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Epidemiology of Congenital Idiopathic Talipes Equinovarus in Iowa, 1997–2005

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Abstract

Congenital idiopathic talipes equinovarus (ITEV), also known as clubfoot, is a well-recognized foot deformity. To date, prevalence estimates and descriptive data reported for ITEV have varied due to differences in study methodology. Using population-based surveillance data collected by the Iowa Registry for Congenital and Inherited Disorders, we examined isolated ITEV births delivered from 1997 through 2005 and compared to live births in Iowa during the same time period. An overall prevalence was calculated for live, singleton full-term births only. Prevalence odds ratios (POR)s and 95% confidence intervals (CI)s were examined for selected infant and parental characteristics. The prevalence of isolated ITEV was 11.4 per 10,000 live, singleton full-term births (95% CI =10.3, 12.6), with no significant variation in prevalence during the study period. Increased PORs were found for males (POR 1.8; 95% CI =1.5, 2.3) and maternal smoking during pregnancy (POR =1.5, 95% CI =1.2, 1.9); low birth weight (< 2,500 g) showed an increase among females (POR =3.2, 95% CI =1.5, 6.9) but not males (POR =0.9, 95% CI =0.3, 2.8). Elevated, but non-significant, PORs were found for season of birth, maternal education, and trimester prenatal care was initiated; decreased PORs were found for fetal presentation, maternal race/ethnicity, parity, area of residence, and parental age at delivery. Our study of a well-defined, homogenous sample suggested that prevalence of isolated ITEV in Iowa was similar to that reported in other population-based studies and provided support for some, but not all, previously reported associations with infant and parental characteristics. More detailed, longitudinal studies of isolated ITEV are recommended.

Keywords

clubfoot; epidemiology; pregnancy; prevalence; risk factors; smoking

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INTRODUCTION

Congenital idiopathic talipes equinovarus (ITEV), also known as clubfoot, is a well-recognized foot deformity estimated to affect approximately 1 in 1,000 live births [Chung et al., 1969]. ITEV is characterized by adduction of the forefoot and midfoot, adduction (varus) of the heel or hind foot, and a fixed plantar flexion (equinus) of the ankle [Miedzybrodzka, 2003]. Approximately one-half of cases present with bilateral deformity; unilateral cases are predominantly right-sided [Roye and Roye, 2002].

ITEV is commonly associated with joint laxity, congenital dislocation of the hip, tibial torsion, oligodactyly, and a family history of other foot anomalies [Wynne-Davies, 1964]. Treatment of ITEV often includes multiple serial castings or splintings; surgery is used when non-surgical procedures fail [Roye et al., 2004]. The success rates for treatments vary greatly by ITEV severity and procedure used [Harrold and Walker, 1983]. Complications of treatments include pressure sores, fractures, scarring, and iatrogenic injuries during surgery [Laaveg and Ponseti, 1980; Crawford and Gupta, 1996].

Descriptive data reported for ITEV have repeatedly shown an excess among males [Chung et al., 1969; Roye and Roye, 2002; Carey et al., 2005; Carney and Coburn, 2005; Krogsgaard et al., 2006] and among Hawaiians and Maoris [Stewart, 1951; Morton et al., 1967; Chung et al., 1969]. Inconsistent associations have been reported for infant birth weight [Chung et al., 1969; Byron-Scott et al., 2005; Carey et al., 2005] and month of birth [Pryor et al., 1991; Lochmiller et al., 1998; Barker and Macnicol, 2002; Carey et al., 2005]; a slightly higher proportion of breech deliveries have been reported among ITEV cases [Lochmiller et al., 1998]. Inconsistent associations have also been reported for maternal age, education, and parity [Honein et al., 2000; Skelly et al., 2002; Carey et al., 2005; Moorthi et al., 2005; Dickinson et al., 2008]; several studies have reported a positive association for maternal smoking during pregnancy [Van den Eeden et al., 1990; Alderman et al., 1991; Cornel et al., 1996; Reefhuis et al., 1998; Honein et al., 2000; Skelly et al., 2002; Dickinson et al., 2008]. No consistent associations have been identified between paternal risk factors and ITEV [Savitz et al., 1991; Olshan et al., 2003].

