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Review Article

Latent Risk Factors Associated With the Worldwide Occurrence of Congenital Talipes Equinovarus: A Review

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Abstract

Congenital Talipes Equinovarus (CTEV) is the most frequently reported congenital abnormalities that influence children's lower limbs in particular. With the prevalence of 1-2 percent per 1000 births worldwide, it occurs mainly in males as opposed to females in a 2:1 ration and is bilateral in about half of cases. The etiology of CTEV can eventually play a role in determining the prognostic and the choice of therapeutic interventions for an individual patient. According to available literature, there was the number of risk factors reported to be associated with its occurrence. However, some of them are popularly known to the world, while some still remained latent. CTEV has been positively linked in the latest literature with the genes of Homeobox family, collagen-family, GLI3, T-Box family, muscle contractile family and apoptotic pathway genes mainly due to its unknown etiology.

The recent advances in clubfoot genetics are aimed at examining and explaining the impact of how a demographic, environmental and genetic classification involves itself and how it could result in advanced strategies for individualized therapy. Also, CTEV is thought to be associated during pregnancy with certain maternal environmental interferences, dietary intake, metabolism including mainly folate metabolism, and related activities of the promoter-inducer gene. Hence, the principle objective of this study is to get an overview of all the known and latent risk factors of CTEV, based on the available studies and then update the information as well as hypothesis accordingly.

Abbreviations

CTEV: Congenital Talipes Equinovarus
MTHFR: Methylene Tetra Hydro Folate Reductase
HOX: Homeobox Gene
PITX1: Paired Like Homeodomain 1 Gene
CASP10: Caspase 10 Gene
COL9A1: Collagen Type 9 Alpha 1 Chain
NAT2: N-Acetyltransferase 2
DNA: Deoxyribonucleic Acid
HPA: Hypothalamic Pituitary Adrenal Axis
UK: United Kingdom
ANC: Antenatal Care
CVS: Chorionic Villus Sampling

Introduction

Clubfoot is one of the most prevalent congenital limb deformities, also called congenital talipes equinovarus. It is often an isolated congenital condition and is believed to be idiopathic [1]. It can also be acquired and is referred to as A CTEV i.e. Acquired Equinovarus Congenital Talipes (Table. 1) [1-3]. It appears with a proportion of 2:1 between males and females and is bilateral in about half of the cases [4,5]. Congenital talipes equinovarus (CTEV) affects 1-2 per 1,000 births worldwide. This 3-D deformation is recognizable after delivery. The foot is held in a fixed equinus with adduct us and cavus of the midfoot and a varus of the hindfoot [4].

Table 1: *Difference between CTEV and ATEV i.e. Congenital talipes equinovarus and Acquired talipes equinovarus*

CTEV	ATEV
1. Present since birth.	1. Not present from birth.
2. May be associated with spina bifida.	2. May be due to polio, cerebral palsy etc.
3. Bilateral.	3. Usually unilateral.

4. Skin, subcutaneous tissue, muscles are normal.	4. Tropic changes in the skin, muscles are flaccid (LMN lesion) or spastic (UMN lesion).
5. Transverse crease is seen across the sole on the medial side.	5. No transverse crease.
6. Bone are normal in thickness.	6. Bone are thinner than normal.

In some cases, CTEV may occur as part of a genetic syndrome in combination with other characteristics or congenital anomalies, but in the majority of cases, it may occur in isolation and is considered to be isolated CTEV (Figure 1) [3,4]. CTEV's etiology is not yet known [5]. There was no clarification of either the environmental or genetic factors [6]. Mutations in genes involved in limb and muscle development are risk factors for clubfoot [5], specifically those encoding the contractile muscle complex and those regulating the expression of these many genes [6]. Common genetic variants such as HOX homeobox genes, insulin such as protein binding growth factor, MTHFR gene and Caspase gene family have either been reported to be directly associated with isolated clubfoot or to regulate the expression of other genes involved. According to the latest research by Wang *et al.* HOXD-12 and 13 gene is liable to cause congenital talipes equinovarus [7]. Many studies showed that smoking cigarettes are one of the most significant and coherent determinants in raising a child's risk for CTEV during pregnancy [8]. In the presence of a favorable history of CTEV, smoking also raises the danger to 20 times, thus supporting the function of the gene in CTEV [9]. Environmental factors have been suggested as contributing to CTEV development, such as a small uterine cavity, mother-ingested drugs during pregnancy and herbicide aerial spraying [10].

