

Perinatal and orthopedic outcomes of patients diagnosed with pes equinovarus by mid-trimester fetal ultrasonographic imaging

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Abstract

Objective: In this study, we aimed to evaluate the perinatal and orthopedic outcomes of pregnant women diagnosed with pes equinovarus by mid-trimester fetal ultrasonographic screening in our clinic, and to compare the perinatal and neonatal outcomes of pregnant women complicated with isolated and non-isolated pes equinovarus.

Methods: The pregnancy and newborn medical records of the pregnant women, who were diagnosed with pes equinovarus by mid-trimester fetal ultrasonographic screening at the Perinatology Department of İnönü University between April 1st, 2014 and January 1st, 2017 and followed up to the delivery, were reviewed retrospectively. The patients with terminated pregnancies who had congenital syndromes in addition to pes equinovarus were also included in the study.

Results: During the study period, the data of 71 patients who were prenatally diagnosed with pes equinovarus by mid-trimester fetal ultrasonographic imaging were evaluated. While bilateral pes equinovarus was found in 59.3% of the fetuses in isolated group, it was 79.4% in the non-isolated group ($p=0.084$). The median diagnosis week was 22 weeks in the isolated group while it was 20 weeks in the non-isolated group ($p=0.041$). Fetal karyotyping was performed on 37.5% of the patients in the isolated group during prenatal period while this rate was 38.4% in non-isolated group ($p=0.802$). The patients in the isolated group did not have aneuploidy as a result of karyotyping whereas trisomy 18 was found in three patients and 46,XX,inv(9)(p12q13) in one patient in the non-isolated group ($p=0.053$). In the group complicated with isolated pes equinovarus during neonatal period, 81.2% of the newborns were treated by conservative therapy (corrective casting - Ponseti's or Kite's method), and this rate was 27.2% in the non-isolated group. Surgical requirement was higher in the non-isolated group, and posteromedial release was the most frequent operation.

Conclusion: Distinguishing the fetuses, which are diagnosed with pes equinovarus during prenatal period, as isolated and non-isolated cases has a critical significance in the prediction of neonatal outcomes. The incidence of chromosomal alteration and possibility of poor neonatal and orthopedic outcomes are higher in the non-isolated group. The results of our study will contribute to inform pregnant women properly, who are complicated with isolated and non-isolated fetal pes equinovarus during prenatal period, in terms of follow-up, treatment options and outcomes during perinatal and neonatal periods.

Keywords: Fetal ultrasonography, pregnancy, gestational outcomes, pes equinovarus.

Özet: Mid-trimester fetal ultrasonografik taramada pes ekinovarus saptanan hastaların perinatal ve ortopedik sonuçları

Amaç: Bu çalışmada kliniğimizde mid-trimester fetal ultrasonografik taramada pes ekinovarus saptanan gebelerin perinatal ve ortopedik sonuçlarını değerlendirmeyi, izole ve izole olmayan pes ekinovarus saptanan gebelerin perinatal ve neonatal sonuçlarını karşılaştırmayı amaçladık.

Yöntem: İnönü Üniversitesi Tıp Fakültesi Hastanesi Perinatoloji Bilim Dalı'nda 01.04.2014 – 01.01.2017 tarihleri arasında, mid-trimester ultrasonografik taramada fetüste pes ekinovarus saptanan ve doğuma kadar izlenen hastaların gebelik ve yenidoğan dosyaları retrospektif olarak tarandı. Ayrıca pes ekinovarus konjenital sendromların eşlik ettiği gebelik terminasyonu yapılan hastalar da çalışmaya dahil edildi.

