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Results of fetal anomaly screening performed at 11–14 weeks of gestation at a tertiary center

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Abstract

Objective: The aim of the study is to determine and analyze the incidence of congenital structural anomalies which can be identified by fetal anomaly screening at 11–14 weeks of gestation.

Methods: The patients (except those with cardiac anomalies) found to have fetal anomaly during nuchal translucency (NT) measurement performed at 11–14 weeks of gestation in the ultrasonographic examination at a tertiary center between 2014 and 2016 were included in the study designed as a retrospective cohort study. The demographic characteristics, ultrasonographic findings and gestational outcomes were obtained from medical records.

Results: Congenital structural anomaly (except cardiac anomaly) was identified in 57 (0.46%) out of 12,352 pregnant women who underwent anomaly screening. In the study group, the most common anomaly was neural tube defect (53.4%) followed by anterior abdominal wall defects (15.5%), cystic hygroma (12.1%), hydrops fetalis (6.9%), urinary system anomaly (6.9%) and twin reversed arterial perfusion (TRAP) syndrome (3.4). NT was measured over 95th percentile in all cystic hygroma and hydrops fetalis cases and in 77.8% of anterior abdominal wall defects.

Conclusion: With fetal anomaly screening performed together with first trimester NT measurement, neural tube defect in particular and most of the anomalies can be detected in early weeks of gestation.

Keywords: First trimester, nuchal translucency, fetal anomaly.

Özet: Üçüncü basamak bir merkezde 11–14. gestasyonel haftada yapılan fetal anomali taraması sonuçları

Amaç: Çalışmanın amacı 11–14. gebelik haftasında fetal anomali taraması ile saptanabilen konjenital yapısal anomalilerin insidansını belirlemek ve analizini yapmaktır.

Yöntem: Retrospektif kohort çalışması olarak tasarlanan çalışmaya 2014–2016 yılları arasında üçüncü basamak bir merkezde yapılan ultrasonografik incelemede 11–14. gebelik haftalarında ense saydamlığı (NT) ölçümü sırasında fetal anomali saptanan hastalar (kardiyak anomaliler hariç) dahil edildi. Olguların demografik özellikleri, ultrasonografi bulguları ve gebelik sonuçları tıbbi kayıtlardan elde edildi.

Bulgular: Anomali taraması yapılan 12.352 gebenin 57'sinde (%0.46) konjenital yapısal anomali (kardiyak anomali hariç) tespit edildi. Çalışma grubunda en sık nöral tüp defekti (%53.4) ve daha sonra sırasıyla batın ön duvarı defektleri (%15.5), kistik higroma (%12.1) hidrops fetalis (%6.9), üriner sistem anomalisi (%6.9) ve ikizde ters arteryel kanlanma *(twin reversed arterial perfusion*, TRAP) sendromu (%3.4) izlendi. Kistik higroma ve hidrops fetalis olgularının hepsinde, batın ön duvarı defektlerinin %77.8'inde NT 95 persentilin üzerinde ölçüldü.

Sonuç: İlk trimester NT ölçümü ile birlikte yapılan fetal anomali taraması ile başta nöral tüp defekti olmak üzere çoğu anomali erken gebelik haftalarında saptanabilir.

Anahtar sözcükler: Birinci trimester, ense saydamlığı, fetal anomali.

Introduction

Although the screening of congenital structural anomalies is performed by ultrasonographic examination between 18 and 23 weeks of gestation,[1,2] the improvements in the resolution of ultrasound devices and common use of first trimester screening tests have enabled to diagnose particular major anomalies at the first trimester during nuchal translucency (NT) measurement.[3] In the

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beginning, first trimester ultrasonographic examinations were only used to determine gestational age, to detect fetal heartbeat and to identify chorionicity in twin pregnancies.[3] However, 49–68% of fetal anomalies can be detected by first trimester ultrasonographic examination today.[4–7]

Fetal structural anomalies are seen approximately in 3–5% of all pregnancies.[8] Since most of the fetal organs develop in the first 12 weeks,[9] ultrasonographic examination performed between 11 and 14 weeks of gestation enables to establish early diagnosis of most of the fetal anomalies.[4–7] Early diagnosis may help to take early decisions on the management of patient, and to carry out early karyotyping for the diagnosis of chromosomal anomalies which may cause anomaly and spontaneous abortions. The aim of this study was to determine fetal anomaly incidence except cardiac anomaly which can be detected between 11 and 14 weeks of gestation, and to analyze these anomalies.