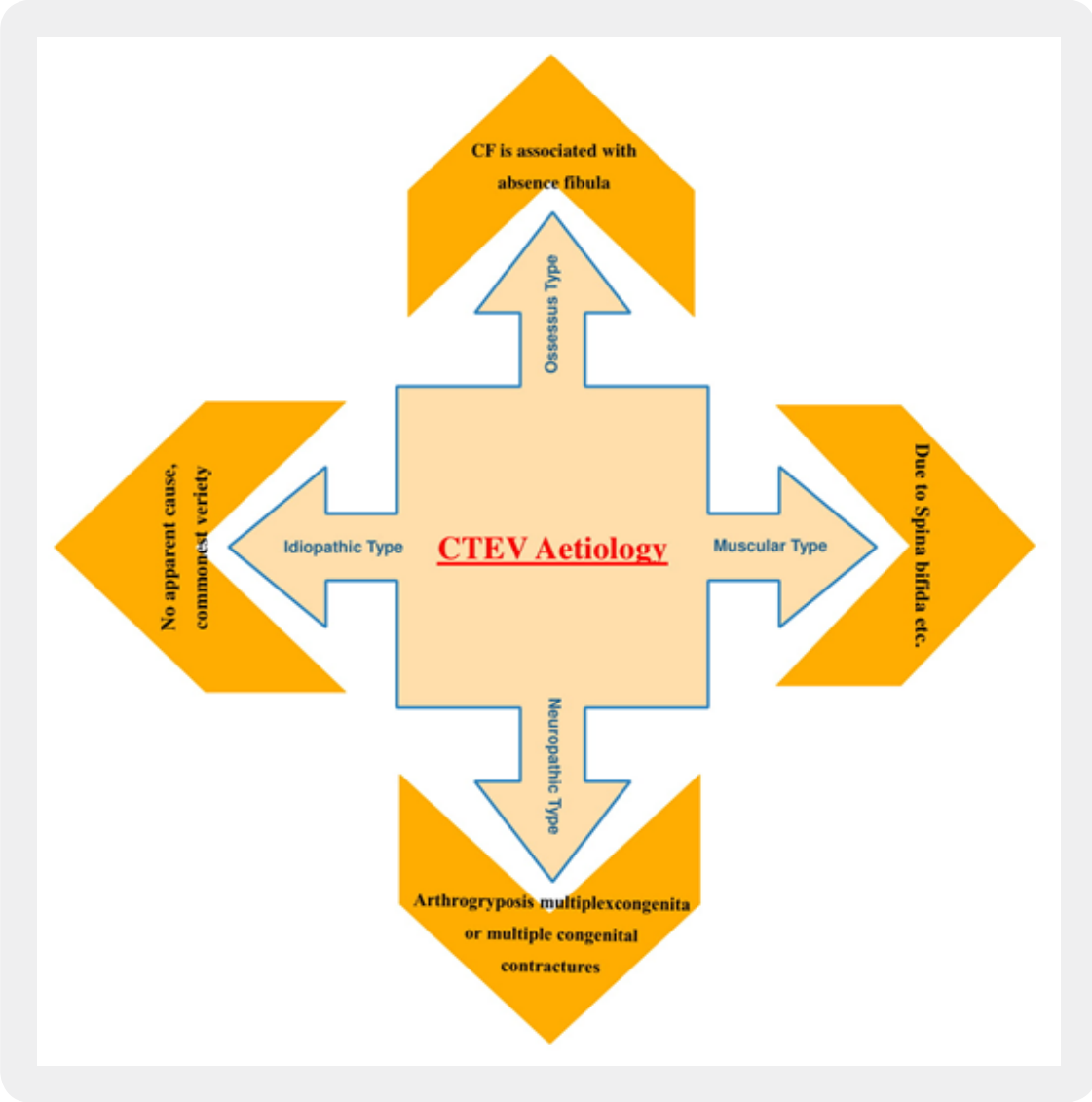

Figure 1: *On the basis of certain etiological parameters the Congenital talipes equinovarus could be of various types, including idiopathic, ossessus, muscular and neuropathic type. Out of all the idiopathic CTEV is the one which is most frequently observed, and the ossessus CTEV is the one which is least observed.*

A clubfoot prenatal diagnosis gives parents the opportunity to know about treatment and prognosis in advance, including prenatal counselling services, and this may allow clinicians to set up their network for optimal management of the disease. [11,12] However, the accuracy of this examination depends on a number of factors, including physician experience, gestational age, equipment quality and methodology [12].