Bulgular: Çalışma periyodunda mid-trimester fetal ultrasonografik taramada prenatal olarak pes ekinovarus saptanan 71 hastanın verileri değerlendirildi. İzole olan grupta fetüslerin %59.3'ünde bilateral pes ekinovarus saptanırken, izole olmayan grupta bu oran %79.4 olarak izlendi ($p=0.084$). İzole grupta medyan tanı haftası 22 hafta olarak saptanırken izole olmayan grupta medyan tanı konulan hafta 20 hafta idi ($p=0.041$). İzole gruptaki hastaların %37.5'ine prenatal dönemde fetal karyotipleme uygulanırken izole olmayan grupta fetal karyotipleme oranı %38.4 olarak saptandı ($p=0.802$). İzole gruptaki hastaların karyotip sonucunda anöploidisi saptanmaz iken, izole olmayan grupta 3 hastada trizomi 18, 1 hastada 46,XX,inv(9)(p12q13) saptandı ($p=0.053$). Neonatal dönemde izole pes ekinovarus saptanan gruptaki yenidoğanların %81.2'i konservatif tedavi (düzeltici alçılama - Ponseti veya Kite yöntemi) ile tedavi edilirken, izole olmayan grupta bu oran %27.2 izlendi. İzole olmayan grupta cerrahi gereksinimi daha fazla olup, en sık posteromedial gevşetme operasyonu uygulandı.

Sonuç: Prenatal dönemde pes ekinovarus tanısı konulan fetüslerde izole ve izole olmayan ayrımının yapılması, neonatal sonuçları öngörmeye kritik öneme sahiptir. İzole olmayan grupta kromozom değişikliklerinin görülme sıklığı, olumsuz neonatal ve ortopedik sonuçlar ile karşılaşma olasılığı daha yüksektir. Çalışmamızın sonuçları, prenatal dönemde fetüste izole ve izole olmayan pes ekinovarus saptanan gebelerin perinatal ve neonatal dönemdeki izlem, tedavi seçenekleri ve sonuçları açısından doğru bilgilendirilmesine katkıda bulunacaktır.

Anahtar sözcükler: Fetal ultrasonografi, gebelik, gebelik sonuçları, pes ekinovarus.

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Introduction

Congenital pes equinovarus (PEV), also known as talipes or clubfoot, is one of the most common congenital orthopedic deformities for feet which is seen in 2–3 cases out of 1000 live births, and requires sequential therapy.^[1] PEV is seen two times more common in male fetuses than female fetuses.^[2] PEV is considered to have more than one reason, and it is characterized by adduction on the anterior side of foot, cavus on middle part, and equinism and varus (internal rotation) deformity on the posterior side.^[3] Twenty percent of the fetuses with pes equinovarus also have other symptoms, and 80% of them do not have any chromosomal disorder or any other congenital anomaly.^[4] Although various factors such as genetic reasons, vascular disorder and fetal restriction are suggested for the etiology of PEV, it has not been fully clarified yet.^[5] Conservative and surgical methods are referred in its treatment. Different rates have been reported for the success of conservative therapy alone including the serial manipulation and casting. While there are studies reporting high success rate for conservative therapy (about 90%), some other studies report low rates (about 50%).^[6] Two main methods are used most frequently as good long-term outcomes are reported. These are Ponseti's method, which includes serial long leg casting following weekly corrective manipulations, and Kite's method, in which splints keeping legs in dorsiflexion and mild abduction during nights are applied as well as serial manipulation and casting.^[7,8] Although surgical treatment modalities have been used more frequently when the biomechanics of the disease

was not clear enough, surgical methods are still referred which include soft tissue releases in cases that cannot be provided sufficient recovery by conservative methods.^[9]

There is limited number of studies in the literature investigating obstetric and orthopedic outcomes of fetuses with pes equinovarus. Therefore, we aimed in our study to evaluate the perinatal and orthopedic outcomes of pregnant women diagnosed with pes equinovarus by mid-trimester fetal ultrasonographic imaging in our clinic, and to compare the perinatal and neonatal outcomes of isolated and non-isolated cases.

