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

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• PURPOSE: To report the population-based birth prevalence of pseudostrabismus in the first year of life and the subsequent diagnosis of strabismus.
• DESIGN: Retrospective population-based cohort study.
• METHODS: All residents of Olmsted County, Minnesota ≤1 year old diagnosed with pseudostrabismus from January 1, 2005 through December 31, 2014, were identified using a medical record linkage system that captures virtually all medical care provided in a single Midwestern United States county population. The birth prevalence of pseudostrabismus and the subsequent diagnosis of strabismus were assessed.
• RESULTS: A total of 184 infants were diagnosed with pseudostrabismus during the 10-year study period, which yielded a birth prevalence of 1 in 113 children in the first year of life. There were 165 (89.7%) infants initially diagnosed by a non-ophthalmology care provider (NOCP) and confirmed by an ophthalmologist, 13 (7.1%) patients were diagnosed by an ophthalmologist alone, and 6 (3.3%) patients were diagnosed by a NOCP alone. Eighty-eight (49.4%) infants had at least 1 follow-up visit with an ophthalmologist, 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) (7 with esotropia and 2 with exotropia).
• CONCLUSION: Pseudostrabismus is a relatively frequent diagnosis in the first year of life. The prevalence of strabismus among infants with pseudostrabismus in this cohort was lower than those in previous reports and similar to strabismus rates reported in the same population. (Am J Ophthalmol 2020;218:242–246.

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PSEUDOSTRABISMUS IS A COMMON CONDITION among infants in which orthotropic eyes appear misaligned due to facial morphologic features.[1] Pseudostrabismus appears more often as esotropic rather than exotropic, 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 with strabismus rates in the general pediatric population, which ranges from 2.1% to 3.9%.[8–14] The purpose of this study was to investigate the birth prevalence of pseudostrabismus over a 10-year period and to report the subsequent diagnosis of strabismus among a population-based birth cohort of infants with pseudostrabismus.

METHODS

THE MEDICAL RECORDS OF ALL PATIENTS 1 YEAR OLD OR younger, who resided in Olmsted County, Minnesota from January 1, 2005, to December 31, 2014, and who were 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 the Mayo Clinic, the Olmsted Medical Group, and affiliated hospitals.[16] The institutional review boards of the Mayo Clinic and the 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 first entered into the medical system. Because the present study was retrospective and considered minimal risk, waivers of consent were granted by the institutional review boards. This study was conducted in accordance with

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TABLE 1. Demographic Characteristics of All Infants in Olmsted County Compared With Those Diagnosed With Pseudostrabismus

Characteristic	All Infants Born in Olmsted County 2005– 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)	9,687 (48.8%)	93 (50.5%)	.65
Race			
Asian	1,060 (5.8%)	14 (7.6%)	.32
Black	1,450 (8.0%)	9 (4.9%)	.12
White	13,348 (67.3%)	128 (70.0%)	.18
Other (American Indian, Hispanic, unknown, or refused to respond)	2,162 (12.0%)	33 (17.9%)	.002
Born prematurely	1,668 (8.4%)	29 (15.8%)	<.001
Born via Caesarean delivery	4,855 (24.5%)	41 (22.3%)	.49
Family history of strabismus	-	9 (4.9%)	-
Other medical, systemic, or genetic conditions[a]	-	12 (6.5%)	-

[a]Developmental delay, cerebral palsy, neurofibromatosis type 1, Williams syndrome, Duane's syndrome, Ras-MAPK pathway disorder, and Malonic aciduria.

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 that occurred in infants. Using the Rochester Epidemiology Project, we conducted a diagnostic code search using 1,007 ocular-related *International Classification of Diseases, Ninth Revision* (ICD-9) codes to identify all patients 1 year old or younger who were diagnosed with any ocular disease, including pseudostrabismus, during the 10-year study period. Patients were excluded from the study if they lived 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 sex-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% CIs) for overall incidence were calculated assuming Poisson error distribution. Statistical analysis was performed using SAS Version 9 (SAS Institute; Cary, North Carolina).

RESULTS

THERE WERE 19,833 NEWBORN BIRTHS IN OLMSTED COUNTY, MN 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 1 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 1,009) 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); 93 (50.5%) of the infants 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), which was >8.4% premature birth rate observed in the general study population without

TABLE 2. *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%)

ICD-9 = *International Classification of Disease, Ninth Revision.*

pseudostrabismus ($P < 0.001$). Nine (4.9%) infants with pseudostrabismus had a family history of strabismus. Of the 1,007 ICD-9 codes initially used to search for all ocular conditions, 6 (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 6 (3.3%) cases. Of the 178 patients examined by an ophthalmologist, 156 (87.6%) patients were diagnosed by a pediatric ophthalmologist and 22 (12.4%) patients by a comprehensive ophthalmologist. Eighty-eight (49.4%) patients had at least 1 follow-up visit with ophthalmology at a mean age of 2.3 years (range: 4.8 months to 9.0 years), whereas 45 (25.7%) patients had at least 2 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, regardless 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 9 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: 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 9 (5.1%) cases.

