

# Descriptive epidemiology of clubfoot in Romania: a clinic-based study

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**Abstract. – OBJECTIVE:** Congenital clubfoot affects 1 per 1000 live births per year in Romania. To date, no epidemiological studies have been conducted in this country to assess risk factors associated with the deformity. The aim of this study was to evaluate specific environmental and socio-demographic factors that may increase the risk of an infant to be born with clubfoot.

**PATIENTS AND METHODS:** A descriptive clinic-based study over a twelve-week period was conducted using structured questionnaires given to biological parents of clinically confirmed clubfoot and control subjects. 62 parents of probands and 66 parents of control patients were enrolled for risk factor questionnaires. Phenotypic data from clubfoot children was also collected.

**RESULTS:** 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 and old maternal age at conception.

**CONCLUSIONS:** Our results support reported literature data that males are two times as likely to have clubfoot which indicates a genetic influence. Previous reports suggest clubfoot babies are born to young mothers but in Romania advanced maternal age ( $\geq 35$  years) was an indicator which may suggest genetic influence. This clinic-based study does not support previously recorded data of a positive association for maternal or household smoking. Data from this Romanian population also does not support previous data suggesting strong associations with maternal diabetes.

*Key Words:*

Clubfoot, Etiology, Epidemiology, Risk factors.

## Introduction

Congenital talipes equinovarus (clubfoot) is a birth defect characterized by equinus of the an-

kle, varus of the hindfoot, cavus and adductus of the forefoot, and atrophy of the calf muscles<sup>1</sup>. Most clubfeet are isolated and idiopathic, but the deformity can be associated with a neuromuscular disorder or a generalized syndrome such as spina bifida, arthrogryposis, or dystrophic dwarfism<sup>2</sup>.

The incidence of clubfoot is approximately 1 in 1000 live birth per year, being the seventh most common congenital birth defect and the most common of the musculoskeletal system, with the global burden of this birth defect affecting more than 150.000 infants every year<sup>3-5</sup>. Eighty percent of infants born with clubfoot live in developing countries where limited medical knowledge and resources prevent them from receiving adequate care. Considering that up to fifty percent of those who are affected have bilateral clubfoot, it becomes evident that neglected clubfoot is a very common physical disability worldwide<sup>6,7</sup>.

Currently the etiology and pathogenesis of clubfoot remains unknown despite in depth epidemiological, clinical, and basic science research. While clubfoot is considered to have a multifactorial origin, data from recent studies implies a major genetic influence<sup>8</sup>. Additional studies have suggested specific risk factors to be associated with clubfoot such as male gender<sup>9-11</sup>, maternal smoking<sup>4,10-14</sup>, maternal age<sup>12</sup>, maternal marital status<sup>11,12</sup>, maternal education<sup>4,10,12</sup>, and maternal diabetes<sup>10,12</sup>. As of today, no epidemiological studies concerning congenital clubfoot have been conducted in Romania.

This study was designed to describe any specific factors that may be associated with increased risk of an infant being born with idiopathic clubfoot in Romania. A greater understanding of specific genetic components and risk factors will play an important role in understanding the pathogenesis of this deformity, ultimately

allowing new insights in avoiding risk factors through education and offering specific targeted therapies.

### Patients and Methods

The proposal for this study was approved through our institutions review board. The study was explained in detail to the parents of each patient and then written consent was acquired for the risk factor questionnaire completion. Subjects aged 0 to 6 years old needed only parental consent, subjects 7 to 12 years old gave written assent, and subjects 13 to 18 years old co-signed a written consent with their parents.

The inclusion criteria for risk factor questionnaires collection were: (1) patients with a pediatric orthopedic surgeon confirmed diagnosis of idiopathic clubfoot and their biological parents/relatives; (2) healthy control patient volunteers who do not have a family history of clubfoot and their biological parents/relatives.

This study utilized a structured questionnaire to describe specific risk factors that could be associated with clubfoot. The questionnaire was conducted in Romanian with a biological parent. It asked for specific information about the infant, details about the pregnancy, and details about both maternal and paternal characteristics. Information regarding the patient included gestation age, sex, birth weight and birth month. For those with clubfoot laterality and family history were also recorded. Information regarding the mother and her pregnancy included age at conception, mode of delivery, presence of breech presentation, smoking history, education and diabetes. Finally, information recorded about the biological father included age at time of conception, military service history and smoking history.