Methods

In this retrospective cohort study, the medical records of pregnant women who admitted to Etlik Zübeyde Hanım Gynecology Training and Research Hospital for first trimester screening tests at 11–14 weeks of gestation between April 2014 and April 2016 were reviewed. The demographic characteristics, ultrasonography reports and gestational outcomes of the cases were obtained from the computer record system of the hospital. The patients who were found to have fetal anomaly during NT measurement when undergoing first trimester screening test were included in the study. Women having molar pregnancy and ectopic pregnancy, measured to have crown-rump length (CRL) <45 mm or >84 mm and detected to have fetal cardiac anomaly were exclude from the study. The study was approved by Training Planning Council of the hospital and informed consent was received from all patients to use medical records in scientific studies.

Ultrasonographic examination was primarily carried out with transabdominal probe (2–5 MHz, Hi Vision Preirus, Hitachi Medical Corporation, Tokyo, Japan). In cases where all fetal anatomic structures could not be evaluated in a clear way transabdominally, 6–9 MHz probe was used and transvaginal ultrasonography was performed. With the CRL measurement among ultrasonography reports, information on gestational age, fetal viability, fetus number and fetal anatomy were obtained. Cranium, cerebral structures, orbita, facial profile, nasal bone, spinal column, lungs, diaphragm, kidneys, bladder, lower and upper extremities (long bones, hands and feet), anterior body wall and cord insertion were the anatomic structures evaluated during fetal anomaly screening. NT values of all fetuses, except those found to have anencephaly, measured according to the standards determined by Fetal Medicine Foundation (FMF) were recorded.[10] If not associated with cystic hygroma, isolated NT increase was not considered as fetal anomaly. Ultrasonographic findings were confirmed with abortion, termination or postnatal macroscopic examination of fetus in all cases except those not maintained their gestational follow-up in the study hospital.

The statistical analysis was done by using SPSS 17 (IBM Corp., Armonk, NY, USA). The continuous variables were presented as mean ± standard deviation or median (minimum–maximum) according to the conformity to normal distribution, and categorical variables were presented as number and percentage.

Results

Congenital anomaly was found in 57 of 12,352 cases who underwent fetal anomaly screening during NT measurement at 11–14 weeks of gestation. Fetal anomaly incidence found during first trimester screening test was 0.46%.

The demographic characteristics and ultrasonographic findings of the cases included in the study are given in **Table 1**. The distribution of fetal anomalies found is shown in **Fig. 1**. The most common fetal anomaly found in first trimester except cardiac anomalies was neural tube defect (53.4%). The second com-

Table 1. Demographic characteristics and ultrasonographic findings of the cases found to have first trimester fetal anomaly.

Characteristics	
Age (year)	25.9±5.9
Gravida	2.2±1.3
Parity	1 (0–3)
Abortion	0 (0–2)
Gestational age (day)	87.9±5.5
CRL, mm	59.5±11.5
NT, mm	3.1 (0.7–19)

The data was presented as mean ± standard devition or median (minimum–maximum). **CRL:** crown-rump length; **NT:** nuchal translucency

mon anomaly was anterior abdominal wall defect (15.5%). Ultrasonographic views of some fetal anomalies are shown in **Fig. 2**.

The detailed description of fetal anomalies, gestational outcomes and the relationship with NT measured above 95th percentile are given in **Table 2**. 66.7% (n=38) of pregnancies resulted with termination, 10.5% (n=6) of them resulted with delivery and 5.3% (n=3) of them resulted with abortion. It was found that ten pregnant women (17.5%) did not undergo their follow-up and treatment at study hospital. The most common anomaly among neural tube defects was anencephaly (24.1%). Among anterior abdominal wall defects, omphalocele was the most common anomaly diagnosed (8.6%). 5.2% of the cases had wide anterior wall defect. In these cases, liver, stomach and intestine were out of abdomen and they also had ectopia cordis.