Methods

Approval was obtained for the study from Scientific Research and Publication Ethics Committee of Health Sciences, İnönü University (approval number of Ethics Committee: 2016/10–11). The pregnancy and newborn files of the pregnant women, who were diagnosed with pes equinovarus by mid-trimester fetal ultrasonographic imaging at the Perinatology Department of Medicine Faculty Hospital at İnönü University between April 1st, 2014 and January 1st, 2017 and followed up to the delivery, were reviewed retrospectively. The patients who had congenital syndromes in addition to pes equinovarus and chose termination of pregnancy were also included in the study. In all patients, the diagnosis of pes equinovarus was established by observing tibia and fibula on the same plane during the imaging of foot on plantar level in the fetal ultrasonographic examination at prenatal period (**Fig. 1**). During the study period, invasive prenatal diag-

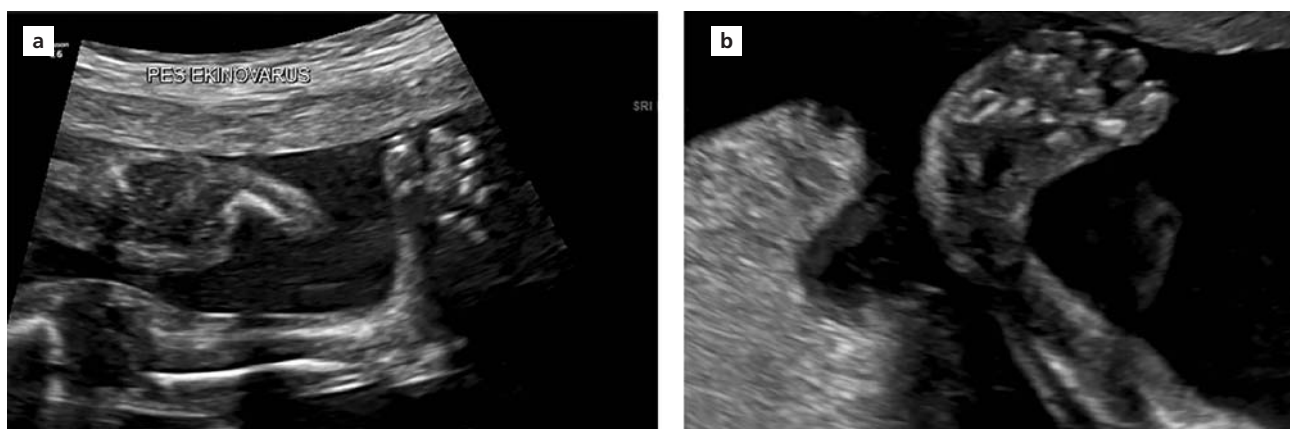


Fig. 1. Gray-scale ultrasonography images (**a** and **b**) where tibia and fibula are on the same plane during ultrasonographic imaging of fetal foot on plantar level.

nosis was recommended to isolated cases and non-isolated cases which had concomitant fetal malformations. The cases with pes equinovarus developed secondary to oligohydramnios/anhydramnios, which developed due to preterm premature rupture of membranes or congenital renal anomalies, were excluded from the study. Termination option was offered in the presence of fetus with fetal chromosomal anomaly or near-fatal congenital anomaly. During the study period, the antenatal follow-ups and deliveries of pregnant women were performed in accordance with the follow-up and delivery protocols established in the Antenatal Care Management Guide and Delivery and Cesarean Section Guide of Health Ministry.^[10,11] All newborns with pes equinovarus accompanied with isolated or congenital syndromes and born in our hospital were referred to newborn intense care unit and the Department of Orthopedics and Traumatology for examination, and the conservative therapy was initiated for these newborns within the first 3 days of life for pes equinovarus deformity (**Fig. 2**). Surgical treatment was conducted in cases where conservative therapy was insufficient or failed.

Inclusion criteria were (i) 18–39 years old, (ii) single live fetus, (iii) diagnosis of pes equinovarus concurrent

with isolated or other anomalies in the mid-trimester fetal ultrasonographic imaging, and (iv) carrying out gestational follow-up and delivery or termination in our clinic.

Exclusion criteria were (i) multiple pregnancies and (ii) intrauterine fetal death.

