DESCRIPTIVE EPIDEMIOLOGY OF CLUBFOOT IN VIETNAM: A CLINIC-BASED STUDY

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ABSTRACT

The prevalence of congenital talipes equinovarus (clubfoot) in Vietnam is estimated to be approximately one in 1000 births. To date, no epidemiological studies have been conducted in this country to assess risk factors associated with this deformity. The purpose of this study was to evaluate specific environmental and socioeconomic factors that may increase the risk of an infant being born with clubfoot. A descriptive clinic-based study was conducted using structured questionnaires given to biological mothers of clinically confirmed clubfoot subjects (n=99) and biological mothers of children between ages 0-18 with no first or second degree family history of clubfoot as controls (n=97). Phenotypic data from clubfoot subjects was also collected. We found that males were twice as likely to have clubfoot and half of clubfoot subjects were affected bilaterally. There was no significant difference in the rate of left versus right clubfoot. Infant and maternal characteristics showing a strong association with clubfoot included breech presentation at birth (p=0.026) and young maternal age (p=0.033). Although there were no strong correlations with any sociodemographic paternal characteristics, a higher percentage of case fathers were younger at the age of conception compared to control fathers. The information from this preliminary study provides a framework for future epidemiologic studies in this population. An understanding of the risk factors associated with clubfoot will play an important role in understanding the pathophysiology of this disabling deformity.

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INTRODUCTION

Congenital talipes equinovarus (clubfoot) is a birth defect characterized by atrophy of the calf muscles and equinus of the ankle, varus of the hindfoot, cavus and adductus of the forefoot[1]. The defect can be associated with a neuromuscular disorder or a generalized syndrome such as spina bifida, arthrogryposis, or dystrophic dwarfism, but most clubfeet are isolated and idiopathic[2]. The severity of the deformity is variable, ranging from mild to extremely rigid foot, and correction usually requires serial manipulation and castings followed by surgical procedures for the rare resistant cases. The prevalence of congenital clubfoot is approximately one in every 1000 live births[3-6]. Numerous studies have reported different birth prevalences between racial and ethnic groups with 0.39 cases per 1000 live births among Chinese populations, 0.76 per 1000 live births in Hispanic populations, 1.12 per 1000 live births among white populations, and 6.8 per 1000 live births among Polynesion populations[6-8]. In Vietnam, the prevalence of clubfoot is estimated to be one per 1000 births[9].

Despite extensive epidemiological, clinical, and basic science research, the etiology and pathogenesis of clubfoot remains unknown. Multiple studies have proposed certain risk factors to be associated with clubfoot, including male gender[5, 10, 11], maternal smoking[10-16], maternal age[12], maternal marital status[11, 12], parity[12, 13], maternal education [10, 12, 13] and maternal diabetes [10, 12]. As of today, no epidemiological studies regarding congenital clubfoot have been conducted in the Asian population.

This study attempts to describe any specific factors that may be associated with increased risk of an infant being born with idiopathic clubfoot in Vietnam. Understanding interactions of specific factors will allow educational approaches to avoid them and provide a better understanding of the etiology and pathophysiology of this deformity.

MATERIALS AND METHODS

The proposal for this study was approved through the University of Iowa Institutional Review Board. After the study was explained in detail, interviewee consent was given verbally before questionnaires were collected. Structured questionnaires were used in this study to evaluate the rate of specific risk factors possibly associated with idiopathic clubfoot.

TABLE 1
Descriptive Statistics of Cases

Phenotypic Characteristics	Cases (n=99)
Gender	
Male	62 (63%)
Female	33 (33%)
Missing	4 (4%)
Laterality	
Bilateral	51 (52%)
Unilateral	45 (45%)
Left	20 (44%)
Right	22 (49%)
Missing	3(7%)
Missing	3(3%)

Questionnaires were given to cases and controls. Cases were biological mothers of live, singleton births with physician confirmed diagnosis of idiopathic clubfoot. Controls included a cluster sample of biological mothers of children between the ages of 0-18 who do not have a first or second-degree family history of congenital clubfoot and no other congenital abnormalities. The questionnaire asked for specific infant information including gestational age, birth weight, and birth month. Maternal and pregnancy information collected included age at conception, mode of delivery, presence of breech presentation, smoking history, education, and diabetes. Information collected about the biological father included age at the time of conception and smoking history. Clubfoot phenotype including laterality of the defect and infant sex was collected as well.