The equivocal results from previously published studies might be due to differences in study methodology. In particular, diagnostic specificity can be limited when non-orthopedic providers assign ITEV case definitions [Byron-Scott et al., 2005]. Also, population-based studies with electronic data linkage to medical or birth records have presented more consistent prevalence and risk estimates for ITEV compared to hospital-based studies. Additionally, prevalence estimates for ITEV have varied by geographic location and racial and ethnic characteristics with estimates among far easterners (Maoris and Polynesians) [Hanify et al., 1980; Boo and Ong, 1990], native Hawaiians [Chung et al., 1969], and South African blacks [Pompe van Meerdervoort, 1976] found to consistently differ from those for Caucasians.

The objectives of our study were to estimate prevalence and describe the epidemiology of ITEV in a Midwestern U.S. population-based sample using data collected from an active, population-based surveillance system and to compare the prevalence to published estimates.

To address methodologic limitations in existing studies, we have uniquely restricted our sample to live, singleton full-term births with a confirmed diagnosis of isolated ITEV.

METHODS

The Iowa Registry for Congenital and Inherited Disorders (IRCID) is an active, population-based surveillance system which ascertains pregnancies (live births, stillbirths, and elective terminations) diagnosed with a birth defect among Iowa residents. The IRCID conducts surveillance on over 38,000 births annually. Surveillance activities conducted by the IRCID are governed by Iowa state law, which specifies that a birth defect is a reportable condition in Iowa [State Legislative Code 641-1.3(139A)].

Subject Selection

IRCID records showed 708 clubfoot deliveries from January 1, 1997 through December 31, 2005. Of these, 257 were classified as ITEV (Centers for Disease Control/British Pediatric Association [CDC/ BPA] classification code 754.50), and 451 were classified as club-foot—not otherwise specified (NOS) (CDC/BPA classification code 754.73). Using multiple criteria, including a history of surgical repair or splinting, the 451 clubfoot—NOS deliveries were further reviewed by an orthopedic surgeon and co-author (J.A.M.), and 374 were reclassified as ITEV. From the 631 (257 +374) ITEV deliveries identified, those diagnosed with a known chromosomal or single gene etiology (e.g., trisomy, chromosomal deletion syndrome, arthrogryposis) or at least one other major structural birth defect in a separate organ system (e.g., spina bifida, cleft lip) (n =230), or with a pregnancy outcome of stillbirth or elective termination (n =4) were excluded. To increase case homogeneity, multiple births (n =18) were also excluded. To control for over-adjustment due to interdependence between gestational age at birth and infant birth weight, preterm births (<37 weeks gestation) (n =32) were also excluded. These exclusions produced a final sample of 347 isolated, live, singleton full-term ITEV births. The comparison sample of 304,308 was comprised of all Iowa live births during the study period (n =340,649) minus multiple (n =11,365) and pre-term births (n =24,976).

Subject Characteristics

Eligible births were linked to birth certificates provided by the Iowa Department of Public Health. Information on infant (sex, birth weight, month of birth, and fetal presentation), maternal (age at delivery, race/ethnicity, education, parity, history of diabetes, trimester at which prenatal care was initiated, smoking during pregnancy and area of residence), and paternal (age at delivery) characteristics was obtained. Maternal area of residence at delivery was further defined using the Rural-Urban Commuting Area (RUCA) (version 1.11) codes [Hart et al., 2005], and were classified into four tiers of residential groups: urban city, large rural town or city, small rural town or city, and isolated small rural town. For our study, RUCA codes were primarily determined using zip codes. When zip codes were missing, Federal Information Processing Standard codes were used to determine the zip code and the corresponding RUCA code.

Statistical Analyses

The prevalence for isolated, live, singleton full-term ITEV was calculated per 10,000 live, singleton full-term births for each year from 1997 through 2005. Both crude and adjusted prevalence odds ratios (POR)s and corresponding 95% confidence intervals (CI)s were estimated using logistic regression. Covariates included in the multivariable logistic regression models were selected if a statistically significant bivariate association ($p < 0.05$) was identified between the variable and ITEV or if a covariate was shown to be associated with ITEV in previous studies. Variables identified as covariates were infant sex and birth weight and maternal age at delivery, education, and smoking during pregnancy. All analyses were conducted using SAS (version 9.2; SAS Institute, Cary, NC).

