THE JOURNAL OF MATERNAL-FETAL & NEONATAL MEDICINE

http://informahealthcare.com/jmf
ISSN: 1476-7058 (print), 1476-4954 (electronic)

J Matern Fetal Neonatal Med, Early Online: 1–4
© 2014 Informa UK Ltd. DOI: 10.3109/14767058.2014.977861

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ORIGINAL ARTICLE

Prevalence and prenatal ultrasound detection of clubfoot in a non-selected population: an analysis of 549 931 births in Tuscany

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Abstract

Objective: To evaluate the prevalence and prenatal ultrasound detection of clubfoot in Tuscany during a period of 20 years.
Methods: This is a descriptive analysis on data from the Tuscan register of congenital defects, covering a 20-year period from 1992 to 2011. The Tuscan registry of congenital defects is a population-based register for the epidemiologic surveillance of congenital anomalies. The study included all cases of pre- or postnatally diagnosed clubfoot (isolated clubfoot and cases associated with other congenital defects). Overall prevalence and pre-natal detection rates were calculated.
Results: Among the 549 931 deliveries recorded in Tuscany between 1992 and 2011, 858 cases of clubfoot were registered, with a prevalence of 1.56/1000. Seventy-eight percent of cases were isolated. The detection rate was higher when the defect was associated with other anomalies compared to isolated forms. Over the study period, there was a substantial improvement in the prenatal detection of clubfoot (from 11 to 31% overall). For isolated forms, detection rate improved from 4 to 16%, and for cases associated with other congenital defects, it increased from 43 to 73%.
Conclusion: Prevalence of clubfoot in Tuscany is 1.56 per 1000 births, in agreement with the incidence reported in epidemiological studies in Europe. Prenatal detection of clubfoot improved over time. The detection rate was higher in cases associated with other anomalies.

Keywords

Clubfoot, congenital abnormalities, prenatal diagnosis, ultrasound

History

Received 9 April 2014
Accepted 14 October 2014
Published online 11 November 2014

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Introduction

Clubfoot, or talipes equinovarus, is a positional deformity of the fetal foot resulting in the foot being fixed in adduction, supination and varus position. It is characterized by a subluxation of the talo-calcaneo-navicular joint, with under-development of the soft tissues on the medial side of the foot and frequently of the calf and peroneal muscles [1]. It is one of the most common congenital birth defects, with an incidence of approximately one per 1000 newborns [2]. It is almost twice as common in males than in females [3]. The incidence may vary between countries and population, suggesting differences in genetic disposition [4].

The foot development is influenced by many factors, such as neuromuscular conditions, genetic syndromes, aneuploidy, amniotic fluid volume, multiple gestations and hereditary factors [4–6].

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In most cases the defect is isolated and the exact etiology is unknown (idiopathic). In 20% of cases, clubfoot is associated with distal arthrogryposis, congenital myotonic dystrophy, myelomeningocele, amniotic band sequence or other genetic syndromes, such as trisomy 18 or chromosome 22q11 deletion syndrome [7]. In addition, some studies highlight the importance of early limb developmental pathways in clubfoot etiology, as for example the anterior tibial artery hypoplasia present in more than 80% of clubfoot patients though the genetic basis of this abnormality is unknown [8].

Clubfoot can be diagnosed prenatally by ultrasonography. Even if its diagnosis *in utero* has been reported as early as 12 weeks of gestation [9], it is more commonly detected at 19–23 weeks, during the routine second-trimester ultrasound. Overall detection of clubfoot prenatally is reported to be around 60% [9,10].

The objective of our study was to evaluate the prevalence of clubfoot in a non-selected population in Tuscany during 20 years and to study trends in prenatal detection rate over time.

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Materials and methods

This is a descriptive analysis on data from the Tuscan register of congenital defects, covering a 20-year period from January 1992 to December 2011. The Tuscan registry of congenital defects is a population-based register for the epidemiologic surveillance of congenital anomalies.

A detailed description of the registry, method of case ascertainment, data collection and processing is available elsewhere (http://www.eurocat-network.eu/content/Reg-Des-Tuscany.pdf). The study included all cases of pre- or postnatally diagnosed clubfoot (both cases of isolated clubfoot and those associated with other congenital defects). Prenatal diagnosis of clubfoot was based on ultrasound performed by physicians. All cases of clubfoot were confirmed postnatally either through a physical examination by a pediatrician or at autopsy. The study included all deliveries occurred in Tuscany during the study period, including miscarriages, terminations of pregnancy for fetal anomaly (TOPFA) following prenatal diagnosis and intrauterine fetal deaths (FD) of fetuses beyond 16 weeks' gestation.

All cases were coded according to the International Classification of Diseases (ICD) version 9 with 1-digit BPA extension (from 1992 to 2001) or version 10 (from 2002 to 2009) [11,12].