For the patients included in the study, age, gravida, parity, body mass index, week of gestation for diagnosis, whether pes equinovarus is unilateral or bilateral, fetal karyotyping results, how pregnancy was ended, delivery, gestational age at delivery, birth weight, sex, neonatal intensive care unit requirement, therapy type for pes equinovarus and prognosis parameters were recorded. Statistical Package for the Social Sciences (SPSS) version 22.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. For statistical comparison of the cases, the normality distribution of the data obtained from the patients was analyzed by Shapiro-Wilk test. In isolated and non-isolated PEV groups, the data displaying normal distribution were defined as mean and standard deviation, and the data not displaying normal distribution were defined as median, minimum and maximum. While t-test was used for the data complying with normal distribution, the non-compli-



Fig. 2. In pes equinovarus deformity (a), the image of long leg casting (b) applied after corrective manipulations performed during Ponseti's method in the conservative treatment.

ant data were compared and analyzed by Mann-Whitney U test. The categorical variables were summarized by numbers and percentages, and Pearson's exact chi-square and chi-square tests with correction for continuity were used for the comparisons. In all analyses, 0.05 was considered as the significance level.

Results

Of 71 patients who were diagnosed with pes equinovarus in the mid-trimester fetal ultrasonographic imaging during the study period, no fetal malformation was found in 32 (45.1%) (isolated group), and additional fetal anomaly was observed together with PEV in 39 (54.9%) (non-isolated group). Pregnancy termination was decided in 17 (43.6%) patients in the non-isolated group due to chromosomal anomaly and concurrent major fetal malformations. Flow chart for pregnant women diagnosed with pes equinovarus in the fetus in mid-trimester ultrasonographic imaging between April 1st, 2014 and

January 1st, 2017 is shown in **Fig. 3**. When isolated PEV cases and non-isolated PEV cases were compared in terms of maternal characteristics, no statistically significant difference was found between the groups in terms of age, gravida, parity and body mass index ($p=0.182$, $p=0.079$, $p=0.149$, and $p=0.125$, respectively). When the week of gestation established with median diagnosis in the non-isolated group was compared with isolated PEV group, it was found lower which was statistically significant [20.0 (16.0–26.0) and 22 (19.0–25.0); $p=0.041$]. Fetal karyotyping was performed on 37.5% of the patients in the isolated group during prenatal period while this rate was 38.4% in non-isolated group ($p=0.802$). While no chromosomal change was found in the invasive prenatal diagnosis performed for all patients in the isolated group, trisomy 18 was found in 3 patients and 46,XX,inv(9)(p12q13) in 1 patient in the non-isolated group ($p=0.053$). The characteristics of pregnant women found to have isolated and non-isolated PEV are summarized in **Table 1**.

