

**EARLY SCREENING FOR ANTENATAL CONGENITAL FETAL LIMB ANOMALIES  
AND IMPLICATIONS IN THE PEDIATRIC SURGERY****Dominic Gabriel Iiescu<sup>1,2</sup>, Ciprian Laurențiu Pătru<sup>\*</sup>, Roxana Drăgușin<sup>1</sup>, Maria Florea<sup>1</sup>, George Lucian Zorilă<sup>1</sup>,  
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**ABSTRACT**

**Introduction:** Congenital limb anomalies may be isolated, or may be associated with genetic syndromes. Literature shows that over 90% of them can be detected in the first trimester. The treatment of congenital limb anomalies is still a therapeutic challenge requiring multidisciplinary management to improve function and quality of life. **Aim:** The aim of the study was to determine the accuracy of the antenatal ultrasound in the detection of fetal limb anomalies in the first trimester of pregnancy for a better counselling and an earlier surgical correction. **Methods:** The study enrolled patients referred consecutively to the Antenatal Diagnosis Unit with gestational age between 11 weeks + 0d and 13W + 6d, over a 6 years period. In all cases an extensive protocol of morphological evaluation was applied. We correlated the first trimester findings with the second trimester examination, histopathological examination, postnatal clinical examination and surgical correction. **Results:** The average gestational age at diagnosis was 12w+4d. Of the study group, 34 fetuses had limb anomalies. 9 fetuses had major limb anomalies. In these cases, the diagnosis was suspected / stated in the first trimester of pregnancy (detection rate 100%). They highest incidence had the congenital club foot and skeletal dysplasia. Isolated anomalies were rare (7 cases). Most cases associated other structural anomalies (18 cases), increased nuchal translucency and chromosomal anomalies. In one case, it has been demonstrated the dynamics of the musculoskeletal structures (fetal akinesia deformation sequence - FADS) between two successive examinations: 12 weeks and 22 weeks. Early surgical correction was possible for all 7 cases suspected with minor isolated limb anomalies. **Conclusions:** An early antenatal diagnosis of fetal limb anomalies can change the counselling of the couple, the outcome of the pregnancy and improve the surgical management. However, prospective studies on samples with adequate statistical significance are needed.

**KEYWORDS:** Limb Anomalies, Prenatal Diagnosis, Pediatric Surgery, Genetic Disorder.**INTRODUCTION**

Congenital limb abnormalities may be isolated or, more commonly, associated with other structural anomalies and genetic syndromes. Literature suggests that up to 90% of fetal limb structures (excluding fingers) can be seen on first trimester ultrasound using a combined transabdominal and transvaginal scan.<sup>[1,2]</sup> Over the past decade the prevalence and accuracy of first-trimester ultrasound have increased. Although evaluation of fetal limbs is not routinely recommended in the first trimester of pregnancy,<sup>[3,4,5]</sup> an early detection of fetal limb anomalies will allow a better counseling and choices for the affected couples.

By performing a morphological scan in the first trimester of pregnancy, a number of limb anomalies can be

diagnosed, including amelia, radial aplasia and club hand, clubfoot, sirenomelia and phocomelia.<sup>[6,7,8,9,10]</sup>

For some conditions therapy should begin in the neonatal period.<sup>[11,12]</sup> An early referral to the surgeon is important.