Because a strict birth-registry is not currently in place in Vietnam, the cohort for this case-control study was hospital-based. Collaborations with Dr. Huynh Manh Nhi and Dr. Vo Quang Nam, orthopaedic surgeons in Ho Chi Minh City (Vietnam's largest metropolis), specializing in the care of clubfoot patients, provided us with access to their clubfoot patient lists. Additional clubfoot patient lists were compiled through extensive networking with other orthopaedic surgeons throughout major cities in Southern Vietnam. The biological mothers of these patients were informed about this study by their physician and were asked to bring their child back to the clinic for a follow-up visit at which time questionnaires were collected by a medical student fluent in Vietnamese and English. Questionnaires for controls were collected in pediatric departments of two major hospitals in Ho Chi Minh City. Recruitment of subjects and collection of questionnaires occurred within a 10-week period.

Statistical Analysis

Cochran-Mantel-Haenszel Statistics was used to determine association between particular risk factors and clubfoot. *P*-values <0.05 indicate statistical significant associations.

RESULTS

Ninety-nine biological mothers of clubfoot and 97 mothers of non-clubfoot children were enrolled and phenotypic data was collected from 99 clubfoot cases.

Phenotypic data of all the clubfoot cases is shown in Table 1. Sixty-three percent of all clubfoot cases were males and 33% were females. There was no significant difference in the proportion of bilateral vs. unilateral clubfoot (53% bilateral and 47% unilateral) within all cases. No significant difference was seen in the proportion of bilateral vs. unilateral clubfoot within male cases (52% bilateral, 49% unilateral) or within female cases (58% bilateral, 42% unilateral) (data not shown). Of the 45 unilateral clubfoot cases, 20 (44%) had left clubfoot and 22 (49%) had right clubfoot (missing data for 3 cases).

Descriptive statistics describing possible risk factors associated with clubfoot are presented in Table 2. There was no association with infant characteristics (gestational age and birth weight) and clubfoot. Eleven percent of clubfoot cases did not have full-term births (<37 weeks gestational age) compared to 7% of controls. Nine percent of clubfoot cases were born less than 2500 grams compared to 4% of controls. However, breech presentation did show a strong association with clubfoot: 9% of clubfoot cases were born breech compared to only 2% of controls, corresponding to a p value of 0.026. We found no seasonal variation associated with increasing risk for clubfoot. Forty-seven percent of both cases and controls were born between November-April and 48% of cases were born between May-October vs. 49% of controls.

The socio-demographic maternal characteristic that showed significant association with clubfoot was maternal age at conception: 35% of case mothers were <25 years old compared to only 18% of control mothers. 46% of case mothers were between the ages of 25-34, and 8% were 35 or older when they conceived a baby with clubfoot compared to 58% and 15% of control mothers, respectively (p=0.033). The percentages of maternal smoking, diabetes, and education were similar between cases and controls. Socio-demographic paternal characteristics did not show strong associations with clubfoot, although a higher percentage of case fathers were younger than 25 years old at the time of conception compared to control fathers (9% and 3%, respectively). 55% of case fathers were between the ages of 25 and 34, and 23% were 35 years or older compared to 56% and 32% of control fathers, respectively. 62% of case fathers and control fathers reported a history of smoking.

DISCUSSION

Congenital idiopathic clubfoot is the most common musculoskeletal deformity affecting 1 to 7/1000 newborns[3, 6, 7, 17-27]. Although it is a well-recognized foot

TABLE 2
Descriptive Statistics of Cases and Controls

Demographic Characteristics	Cases (n=99)	Controls (n=97)
Gestational Age		
<37 weeks	11 (11%)	7 (7%)
37+ weeks	84 (85%)	90 (93%)
Missing	4 (4%)	0
Birth Weight (grams)		
<2500	9 (9%)	4 (4%)
2500-3500+	86 (87%)	92 (95%)
Missing	4(4%)	1 (1%)
Birth Month		
Nov-Apr	47 (47%)	47 (47%)
May-Oct	48 (48%)	49 (49%)
Missing	4 (4%)	1 (1%)
Breech Presentation (p= 0.026)		
Yes	9 (9%)	2 (2%)
No	84 (85%)	94 (97%)
Missing	6(6%)	1 (1%)
Maternal Age at Conception (p=0.033)		
<25	33 (35%)	17 (18%)
25-34	46 (46%)	56 (58%)
35+	8 (8%)	15 (15%)
Missing	12(12%)	9 (9%)
Maternal smoking during pregnancy		
Yes	1 (1%)	0
No	96 (97%)	97 (100%)
Missing	2 (2%)	0
Maternal diabetes		
Yes	0	1 (1%)
No	95 (96%)	64 (66%)
Missing	4 (4%)	32 (33%)
Maternal Education (years)		
<12	64 (65%)	60 (62%)
>12	32 (32%)	36 (37%)
Missing	3 (3%)	1 (1%)
Maternal Marital Status		
Married	96 (97%)	97 (100%)
Single	1 (1%)	0
Missing	2 (2%)	0
Paternal age at conception		
<25	9 (9%)	3 (3%)
25-34	54 (55%)	54 (56%)
35+	23 (23%)	31 (32%)
Missing	13 (13%)	9 (9%)
Paternal smoking		
Yes	61 (62%)	60 (62%)
No	28 (28%)	36 37%)
Missing	10 (10%)	1 (1%)