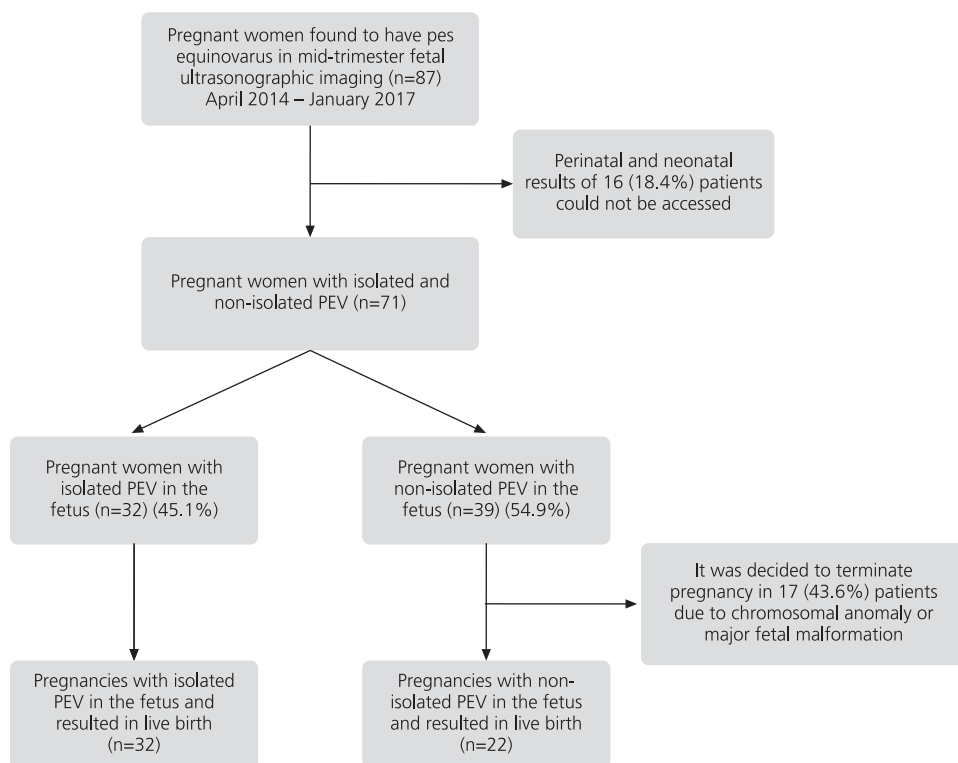


Fig. 3. Flow chart for pregnant women diagnosed with pes equinovarus in the fetus in the mid-trimester ultrasonographic screening between April 2014 and January 2017.

Table 1. The characteristics of the groups found to have isolated and non-isolated pes equinovarus.

	Isolated group (n=32)	Non-isolated group (n=39)	p-value
Age*	28.34±5.64	30.10±5.32	0.182
Gravida†	2.0 (1.0–4.0)	2.0 (1.0–13.0)	0.079
Parity†	1.0 (0.0–3.0)	1.0 (0.0–5.0)	0.149
Abortion†	0.0 (0.0–2.0)	0.0 (0.0–7.0)	0.329
Body mass index (kg/m ²)†	26.0 (22.0–32.0)	27.0 (18.4–38.0)	0.403
Gestational age at diagnosis†	22.0 (19.0–25.0)	20.0 (16.0–26.0)	0.041
Laterality†			0.084
Unilateral	13.0 (40.7)	8.0 (20.6)	
Bilateral	19.0 (59.3)		
	31.0 (79.4)		
Fetal karyotyping†	12.0 (37.5)	15.0 (38.4)	0.802
Normal karyotyping	12.0 (100)	11.0 (73.3)	0.053
Trisomy 18	-	3.0 (20.0)	
46,XX,inv(9)(p12q13)	-	1.0 (6.7)	

*Mean ± standard deviation; †Median (min–max); ‡n (%)

Gestational age at delivery was significantly lower in non-isolated PEV group compared to isolated group ($p<0.001$). When newborns' birth weight, 1-minute and 5-minute APGAR scores and pH values of cord blood in the non-isolated PEV group were compared to isolated-PEV group, statistically significant reduction were found in all parameters ($p<0.001$ in all parameters). Neonatal intensive care unit need in the isolated PEV group was significantly lower compared to the newborns with non-

isolated PEV ($p<0.001$). PEV anomaly was more common among male fetuses in both groups whereas there was no significant difference among the groups in terms of female-male ratio ($p=0.332$). Perinatal outcomes of the patients in isolated and non-isolated pes equinovarus groups are given in **Table 2**.

In the group complicated with isolated pes equinovarus during neonatal period, 81.2% of the newborns

Table 2. Delivery results of the groups found to have isolated and non-isolated pes equinovarus.

	Isolated group (n=32)	Non-isolated group (n=39)	p-value
Gestational age at delivery*	38.0 (34.0–39.0)	34.5 (25.0–39.0)	<0.001
Delivery type†			0.583
Vaginal	17 (53.2)	10 (45.5)	
Cesarean section	15 (46.8)	12 (54.5)	
Birth weight*	3150.0 (1500.0–3900.0)	1565.0 (520.0–3600.0)	<0.001
Sex†			0.332
Female	9 (28.2)	9 (40.9)	
Male	23 (71.8)	13 (59.1)	
1-minute APGAR score*	8.0 (6.0–9.0)	6.5 (1.0–8.0)	<0.001
5-minute APGAR score*	9.0 (8.0–10.0)	7.5 (1.0–9.0)	<0.001
Cord pH*	7.33 (7.20–7.42)	7.20 (6.90–7.40)	<0.001
Newborn's intense care unit need†	5 (15.6)	18 (81.8)	<0.001

