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Pseudostrabismus in the First Year of Life and the Subsequent Diagnosis of Strabismus

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Abstract

Purpose: To report the population-based incidence of pseudostrabismus in the first year of life and the subsequent diagnosis of strabismus.

Design: Retrospective population-based cohort study.

Methods:

Setting: A medical record linkage system that captures virtually all medical care provided to residents of Olmsted County, Minnesota.

Study population: Residents of Olmsted County, Minnesota 1 year of age diagnosed with pseudostrabismus from January 1, 2005, through December 31, 2014.

Main Outcomes and Measures: The prevalence of pseudostrabismus in the study cohort and the subsequent diagnosis of strabismus.

Results: A total of 184 infants were diagnosed with pseudostrabismus during the 10-year study period, yielding a birth prevalence of one in 113 children in the first year of life. One hundred sixty five (89.7%) were diagnosed by a non-ophthalmology care provider (NOCP) and confirmed by an ophthalmologist, 13 (7.1%) by an ophthalmologist alone, and six (3.3%) by a NOCP alone.

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Eighty-eight (49.4%) had at least one follow-up visit with ophthalmology, and the median follow-up time from pseudostrabismus diagnosis to the last health care visit that included an eye examination was 7.7 years (interquartile range: 5.8 years). Nine (4.9%) of the 184 infants were subsequently diagnosed with strabismus at a mean age of 4.5 years (range: 1.3 to 8.7 years); seven with esotropia and two with exotropia.

Conclusions: Pseudostrabismus is a relatively frequent diagnosis in the first year of life. The prevalence of strabismus among pseudostrabismic infants in this cohort is lower than prior reports and similar to strabismus rates reported in the same population.

Abstract

In this population-based cohort, pseudostrabismus was diagnosed in nearly 1% of infants during the 10-year study period. Strabismus was subsequently diagnosed in 4.9% of pseudostrabismic infants, a rate that was lower than prior reports but similar to those observed in the same pediatric population. These findings suggest that the apparent elevated strabismus risk among pseudostrabismic patients may not be causal, but instead, due to confounding factors.

Introduction

Pseudostrabismus is a common condition among infants in which orthotropic eyes appear misaligned due to facial morphologic features.¹ More often esotropic-appearing than exotropic, pseudostrabismus is diagnosed relatively frequently and generally resolves over the first several years of life.² The prevalence of pseudostrabismus remains unknown and may depend on a variety of factors including race, age at diagnosis, and experience of the examiner. Although it is unclear whether pseudostrabismus is associated with or a risk factor for the development of strabismus later in life, reported rates of ocular misalignment among children initially diagnosed with pseudostrabismus have varied from 9.6% to 19%,^{2–7} compared to strabismus rates in the general pediatric population ranging from 2.1% to 3.9%.^{8–14} The purpose of this study was to investigate the prevalence of pseudostrabismus diagnosed over a 10-year period and to report the subsequent diagnosis of strabismus among a population-based birth cohort of pseudostrabismic infants.

Methods

The medical records of all patients 1 year of age residing in Olmsted County, Minnesota from January 1, 2005, through December 31, 2014, when diagnosed with pseudostrabismus were retrospectively reviewed. Patients were identified using the Rochester Epidemiology Project, a medical record linkage system that tracks medical care delivered to residents of Olmsted County, Minnesota using diagnostic and surgical procedure codes.¹⁵ The patient population in Olmsted County, Minnesota is relatively isolated from other urban areas, and the Rochester Epidemiology Project captures virtually all medical care provided by Mayo Clinic, Olmsted Medical Group, and affiliated hospitals.¹⁶ The Institutional Review Boards (IRB) of Mayo Clinic and Olmsted Medical Center approved this retrospective cohort study. Participants in the Rochester Epidemiology Project were asked to give authorization for minimal risk research when they are first entered into the medical system. Since the present study was retrospective and considered minimal risk, waiver of consent was granted by the

IRBs. This study was in accordance with Health Insurance and Portability and Accountability Act and adhered to the tenets of the Declaration of Helsinki.

This investigation was part of a larger study of all ocular disorders occurring in infants. Using the Rochester Epidemiology Project, we conducted a diagnostic code search utilizing 1,007 ocular-related International Classification of Diseases, Ninth Revision (ICD-9) codes to identify all patients 1 year old diagnosed with any ocular disease, including pseudostrabismus, during the 10-year study period. Patients were excluded from the study if they were living outside Olmsted County at the time of diagnosis, if their birth date was outside the study period, or if they were older than 12 months when diagnosed with pseudostrabismus. The medical records of all patients identified via the ICD-9 code search were individually reviewed to assess diagnoses, demographic data, underlying medical conditions, and ICD-9 codes associated with the diagnosis of pseudostrabismus. Confirmed diagnoses were based on ocular conditions documented in the medical record.