Because a strict birth-registry is not currently in place in Romania, the cohort for this case-control study was hospital based. The patients were recruited from two pediatric orthopedic hospitals from major cities in Romania: Cluj-Napoca and Bucharest, and also from the patients who attended the Ponseti Workshop in Cluj. The population of controls included patients receiving treatment in the pediatric orthopedic outpatient clinics who did not have a diagnosis of idiopathic clubfoot. Additionally, the controls did not have a first- or second-degree family of clubfoot or any other congenital disorders. Recruitment of subjects and the collection of the questionnaires occurred over a 12-week period.

### Statistical Analysis

The data were recorded in Romanian, translated into English, and analyzed with EpiInfo version 7 (Centers for Disease Control and Prevention, Atlanta, USA), using a Student's *t*-test. A *p*-value of < 0.05 indicated a statistically significant association.

### Results

Sixty-two biological parents of clubfoot and 66 parents of control patients were enrolled for the risk factor questionnaires and phenotypic data was collected from 62 clubfoot patients.

Phenotypic characteristics specific to clubfoot patients are shown in Table I. Of all clubfoot cases, 65% were males and 35% were females. This difference corresponds with a *p*-value of 0.0008. Forty-two percent of the cases presented bilaterally while 58% presented unilaterally, which implies no significant difference in proportion. Of the 30 unilateral clubfoot cases, 43% had left clubfoot and 57% had right clubfoot. Finally, 6% of the cases reported known family history of clubfoot.

**Table I.** Descriptive statistics of clubfoot cases.

Phenotypic characteristics		Cases (n = 62)	<i>p</i> -value
Gender	Male	40 (65%)	–
	Female	22 (35%)	0.0008
Laterality	Bilateral	32 (52%)	–
	Unilateral	30 (48%)	> 0.05
	Left	13 (43%)	–
	Right	17 (57%)	> 0.05
Known Family History	Yes	4 (6%)	–
	No	58 (94%)	> 0.05

Table II contains the statistics describing possible risk factors associated with clubfoot. Seventy-seven percent of the clubfoot children had full-term births compared to 82% of controls and 90% of clubfoot patients were born > 2500 grams compared to 85% of controls. Neither of these infant characteristics showed an association with clubfoot. There was also no association found between clubfoot and season of birth. Fifty-six percent of clubfoot patients were born in the fall and winter months (September-February) compared with 60% of control patients. Of clubfoot patients 16% were breech versus 5% of control subjects which indicates a strong association between clubfoot and breech presentation. This data corresponds with a *p*-value of 0.031. Forty-six percent of clubfoot subjects were delivered by Caesarean section compared to 24% of control subjects which also

indicated a strong association and corresponds to a *p*-value of 0.0076.

Of socio-demographic maternal characteristics measured by the study, maternal age at conception was statistically associated with clubfoot. While 18% of mothers of clubfoot patients were older than 35 years at conception, only 6% of control mothers were of old maternal age, corresponding to a *p*-value of 0.040. The percentages of the other maternal socio-demographic characteristics were similar between clubfoot and control populations: maternal smoking (32% clubfoot cases vs. 21% control cases), maternal diabetes (2 mothers in control group compared to null in clubfoot group), nulligravida before conception of subject, and education level less than or equivalent to a high school degree (53% clubfoot cases vs. 52% control cases). Socio-demographic paternal characteristics did not show

**Table II.** Descriptive statistics of clubfoot cases and controls.

Demographic characteristics		Clubfoot (n = 62)	Controls (n = 66)	<i>p</i> -value
Gestational age	< 37 weeks	14 (23%)		–
	37+ weeks	48 (77%)		> 0.05
	Missing	0		
Birth weight (grams)	0-2500	5 (8%)		–
	> 2500	56 (90%)		> 0.05
	Missing	1 (2%)		
Birth month	Sept-Feb	35 (56%)		–
	Mar-Aug	27 (44%)		> 0.05
	Missing	0		
Breech presentation	Yes	10 (16%)		0.026
	No	47 (76%)		–
	Missing	5 (8%)		
Maternal age at conception	< 23	8 (13%)		–
	24-34	43 (69%)		–
	35+	11 (18%)		0.040
	Missing	0		
Maternal smoking during pregnancy	Yes	20 (32%)		> 0.05
	No	40 (65%)		–
	Missing	2 (3%)		
Maternal diabetes mellitus	Yes	0		
	No	62 (100%)		
	Missing	0		
Maternal education (years)	≤ 12	33 (53%)		–
	> 12	29 (47%)		> 0.05
	Missing	0		
Maternal marital status	Married	58 (94%)		> 0.05
	Single	4 (6%)		–
	Missing	0		
Paternal age at conception	< 23	1 (2%)		> 0.05
	24-34	40 (64%)		–
	35+	20 (32%)		–
	Missing	1 (2%)		
Household smoking	Yes	15 (24%)		
	No	46 (74%)		–
	Missing	1 (2%)		

strong associations with clubfoot, including smoking, military service and age at conception.