Four cases had spontaneous multiple pregnancy (twin pregnancy in three cases and triple pregnancy in one case). In all twin pregnancies, it was found during anomaly screening that one of the fetuses was dead. The living fetuses had megacystis, anencephaly and hydrops fetalis. Megacystis case resulted with delivery and hydrops fetal-

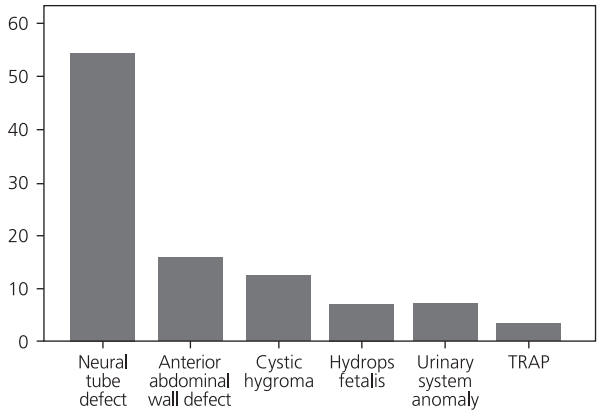

Fig. 1. Distribution of fetal anomalies.

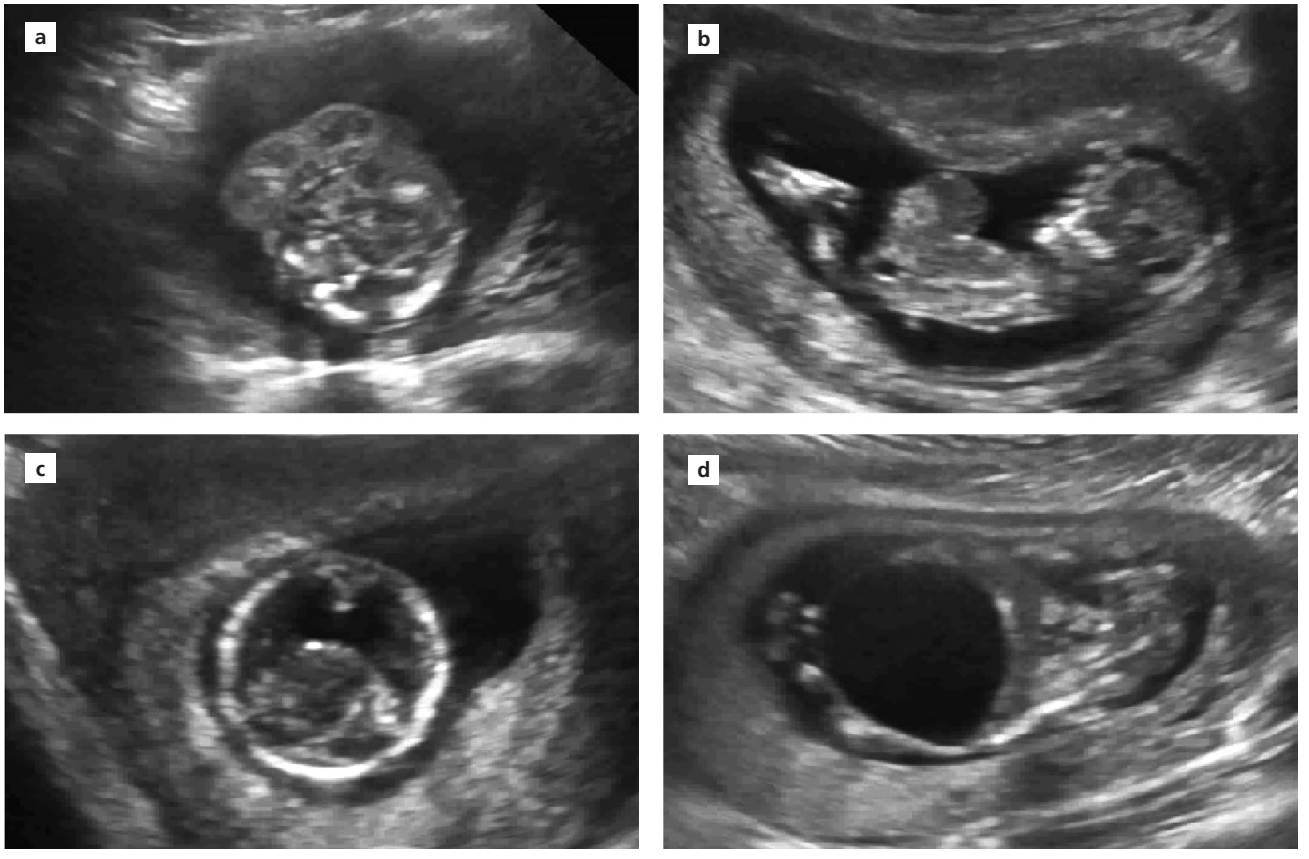

Fig. 2. Fetal anomaly examples found at first trimester. (**a**) Encephalocele, (**b**) omphalocele, (**c**) semilobar holoprosencephaly and (**d**) megacystis.

is cases resulted with termination; the case found to have anencephaly did not maintain the treatment in the study hospital. One case with triple pregnancy had twin reversed arterial perfusion (TRAP) syndrome.