Etiology of Clubfoot With Its Management Trends

CTEV is by far the most prevalent congenital foot defect that gives club-like appearance [1] In clubfoot patients the prevalence of congenital anomalies or chromosome abnormalities varies greatly from 24% of

50% according to population [13]. According to the Turco's theory medial displacement of navicular and calcaneus around the talus could be the cause of CTEV, according to Brockman's theory the congenital atresia of the talonavicular joint could be the cause of CTEV, according to the Mc-Kay's theory the three-dimensional bony deformity of the subtalar complex could be one of the cause behind CTEV [12,13], and etc. Furthermore, there are also many more theories emphasizing the link between mother-child and deformity, including The Intrauterine theory which states that CTEV could be due to compression by malposition of the fetus in utero and The Prenatal muscle imbalance theory which states that CTEV could be due to weak pronators and overacting extensors and inverters etc (Figure 2). With advancing age, the cosmetically unsightly clubfoot starts posing functional problems like altered gait (stumbling gait), callosities, and degeneration and arthritic changes in the ankle with foot joints. CTEV can be assessed by Dorsiflexion Test, Plumb Line Test and Scratch test etc. Pirani's classification is the most accepted findings for severe abnormality [14]. Since CTEV is a mechanical problem (Table. 2), radiography is by far the most important investigation. However, as per the recent studies, the laboratory data actually help us to find the positive link between genetic malfunctioning and occurrence of CTEV. This, in turn, forces us to establish a new approach of laboratory diagnostic parameters too [11,14]. CTEV can be managed by conservative management, surgical management. It is the treatment of choice in infants less than 6 months of age. Ponseti in the year 1950 described a very effective conservative method of treating clubfeet with very few recurrence rates. The Ponseti method is now successfully used to treat severe non-idiopathic deformities of the clubfoot [8,12].

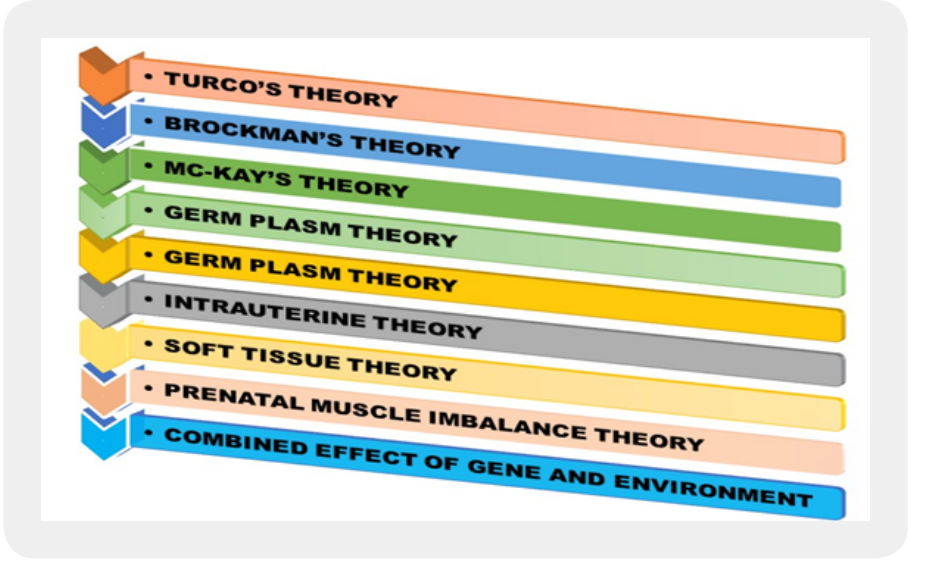

Figure 2: *Till date proposed theories of Congenital Talipes Equinovarus. Out of which the most primitive one is Turco's theory which suggest that the medial displacement of navicular and calcaneus around the talus could be cause of CTEV, then according to Brockman's theory the congenital atresia of the talonavicular joint could be the cause of CTEV, according to the Mc-Kay's theory the three-dimensional bony deformity of the subtalar complex could be one of the cause behind CTEV. The Intrauterine theory states that CTEV could be due to compression by malposition of fetus in utero and The Prenatal muscle imbalance theory which states that CTEV could be due to weak pronators and overacting extensors and invertors.*

Table 2: *The complexities of Congenital talipes equinovarus with its primary and secondary deformities*