## Discussion

The results of this study support previously reported data in the literature indicating that males are twice as likely as females to be affected by clubfoot (65% of males and 35% of females,  $n=62$ ), indicating that there is a genetic influence for male sex as a strong risk factor for clubfoot<sup>1-3</sup>. Approximately 50% of children had bilateral clubfoot and this also aligns with previously recorded data<sup>2,3,6,7</sup>, however there was no significant difference in the percentage of right vs. left unilateral clubfoot in our study population (57% right, 43% left). Some studies have reported a higher prevalence of right-side clubfoot<sup>10,15-17</sup>.

We found no significant associations between clubfoot and low birth weight (< 2500 g) or pre-term birth (< 37 weeks), both of which have been shown to have associations with clubfoot in previous studies<sup>10,12</sup>. A seasonal variation for the incidence of clubfoot has been reported<sup>3,18-20</sup>. Pryor et al<sup>19</sup> and Palma et al<sup>3</sup> reported an increase in the prevalence of clubfoot children born in the winter quarter. Robertson and Corbett<sup>20</sup> reported a significant seasonal variation in clubfoot, with a peak month of conception determined to be in June. Barker and Macnicol<sup>18</sup> reported a seasonal increased incidence of idiopathic congenital clubfoot in children born in March and April. In contrast, Lochmiller et al<sup>15</sup> did not find any seasonal variation in the month of birth of 285 children treated in Texas and Loder et al<sup>21</sup> also did not find seasonal variation in clubfoot in industrialized populations. Our results did not show any seasonal variation with the births of clubfoot cases and controls.

Previous data<sup>2,12</sup> support the association between breech presentation and clubfoot. On the other hand, Palma et al<sup>3</sup> did not find any association between clubfoot and breech presentation in the Peru-born clubfoot children. Our study did find a significant association between breech position and clubfoot and between Caesarean section delivery and clubfoot. This is likely an issue of patient care and may indicate that physicians are likely to elect for a Caesarean section if they are aware of a child's clubfoot malformation. We are currently informally surveying Romanian physicians to get their opinion concerning this association.

Many descriptive studies have reported specific socio-demographic factors to be associated with an increase risk of an infant being born with clubfoot. One of the most consistently reported associations with clubfoot is maternal smoking<sup>4,10-14</sup>. According to a 1995 prevalence study<sup>22</sup>, 25% of Romanian females' ages 25 to 44 years old smoke. Our study aligned approximately with this data and found that 21% of control mothers smoked compared to 33% of clubfoot mothers. While there is a slight difference the data did not prove to be statistically significant. Twenty-five percent of both the control and clubfoot mothers reported living in a household with a smoker which would indicate the presence of second hand smoke. These data sets do not support previous hypothesis of second-hand smoke as a risk factor<sup>23</sup>. Data from this Romanian population also does not support previous data suggesting strong associations with maternal diabetes<sup>10,12</sup> and maternal education<sup>4,10,12</sup>.

Palma et al<sup>3</sup> and Nguyen et al<sup>2</sup> reported young maternal age to be a significant risk factor for clubfoot in Peru, and respectively, Vietnam, confirming findings from several studies<sup>12,24</sup>, but in Romania advanced maternal age (more than 35 years old) has been found to be a strong risk factor for clubfoot, that may suggest genetic influence<sup>10</sup>. Maternal marital status and paternal age at conception were not found to have significant association with clubfoot in our study population.

## Conclusions

This study supports previous data stating that males are twice as likely to be affected by clubfoot and approximately 50% of clubfoot patients are affected bilaterally. In our study, there was no significant difference between left and right clubfoot in patients that are unilaterally affected. Many of these findings are reported by numerous studies, suggesting a strong genetic association with clubfoot. Our findings also confirm previous studies reporting associations with breech presentation and Caesarean section. The absence of the association between maternal smoking and clubfoot in our study contradicts numerous studies that have shown a strong association. Differences in culture may have led to this disagreement. In the same time, our data contradicts the association between young maternal age and

clubfoot, suggesting the old maternal age as a risk factor for clubfoot in the Romanian population. These preliminary findings provide the foundation for future epidemiologic studies in the Romanian population.

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### Conflict of Interest

The Authors declare that there are no conflicts of interest.

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