Cases can have one syndrome and/or up to eight malformation codes. The data were extracted from the Tuscan database on the basis of the ICD/BPA codes (754.5, 754.6, 754.7, Q66.0–Q66.8) assigned to cases of clubfoot.

In Tuscany, routine fetal ultrasound examinations are offered to all pregnant women between 10 and 12^{+6}, 19 and 22^{+6}, 30 and 33^{+6} weeks of gestation.

The study period was divided into four 5-year periods: the first period from 1992 to 1996, the second from 1997 to 2001, the third from 2002 to 2006 and the fourth from 2007 to 2011. Prevalence and detection rates were calculated for each period. Prevalence rates were calculated as: number of cases (live births + FD + TOPFA)/number of births (live and stillbirths). The reason why we chose to divide the study period in these four intervals is that during the last 20 years important changes in prenatal diagnosis occurred: first, an increase in the number of women having access to prenatal ultrasound, and second, an improvement in the skills of the examiners and in the ultrasound technology, which led to an increase in the detection rate of fetal anomalies in general.

Results

A total of 549 931 deliveries occurred in Tuscany between 1992 and 2011. Data on prevalence of clubfoot and detection rates are reported in Tables 1 to 3. A total of 858 cases of clubfoot, isolated or associated to other congenital defects, were reported, with a prevalence of 1.56/1000 (Table 1). Prenatal diagnosis was overall made in 168 cases (19.7%) and showed an increase over the years.

Of the 858 cases of clubfoot, 672 (78.3%) were isolated (idiopathic), with a prevalence of 1.22/1000 (Table 2) and a prenatal diagnosis was made in 68 cases of 666 (10.2%) (in six cases the time at which the diagnosis was made was not reported). The other 186 cases were associated with other congenital defects (Table 3), with a prevalence of 0.34/1000 and the prenatal diagnosis was made in 100 cases (53.8%). Of these 186 cases, 33 (3.8% of total cases) were associated with a chromosomal abnormality. The type of abnormality and the outcome is reported in Table 4.

Table 1. Total cases of clubfoot.

Period	Total live births	Cases	Prevalence (on 1000 births)	Prenatal diagnosis	Detection rate**
1992–1996	123 738	211	1.7	24	11.4%
1997–2001	129 710	226	1.74	41	18.3%
2002–2006	142 776	213	1.49	39	18.3%
2007–2011	153 707	208	1.35	64	31.2%
Total	549 931	858*	1.56	168	19.7%

*In seven cases the time at which the diagnosis was made was not reported.
**Percentages are calculated on the total cases with known time of diagnosis.

Table 2. Cases of isolated clubfoot.

Period	Total live births	Cases	Prevalence (on 1000 births)	Prenatal diagnosis	Detection rate**
1992–1996	123 738	169	1.36	6	3.6%
1997–2001	129 710	178	1.37	18	10.3%
2002–2006	142 776	172	1.2	20	11.6%
2007–2011	153 707	153	0.99	24	15.9%
Total	549 931	672*	1.22	68	10.2%

*In six cases the time at which the diagnosis was made was not reported (one in the period 1992–1996, three in the period 1997-2001 and two in the period 2007–2011).
**Percentages are calculated on the total cases with known time of diagnosis.

Table 3. Cases of clubfoot associated with other congenital defects.

Period	Total live births	Cases	Prevalence (on 1000 births)	Prenatal diagnosis	Detection rate**
1992–1996	123 738	42	0.34	18	42.9%
1997–2001	129 710	48	0.37	23	47.9%
2002–2006	142 776	41	0.29	19	46.3%
2007–2011	153 707	55*	0.35	40	72.7%
Total	549 931	186*	0.34	100	54.1%

*In one case the time at which the diagnosis was made was not reported (in the period 2007–2011).
**Percentages are calculated on the total cases with known time of diagnosis.

In order to show the improvement of prenatal diagnosis throughout the years, Tables 1–3 report data grouped by period. The detection rate of clubfoot showed a substantial increase over the study period, from 11.4% in the period 1992–1996 to 31.2% in the period 2007–2011. The increase in the detection rate was observed for both the isolated forms (from 3.6 to 15.9%) and the cases associated with other congenital defects (from 42.9 to 72.7%).

Concerning the period in which the defect was detected, of the 858 cases, 168 had prenatal diagnosis, 634 were diagnosed at birth, 30 in the first week of life, 8 in the first month of life, 5 in the first year of life, 4 were detected after spontaneous abortion and 2 were detected at autopsy. In 7 cases the time of diagnosis was not reported.

Therefore, in a large percentage of cases the diagnosis of clubfoot was performed after birth while less frequently the

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Table 4. Types of chromosomal abnormalities and outcome.