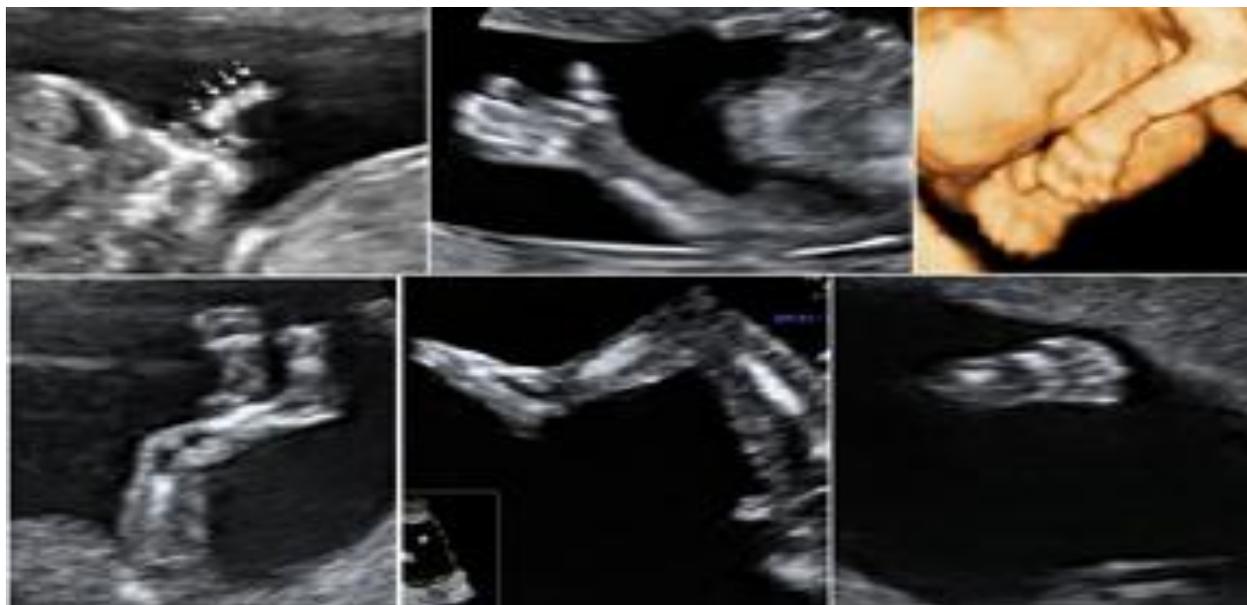
**MATERIAL AND METHODS**

Between 1 January 2009 and 31 January 2015, 1123 pregnancies with gestational age between 11–0 and 13–6 weeks were assessed by ultrasound at the Prenatal Diagnosis Unit in the Clinical Emergency Hospital in Craiova, Romania.

All fetuses were scanned transabdominally and transvaginally using high-resolution ultrasound machines (Voluson 730 and E8-GE Healthcare Systems). Fetal gestational age based on ultrasound Crown Rump Length

(CRL) measurements, location and type of limb anomalies and associated anatomic anomalies were obtained. The fetal limbs were examined using a sequential scan. The upper extremities were examined starting with the humerus, followed by the forearms and

the hands in a proximal-to-distal direction. The lower extremities were examined starting with the femur, tibia and fibula, and the feet in a proximal-to-distal direction. Coronal sections were also taken. The limb positions and movements were lastly examined. (Figure 1)

