Congenital talipes equinovarus: A literature review

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ABSTRACT

Congenital talipes equinovarus (CTEV) is a congenital disability characterized by leg deformities in the cavus, adducts, varus, and equinus. The etiology of CTEV is poorly understood, despite its incidence ranging from 0.76 to 3.49 cases per 1000 live births in Indonesia. CTEV involves the fixation of the foot in the adducts, varus, and equinus with concurrent soft tissue anomalies. Despite advances in treatment, disability often persists. Theoretical models have been proposed for neurological, vascular, connective tissue, bone, and muscular causes; however, the currently available data suggests that mild cases are associated with intrauterine position. CTEV’s etiology appears to involve a hereditary component, as its prevalence varies by ethnic group. Genetic factors have been identified in 24–50% of cases, depending on the community studied. Based on a complex segregation analysis, the most plausible inheritance pattern is a single large-effect gene interacting with a polygenic background.

1. Introduction

Congenital talipes equinovarus (CTEV) is a congenital disability characterized by leg deformities in the cavus, adducts, varus, and equinus. The deformity can affect one or both legs [1–3]. CTEV is one of the most common congenital disabilities of the musculoskeletal system [2]. In Indonesia, its incidence ranges from 0.76 to 3.49 cases per 1000 live births [4]. The deformities associated with CTEV cannot resolve independently. Without treatment, they will worsen until adulthood, causing side effects such as pain and long-term dysfunction [5–7].

In Europe, CTEV is twice as common in males compared with females [8]. A family history of CTEV increases the risk of an individual being born with CTEV. Siblings of a CTEV patient have a 2–4% chance of also having CTEV. If both parents and a previous child or other family member have CTEV, the probability of another child having CTEV increases from 10% to 20%. The more family members who have CTEV, the greater the chance that a new family member would be born with CTEV [8,9].

In a study of 346 CTEV neonates and 3029 control births, Honein et al. (2000) discovered a connection between CTEV and maternal smoking during pregnancy. The adjusted odds ratios for smoking alone were 1.34 (95% CI; 1.04, 1.72), 6.52 for only a family history (95% CI; 2.95, 14.41), and 20.30 (95% CI; 7.90, 52.17) for combined maternal smoking and family history. This indicates an interaction between genetic factors and tobacco exposure [6]. Similarly, a systematic review by Hackshaw et al. also identified a relationship between maternal smoking and CTEV (odds ratio 1.28; 95% CI; 1.11–1.48) [10].

Despite most cases of idiopathic CTEV (ICTEV) being delivered breech compared to control births, the majority of ICTEV cases have a cephalic presentation at delivery [6,11]. Pavone et al. (2012) found a pattern of seasonality in ICTEV births in Sicily, observing an increase from January to March and a decline from August to October. This finding warrants further research to determine whether this pattern is present in other populations [12].

The Canadian Early and Mid-Trimester Amniocentesis Trial (CEMAT) found a clear link between ICTEV and early amniocentesis (EA) performed during the first 11–12 weeks of pregnancy, with 1.3% of births within the EA group having CEVT (29/2172). This rate was far higher than the incidence associated with mid-trimester amniocentesis (MA) procedures, which occur during weeks 15–16 (0.1%; 2/2162). Therefore, the EA group experienced a 10-fold increase in ICTEV compared to the MA group. ICTEV was more likely to occur if amniotic
fluid leakage occurred: 15% (9/60) of cases with amniotic leakage resulted in ICTEV, compared to 1.1% (19/1735) of cases with no leakage. The significant number of cases where no leakage was detected may be due to unnoticed fluid loss and other factors. Of note, several ICTEV cases in the study exhibited chronic oligohydramnios at 18–20 weeks, implying that 11–12 weeks may be a key developmental period during which ICTEV susceptibility increases [6].

2. Pathoanatomy

As shown in Fig. 1, there are several anatomical abnormalities that occur in the feet of CTEV patients [13]:

- Malpositioned tarsal bones.
- Calf muscle atrophy.
- Leg shortening.

Malpositioned tarsal bones impact the shape of the tarsal joints. As the foot is in a pronated position, the planter arch is more curved (cavus). In the lateromedial direction, this results in increased meta-tarsal bone flexion [8,13].

In CTEV, the gastrosoleus complex, tibialis anterior, tibialis posterior, and flexor digitorum longus appear to exert excessive traction. The muscles in a foot affected by CTEV are smaller and shorter than those in an unaffected foot. There is more collagen-rich connective tissue near muscles in a foot affected by CTEV are smaller and shorter than those in an unaffected foot. There is more collagen-rich connective tissue near the distal tip of the gastrosoleus muscle, and the fibers of this connective tissue typically extend into the deep fascia and Achilles tendon [5,14].