deformity, the etiology and pathophysiology of congenital clubfoot remains unknown. Based on previously published data, there is likely etiologic heterogeneity involving both genetic and environmental influences. The results of our study confirm male sex as a strong risk factor for clubfoot (63% of males compared to 33% of females, n=96)[5, 15]. The proportion of cases with bilateral clubfoot was similar to those previously reported [2]. Prior studies have demonstrated a higher prevalence of right-sided clubfoot[10, 22, 28, 29], however there was no significant difference in the percentage of right unilateral vs. left unilateral clubfoot in our study population (22% right, 20% left). No statistically significant differences for laterality were identified between males and females (data not shown). We did not find associations between low birth weight and preterm birth with clubfoot, contradicting previous reports[10, 12]. We did find, however, a strong association between breech presentation and congenital clubfoot, confirming findings in a previous study[12].

A seasonal variation for the incidence of clubfoot has been reported [30-32]. Pryor et al. reported an increase in the prevalence of clubfoot babies born in the winter quarter, from December to February[31]. Robertson and Corbett reported a significant seasonal variation in clubfoot, with the peak month of conception determined to be in June[32]. Barker and Macnicol reported a seasonal

increased incidence of idiopathic congenital clubfoot in neonates born in March and April[30]. The extrinsic factor of seasonal variation may be linked to increasing incidence of certain infections during specific seasons. In contrast, Lochmiller et al. did not find any seasonal variation in the month of birth of 285 children treated in Texas [22] and Loder et al. also found a lack of seasonal variation in idiopathic clubfoot in industrialized populations [33]. In Vietnam, there are two main seasons: the rainy season from May to September/October and the dry season from October/November to April. Our results did not show any seasonal variation with the births of clubfoot cases and controls.

Many descriptive studies have reported specific socio-demographic characteristics to be associated with an increase in the risk of an infant being born with clubfoot. However, findings among these studies have varied due to differences in methodology or study population. One of the most consistently reported associations with clubfoot is maternal smoking[10-16]. Smoking in Vietnam is strongly sex-linked. A 1997 national prevalence survey found about half of males but just 3.4% of females used tobacco smoke regularly. A study in 2002 by Morrow et al. confirmed that this low prevalence of female smokers is strongly enduring and mainly attributed to its "inappropriateness" [34]. This finding holds true in our study population; of 196 women questioned in our study, only 1 woman reported having a smoking history. Therefore, our results do not confirm the linkage of maternal smoking and congenital clubfoot. However, 62% of fathers with clubfoot children reported a history of smoking thus complicating the interpretation of our results by the addition of likely second hand smoke exposure to these mothers.

Our study also shows young maternal age to be significantly associated with increased risk of clubfoot (35% of case mothers younger than 25 years old compared to 18% of control mothers, p=0.033), confirming findings from several studies including a multistate epidemiologic study of clubfoot [12, 35]. Maternal diabetes, marital status, and education did not show associations with clubfoot within our study population.

CONCLUSIONS

This study supports previously reported findings that males are more commonly affected by clubfoot by a 2:1 ratio and that 50% are affected bilaterally. These findings are virtually unanimous across every study, suggesting a strong genetic association with clubfoot. Our findings also confirm previous research reporting strong associations with breeched presentation and young maternal age. The absence of the association between maternal smoking and clubfoot in our cohort contradicts numerous findings that have shown a strong association. Differences in culture may have led to this disagreement. However, paternal smoking and second hand smoking should be considered in future investigations. These preliminary findings provide a foundation for more sophisticated epidemiologic studies in the Vietnamese population as well as in the general Asian population in the future.

ACKNOWLEDGEMENTS

Funding for research was provided by The Carver College of Medicine Summer Research Fellowship award. The authors would like to thank Dr. Huynh Manh Nhi, Dr. Vo Quang Dinh Nam, Dr. Do Van Thanh, Dr. Nguyen Ba Minh Phuoc, Dr. Pham Dong Doai, Dr. Tran Cong Toai, Dr. Duong Thanh Binh and Dr. Nguyen Thi Phuong Tan for providing their clubfoot patient lists. Special thanks to Dr. Huynh Manh Nhi and Dr. Vo Quang Dinh Nam for their assistance in contacting the other regional doctors.

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