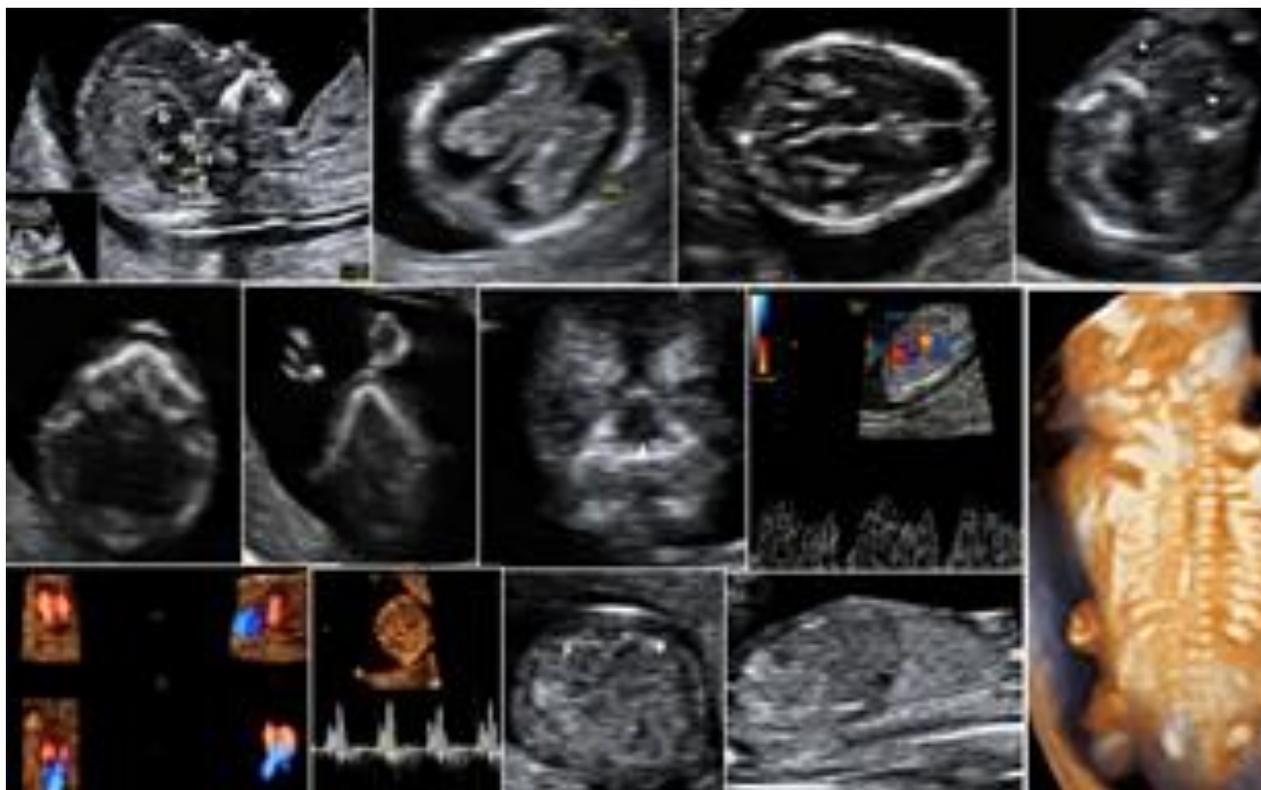


**Figure 1. Assessment of the fetal limbs at the first trimester ultrasound scan.**

An extensive protocol of morphological evaluation was applied including visualization of the fetal skull, choroid plexuses, cerebellum, orbits, lips, nose, heart (four chamber and three-vessel view both in grey scale and color Doppler and pulse Doppler of the ductus venosus-

DV), diaphragm, stomach, abdominal wall, the umbilical cord insertion, kidneys, bladder and spine. (Figure 2)

All patients had also a fetal anatomy scan in the second trimester at 18 to 20 weeks of gestation. (Figure 3)



**Figure 2: First trimester fetal anatomy scan.**



**Figure 3: Second trimester fetal anatomy scan.**

We correlated the first trimester data with the second trimester examination, postnatal examination, surgical correction and histopathological results (in cases of pregnancy termination where genetic tests and autopsy were abstracted).

## RESULTS

Between 1 January 2009 and 31 January 2015, a total of 1123 patients had early fetal anatomy scans. The mean gestational age at the time of the first trimester ultrasound scan was 12 weeks +4 days. A total of 34 limb anomalies were identified, 27 in the first trimester and 7 in the second trimester of pregnancy. In all major anomalies (9 cases) the detection rate was 100% for the first trimester of pregnancy. (Figure 4,5).



**Figure 4: Club foot.**



Figure 5: A case of tetramelia diagnosed in the first trimester. 3D reconstruction and anatomopathological aspects.

**Types of fetal limb anomalies**

Club foot was the most common anomaly detected (8 cases) followed by skeletal dysplasia (6 cases), club hand (5 cases), sirenomelia (4 cases) and limb dysplasia (2

cases). In one case we demonstrated the dynamics of the musculoskeletal structures (fetal akinesia deformation sequence - FADS) between two successive examinations: 12 weeks and 22 weeks.(Figure 6,7)



Figure 6: Second trimester scan. Missing fingers at both hands and club foot.