In CTEV patients, the ligaments on the medial and posterior sides of the tarsal and ankle joints are extremely thick and stiff, causing the foot to remain in an equinus position with the calcaneus in inversion and the navicular in adduction [13,15]. The severity of a CTEV malformation is inversely proportional to leg muscle size. In the most severe cases, the gastrosoleus muscle appears as a minute muscle in the proximal portion of the calf. Excess collagen formation in the muscles, tendons, and ligaments can result in relapses up until the age of 3–4 [16,17].

Under microscopic examination, the ligaments of newborns with CTEV have more collagen fibers and cells [17]. The knots of collagen fibers have a crimped (wavy) pattern. This pattern allows the ligaments to stretch. Careful ligament stretching will not negatively impact a newborn. Stretching removes the crimp pattern for a few days later; once this has reappeared, more stretching can occur. This stretching ability enables CTEV to be manually corrected [18].

CTEV deformities primarily occur in the tarsal bones. The tarsal bones are primarily made up of cartilage and are typically in adduction, inversion, or flexion. The talus is in a highly plantar flexed position, while the neck of the talus is deflected medially and plantarly. The neck intersects with the medial portion of the talus head as it approaches the middle malleolus. The calcaneus is inverted and adducted below the talus [16].

In CTEV, the anterior side of the calcaneus is behind the talar head. This causes heel varus and equinus deformities. Attempting to evert the calcaneus without abducting it will result in the compression of the calcaneus against the talus. In turn, this will not correct the heel varus. The heel varus deformity in CTEV can be corrected by abducting the calcaneus into a normal position in relation to the talus [19].

3. A multifactorial genetic basis

The etiology of ICTEV is largely unknown, although it is known to involve a genetic component [20]. In a twin study, 32% of monozygotic twins had ICTEV concordance (i.e., both twins had ICTEV), compared to 2.9% of dizygotic twins. The frequency of ICTEV in dizygotic twins has been shown to be similar to the background population rate [2,6,21]. While a family history of ICTEV is seen in many cases, the heredity nature appears to vary by population. For example, a familial history is seen in 25–30% of Caucasian cases versus in 54% of Polynesian cases [21–23]. Furthermore, the incidence of ICTEV varies globally (Table 1), implying the presence of a genetic factor.

The uneven sex ratio (1:2.0–2.5 female: male) and pedigree analysis suggests that the heredity nature of CTEV does not follow a typical Mendelian inheritance pattern [35,36]. CTEV is unlikely to be caused by a single gene. Instead, the cause is likely to be polygenic in character and/or multifactorial based on complicated inheritance patterns [37].

4. Etiology

While the cause of CTEV is not yet known, it is not caused by embryonic malformation [38]. The development of CTEV occurs in the second trimester of pregnancy [39].

Table 1
Incidence of idiopathic congenital talipes equinovarus in various populations.

| Author | Country | Year | Population | Birth prevalence per 1000 births |
|--------|---------|------|------------|----------------------------------|
| Mathias et al. [24] | Uganda | 2010 | Live births | 1.18 |
| Pachajoa et al. [25] | Columbia | 2011 | Births | 1.76 |
| Goyalpouri et al. [26] | Iran | 2013 | Live births | 0.81 |
| El Koumi et al. [27] | Egypt | 2013 | Live births | 2.38 |
| Orimolade et al. [28] | Nigeria | 2014 | Live births | 3.22 |
| Sachdeva et al. [29] | India | 2014 | Births | 2.80 |
| Baruah et al. [30] | India | 2015 | Live births | 1.35 |
| Xia et al. [31] | China | 2015 | Births | 0.42 |
| Barik et al. [32] | India | 2020 | Live births | 0.7 |
| Fakheeta et al. [33] | Saudi Arabia | 2021 | Births | 2.3 |
| Edbjornsson et al. [34] | Sweden | 2021 | Live births | 1.24 |

Fig. 1. A) Bilateral congenital clubfoot in a newborn, B) Post-manipulation and initial casting of the left and right foot.
Several theories have been proposed regarding the underlying factors that drive CTEV development. Proposed factors include joint and/or bone formation abnormalities, uterine restriction, neurological development, distal limb vasculature, connective tissue, and developmental arrest [37].