Primary Deformities	Secondary Deformities
1.Equinus	1.Foot size is decreased to 50%
2.Varus	2. Medial border is concave, lateral border is convex
3. Cavus	3.Forefoot is plantarflexed upon hindfoot
4.Forefoot adduction	4.Skin is stretched over the dorsum of the foot
5.Internal tibial torsion	5.Callosities are present over the dorsum of the foot
Late Changes	6.Stumbling gait
1.Degeneration of joints	7.Hypotrophic anterior tibial artery
2.Fusion of joints	8.Atrophy of muscles in anterior or posterior compartments of the leg

Environmental Interference in Occurrence of Clubfoot

Multi-factor involvement, including genetic and environmental factors, has been proposed by epidemiological studies to contribute collectively to CTEV etiology (Figure 3(a) & 3(b)) [14]. Various studies have shown a greater risk of CTEV in infants due to smoking during pregnancy because it involves an enhanced possibility of other birth defects like limb reduction defects, abdominal wall defects, and certain heart defects [15]. In the absence of a club foot's family history, maternal smoking exposure is associated with isolated clubfoot. Vascular disruptions or compromise associated with smoking can be a probable factor contributing to the incidence of clubfoot.

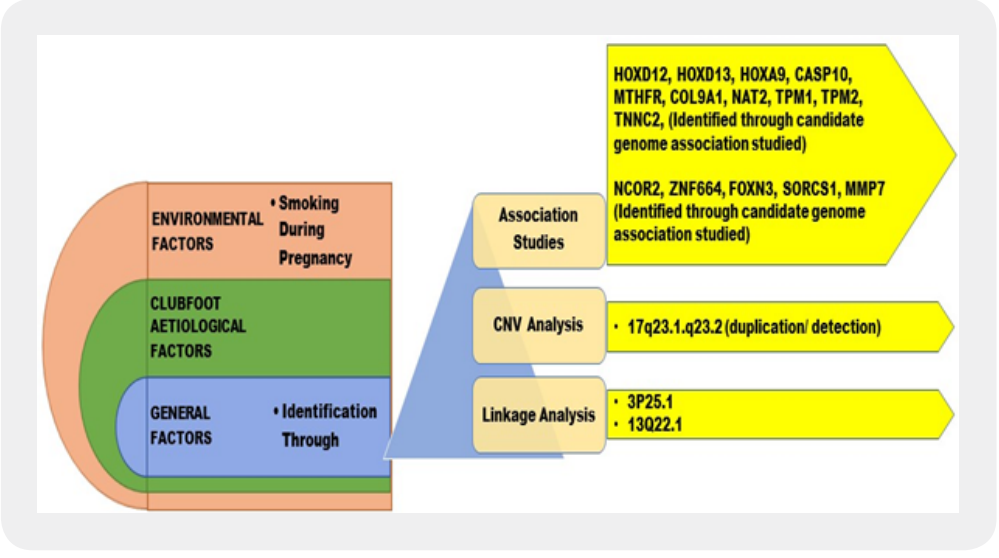

Figure 3(a): *Prominent known etiological factors of congenital talipes equinovarus: As per the latest trending theory the possible risk factors include genetic as well as environmental. However, we are suggesting further classification and sub division of genetic and environmental factors, including smoking during pregnancy a prominent one.*