Figure 7: Fetal akinesia deformation sequence – FADS.

**Nuchal translucency (NT) with limb abnormalities**

Nuchal translucency measurements were obtained in all cases. 29 fetuses diagnosed with limb anomalies associated an NT  $\geq$  95th percentile. A significantly increased NT was observed in all cases of lethal skeletal dysplasia and in 8 cases of clubfoot.

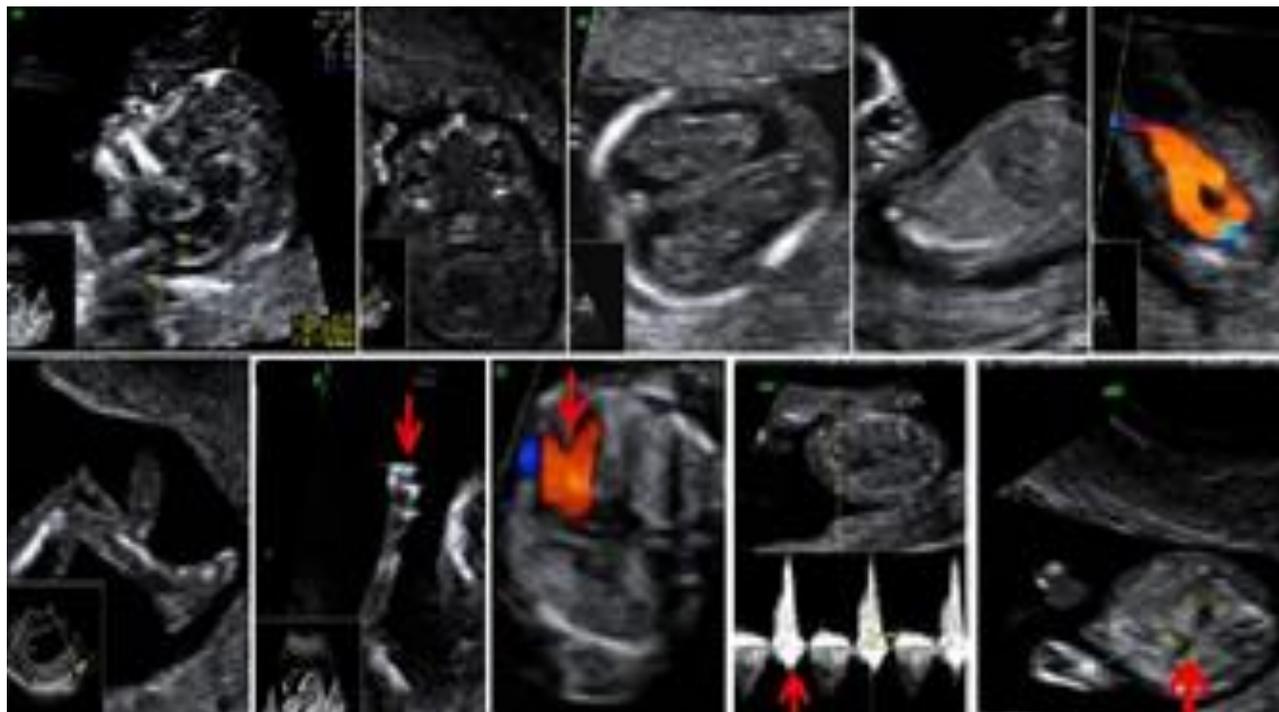
**Associated abnormalities**

Most cases associated other structural anomalies (18 cases), whereas the remaining 7 cases had otherwise normal anatomy (only isolated minor limb anomalies-club hand and club foot). These cases were operated by

the pediatric surgeon and the follow-up at 3 years was very good. The most common associated anomalies included hydrops (11 cases) cardiac abnormalities (9 cases), abdominal wall defects (6 cases), a single umbilical artery (4 cases) and megacystis (2 cases).