Additional collected data included comorbid ocular disease, medical specialty of the provider who made the pseudostrabismus diagnosis, and any subsequent diagnosis of strabismus. For medical specialty of provider, a non-ophthalmology care provider (NOCP) was defined as examiners whose specialty was family medicine, pediatrics, optometry, or nursing. Longitudinal findings were ascertained from follow-up examinations with ophthalmology and any health care visit in which an eye examination was performed, including visits with NOCPs. Ophthalmology follow-up visits were defined as any examination by an ophthalmologist after the initial diagnosis of pseudostrabismus. The medical records were reviewed through March 31, 2020.

The incidence and birth prevalence of pseudostrabismus and the subsequent diagnosis of strabismus were estimated using the age- and gender-specific population figures for Olmsted County population data for 2005 through 2014. Population data are obtained at each census, and the population for each year between census years is calculated using a linear interpolation of the data. The 95% confidence intervals (95% CI) for overall incidence were calculated assuming Poisson error distribution. Statistical analysis was performed using SAS (SAS Institute; Cary, North Carolina).

Results

There were 19,833 newborn births in Olmsted County, Minnesota during the 10-year study period. The diagnostic code search of 1,007 ocular-related ICD-9 codes identified 4,764 potential ocular diagnoses during the 10-year study period, of which 4,393 (92.2%) infants were confirmed to have at least one ocular diagnosis after review of the medical records. Of the 4,393 confirmed diagnoses, 184 (4.2%) infants were diagnosed with pseudostrabismus, yielding a birth prevalence of 882.0 per 100,000 per year (95% CI: 755 to 1009), or 1 in 113 live births (95% CI: 99 to 132). The historical and initial clinical characteristics of the 184 infants are described in Table 1. The mean age at pseudostrabismus diagnosis was 7.5 months (range: 20 days to 12.0 months), and 93 (50.5%) were female. A history of premature birth (<37 weeks) was observed in 29 (15.8%) patients (diagnosed with pseudostrabismus at a mean age of 7.7 months), greater than the 8.4% premature birth rate

observed in the general study population without pseudostrabismus ($p<0.001$). Nine (4.9%) pseudostrabismic infants had a family history of strabismus. Of the 1,007 ICD-9 codes initially used to search for all ocular conditions, six (0.60%) ICD-9 codes were used to code for pseudostrabismus (Table 2). The ICD-9 code most commonly associated with pseudostrabismus was 378.87 (Other dissociated deviation of eye movements) in 155 (84.2%) cases.

The diagnosis of pseudostrabismus was made by a NOCP initially and confirmed later by an ophthalmologist in 165 (89.7%) cases, by an ophthalmologist alone in 13 (7.1%) cases, and by a NOCP alone in six (3.3%) cases. Of the 178 patients examined by an ophthalmologist, 156 (87.6%) were diagnosed by a pediatric ophthalmologist and 22 (12.4%) by a comprehensive ophthalmologist. Eighty-eight (49.4%) patients had at least one follow-up visit with ophthalmology at a mean age of 2.3 years (range: 4.8 months to 9.0 years), while 45 (25.7%) had at least two visits at a mean age of 4.9 years (range: 9.2 months to 11.4 years). The remaining 90 (50.6%) patients had no further follow-up with ophthalmology after pseudostrabismus diagnosis. Virtually all patients, irrespective of whether they were evaluated by an ophthalmologist or a NOCP alone, received regular health care follow-up that included an eye examination by NOCPs. Excluding nine patients who were ultimately diagnosed with strabismus, the median follow-up time from pseudostrabismus diagnosis to last health care follow-up visit that included an eye examination was 7.7 years (interquartile range [IQR]: 5.8 years). The specialty of the provider who conducted the last health care follow-up visit was pediatrics in 114 (65.1%) cases, family medicine in 52 (29.7%) cases, and ophthalmology in nine (5.1%) cases.