*Median (min–max); †n (%)

were treated by conservative therapy (corrective casting - Ponseti's or Kite's method), and this rate was 27.2% in the non-isolated group ($p<0.001$). In the conservative therapy, Ponseti's method was used more frequently in both groups; surgical treatment need after conservative therapy was higher in non-isolated group compared to isolated PEV group which was statistically significant (18.8% and 72.8%, respectively; $p<0.001$). Posteromedial release operation was the most frequent practice in the newborns who needed surgery in both groups. Orthopedic treatment results of the patients during neonatal period in isolated and non-isolated pes equinovarus groups are summarized in **Table 3**.

Discussion

Mid-trimester fetal ultrasonographic imaging is routinely recommended for all pregnant women at prenatal care. In parallel to advanced ultrasonographic technologies, it has become possible to establish early diagnosis during prenatal period for many congenital malformations including fetal musculoskeletal deformities.^[12,13] Also, it has been claimed that the use of 3D ultrasonography in prenatal ultrasonographic imaging has helped to establish early and accurate diagnosis for congenital malformations.^[14] Although different rates are reported in various studies, the diagnosis rate of pes equinovarus during prenatal period is reported about 60%.^[15] In our study, we found that median week of gestation when pes equinovarus was diagnosed was 22 weeks in isolated PEV cases and 20 weeks in non-isolated PEV cases. Similar to our study, Hartge et al. retrospectively analyzed the prenatal and postnatal results of 106 fetuses with congenital PEV and they reported median prenatal diagnosis time as 23 weeks for those who gave live births, and as 18 weeks in the group who were found to have many congenital mal-

formations and gave stillbirth.^[16] In the epidemiological case control study conducted in the USA, Mahan et al. found PEV diagnosis rate 62.3% at prenatal period even though there were different rates in various states. As a result of their multivariate analysis, they showed that maternal age <35 years, presence of concomitant congenital malformations and PEV anomaly being bilateral were the strongest predictors to establish PEV diagnosis at prenatal period.^[17] In our study, we found concomitant congenital malformation in 54.9% of the patients diagnosed with PEV in mid-trimester ultrasonographic screening, and we observed that invasive prenatal diagnosis was established in 37.5% of the fetuses with isolated PEV and in 38.4% of the fetuses with non-isolated PEV. While there was no chromosomal alteration in cases with isolated PEV who underwent invasive prenatal diagnosis, we observed chromosomal alteration in 26.7% of the fetuses with concomitant malformation. While there are studies in the literature which define 46,XX,inv(9)(p12q13) chromosomal alteration observed in a patient in non-isolated patient group as a chromosomal polymorphism, which is clinically insignificant, there are also other studies associating this chromosomal alteration with fascial dysmorphism, neurodevelopmental retardation and congenital anomalies.^[18] A recent study found that abnormal karyotype rate was 2.2% in isolated cases with fetuses diagnosed with congenital PEV and 30.3% in cases with concomitant malformations, and the study showed that the laterality of PEV anomaly is not associated with high chromosomal anomaly incidence.^[19] On the other hand, the researchers reported that a detailed ultrasonographic imaging should be performed in order to identify concomitant malformations in fetuses diagnosed with PEV during congenital period, karyotyping should be recommended in the presence of concomitant

Table 3. Orthopedic results of the groups found to have isolated and non-isolated pes equinovarus.

	Isolated group (n=32)	Non-isolated group (n=22)	p-value
Conservative therapy (Corrective casting)*	26 (81.2)	6 (27.2)	<0.001
Ponseti	19	5	
Kite	4	1	
Conservative + Surgical therapy*	6 (18.8)	16 (72.8)	<0.001
Posteromedial release	4	7	
Posteromedial and lateral release	2	4	
Subtalar release	-	3	
Tibialis anterior tendon transfer	-	2	