**Diagnosis**

After counseling the couples, only 26 patients had fetal karyotyping. Of these, 2 fetuses had a normal karyotype, 12 fetuses had trisomy 18, 10 fetuses had trisomy 21 and in 2 cases the karyotype was euploid with mosaicism. (Figure 8).



**Figure 8:** A case of trisomy 18. First trimester scan suspected only clenched hands, a possible atrio-ventricular septal defect with normal tricuspid valve and renal dilatation over 2 mm.

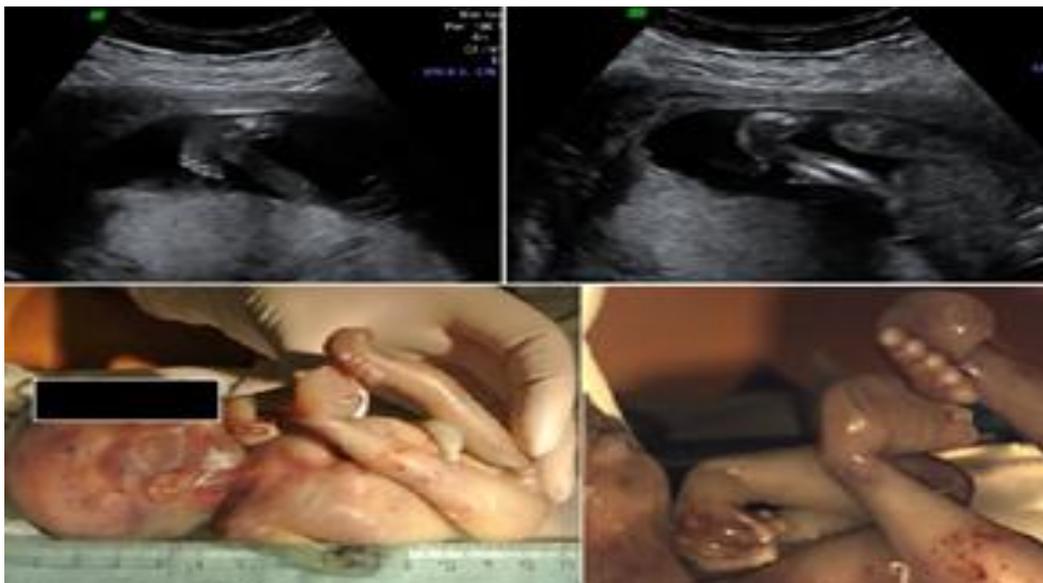
**Pregnancy Outcomes**

Pregnancy outcome was known in all cases. 22 of the patients obtained for therapeutic abortion, 9 patients had spontaneous abortions and there were 3 cases of

intrauterine death at 17 weeks of gestation. There were no live births. Fetal autopsy reports were available in all cases and confirmed the suspected anomalies.(Figure 9,10).



**Figure 9:** Same case of trisomy 18. Fetal autopsy confirmed the ultrasound findings: Clenched hands (A), Atrio-ventricular septal defect (B) and kidney malformations (C).



**Figure 10: Bilateral club hand and club foot.**

## DISCUSSION

According to literature, many limb abnormalities are detectable before 15 weeks of gestation, including long bone shortening or aplasia, absent digits, syndactyly, abnormal positioning of wrists and ankles, club hands and feet, overlapping digits, and fused lower extremities.<sup>[13,14,15]</sup> Our study results are consistent to literature showing that congenital club foot and skeletal dysplasia can be detected in the first trimester.

Recent studies<sup>[16]</sup> have demonstrated that the first trimester diagnosis of the club foot may be difficult because the visualization of the long axis of the foot should be visualized in the same plane as the full length of the tibia and fibula.<sup>[17]</sup> Our study showed that club foot had the highest detection rate, maybe due to the association of other fetal anomalies that may have helped the the rate of missed diagnoses.