RESULTS

From 1997 through 2005, 304,308 unaffected live, singleton full-term births and 347 isolated, live, singleton full-term ITEV births were identified. Of the ITEV births, 184 (53%) were unilateral (106 right-sided, 77 left-sided, 1 unreported) and 158 (46%) were bilateral with the remaining 5 (1%) of unknown laterality. No statistically significant differences for laterality were identified between males and females (data not shown).

During the 9-year time period, the prevalence estimate for isolated ITEV was 11.4 per 10,000 live, singleton full-term births (95% CI = 10.3, 12.6) with no significant variation in prevalence between the birth years ($p = 0.40$). The unadjusted POR for males was nearly twice that for females (Table I). The POR for deliveries less than 2,500 g was elevated, but non-significant, compared to deliveries of 2,500–3,500 g. Using “spring” births (i.e., conception months June–August) as the reference group, PORs for “summer” and “fall” births were weakly, but non-significantly, elevated. Breech presentation showed a decreased POR, although the estimate was based on a small number of deliveries.

Among maternal characteristics, maternal age of 35 years or older at delivery was associated with a significantly decreased POR compared to mothers 20–34 years of age. Conversely, a significantly increased POR was found for infants born to mothers who smoked during pregnancy versus those born to non-smoking mothers. Additionally, weak but non-significant elevation in PORs were found for mothers with less than a high school education compared to those with a high school education or higher and for mothers who initiated prenatal care in the second or third trimester rather than the first trimester. PORs for the remainder of maternal characteristics, including area of residence determined by RUCA codes, and paternal age tended to be near or below unity.

Values for adjusted PORs of selected infant and maternal characteristics tended to reflect the unadjusted values with a reduced estimate for older mothers and elevated estimates for males, low birth weight deliveries, lower educated mothers, and mothers who smoked during pregnancy (Table II). For infant birth weight, stratification by infant sex and adjustment for the maternal characteristics produced an elevated POR for low birth weight females (POR = 3.2; 95% CI = 1.5, 6.9), but not males (POR = 0.9; 95% CI = 0.3, 2.8). PORs for each maternal characteristic did not appreciably differ when stratified by infant sex and adjusted for infant birth weight and the remainder of maternal characteristics (data not shown).

DISCUSSION

The prevalence of isolated ITEV in this 9-year population-based Midwestern sample was 11.4 per 10,000 live, singleton full-term births. Approximately one-half of all ITEV births were bilateral; unilateral births tended to be right-sided. Both crude and adjusted analyses supported an excess risk of isolated ITEV among all males, low birth weight females, and among infants born to mothers who reportedly smoked during pregnancy. A reduced, crude prevalence of isolated ITEV was found among mothers 35 years or older, which was attenuated in adjusted analyses. No significant associations were noted for season of birth and fetal presentation; maternal race/ ethnicity, parity, diabetes during pregnancy, trimester at which prenatal care was initiated, and area of residence; or paternal age.

Our prevalence estimate was somewhat higher than that reported in a population-based prevalence study on isolated ITEV among live, singleton births in Texas [Moorthi et al., 2005], comparable to those reported in population-based studies in Australia [Byron-Scott et al., 2005; Carey et al., 2005] and Denmark [Krogsgaard et al., 2006] that did not restrict isolated cases to ITEV, and somewhat lower than that reported in a multi-state population-based study that did not restrict cases to isolated ITEV or singleton births [Parker et al., 2009]. This latter study included a subset of births from Iowa (birth years 2001–2005), but the methodological differences between studies could account for the difference in prevalence estimates. In addition, each ITEV birth included in the current study had diagnostic confirmation of clubfoot NOS as ITEV by an orthopedic surgeon.

Among published population-based studies of isolated ITEV [Skelly et al. 2002; Moorthi et al., 2005], isolated congenital TEV [Alderman et al., 1991; Byron-Scott et al., 2005], or isolated TEV/ clubfoot NOS [Honein et al., 2000; Carey et al., 2005; Krogsgaard et al., 2006; Dickinson et al., 2008], our findings of male excess and right-sided predominance were consistent with those previously reported [Skelly et al., 2002; Moorthi et al., 2005]. The increased POR among low birth weight females was observed for extreme low birth weight (<999 g) in crude but not adjusted estimates in one study of isolated congenital TEV [Byron-Scott et al., 2005]. The lack of an association between increased birth weight and ITEV in our sample was consistent with previous findings for isolated congenital TEV [Byron-Scott et al., 2005; Carey et al., 2005], as was the finding of no association with breech births [Alderman et al., 1991; Carey et al., 2005]. One study of isolated congenital TEV examined season of birth and supported our finding of no association [Alderman et al., 1991].