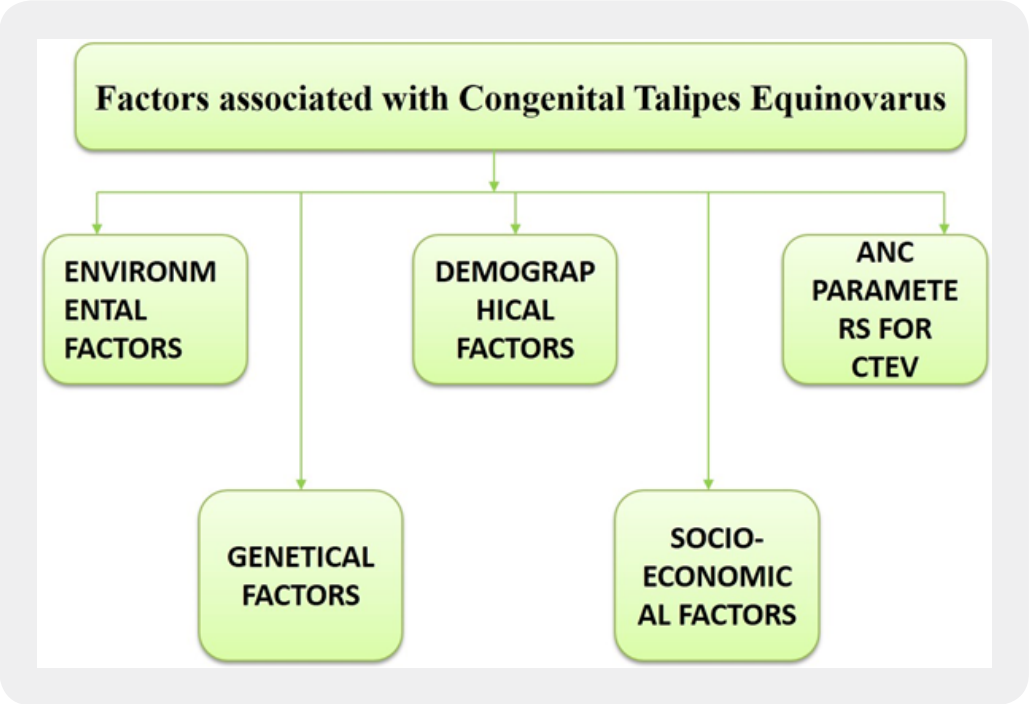

Figure 3(b): *Overall studied factors associated with congenital talipes equinovarus: According to the available literature the prominent factors are only environmental and genetic, however still the overall factors includes all the parameters of the society with income status, education level, cohabitation status, races etc. Hence, we are suggesting the new classification of associative factors for clubfoot.*

Maternal Smoking (Active & Passive) as a Risk Factor of CTEV

The potential for gene-environment interaction in clubfoot etiology on the Asian population has not been examined yet. Indeed, available researches also demonstrate that both maternal smoking and the history of the family are essential causes for clubfoot and that these two variables can have a substantial potential relationship. It also offers a further indication of etiology of clubfoot and emphasizes the significance of considering interactions of sex, laterality, and higher-order in etiological studies of defects.

Genetic Mis-Functioning as a Reason Behind CTEV

Genetic factors make a substantial contribution to CTEV etiology. The genetical cause indicated that CTEV is prone to segregate in families [16]. As per the available literature, it has been found that there is a link between family history of CTEV, with the occurrence of CTEV in neonates [17,18]. The significance of genes involved in the growth of premature limbs was recently identified by the discovery of an unusual mutation in the transcription factor PITX1 [19]. PITX1 is the first gene involved in clubfoot explaining the foot's unique involvement [19]. Mainly Hox-Gene Family, MTHFR Gene, Caspase-Gene Family, etc. are the genetically identified factors through associative studies (Table. 3). Genes with apoptosis, homeobox A and D (HOXA and HOXD) and the genes involved in muscle contraction, have suggested the contribution

of genetic in the accountability of CTEV [20,21]. Heck and colleagues [22] detected evidence that a rare CASP10 gene allele was linked and associated with simplex CTEV cases. Polymorphism of methylenetetrahydrofolate reductase gene (MTHFR) in mothers was also associated with CTEV [21]. The gene COL9A1 is the significantly susceptible gene for CTEV, as the elevated expression of COL9A1 was noted relative to ordinary people [20]. NAT2 (N-acetyltransferase 2) contributes to the biotransformation of N-acetylation tobacco smoke [23]. Functional analysis has shown that the variants associated with CTEV result in allele-specific interactions between nuclear proteins and cause higher promoter activity [9].

Table 3: *Data representation of recent studies accomplished on CTEV in the previous years*

Fisrst Author	Aim of the Study	Methodology	Targetedgene	Result
L Bonafé *et al*, 2002 [24]	To evaluate the relationship between R279 W mutation in DTDST and occurrence of ICTEV	PCR, Genotyping	DTDST	Linkage and association results obtained with GENEHUNTER for D5S1507 were not significant.
Li-li Wang *et al*, 2005 [8]	To study SNPs in HoxD10, HoxD12, HoxD13 and haplotypes distribution in ICTEV pedigree	PCR, Genotyping, TDT	HoxD10 HoxD12 HoxD13	The rs847154 located in 5' flanking sequence of HOXD12 gene and the rs13392701 located in exon 1 of HOXD13 gene were noted to have transmission disequilibrium in 84 nuclear pedigrees ($P < 0.05$).
Zhang X *et al*, 2006 [25]	To explore the association and mutation of GLI3 gene in ICTEV	PCR, Genotyping, TDT	GLI3	rs929387ls located in exon 14 of GLI3 gene have transmission disequilibrium in 84 nuclear pedigrees ($P<0.05$), and rs846266 located in exon 4 have no transmission disequilibrium ($P>0.05$). A mutation in exon 9 was detected in one patient and his mother.
Sharp L *et al*, 2006 [26]	To study MTHFR C677Tpo lymorphism, and maternal periconcep tional folic acid supple ment use, influenced risk of isolated clubfoot	PCR, Genotyping	MTHFR	A significant trend of decreasing clubfoot risk with increasing number of T alleles: relative risk for CT vs. CC = 0.75, 95% confidence interval: 0.57, 0.97; relative risk for TT vs. CC = 0.57, 95% confidence interval: 0.35, 0.91; p trend = 0.006. This association was not modified by maternal folic acid use.