In cases of skeletal dysplasia, an increased NT associated with hypomineralization of the skull, shortening of the long bones, a narrow thorax, fractured ribs and short angulated long bones may suspect the diagnosis, although a second trimester scan is necessary to confirm.<sup>[18]</sup>

Many studies described the association between limb anomalies and aneuploidy. Our data suggest that evaluation of the fetal limbs can be part of the routine first-trimester nuchal scan. In our study 24 of the 34 fetuses had a chromosomal disorder. We conclude that an increased NT in the first trimester may not useful in predicting fetal limb defects. Screening for limb anomalies in the first trimester of pregnancy is very important because they are often associated with other serious fetal anomalies. Many of these anomalies can now be detected on transabdominal and transvaginal scan, although 3D ultrasound may provide a more detailed evaluation.<sup>[18, 19]</sup> In our study, 32 of the 34

fetuses had associated anatomic anomalies. It is important to notice that in this study a very small number (2 cases) had isolated limb malformations.

The association between fetal limb anomalies and aneuploidy is very common.<sup>[20]</sup> In this study the majority of the fetuses associated trisomy 18 (12 cases). Trisomy 18 is a usually lethal chromosomal disorder that affects approximately 1 per 6000 live births (38). It is the most frequent trisomy associated with limb anomalies.<sup>[21]</sup> Because of the high incidence of aneuploidy in fetuses diagnosed with limb anomalies counseling the couples for invasive maneuvers (chorionic villous sampling or amniocentesis) should be considered.

In our study, fetal autopsy reports were possible and confirmed the suspected anomalies in all cases. In some cases, autopsies additionally diagnosed other fetal anomalies: multicystic kidneys, cleft lip and other cardiac malformations.

The first consultation over a newborn with a anomaly of the limbs can be difficult for both the parents and the surgeon specially in cases with major anomalies. Parents do not realise the extent of the malformation and how it will or will not develop. Helping the parents to understand what is involved in the surgical treatment requires time and patience. There are many aspects for the parents to understand (several operations may be necessary; scars may be produced on visible areas). There are good arguments for surgery in the neonatal period. Some operations need to be done in the first few months of life (for instance tight constriction bands, floating polydactyly of the little finger or thumb, and some syndactyly cases with distant bony union and flexion deformities.<sup>[22,23]</sup> The age of the patient at operation is thought to be an important factor in the long-term outcome.<sup>[24,25]</sup>

To conclude, our study results are consistent with the literature suggesting that, in the majority of cases, major limb anomalies can be detected in the first trimester. In most fetuses it is possible to evaluate the limbs at the time of nuchal translucency screening. Physicians should consider performing a more detailed ultrasound scan of the fetus at the time of NT measurement. This can improve the couple's counseling for a better management of the pregnancy and an earlier correction. However, the number of the patients are small and we still need larger cases for further confirmation of these data.

### COMPETING INTERESTS

The authors declare that they have no competing interests.

