, myotonic dystrophy, or any cranial nerve palsy). Patients with syndromic ptosis, including Duane retraction syndrome, Marcus Gunn jaw-winking ptosis, congenital fibrosis of the extraocular muscles, monocular elevation deficiency, or blepharophimosis-ptosis-epicanthus inversus syndrome, were also excluded. Additionally, those with established risk factors for congenital ptosis, such as forceps-assisted delivery, vacuum extraction, or shoulder dystocia, were not included. Finally, patients with a follow-up period of fewer than 12 months or incomplete follow-up were excluded from the study.

Exemption from ethics approval and waiver of informed consent The report adhered to the ethical principles outlined in the Declaration of Helsinki, as amended in 2013. The Institutional Review Board waived the need for ethics approval and obtaining consent for the collection, analysis, and publication of retrospectively obtained and anonymized data for this non-interventional study.

Observation procedures Diagnosis of congenital ptosis was determined through the review of ophthalmologists' reports. Newborns requiring surgical repair were referred to an oculoplastic surgeon.

Statistical analysis Continuous variables were analyzed using Student's t-test, while proportions underwent $\chi 2$ test with Yates' correction. To account for repeated testing, only probabilities less than 0.05 were deemed statistically significant. Data analysis was conducted using SPSS ver.27 (SPSS Inc., Chicago, IL).

Results

A total of 51 newborns diagnosed with SCP during the study period were included. Baseline characteristics significantly differed between the study group (SCP) and the general population. Gestational age was lower in SCP (38.5±2.6 weeks versus 39.1±1.7 weeks, p=0.012), and birth weight was also lower (2998±506 gr versus 3255±484 gr, p>0.001). Comparing maternal age to existing demographic data on maternal primiparous age was challenging due to varying birth orders, but the data appeared reflective of the general population (Table 1).

Data are given as mean±SD. For two-group comparisons, qualitative data were analyzed with the two-factor c^2 with Yates' correction and continuous variables with the Student's T-test. SCP: newborns diagnosed with simple congenital ptosis, i.e., study group. Bold for p-value less than 0.05. *Median maternal age at first birth in Israel

In SCP, a notably higher incidence of preterm deliveries was evident compared to the general population (15.7% versus 0.05%, p<0.001). Rates of caesarean sections were similar to those in the general population.

A significant difference emerged in the incidence of intrapartum fever between SCP and the general population (5.9% versus 0.15%, p<0.001). In all cases, the fever subsided within several hours. No intrauterine infection cases were diagnosed, and the source of fever remained unknown. No significant differences were found in the proportions of Group B Streptococcus (GBS) carrier status, or in the incidence of Cytomegalovirus (CMV) infection (Table 2).

Data are given as absolute numbers and percentages. For two-group comparisons, qualitative data were analyzed with the two-factor c^2 with Yates' correction. Preterm delivery: Before 37 weeks' gestation. Bold for p-value less than 0.05.

Table 1: Baseline characteristics

	SCP (n=51)	Control population	N	p-value
Maternal age (y)	28.8±5.5	27.7[10]*	N/A	N/A
Gestational age (w)	38.5±2.6	39.1±1.7[13]	1,60,079	**0.012**
Birth weight (gr)	2998±506	3255±484[13]	1,60,079	**>0.001**

Data are given as mean±SD. For two-group comparisons, qualitative data were analyzed with the two-factor c^2 with Yates' correction and continuous variables with the Student's T-test. SCP: newborns diagnosed with simple congenital ptosis, i.e., study group. Bold for p-value less than 0.05. *Median maternal age at first birth in Israel

Table 2: Obstetric data

	SCP (n=51)	Control population	N	p-value
Preterm delivery	8 (15.7%)	0.05%[14]	1,60,079	**<0.001**
Caesarean Section	11 (21.6%)	18.1%[15]	1,77,039	0.516
Intrapartum fever	3 (5.9%)	0.15%[16]	3,56,356	**<0.001**
GBS carrier status	6 (11.8%)	21%[17]	25,367	0.107
CMV infection	0 (0%)	0.7%[18]	2,000	0.549

Data are given as absolute numbers and percentages. For two-group comparisons, qualitative data were analyzed with the two-factor c^2 with Yates' correction. Preterm delivery: Before 37 weeks' gestation. Bold for p-value less than 0.05.

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Discussion

The etiology of simple congenital ptosis is intricate and multifaceted. Genetics play a significant role, highlighted by a heritability index of 0.75 established in monozygotic twins [7]. Additionally, a higher incidence of SCP was noted in consanguineous marriages [8], suggesting a possible recessive inheritance pattern. However, the data also reveals that 0.25 of the concordance in monozygotic twins could not solely be explained by Mendelian genetics. This suggests the involvement of either a local in utero environmental factor or de novo genetic defect, emphasizing the importance of our quest for modifiable risk factors for SCP.

While obstetric factors such as shoulder dystocia, vacuum extraction, and forceps-assisted delivery2 have been linked to congenital ptosis, they account for only a fraction of SCP cases. In our pursuit of identifying additional risk factors, we have deliberately excluded these potential confounders from our study.

Older maternal age has been linked to higher rates of SCP [9], posing a potential confounding factor in our study. The mean maternal age within our sample stood at 28.8 years. In Israel, the average primiparous age is 27.7 years, with a fertility rate of 2.9 children per woman [10]. Even under the assumption of consecutive pregnancies with no gaps, the mean age at childbirth would be at least 28.5 years. Therefore, it is evident that our cohort's age was not significantly older than that of the general population.

In our cohort, several associations emerged between SCP and obstetric data. Intrapartum fever rates were significantly higher in SCP versus the general population in Israel. However, GBS carrier status rates were similar to the general population, as were the rates of CMV infection. Therefore, an alternative infectious agent might be implicated.

We have also found an association between younger gestational age, including increased rates of preterm labor, and SCP. These findings align with existing data on prematurity and other congenital anomalies [11]. Prematurity and younger gestational age are known to be associated with variable rates of immune compromise [12-18]. The combination of these findings and the previously mentioned higher rates of intrapartum fever lead us to suspect an immune or infectious component in the pathophysiology of some SCP cases.Our study has several limitations to consider. Its retrospective nature and reliance on a relatively small sample size pose inherent constraints. Additionally, while the majority of our population-based prevalence data were derived from the Ministry of Health Census, certain variables were collected from research on smaller samples.

Further research is imperative to validate our findings in a larger, community-based sample, and identify the infectious culprit. Such investigations have the potential to advance the prenatal diagnosis of congenital ptosis.

In conclusion, our pilot study unveils novel associations between congenital ptosis and obstetric risk factors. We anticipate that these findings will augment the current understanding of congenital ptosis, potentially facilitating early diagnosis and treatment of this vision-threatening condition.

Financial Disclosures: The authors have neither proprietary nor commercial interests in any medications or materials discussed in this study.

Conflict of Interests: The authors have no conflicts of interest to disclose.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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