5. The joint/bone theory

The joint/bone theory proposes that CTEV is caused by positional bony anomalies. In 400 BC, Hippocrates wrote, “the malformation involves the complete combination of bones that make up the skeleton of the foot, all the abnormalities noticed in the soft area are subsequent …” [40]. Researchers have confirmed this notion by linking CTEV to bone abnormalities of the foot [6]. In CTEV, the ossification grooves and related cartilage canals are not found in their regular sites, and the coordination of endochondral and perichondral ossification is disrupted [41].

6. The ‘positional’ hypothesis

Hoffa (1902) established the commonly accepted uterine restriction theory, which states that uterine restriction of fetal foot mobility causes ICTEV [6,42]. Hoffa proposed that ICTEV developed from the oligohydramnios sequence, which is a condition whereby not enough amniotic fluid is present. The findings of the CEMAT report may lend support to this theory. However, the oligohydramnios sequence is frequently linked to other developmental abnormalities and may have a neurological explanation. Furthermore, amniotic fluid leakage was only associated with a low proportion of ICTEV patients in the CEMAT study. Therefore, the cause of ICTEV following EA may differ from that proposed in this theory [6].

CTEV can be discovered as early as the second trimester, before uterine pressure is placed on the growing embryo, forming an argument against the positional theory [43]. To test this, Idelberger (1939) conducted a twin study, comparing ICTEV concordance rates in dizygotic twins to rates in the general population, finding that the rates were identical (approximately 2.9%). While 250 twins were included in this study, no explanation was provided as to how the twins were identified and compared. Therefore, the accuracy of the twin comparisons cannot be assessed. Furthermore, although it was the first reported twin study on ICTEV, the rates reported were high for a European community. Therefore, this study is given little weight [5,6,44,45].

7. The neurological hypothesis

Talipes equinovarus is a common symptom in many neurodegenerative disorders. For example, it is frequently seen in conjunction with neurological disorders caused by spina bifida [46,47]. In one study, 18 out of 44 ICTEV cases also had aberrant nerve conduction, with 8 involving a spinal anomaly [6,46,47].

8. The vascular hypothesis

Atlas et al. (1980) investigated CTEV vasculature and found vascular anomalies in “every deformed foot of 12 fetuses,” with at least one branch of the vascular tree of the foot being blocked at the level of the sinus tarsi [6]. Another study found that four out of 11 patients with unilateral ICTEV exhibited vascular abnormalities and diminished muscle volume in the affected limb [48].

These abnormalities were most noticeable during early fetal development. In older specimens, including stillborns, the abnormalities had been reduced to tangles of fibrous tissue and fatty infiltration [6]. Muscle wasting of the ipsilateral calf is commonly seen in individuals with ICTEV, which may be related to reduced vascularization in the anterior tibial artery during development [6,48]. Vascular insufficiency likely plays a role in the link between ICTEV [6,48] and smoking [6,48], as well as EA [6].

9. The connective tissue hypothesis

The connective tissue theory proposes that ICTEV is caused by a fundamental connective tissue defect. The relationship between ICTEV and joint laxity lends support to this theory, as individuals with ICTEV are often found to have severe plantar fibrosis during surgery [6].

10. The developmental arrest hypothesis

The “physiological clubfoot” and “arrested intrauterine development” theories gained popularity in the early twentieth century. Böhm found that the posture of an unaffected foot was comparable to that of a clubfoot at 8 weeks, despite talus deformities not having yet developed in the clubfoot. It has been postulated that an injury before 8 weeks, such as a teratogen, could cause CTEV by producing aberrant tissue differentiation or a specification deficiency (Fig. 2). The severity of developmental abnormalities in CTEV has also been linked to important “growth spurts” in the foot [36].

Several studies have determined that primary defects in CTEV are calcaneus and talus anomalies [2]. However, once a clubfoot position develops, alterations in the size and angulation of the talus develop, suggesting this may also be a primary defect. Furthermore, questions have been raised regarding whether a cartilage anlage or a bone defect could create the wide range of deformities seen in CTEV. According to the current school of thought, the bone anomalies associated with CTEV are caused by additional deforming stresses, such as those found in poliomyelitis or foot binding [36].

11. Conclusion

CTEV is caused by a confluence of genetic and environmental factors. There is evidence that the pathophysiology of ICTEV is influenced by abnormalities in the development of joint, bone, vasculature, innervation, muscle, and connective tissue. Disturbance of the embryonic medial foot rotation process may be the common link between these developmental characteristics. There are likely several causes of ICTEV, and in certain cases, the phenotype may evolve due to the impact of various factors acting together. In the not-too-distant future, improvements in genetic epidemiology studies, a better understanding of the regulation of developmental processes, genetic mapping techniques, and the development of mouse models are all likely to contribute to elucidating the causes of ICTEV.

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Author contribution

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