In six cases, the pregnancy resulted with delivery. In five of them, it was found that the family did not accept termination. The sixth was a triple pregnancy case. While two fetuses which were intrauterine ex had TRAP syndrome, third fetus did not have any anomaly and resulted with delivery at 40 weeks of gestation. Two of 3 cases with neural tube defect resulted with delivery had spina bifida and the delivery was carried out with cesarean at 37 weeks of gestation. In three cases diagnosed with anencephaly, the labor initiated at 33 weeks of gestation and the case with previous cesarean history delivered 1800 g live baby with cesarean section. In megacystis case with twin sibling, severe dilatation was detected on fetal left renal pelvis and ureter when the term is reached and when labor started at 38 weeks of gestation, the delivery was carried out with cesarean section due to fetal macrosomy. It was found that another pregnancy with cystic hygroma was resulted with live birth at 38 weeks of gestation.

Nuchal translucency was measured over 95th percentile in all cystic hygroma and hydrops fetalis cases and in 77.8% of anterior abdominal wall defects. In urinary system anomalies and neural tube defects, this rate was 25% and 9.6%, respectively (**Table 2**).

Discussion

In the present study, in conformity with the literature, the fetal anomaly incidence found in first trimester ultrasonographic examination was 0.46%. Syngelaki et al. also reported a similar fetal anomaly incidence (0.47%) at 11–13 weeks of gestation.[11] However, their study also included cardiac anomalies unlike our study.

Today, with the ultrasonographic examination performed at 11–14 weeks of gestation, many fetal anomalies can be detected during first trimester. 53% of central nervous system anomalies, 75% of gastrointestinal system and abdominal wall anomalies, 25% of major urinary anomalies, 69% of major skeletal anomalies, 99% of hydrops fetalis, and 49% of major structural anomalies in total can be diagnosed during first trimester.[4] In our study, we found that neural tube defects were the most common anomaly diagnosed during first trimester. Among them, cranial anomalies including anencephaly, holoprosencephaly, iniencephaly and encephalocele were the most common ones (25/31). In the series of

Table 2. Fetal anomalies except cardiac anomaly found at first trimester, gestational outcomes and their relationship with NT >95th percentile.

Anomaly	N (%)	NT >95th persentil / N (%)	Gestational outcomes			
			Termination	Delivery	Abortion	Lost to follow-up
Neural tube defect	31 (53.4%)	3/31 (9.6%)	24/31(77.4%)	3/31 (9.6%)	-	4/31 (13.0%)
Holoprosencephaly	4 (6.9%)	1/4 (25.0%)	4/4 (100%)	-	-	-
Anencephaly	14 (24.1%)	-/14 (-)	12/14 (85.8%)	1/14 (7.1%)	-	1/14 (7.1%)
Spina bifida	6 (10.3%)	0/6 (0.0%)	3/6 (50.0%)	2/6 (33.3%)	-	1/6 (16.7%)
Iniencephaly	3 (5.2%)	1/3 (33.3%)	3/3 (100%)	-	-	-
Encephalocele	4 (6.9%)	1/4 (25.0%)	2/4 (50.0%)	-	-	2/4 (50.0%)
Anterior abdominal wall defect	9 (15.5%)	7/9 (77.8%)	6/9 (66.7%)		1/9 (11.1%)	2/9 (22.2%)
Omphalocele	3 (5.2%)	2/3 (66.7%)	1/3 (33.3%)	-	1/3 (33.3%)	1/3 (33.3%)
Omphalocele containing liver	2 (3.4%)	2/2 (100%)	2/2 (100%)	-	-	-
Gastroschisis	1 (1.7%)	0/1 (0.0%)	1/1 (100%)	-	-	-
Wide anterior wall defect	3 (5.2%)	3/3 (100%)	2/3 (66.7%)	-	-	1/3 (33.3%)
Cystic hygroma	7 (12.1%)	7/7 (100%)	3/7 (42.9%)	1/7 (14.3%)	1/7 (14.3%)	2/7 (28.5%)
Hydrops fetalis	4 (6.9%)	4/4 (100%)	4/4 (100%)	-	-	-
Urinary system anomaly	4 (6.9%)	1/4 (25.0%)	1/4 (25.0%)	1/4 (25.0%)	1/4 (25.0%)	1/4 (25.0%)
Megacystis	3 (5.2%)	1/3 (33.3%)	1/3 (33.3%)	1/3 (33.3%)	1/3 (33.3%)	-
Hydronephrosis	1 (1.7%)	0/1 (0.0%)	-	-	-	1/1 (100%)
TRAP	2 (3.4%)	2/2 (100%)	-	1/2 (50.0%)	-	1/2 (50.0%)