Liu LY *et al*, 2007 [27]	To analyze SNPs within COL9A1 gene in ICTEV	PCR, Genotyping, ETDT	COL9A1	The results showed that rs592121 and rs1135056 loci within COL9A1 gene existed transmission disequilibrium in 84 nuclear pedigrees (P<0.05). Expression of COL9A1 on mRNA levels showed significantly higher in patients with ICTEV than in normal person (t=4.7500, P<0.05) .
Zhao N *et al*, 2008 [28]	To detect the expressions of COL1A1 mRNA in 20 patients with ICTEV	PCR-DGGE, DNA sequencing	COL1A1	Expression of COL1A1 on mRNA levels showed significantly higher in patients with ICTEV than in normal persons (t=12.680, P < 0.05). By DNA sequencing, a -161(T--> C) heterozygous mutation and a+ 274(C-->G) homozygous mutation were detected, and both were new identified mutations. These results indicated that the mutations in transcription regulator sequences of COL1A1 could cause ICTEV.
Shyy W *et al*, 2009 [29]	To test the hypothesis that CAND2 and WNT7a mutation associated with ICTEV	PCR, DNA sequencing	CAND2 WNT7a	A polymorphism was observed in each gene, but the single nucleotide change in CAND2 was a silent mutation that did not alter the amino acid product, and the single nucleotide change in WNT7a was in the upstream, non-coding or promoter region before the start codon.
Audrey R. Ester *et al*, 2009 [30]	To study HoxA, HoxD and IGFBP3 in patients with ICTEV	PCR, Genotyping, In Silico	HoxA HoxD IGFBP3	Tested genes positve Interactions with CASP3
Shyy W *et al*, 2010 [31]	To study MYH genes in ICTEV patients	PCR, DNA sequencing	MYH 1 MYH 2 MYH 3 MYH 8	MYH genes not directly cause ICTEV
W. Lu *et al*, 2012 [32]	To assess whether variation in or around TBX4 is a common cause of non syndromic clubfoot	CGH, PCR, Genotyping, DNA sequencing	TBX4	TBX4 variation negative

Katelyn S. Weymouth *et al*, 2012 [33]	To interrogate muscle con tractile com plex genes in ICTEV	PCR, Genotyping, DNA sequencing	Muscle contractile complex genes	TNNC2 was identified positively
Tian-Xiao Zhang *et al*, 2014 [34]	To identify genetic risk factors associated with clubfoot	Microarray genotyping, GWAS association study	Genome	SNPs replication 12q24.31 FOXN3, SORCS1 MMP7/ TMEM123
Yang H *et al*, 2016 [35]	To determine the disease-causing mutations in Chinese patients and, to evaluate the association of filamin B gene with isolated CTEV	Whole-exome DNA Sequencing & Sanger sequencing	filamin B gene	A putative pathogenic mutation in the FLNB gene noted positively.
Zhang Z *et al*, 2016 [36]	To characterize a previously uncharacterized genetic disorder associated with equinus deformity.	Whole-exome DNA Sequencing	ANXA3 gene & MTHFR gene.	These findings imply that this uncharacterized genetic disorder is not clubfoot, despite sharing some similar symptoms.
Weymouth KS *et al*, 2016 [37]	Four (rs3801776/ HOXA9, rs4075583/TPM1, rs2025126/TPM2, and rs2145925/ TPM2,) SNPs, were evaluated to determine whether they altered promoter activity.	Electrophoretic mobility shift assays were performed on these four SNPs to identify allele-specific DNA-protein interactions.	SNPs, rs3801776/ HOXA9, rs4075583/ TPM1, rs2025126/ TPM2, and rs2145925/ TPM2,	The ancestral alleles of rs3801776/ HOXA9, rs4075583/TPM1, and rs2025126/TPM2 and the alternate allele of rs2145925/TPM2 created allele-specific nuclear protein interactions and caused higher promoter activity.
Alvarado DM *et al*, 2016 [38]	To report chromosome 12q13.13 microdeletions ranging from 13 to 175 kb and involving the 5' HOXC genes	Proband's screening for point mutations, multiplexed direct genomic selection, & SNP genotyping	HOXC genes	HOXC and HOXD gene expression is reduced in fibroblasts from a patient with a 5' HOXC deletion.