Nine (4.9%) of the 184 infants with pseudostrabismus, 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, 2 (22.2%) were female, and 1 (11.1%) had a family history of strabismus. All 9 were diagnosed with pseudostrabismus by a NOCP initially, and this diagnosis was then confirmed by a pediatric ophthalmologist. Four of the children were diagnosed with accommodative esotropia, 2 with non-accommodative esotropia, and 1 each with abnormal central nervous system–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 9 children with strabismus, 5 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 infant with strabismus was diagnosed at the second ophthalmology follow-up visit at 4.2 years old. The 3 remaining infants with strabismus 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 who were younger than 1 year of age. The subsequent diagnosis of strabismus was observed in 4.9% of infants with pseudostrabismus overall, or 10.2% of infants with at least 1 ophthalmology follow-up visit. Strabismus rates in this cohort of children with pseudostrabismus were lower than that of previous reports, which ranged from 9.6% to 19%,[2–7] but was similar to the 3.9% prevalence of strabismus observed in the same population.[12–14]

Previous reports of strabismus rates among children with pseudostrabismus, which varied 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 present study was limited to only infants with pseudostrabismus who had ophthalmology

follow-up, the rate of strabismus would increase 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 nontransient nature of the study population.[16] Of note, 1 of the previous studies also reported a strabismus rate of 6.5% among infants with pseudostrabismus when including both patients with and without ophthalmology follow-up, which was 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 3 years of age were subsequently diagnosed with strabismus, a rate that was nearly twice that reported in the present study. The investigators included children diagnosed with pseudostrabismus up to 3 years of age, whereas only infants up to 1 year of age were included in the present investigation. It was unclear why or if older age at diagnosis was associated with a higher subsequent rate of strabismus development. Furthermore, the investigators relied solely on ICD diagnosis codes without reviewing the medical records to identify pseudostrabismus cases. Previous studies that investigated ICD-9 code accuracy suggested 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 4 (2.2%) had an associated ICD-9 code of 743.63 (other specified congenital anomalies of eyelid), which was 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 8 (4.3%) cases (Table 2). Although the numbers were large in this insurance claim database study, the accuracy of its ICD code–based methodology was a significant limitation.

Studies that reported an increased prevalence of strabismus among children diagnosed with pseudostrabismus as infants suggested that the 2 conditions are somehow associated or that the latter is a risk factor for the former. It remains unclear how or why children with pseudostrabismus would be more prone to developing strabismus because there is no causal or direct pathophysiologic association. A more likely explanation was the selection bias that occurred when excluding children with pseudostrabismus who did not have ophthalmology follow-up. Compared to patients with pseudostrabismus whose condition resolved, those with persistent concerns for an ocular deviation (observed by the parents) might have been more likely to receive follow-up care. It was possible that some of these patients had strabismus although they were initially misdiagnosed with pseudostrabismus, particularly among children who were uncooperative or had an intermittent deviation (e.g., accommodative esotropia or intermittent exotropia), which was observed in 5 of the 9 children subsequently diagnosed with strabismus in this study. Another contributing factor might be the population in which the condition was studied. In Olmsted County, Minnesota, specialty care is relatively abundant because the Mayo Clinic serves a relatively small county population. As a result, NOCPs in this study might have been more likely than providers in other populations to refer infants to ophthalmologists to confirm a diagnosis of pseudostrabismus. This potentially increased the reported prevalence of pseudostrabismus and artificially decreased the observed strabismus rate among children with pseudostrabismus. Furthermore, premature birth might be a confounding factor because it predisposed infants to both pseudostrabismus, as observed in this and other studies, and strabismus.[21,22] Lastly, children with pseudostrabismus may be more likely to experience increased medical surveillance compared with the general population without an ocular condition, which potentially biased the examiner to an elevated rate of strabismus among children diagnosed with pseudostrabismus.

There were several limitations to the findings of this study. The retrospective study design was limited by incomplete data and irregular follow-up. More than one-half of the pseudostrabismus cohort was not evaluated in ophthalmology follow-up because there was no standardized follow-up examination schedule for children diagnosed with pseudostrabismus. However, it was not unreasonable to presume that these patients did not develop strabismus because they received relatively robust health care follow-up with NOCPs who were trained to screen for vision threatening conditions, such as strabismus. NOCP medical records were also reviewed as part of this study. In addition, although the prevalence of strabismus in Olmsted County was reported to be 3.9%, this rate was among children up to 18 years of age. The prevalence among children by 5 years of age in Olmsted County was 2.6%,[12–14] which was nearly one-half the 4.9% rate observed in children with pseudostrabismus 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 was lower than that of previous reports and comparable to the prevalence of childhood strabismus in the Olmsted County, Minnesota population. The apparent elevated risk of strabismus that occurred among children initially diagnosed with pseudostrabismus in previous studies does not appear to be causal, but instead, was more likely the result of confounding factors and the population in which these conditions were studied.

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