Consistent with some previous population-based studies that examined isolated ITEV [Skelly et al., 2002], isolated congenital TEV [Alderman et al., 1991], or isolated TEV/ clubfoot NOS [Honein et al., 2000; Dickinson et al., 2008], a significantly increased POR was found among infants of mothers who reportedly smoked during pregnancy. Our findings of no differences in PORs with respect to maternal age at delivery supported most [Alderman et al., 1991; Honein et al., 2000; Byron-Scott et al., 2005; Carey et al., 2005; Moorthi et al., 2005], but not all [Dickinson et al., 2008] studies. The increased POR among infants born to high school graduates was consistent with one study [Moorthi et al., 2005]. No significant differences were noted in the PORs between non-Hispanic whites and other

racial/ethnic groups supporting one previous study [Moorthi et al. 2005], but not another [Dickinson et al., 2008].

Our study was largely limited to selected non-inherited risk factors for isolated ITEV, as it was primarily a surveillance-based study. Exclusion of stillbirths and elective terminations may have underestimated the prevalence of isolated ITEV; however, this effect was thought to be small due to the rarity of non-live born isolated ITEV deliveries identified in Iowa. Likewise, restriction of births to singleton births may have underestimated prevalence; however, the percentage of isolated ITEV involving multiple births was low and equivalent to that observed among all Iowa non-ITEV live births. Another potential limitation is that Iowa is comprised of predominantly non-Hispanic whites; thus, our prevalence rates do not generalize to other racial/ethnic groups. Also, maternal smoking exposure was obtained from birth certificates; however, the reported smoking rates in our study were slightly lower than maternal interview reports in another population-based study of isolated ITEV [Honein et al., 2000], but higher than ITEV studies that used smoking status collected from birth certificates and questionnaires [Tong et al., 2009]. Lastly, a large proportion of birth certificates lacked information on the biological father, which limited analysis of the relation between paternal characteristics and isolated ITEV.

This study had several strengths. The IRCID used multi-source, active, population-based surveillance to identify ITEV deliveries, and each diagnosis was confirmed by medical geneticists, thereby improving ascertainment and classification. Also, difficulties with interpretation of etiology in mixed samples of isolated and syndromic ITEV were minimized by inclusion of only isolated, live, singleton full-term births. Additionally, we were able to examine the role of urban and rural residence during pregnancy by categorizing maternal residential postal codes using the RUCA classification system.

In conclusion, the prevalence of isolated ITEV in Iowa was similar to that reported in other population-based prevalence estimates published to date. Given the variation in case inclusion criteria between previous studies and the current study, support for some, but not all, reported associations with infant and parental characteristics were found. Continued investigation of these characteristics in larger, but similarly well-defined population samples of isolated ITEV is recommended to further explore subgroups of infants (e.g., low birth weight females) at increased risk for ITEV.

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Prevalence per 10,000 and Prevalence Odds Ratios for Selected Infant and Parental Characteristics of Isolated, Live, Singleton Full-term Idiopathic Talipes Equinovarus Births, Iowa 1997–2005