Nine (4.9%) of the 184 pseudostrabismic infants, or 10.2% of the 88 patients with ophthalmology follow-up, were subsequently diagnosed with strabismus at a mean age of 4.5 years (range: 1.3 to 8.7 years). Three (33.3%) were born prematurely, two (22.2%) were female, and one (11.1%) had a family history of strabismus. All nine were diagnosed with pseudostrabismus by a NOCP initially and confirmed by a pediatric ophthalmologist. Four of the children were diagnosed with accommodative esotropia, two with non-accommodative esotropia, and one each with abnormal CNS-related esotropia, intermittent exotropia, and paralytic exotropia. The average follow-up time from initial pseudostrabismus diagnosis to subsequent strabismus diagnosis was 3.9 years (range: 7.9 months to 7.7 years). Of the nine strabismic children, five were diagnosed with strabismus at their first ophthalmology follow-up visit at a mean age of 5.1 years (range: 1.3 to 8.7 years). One additional strabismic infant was diagnosed at the second ophthalmology follow-up visit at 4.2 years old. The three remaining strabismic infants were diagnosed in subsequent ophthalmology visits after their second ophthalmology follow-up visit at a mean age of 3.4 years (range: 2.5 to 4.5 years).

Discussion

In this population-based retrospective cohort study, pseudostrabismus was diagnosed in nearly 1% of children less than one year of age. The subsequent diagnosis of strabismus was observed in 4.9% pseudostrabismic infants overall, or 10.2% infants among those with at least one ophthalmology follow-up visit. Strabismus rates in this cohort of pseudostrabismic

children were lower than that of previous reports, which ranged from 9.6% to 19%,²⁻⁷ but similar to the 3.9% prevalence of strabismus observed in the same population.¹²⁻¹⁴

Prior reports of strabismus rates among pseudostrabismic children, varying from 9.6% to 19.4%, primarily occurred in small retrospective single center studies.²⁻⁷ A key inclusion criterion for these studies was that all children required a follow-up evaluation by an ophthalmologist. Such cohorts are not necessarily representative of the general population because they are more closely medically surveilled, and ophthalmology follow-up is not routinely recommended following a diagnosis of pseudostrabismus. If the current study was limited to only pseudostrabismic infants who had ophthalmology follow-up, the rate of strabismus increases to 10.2%. However, the true rate of strabismus developing in such patients is likely closer to the 4.9% rate due to the generally high quality and pervasive nature of medical care available to the community and the relatively non-transient nature of the study population.¹⁶ Of note, one of the prior studies also reported a strabismus rate of 6.5% among pseudostrabismic infants when including both patients with and without ophthalmology follow-up, not dissimilar to the 4.9% rate observed in this study.⁵

A more recent investigation by Ryu and Lambert reviewed strabismus rates among children initially diagnosed with pseudostrabismus using insurance claim and ICD code data from a national cohort.⁷ They reported 9.6% of 17,885 children diagnosed with pseudostrabismus before three years of age were subsequently diagnosed with strabismus, a rate that is nearly twice that reported in the present study. The authors included children diagnosed with pseudostrabismus up to three years of age, while only infants up to one year of age were included in the current investigation. It is unclear why or if older age at diagnosis is associated with a higher subsequent rate of strabismus development. More importantly, the investigators relied solely on ICD diagnosis codes without reviewing the medical records to identify pseudostrabismus cases. Prior studies investigating ICD-9 code accuracy suggest ICD-9 codes alone may be insufficient in accurately identifying diagnoses.^{17,18} Numerous factors contribute to ICD-9 coding inaccuracy including inadequate training, coder experience, and unintentional and intentional errors such as upcoding, misspecification, and unbundling of codes.^{19, 20} Because the medical records of all 4,393 infants diagnosed with an ocular disorder in this study were individually reviewed, we were able to confirm or correct all diagnoses. Of the 184 pseudostrabismus cases in this study, only four (2.2%) had an associated ICD-9 code of 743.63 (other specified congenital anomalies of eyelid), the sole ICD-9 code used by Ryu and Lambert to identify their pseudostrabismus cases. Other codes associated with pseudostrabismus in this study included 378.87 (other dissociated deviation of eye movements) in 155 (84.2%) cases, 378.9 (unspecified disorder of eye movements) in 15 (8.2%) cases, and 378 (esotropia) in eight (4.3%) cases (Table 2). Although the numbers are large in this insurance claim database study, the accuracy of ICD code-based methodology is a significant limitation.