TRAP: Twin reversed arterial perfusion

Dane et al., 10 of 17 patients found to have first trimester fetal anomaly had cranial anomaly.[12] Akdeniz et al.[13] reported that the most common anomaly in patients who underwent pregnancy termination due to fetal anomaly at 11–24 weeks of gestation was central nervous system anomaly (23/57). In another series, the most common fetal anomaly at 11–13 weeks of gestation was anterior abdominal wall defect. Omphalocele was found in 60 of 165 fetal anomaly cases and gastroschisis was found in 19 of them.[11]

Nuchal translucency measurement is a part of first trimester screening test. On the other hand, increased NT measurement may be the indication of not only fetal trisomies but also major structural anomalies. While the relationship between NT increase and cardiac anomalies are shown clearly,[14] also other structural anomalies increase NT. In the series we present, cardiac anomalies were excluded from the study. When cystic hygroma and hydrops fetalis cases were also excluded, the NT was found >95th percentile in the most common anterior abdominal wall defects (77.8%). In another series published in 2011, NT was found >95th percentile in the most common megacystis (69%) and lethal skeletal dysplasias (50%).

Although most of the major structural anomalies can be diagnosed with first trimester fetal anomaly screening, second trimester screening test is required doubtlessly. Withlov et al. reported that the rate of fetal anomaly detection rate which was 59% at early pregnancy increased to 81% with second trimester anomaly screening.[15] This rate was similar to the major congenital anomaly rate (79.4%) found with second trimester ultrasonography in the study of Pekin et al.[16] Second trimester fetal anomaly screening should be performed due to the development of some structural anomalies at the late periods of pregnancy or non-evaluation of anatomic structures at first trimester. In the series of 44,859 cases of Syngelaki et al., 100% of acrania, allobar holoprosencephaly, omphalocele, gastroschisis, megacystis and body stalk anomalies could be diagnosed at 11–13 weeks of gestation, none of corpus callosum agenesis, semilobar holoprosencephaly, cerebellar or vermian hypoplasia, echogenic lung lesions, intestinal obstruction, duplex kidney, severe hydronephrosis and talipes could be diagnosed at first trimester.[11] On the other hand, there are also anomalies which can be detected at first trimester but recover as weeks of gestation progress. While omphalocele and megacystis are the anomalies which can be detected at first trimester easily, they can be temporary findings in fetuses without chromosomal anomaly.[17,18] It was shown that 92.5% of omphaloceles including only intestine at 11–13 weeks of gestation recover at 20 weeks of gestation.[17] Megacystis with bladder length smaller than 15 mm has 90% chance to recover in fetuses with normal karyotype.[18]

The retrospective design of the study presented is the main limitation although it has a wide population. Since some of the patients found to have fetal anomaly did not maintain their follow-up and treatment at the study hospital, full information on the gestational outcomes of all patients is not available. Also, being unable to evaluate cases together with karyotype analysis results is another limitation. It is not known how much of the structural malformations found are associated with chromosomal anomalies.

Conclusion

With the ultrasonographic examination performed during NT measurement at first trimester, it is possible to diagnosis a significant number of fetal anomalies. In the study performed, when malformations are excluded, it was found that the neural tube defects are the fetal anomalies which can be diagnosed most commonly at 11–14 weeks of gestation.

Conflicts of Interest: No conflicts declared.

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