Type	Number of cases	Outcome
Trisomy 18	16	13 TOP 3 Births
Trisomy 21	2	1 live birth 1 stillbirth
Trisomy 13	1	Birth
Turner mosaicism	1	Birth
Trisomy 8	1	Birth
Triplody 69XXX	1	TOP
Chromosome 6 abnormality*	1	TOP
Chromosome 13q deletion: 46,XY,13q-?	1	Birth
Chromosome 18q deletion: 46,XX,del18(q22.2-qter)	1	Birth
Chromosome 4p deletion (4p16.3 Wolf-Hirschhorn syndrome)	1	TOP
Chromosome 5p deletion (Cri du chat syndrome)	1	Birth
Chromosome translocation: t(5,22);(q?;q?)	1	Birth
Ring chromosome 9: 46,XX[79]/46XXr(19) [21]	1	TOP
Complex translocation: 46,XY(1;der1;2;4)(p32;q42;q31;p15.2)	1	TOP
Pericentric inversion of chromosome 9: inv(9)(p?;q?)	1	Birth
Autosome anomaly – not specified	2	1 birth, 1 miscarriage
Total	33	

TOP: termination of pregnancy.
*Exact rearrangement is not available; ? indicates uncertainties or unknown items in karyotype description.

diagnosis was made in the prenatal period, with an overall detection rate of 10.2% for isolated clubfoot and of 54.1% for clubfoot associated with other anomalies.

Discussion

The aim of our study was to perform a detailed analysis of clubfoot prevalence in Tuscany in a 20-year period, and to evaluate the prenatal detection rate of this defect. The prevalence of 1.56 per 1000 pregnancies of this report is in agreement with the incidence of 1.0–1.6/1000 reported in epidemiological studies conducted in different European countries [13–16]. Our data show a trend toward a decrease in the prevalence of this condition over the years, mainly related to the isolated forms. A similar decrease has been described in a recent epidemiological study in Sicily [17]. The exact reason is unknown, and it is probably related to multiple causes, with both genetic and environmental factors playing major role.

Our data showed that prenatal diagnosis of clubfoot in Tuscany has improved over the last 20 years, from 11.4 to 31.2%. The ultrasound diagnosis of isolated clubfoot is less frequent than that of clubfoot associated with other defects, as our data confirmed. However, prenatal diagnosis improved for both forms over the years: from 3.6% in the first five-year period, to 15.9% in recent years for isolated clubfoot and from 42.9 to 72.7% for cases associated with other anomalies. The observed increase in prenatal diagnosis of clubfoot is due to an overall improvement in obstetric ultrasound over the last two decades. The accuracy of prenatal diagnosis is related to several factors, such as the skills of the examiner, the quality of the equipment, gestational age and the methodology used [9]. As previously reported, prenatal detection of this anomaly increases the probability of association with other chromosomal or structural defects. Abnormal karyotypes, such as trisomy 13 and 18 and sex chromosome abnormalities [18–20], and different chromosome rearrangements, associated with hip or other limb abnormalities, ventriculoseptal defects and hypospadias, have been reported [18]. Therefore, the prenatal detection of clubfoot is important because it may lead to the discovery of other associated deformities and chromosome anomalies [9]. At the present moment, the array comparative genomic hybridization (aCGH), a technique enabling high-resolution, genome-wide screening of genomic copy number variations, is the best and faster technique, that also in prenatal diagnosis can identify the genetic causes underlying multiple congenital anomalies [21]. Prenatal counseling regarding prognosis and risk of chromosomal defects should be tailored to clubfoot, and more importantly to the presence/absence of associated anomalies. Irrespective of this condition, clinicians should advise invasive genetic testing if associated anomalies are seen prenatally. In the absence of associated anomalies, prenatal conventional karyotyping is not recommended in cases of clubfoot, although aCGH should be considered.

One limitation of our study is the possibility that some cases of clubfoot were missing, resulting in an underestimation of the true incidence. This is a common limitation of epidemiological studies. However, we think the number of missed cases is very small. Clubfoot diagnosis is easy to make at birth, and practically all children in Tuscany are born in hospital. Loss of information may also be caused by failure to properly record and report the diagnosis. However, the Tuscany Register of Congenital Defects is part of the EUROCAT network, a European network of population-based registries for the surveillance of congenital anomalies, which follows specific guidelines for registration to optimize the accuracy of estimation of prevalence rates and achieve standardization across regions.

A strength of our study is that data are collected from a population-based registry, which is a particularly powerful tool for the evaluation of health services, because it represents the experience of a whole community, not the outcomes of hospital units, which may serve only a selected group of women or children.

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In summary, our results demonstrate an improvement in prenatal diagnosis of clubfoot over the years, in accordance with other studies [9,20]. One obvious explanation for the improved detection rates over the years is the improvement in ultrasound equipment. However, still in the larger percentage of cases the diagnosis of clubfoot is performed after birth: this highlights the importance of continuous teaching and training of ultrasound personnel, in order to detect this defect. Accuracy of prenatal diagnosis of this condition is important in order to exclude any other associated abnormalities.

Declaration of interest

The authors report no conflicts of interest.

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