Studies reporting an increased prevalence of strabismus among children diagnosed with pseudostrabismus as infants suggest that the two conditions are somehow associated or that the latter is a risk factor for the former. It remains unclear how or why pseudostrabismic children would be more prone to developing strabismus as there is no causal or direct pathophysiologic association. A more likely explanation is the selection bias that occurred

when excluding pseudostrabismic children without ophthalmology follow-up. Compared to pseudostrabismic patients whose condition resolved, those with persistent concerns for an ocular deviation (observed by the parents) may have been more likely to receive follow-up care. It is possible that some of these patients were truly strabismic although initially misdiagnosed with pseudostrabismus, particularly among children who were uncooperative or had an intermittent deviation such as accommodative esotropia or intermittent exotropia, observed in five of the nine children subsequently diagnosed with strabismus in this study. Another contributing factor may be the population in which the condition was studied. In Olmsted County, Minnesota, specialty care is relatively abundant since Mayo Clinic serves a relatively small county population. As a result, NOCPs in this study may have been more likely than providers in other populations to refer infants to ophthalmologists to confirm a diagnosis of pseudostrabismus, thus potentially increasing the reported prevalence of pseudostrabismus and artificially decreasing the observed strabismus rate among pseudostrabismic children. Furthermore, premature birth may be a confounding factor as it predisposes infants to both pseudostrabismus, observed in this and other studies, and strabismus.^{21, 22} Lastly, pseudostrabismic children may be more likely to experience increased medical surveillance compared to the general population without an ocular condition, potentially biasing the examiner to an elevated rate of strabismus among children diagnosed with pseudostrabismus.

There are several limitations to the findings of this study. The retrospective study design is limited by incomplete data and irregular follow-up. More than half of the pseudostrabismus cohort was not evaluated in ophthalmology follow-up because there was no standardized follow-up exam schedule for children diagnosed with pseudostrabismus. However, it is not unreasonable to presume that these patients did not develop strabismus since they received relatively robust health care follow-up with NOCPs who were trained to screen for vision threatening conditions such as strabismus, and NOCP medical records were reviewed as part of this study. Additionally, while the prevalence of strabismus in Olmsted County has been reported to be 3.9%, this rate is among children up to 18 years of age. The prevalence among children by 5 years of age in Olmsted County is 2.6%,^{11–13} nearly half the 4.9% rate observed in the pseudostrabismic children at the same age.

Pseudostrabismus was diagnosed in nearly 1% of infants in the first year of life in this population-based cohort. The subsequent diagnosis of strabismus in these children is lower than prior reports and comparable to the prevalence of childhood strabismus in the Olmsted County, Minnesota population. The apparent elevated risk of strabismus occurring among children previously diagnosed with pseudostrabismus in prior studies does not appear to be causal, but instead, is more likely the result of confounding factors and the population in which these conditions are studied.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Biography

Timothy T. Xu is a third year medical student at Mayo Clinic Alix School of Medicine in Rochester, Minnesota. He received his undergraduate degree from Emory University in Atlanta, Georgia, where he was an Emory Scholar and graduated *Summa cum laude* and *Phi Beta Kappa*. He is pursuing a career in academic ophthalmology.

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Table 1:

Demographic characteristics of all infants in Olmsted County compared to those diagnosed with pseudostrabismus.

Characteristic	All Infants Born in Olmsted County from 2005 to 2014 (N=19,833)	Pseudostrabismic Infants (N=184)	P-value
Mean age at diagnosis (range)	-	7.5 months (20 days to 12.0 months)	-
Sex (female)	9687 (48.8%)	93 (50.5%)	0.65
Race			
Asian	1,060 (5.8%)	14 (7.6%)	0.32
Black	1,450 (8.0%)	9 (4.9%)	0.12
White	13,348 (67.3%)	128 (70.0%)	0.18
Other (American Indian, Hispanic, Unknown, or Refused to Respond)	2,162 (12.0%)	33 (17.9%)	0.002
Born Prematurely	1,668 (8.4%)	29 (15.8%)	<0.001
Born via Caesarean delivery	4,855 (24.5%)	41 (22.3%)	0.49
Family history of strabismus	-	9 (4.9%)	-
Other medical, systemic, or genetic conditions*	-	12 (6.5%)	-

* Developmental delay, Cerebral palsy, Neurofibromatosis type 1, Williams syndrome, Duane's syndrome, and Ras-MAPK pathway disorder, and Malonic aciduria

Table 2:

International Classification of Disease, Ninth Revision (ICD-9) codes associated with the diagnosis of pseudostrabismus.

ICD-9 code	Number of pseudostrabismus cases
378.87 (Other dissociated deviation of eye movements)	155 (84.2%)
378.9 (Unspecified disorder of eye movements)	15 (8.2%)
378 (Esotropia)	8 (4.3%)
743.63 (Other specified congenital anomalies of eyelid)	4 (2.2%)
368.00 (Amblyopia, unspecified)	1 (0.54%)
367.0 (Hypermetropia)	1 (0.54%)