Yuanhui Wang *et al*, 2018 [39]	To establish a relationship between HOX gene and pediatric congenital clubfoot	RT-PCR and Western Blotting along with Statistical analysis.	HOX gene	The expression of IL-1β, IL-6, TNF-α, Fas, FasL and Bax mRNA in the CCF group was significantly higher than that in the control group.
Jingchun Li *et al*, 2019 [40]	To establish that, HOXA9 rs3801776 and TPM2 rs2025126 genetic polymorphisms may play important roles in regulating muscle development in Chinese children.	Case-Control study to examine the associations between these two polymorphisms and CTEV susceptibility.	HOXA9 rs3801776 and TPM2 rs2025126	rs3801776A was associated with increased CTEV risk.

Homeodomain Gene Family/HOX-Gene Family and Their Role in the Occurrence of CTEV

For many areas of the body, the HOX gene plays a vital function, including the nerves, muscles, bones, and blood vessels. Thus, diseases can occur on the limbs if any HOX gene has mutations or an irregular expression HOXD12 and HOXD13, which are the primary susceptible genes of CTEV also. Genes in the HOXA cluster, i.e., chromosome 7p15, chromosome 2q31,33, and chromosome 12q13.13 are engaged in the patterning of the limb, muscle and axial skeleton [41,42]. A deletion in its region is thought to be associated with clubfoot. The HOX family comprises 39 genes in four A, B, C and D clusters. Ester *et al*. and others [30,43] have shown that variations of the HOXA, HOXC, and HOX-D genes in regulatory regions are correlated with CTEV.

Methylenetetrahydrofolate Reductase (MTHFR) Gene's and Their Role in the Occurrence of CTEV

MTHFR refers to methylenetetrahydrofolate reductase. It causes genetic mutation, which can lead to high blood homocysteine levels and low folate and other vitamins. A maternal genotype MTHFR did not affect the clubfoot risk for the children as a whole, although a possible association with the use of folic acid has been reported as associated with the CTEV risk. This is the first recognized study on unique genetic polymorphism in clubfoot [33]. Many essential metabolic processes include B vitamin folate, including the synthesis and repair of DNA and DNA methylation [43]. The risk of multiple congenital malformations has been observed in pregnant women with poor folate status [30,33]. MTHFR played a part in etiology of many congenital malformations - which includes neural tube defect and orofacial clefts - but, there is a paucity of literature on clubfoot in the Asian population [33]. According to the latest research, researchers proposed that there was an association between the use of maternal genotype, consumption of folic acid and risk of clubfoot in the embryo. However, interaction tests have not yet been clinically established.

Demographic Factors Accountable for Clubfoot

There are a number of population-based orthopedic-confirmed clubfeet patients and controls for assessing the incidence patterns [26,27,44]. The male majority reported in various studies was reported in our study,

including the demonstrations and analysis for isolated cases, those that were associated with other chief malformations, unilateral and bilateral cases, and that could be attributed to fetal constraint or genetics. However, the lowest magnitudes of masculine births have been observed among cases of further major congenital malformations, those associated with fetal constraint, and those with a positive family history in first-degree relatives, possibly due to etiological heterogeneity among them [44].

Sexuality of Child as a Risk Factor of CTEV

There is evidence in both animals and humans that psycho-social and environmental stressors modify the sex ratio in favour of females, possibly by activating the hypothalamic-pituitary-adrenal (HPA) axis [44]. Why more males are born with clubfoot than females remains a mystery, with countably low available literature and hence requires further studies with special emphasis. However, we may suggest that the environmental or psycho-social factors that change the male sex ratio may be worth considering as a risk factor [24].

Maternal Age and Weight During Pregnancy as a Risk Factor of CTEV

Maternal age was reported to be inversely linked to clubfoot [9,45-47]. However, other studies found no association [48-52]. We did not use primiparity as a constraint predictor because almost half of all women fall into that category and would have weakened the sensitivity of any particular constraint. For example, no correlation has been observed for obesity since primiparity was added to the concept of 'constraint.' Clubfoot is well known to recur in some obese families [45], And studies suggest that clubfoot cases had a relative first degree affected [9,45,52-54].

Role of Socio-Economic Factors in Occurence of Clubfoot

Socio-demographic factors in clubfoot have not been consistently related; however, still they have a specific impact on the child and mother both. Hence, we may consider them also as a sub-prominent factor for clubfoot.