*n (%)

malformations, but it is controversial to recommend invasive prenatal diagnosis in isolated cases.^[19,20] Although it is important to establish PEV diagnosis on fetus at ultrasonographic imaging during prenatal period and to distinguish if the case is isolated or not, in terms of invasive prenatal diagnosis and informing the family about postnatal outcomes, the restrictions of ultrasonography also should be mentioned when counselling, and it should be stated to the family that concomitant findings can be identified during further weeks of gestation or postnatal period in about 10% of the cases established with isolated PEV diagnosis at prenatal period.^[21,22]

While the treatment of pes equinovarus deformity during neonatal period may vary, conservative therapy is usually preferred in the beginning, and surgical option is considered when the cases do not respond to conservative therapy. In addition to conservative therapy which includes daily stretching exercises and French functional methods where physiotherapy and splints are used, Ponseti's and Kite's methods also can be used in which serial manipulation and casting are performed. Today, Ponseti's method is the most frequent modality used in conservative therapy, and it is aimed to treat all foot deformities (cavus, varus, and adduction) simultaneously in this technique.^[23,24] In this method, manipulations performed on feet and ankles for 6–8 weeks are followed by long leg casting, where casts are replaced weekly. In more than 90% of the cases, the procedure of Achilles tenotomy is required, which is a minor surgical procedure performed by local anesthesia to fix equinism deformity completely, and this procedure is considered as a part of the routine therapy. At the end of the therapy, the patients are recommended to wear orthopedic boots for 23 hours a day for 3 months and then only during sleep times up until age of 4.^[25] In Kite's method, each deformity of foot is fixed by biweekly manipulation and immobilization procedures one by one, and physicians do not proceed to next deformity until current one is fixed completely.^[26] In our study, we found that Ponseti's method was the most common procedure in the conservative therapy performed on the cases diagnosed with isolated and non-isolated PEV in mid-trimester fetal ultrasonographic screening. While we found that the success rate of conservative therapy was 81.2% in cases with isolated PEV, significantly higher surgery need was observed in cases with concomitant malformations after conservative therapy. A recent study evaluating postnatal outcomes of fetuses with congenital PEV reported that at least one surgical procedure was

needed during postnatal period in 32.6% of the cases.^[16] Rijal et al. compared Ponseti's and Kite's methods in the conservative therapy of isolated PEV cases, and showed that Ponseti's method provided a faster recovery in all deformities of PEV.^[27] He et al. compared Ponseti's method with other conservative therapy options, and they reported that Ponseti's method was safe and effective on PEV treatment and significantly decreased surgery needs compared to other methods.^[28]

Muscle, ligament or joint releases such as tibialis anterior tendon transfer and posteromedial soft tissue release operations, and major surgical procedures such as wedge osteotomy are required in patients who do not respond to conservative therapy or develop relapse later despite the conservative therapy.^[29,30] In this study, we found that the fetuses found to have isolated PEV had significantly less major surgery needs than the fetuses found to have concomitant anomalies, and we observed that posteromedial release operation was the most common procedure in the patients with surgery needs in both groups. Some of the long-term observational studies performed on the cases developing relapses in particular claimed that the success rate for the results of major surgery in such cases is not high, and that repeating conservative methods in these patients increases the treatment success.^[31,32]

Our study has some limitations which are the retrospective study design, being unable to determine the rate of detecting pes equinovarus since it was not possible to access neonatal outcomes of all patients who underwent mid-trimester fetal ultrasonographic screening, and long-term treatment results were not evaluated after conservative and/or surgical therapy.

Conclusion

Consequently, distinguishing the fetuses, which are diagnosed with pes equinovarus during prenatal period, as isolated and non-isolated cases has a critical significance in the prediction of neonatal outcomes. The incidence of chromosomal alterations and possibility of poor neonatal and orthopedic outcomes are higher in the non-isolated PEV cases. Success rate is higher by conservative methods in orthopedic treatment for the cases with isolated PEV, and surgery needs seem higher in non-isolated cases. The results of our study will help to inform pregnant women properly, who are diagnosed with isolated and non-isolated fetal pes equinovarus during prenatal period, in terms of follow-

up, treatment options and treatment outcomes during perinatal and neonatal periods.

Conflicts of Interest: No conflicts declared.

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