Fetal Ultrasound Scanning at 11-13 weeks Gestation for Detection of Fetal Abnormalities at Low Risk Pregnancy

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Abstract

Background: Fetal structural anomalies are present in up to 2- 3% of all pregnancies. Worldwide, second trimester scan between 18 and 22 weeks is the standard of care for fetal anatomical assessment; however, first-trimester screening can detect almost half of all severe fetal anomalies at an early stage of pregnancy. The prenatal detection of fetal anomalies during first trimester of pregnancy allows for optimal perinatal management, providing expectant parents with opportunities for additional imaging, genetic testing, and the provision of information regarding prognosis and management options.

Objective: To determine the effectiveness of the fetal ultrasound scanning at 11-13 weeks gestation in the early diagnosis of structural fetal anomalies in an unselected low-risk population.

Patients and Methods: This prospective follow-up study included 195 pregnant women at first trimester with low risk pregnancy at the fetal medicine unit of Obstetrics and Gynecology Department in Mansoura University Hospital during 2021. Ultrasound screening was performed at 11-13 Weeks in all pregnant women. For those who had normal scans a follow up scan was done at 18-22 weeks. Fetal viability was examined and crown rump length was measured.

Results: In this study, we have shown the prevalence and types of congenital anomalies in the studied cases during 11-13 weeks gestation and the associations of such anomalies with the demographic characteristics, obstetric history and CRL.

Conclusion: This study shows that ultrasound diagnosis at 11–13th week gestational age is possible for some severe anomalies. We recommend the introduction of an 11–13th week scan as first part of the routine anomaly screening in pregnancy, as this enables early identification of severe anomalies.

Keywords: First trimester, Fetal anomalies, Low risk pregnancy.

INTRODUCTION

Fetal structural anomalies are found in up to 2- 3% of all pregnancies. The etiology is unknown in about two –thirds of cases. A revolutionary technological achievement and the use of high-frequency ultrasound enabled detailed and accurate imaging of the structure of the fetus, such as fetal viability, dating, development, any chromosomal or structural abnormalities, and multiple pregnancies, even in early pregnancy at 11-13 weeks. (1)

Ultrasound-based screening is an integral part of routine prenatal care. The prenatal detection of fetal anomalies allows for optimal prenatal management, providing expectant parents with opportunities for additional imaging, genetic testing, and the provision of information regarding prognosis and management options. (2)

In majority of countries worldwide, second trimester scan between 18 and 22 weeks remains the standard of care for fetal anatomical assessment; however, most recent literature shows a significant improvement in detection of fetal abnormalities in first trimester of pregnancy. (3)

First-trimester screening can detect almost half of all severe fetal anomalies at an early stage of pregnancy with positive predictive values of 90% and more. Sensitivities varied depending on the organ system and reached the highest figures for anomalies of the heart, the abdomen, the spine and the skeletal system. (4)

Major abnormalities are classified into three groups according to the probability of their detection rate by 11-14th weeks' ultrasound. The first group includes anomalies that can be easily detected in the first trimester such as anencephaly, the second group comprises anomalies that reveal ultrasonography signs later in gestation and have no possibility of early detection such as hypoplasia of cerebellum. The third group anomalies can be detected in first trimester with meticulous examination using high-tech devices. This group of anomalies includes spina bifida occulta, skeletal dysplasia, and some kinds of cardiac defects, which sometimes need to be examined using transvaginal ultrasound. (5)

Screening in the first and early second trimester and early detection of major anomalies will lead to early decisions of pregnancy termination. Moreover, doing it before the 16th gestational week brings the advantage of early termination before women feel movements of the fetus. This is important for women, especially in cultures in which beliefs strongly affect social life rules. Furthermore, early termination of pregnancy has physical and physiological advantages for women and their families compared with late termination. (6)

AIM OF THE WORK

The aim of the present study was to determine the effectiveness of the fetal ultrasound scanning at 11-13 weeks gestation in the early diagnosis of structural fetal anomalies in an unselected low-risk population.

PATIENTS AND METHODS

This prospective follow-up study included 195 pregnant women at first trimester with low risk pregnancy at the fetal medicine unit of Obstetrics and Gynecology Department in Mansoura University Hospital during 2021.

Sample size justification: The calculated sample size of the study was 176 participants at 5% level of significance and 95% power of the study, using G*Power 3 sample size calculator. The estimation of sample size based on the previously reported incidence of Fetal non-chromosomal abnormalities detected in the first trimester= 27.6% and percentage of Fetal non-chromosomal abnormalities detected in the second trimester = 53.8%. The sample size was increased to 195 participants to compensate

for the incomplete data and to increase the study power.

Ultrasound screening was performed at 11-13 Weeks in all pregnant women. For those who had normal scans a follow up scan was done at 18-22 weeks for confirmation. Fetal viability was examined and crown rump length was measured.

Inclusion Criteria: Age between 19-40 years old. Healthy pregnant women with singleton pregnancy attending for a routine hospital visit at 11-13th week gestation.

Exclusion Criteria: Gestational age <11 weeks or >14 weeks. Multiple gestations. Maternal disease/ disorder, IVF or induced pregnancies. Incomplete pregnancy outcome information, unexplained miscarriages, and fetal death.