TABLE I

Characteristics	ITEV births (n =347)		Iowa births (n =304,308)		Prevalence per 10,000	POR (95% CI)
	No. ^a	%	No. ^a	%		
Infant						
Sex						
Female	120	34.6	148,993	49.0	8.1	Reference
Male	227	65.4	155,315	51.0	14.6	1.8 (1.5, 2.3)
Birth weight (g)						
<2,500	10	2.9	4,907	1.6	20.4	1.8 (0.9, 3.3)
2,500–3,500	181	52.2	155,003	51.0	11.7	Reference
>3,500	156	44.9	144,342	47.4	10.8	0.9 (0.8, 1.1)
Season of birth						
Summer (June–August)	101	29.1	79,250	26.0	12.7	1.3 (0.9, 1.7)
Fall (September–November)	102	29.4	76,186	25.0	13.4	1.3 (1.0, 1.8)
Winter (December–February)	71	20.5	76,211	25.1	9.3	Reference
Spring (March–May)	73	21.0	72,661	23.9	10.1	0.9 (0.7, 1.3)
Fetal presentation						
Cephalic	337	97.4	290,387	95.6	11.6	Reference
Breech	9	2.6	13,312	4.4	6.8	0.6 (0.3, 1.1)
Maternal						
Age at delivery (years)						
<20	30	8.7	29,111	9.6	10.3	0.9 (0.6, 1.3)
20–34	293	84.4	243,125	79.9	12.1	Reference
35	24	6.9	32,048	10.5	7.5	0.6 (0.4, 0.9)
Race/ethnicity						
Non-Hispanic White	301	87.5	265,705	87.9	11.3	Reference
Non-Hispanic Other	19	5.5	18,257	6.0	10.4	1.2 (0.8, 1.7)
Hispanic	24	7.0	18,493	6.1	13.0	0.9 (0.6, 1.5)
Education (years)						

Characteristics	ITEV births (n =347)		Iowa births (n =304,308)		Prevalence per 10,000	POR (95% CI)
	No. ^a	%	No. ^a	%		
<12	62	17.9	43,136	14.3	14.4	1.3 (1.0, 1.7)
12 or more	285	82.1	258,798	85.7	11.0	Reference
Parity						
0	149	42.9	117,571	61.3	12.7	Reference
1 or more	198	57.1	186,565	38.7	10.6	0.8 (0.7, 1.0)
History of diabetes						
No	338	97.4	292,859	96.4	11.5	Reference
Yes	9	2.6	10,820	3.6	8.3	0.7 (0.4, 1.4)
Prenatal care initiation						
First trimester	300	87.0	266,221	88.5	11.3	Reference
Second/third trimester	45	13.0	34,509	11.5	13.0	1.2 (0.9, 1.6)
Smoking during pregnancy						
No	263	76.0	249,906	82.8	10.5	Reference
Yes	83	24.0	51,737	17.2	16.0	1.5 (1.2, 2.0)
Area of residence						
Urban	189	55.9	165,953	55.7	11.4	Reference
Large rural town/city	49	14.5	40,897	13.7	11.9	1.0 (0.8, 1.4)
Small rural town	51	15.1	48,355	16.2	10.6	0.9 (0.7, 1.3)
Isolated small rural town	49	14.5	42,573	14.3	11.5	1.0 (0.8, 1.4)
Paternal						
Age at delivery (years)						
<35	240	79.5	208,537	78.5	11.5	Reference
35	62	20.5	57,000	21.5	10.9	1.0 (0.7, 1.3)

POR, prevalence odds ratio; ITEV, idiopathic talipes equinovarus; CI, confidence interval.

^aFrequencies of ITEV births and Iowa births may not total 347 and 304,308, respectively, due to missing responses.

TABLE II

Adjusted Prevalence Odds Ratios for Isolated, Live Singleton Full-term Idiopathic Talipes Equinovarus Births, Iowa 1997–2005

Characteristics	ITEV births (n =347) ^a	Iowa births (n =304,308) ^a	aPOR (95% CI) ^b
Infant			
Sex			
Female	120	148,993	Reference
Male	227	155,315	1.8 (1.5, 2.3)
Birth weight (g)			
<2,500	10	4,907	1.8 (0.9, 3.3)
2,500–3,500	181	155,003	Reference
>3,500	156	144,342	0.9 (0.7, 1.1)
Maternal			
Age at delivery (years)			
<20	30	29,111	0.7 (0.5, 1.1)
20–34	293	243,125	Reference
35	24	32,048	0.6 (0.4, 1.0)
Education (years)			
<12	62	43,136	1.4 (1.0, 1.8)
12 or more	285	258,798	Reference
Smoking during pregnancy			
No	263	249,906	Reference
Yes	83	51,737	1.5 (1.2, 1.9)

aPOR, adjusted prevalence odds ratio; ITEV, idiopathic talipes equinovarus; CI, confidence interval.

^aFrequencies of ITEV births and Iowa births may not total 347 and 304,308, respectively, due to missing responses.

^bEach variable adjusted for all other variables in the table.