Impact of Parental Qualification and Combined Family Income Status on CTEV

Level of education positively associated with clubfoot [9,45-47], however, other studies found no association [48-52], as we observed. Further, the combined family income and its stability source have both direct as well as indirect impact on clubfoot [9,47-49], by deciding the means of basic requirements for pregnant women and infant both such as food, water, shelter, hygiene and early age medication etc [9,47-49].

Impact of Parental Cohabitation Status on CTEV

We analyzed the status of cohabitation as a further measure of socioeconomic status in comparison to a higher risk of unmarried mothers in a UK study, and it was also not associated with clubfoot [45]. Two studies have identified a higher risk of clubfoot in White mother's offspring compared to non-White mothers [9,46], which was not substantiated in four other studies [47,49,50,52].

Proposed ANC Parameters Associated With Clubfoot

In at least some cases, clubfoot was accused of arising from fetal constraint and also thought to be associated with ANC managements, including gestational age and medication also.

Number of Previous Pregnancies as a Risk Factor of CTEV

Based on clinical findings of cases involving oligohydramnios, uterine bicornuate, breech presentations, and multiple births, i.e. females with no prior births are at increased risk of clubfoot. Past epidemiological studies have, however, found contradictory findings, with positive, inverse and null associations [47-49,55]. Increased clubfoot risks associated with breech delivery and uterus bicornuate and 60 to 80% increased risks for oligohydramnios and multiple births, in favour of a framework for limiting a minority of cases [47-49,55]. The relation between clubfoot and primiparity which is regularly observed [45-52]. Was raised as evidence to support fetal pathogenesis, on the premise that after the first birth, by holding the fetus, the intrauterine area is extended [45,49].

Gestational Age as a Risk Factor of CTEV

Another potential pathogenetic mechanism for clubfoot is the vascular disturbance, leading to increased risk of clubfoot in women with early gestational amniocentesis [55,56] Or is it exposed to abortive misoprostol [57,58]. In a few studies, we found that if there is a 16 Weeks of gestation, amniocentesis, CVS, or the fetal loss of a twin or triplet to be vascular disturbance markers. Such factors were correlated with an increased risk of clubfoot 5.6, 2.2, and 4.1 times respectively, Supporting potential vascular disruption pathogenesis [55-58].

Proposed Outcomes of Prenatally Diagnosed Clubfoot

Based on more systemic or neurological developmental abnormalities, it is suggested that the Prenatally diagnosed isolated clubfoot cases will postnatally have complex clubfoot [26,27]. While advising women on isolated clubfoot prenatally diagnosed, it is necessary to reassure them that approximately 10 percent of people would have a normal foot or foot deformity that needs minimal treatment [26,33]. Clubfoot may be diagnosed prenatally on a thorough ultrasonography scan performed in the second or third trimester by visualizing Tibia and fibula in the same longitudinal plane as the foot's lateral portion [47-49].

Conclusion With Future Perspectives

Clubfoot is one of the most prevalent birth defects in the musculoskeletal system; its etiology and controversies related to optimal treatment strategies are still unknown. The aim of the study was to update the latest progress in the awareness of the genetic and environmental etiology of clubfoot and explore the future research required for this disorder to achieve a genetic classification scheme. The objective was also to examine the development of clubfoot management and clarify How it revolutionized the Ponseti process childcare worldwide (Figure 4). Although current methods of treatment seem to be beneficial in maximum cases, regardless of heir etiology, co-morbidity risks, i.e. hip dysplasia. Future genome associative research

will provide an uneven alternative in the Identifying Clubfoot susceptibilities, and Large Samples Using Identify the susceptibility of both major and minor genes where present. Individualized interventions based on etiology may also lead to decreased use of braces if etiology or genetic profile correlates with risk of relapse. The primary aim of treatment is to deliver a fully functional, painless foot for long-term correction. In order to achieve this, more progressive research-based studies may need to combine approaches which apply the strengths of different methods.

Figure 4: *Images of first time presented patient with CTEV, patient with bilateral cast, unilateral cast, and FAB: (a) The image depicted the first time presented bilateral clubfoot of 2 months child (b) First bilateral cast as a part of Ponseti management (c) as the right foot score remained unchanged, hence the right foot require one more additional cast and (d) After completion of total six casts, FAB (foot adjustment braces) are provided to the child and advised till the age 5 years.*

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Conflicts of Interest

The authors declare that they have no competing interests in this article.

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