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### REFERENCES

1. Ebrashy A, El KA, Momtaz M, et al. 13–14-week fetal anatomy scan: a 5-year prospective study. *Ultrasound Obstet Gynecol.*, 2010; 35(3): 292–6.
2. Timor-Tritsch IE, Bashiri A, Monteagudo A, et al. Qualified and trained sonographers in the US can perform early fetal anatomy scans between 11 and 14 weeks. *Am J Obstet Gynecol.*, 2004; 191(4): 1247–52.
3. Salomon LJ, Alfirevic Z, Bilardo CM, Chalouhi GE, Ghi T, Kagan KO, Lau TK, Papageorgiou AT, Raine-Fenning NJ, Stirnemann J, Suresh S, Tabor A, Timor-Tritsch IE, Toi A, Yeo G -ISUOG Practice Guidelines: performance of first-trimester fetal ultrasound scan. *Ultrasound Obstet Gynecol.*, 2013; 41: 102-113.
4. NICE. Antenatal care: Routine care for the healthy pregnant woman. National Institute for Health and Clinical Excellence: London, 2010.
5. Nicolaidis KH, Sebire NJ, Snijders RJM. The 11-14 week scan. Diploma in Fetal Medicine Series. The Parthenon Publishing Group, London., 1999.
6. Rice KJ, Ballas J, Lai E, et al. Diagnosis of fetal limb abnormalities before 15 weeks: cause for concern. *J Ultrasound Med.*, 2011; 30(7): 1009–19.
7. Souter V, Nyberg D, Siebert JR, et al. Upper limb phocomelia associated with increased nuchal translucency in a monochorionic twin pregnancy. *J Ultrasound Med*, 2002; 21(3):355.
8. Bianca S, Bartoloni G, Libertini C, et al. Fetal upper limb amelia with increased nuchal translucency. *Congenit Anom (Kyoto)*, 2009; 49(3): 121–2.
9. Singh C, Lodha P, et al. Diagnosis of sirenomelia in the first trimester. *J Clin Ultrasound.*, 2014; 6: 355–9.
10. Bronshtein M, Keret D, Deutsch M, et al. Transvaginal sonographic detection of skeletal anomalies in the first and early second trimesters. *Prenat Diagn* 1993; 13(7): 597–601.
11. Green DP, Hotchkiss RN, Pederson WC, eds. Green's operative hand surgery, Vol. 1, 4th edition. London: Churchill Livingstone, 1999.
12. Nather A, Bose K. Conservative and surgical treatment of clubfoot. *J Pediatr Orthop.*, 1987; 7: 42-8.
13. Bianca S, Bartoloni G, Libertini C, et al. Fetal upper limb amelia with increased nuchal translucency. *Congenit Anom (Kyoto)* 2009; 49: 121–122.
14. Akbayir O, Gungorduk K, Sudolmus S, Gulkilik A, Ark C. First trimester diagnosis of sirenomelia: a case report and review of the literature. *Arch Gynecol Obstet* 2008; 278: 589–592.
15. Gundogan M, Fong K, Keating S, Pierre-Louis J, Chitayat D. First trimester ultrasound diagnosis of lethal multiple pterygium syndrome. *Fetal Diagn Ther.*, 2006; 21: 466–470.
16. Souka AP, Pilalis A, Kavalakis Y, et al. Assessment of fetal anatomy at the 11–14-week ultrasound examination. *Ultrasound Obstet Gynecol.*, 2004; 24(7): 730–4.
17. Viora E, Sciarrone A, Bastonero S, et al. Increased nuchal translucency in the first trimester as a sign of osteogenesis imperfecta. *Am J Med Genet.*, 2002; 109(4): 336–7.
18. Benoit B, Hafner T, Bekavac I, Kurjak A. Three-dimensional sonoembryology. *Ultrasound Rev Obstet Gynecol.*, 2001; 1: 111–119.
19. McAuliffe FM, Fong KW, Toi A, et al. Ultrasound detection of fetal anomalies in conjunction with first-trimester nuchal translucency screening: a feasibility study. *Am J Obstet Gynecol.*, 2005; 193: 1260–5.
20. Dyson RL, Pretorius DH, Budorick NE, et al. Three-dimensional ultrasound in the evaluation of fetal anomalies. *Ultrasound Obstet Gynecol.*, 2000; 16: 321–328.
21. Luchi C, Schifano M, Sacchini C, et al. Detailed fetal anatomy assessment in the first trimester at 11, 12 and 13 weeks of gestation. *J Matern Fetal Neonatal Med.*, 2012; 25(6): 675.
22. Zelop C, Benacerraf B. Sonographic diagnosis of fetal upper extremity dysmorphism: significance and outcome. *Ultrasound Obstet Gynecol.*, 1996; 8: 391–396.
23. Bradbury ET, Kay SPJ, Tighe C, Hewitson J. Decisionmaking by parents and children in paediatric hand surgery. *Br J Hand Surg.*, 1994; 47: 324–30.
24. Wicart PR, Barthes X, Chanem I, Sezing R. Clubfoot posteromedial release: advantages of tibialis anterior tendon lengthening. *J Pediatr Orthop.*, 2002; 22: 536-532.
25. Laaveg SJ, Ponseti SV. Long-term results of treatment of congenital clubfoot. *J Bone Joint Surg [Am]*, 1980; 62-A: 23-31.