Full medical history including: Personal history. Past history of common medical disorder such as hypertension, diabetes, chronic kidney disease and cardiac patients. Past history of parity and gravidity. Family history of fetal anomalies.

Physical examination: a careful general and obstetric examination was done.

Ultrasound protocol: subjects were asked to remove their clothes and put on a gown or cover for the procedure. Ultrasound screening was performed by experienced radiologist transabdominally using ultrasound machine (Samsung H60, Korea). Whenever visualization of fetal structure was suboptimal or a structural abnormality was suspected during transabdominal scan, transvaginal scan was always performed. Ultrasound screening was performed at 11-13 Weeks in all 195 pregnant women. For those who had normal scans a follow up scan was done at 18-22 weeks for confirmation. Fetal viability was examined and crown rump length was measured. Evaluation of fetal anatomy was done according to the following check list.

- Skull and brain
- Face (Facial Profile, Nasal Bone and orbits)
- Neck (Nuchal translucency measurement, presence of Cystic hygroma)
- Spine (Examination of overlying skin and neural tube in longitudinal and transverse planes)
- Heart (Four chamber view, three vessel view, and heart rhythm)
- Stomach (its existence in left upper abdomen)
- Abdominal wall defect
- Kidney (existence, size, and shape)
- Urinary bladder (existence, size, and shape)
- Extremities (existence, size, and shape)

Along with the evaluation of the anatomy, the Nuchal translucency measurement was done according to the guidelines established by the Fetal Medicine Foundation, in fetuses with CRL between 45mm and 84mm at 11 to 13 weeks gestational age. The cut off value of NT measurement was taken as ≥ 3 mm. When NT measurement was abnormal a further confirmatory test was combined. The following confirmatory that were offered are, first trimester serum markers (free βhCG, PAPP-A), chorionic villous sampling, amniocentesis and triple screening or quadruple screening and it was left to the patients choice.

Women were fully counselled before their ultrasound examination and written informed consent was obtained. Based on the anomalies detected, the patients were counselled regarding termination or continuation of pregnancy. All the patients were followed up till delivery.

Pregnancy outcome was obtained from our maternity unit or the patients themselves.

Analytical statistics: Data were analyzed using the Statistical Package of Social Science (SPSS) program for Windows

(Standard version 21). The normality of data was first tested with one-sample Kolmogorov-Smirnov test. Qualitative data were described using number and percent. Associations between categorical variables were tested using Fisher exact and Monte Carlo tests when expected cell count less than 5. Continuous variables were presented as mean ± SD (standard deviation) for normally distributed data and compared with independent t test. The results was considered significant when $p \leq 0.05$. The smaller the p-value obtained, the more significant are the results.

Results

Table 1: Demographic data among the studied group

Demographic data	The study group (n=195)
Age (years) Mean ± SD Min-Max	 27.67±4.21 20-40
Age classes 20-25 y >25-30 y >30-35 y >35-40 y	 65 (33.3%) 85 (43.6%) 39 (20.0%) 6 (3.1%)
Residence Urban Rural	 66 (33.8%) 129 (66.2%)
Consanguinity Positive Negative	 59 (30.3%) 136 (69.7%)

Table 2: Anthropometric measurements among the studied group

Anthropometric measurements	The study group (n=195)
Weight (kg) Mean ± SD	 78.41± 8.75
Height (cm) Mean ± SD	 166.78± 4.95
BMI (kg/m^2) Mean ± SD	 28.19± 2.70

The present results demonstrated that at the mean gestational age of 12.16±0.68, the mean CRL was 68.95±12.57. Normal US represented 97.9% while abnormal US represented 2.1% as illustrated in table 3.

Table 3: First two dimensional ultrasound scan results among the studied group .

First two dimensional ultrasound scan	The study group (n=195)
Gestational age(wk) Mean ± SD	 12.16±0.68
US Normal US Abnormal US	 191 (97.9%) 4 (2.1%)
CRL(mm) Mean ± SD	 68.95±12.57
Gestational age(wk) Mean ± SD	 12.16±0.68

The present results demonstrated that at the mean gestational age of 20.51 ± 1.42, the mean FL was 34.71±3.94. Normal US represented 91.8% while abnormal US represented 2.6%, terminated pregnancy, missed abortion occurred in 1% of cases and 4.6% of cases lost follow-up, as seen in Table 4.

Table 4: Second two dimensional ultrasound scan results among the studied group.

Second two dimensional ultrasound scan	The study group (n=195)
Gestational age(wk) Mean ± SD	 20.51 ± 1.42
US Normal Abnormal Terminated/ missed abortion Lost follow up	 179 (91.8%) 5 (2.6%) 2 (1.0%) 9 (4.6%)
FL(mm) Mean ± SD	 34.71±3.94

In this study, The present results demonstrated that the agreement percentage between the first and second US scans was 83.9% as demonstrated in Table 5.

Table 3: First two dimensional ultrasound

Table 5: Agreement % between first and second US scan.

	First US scan (n=195)	Second US scan (n=186)	Agreement %
Normal US	191 (97.9%)	179 (96.2%)	83.9%
Abnormal US/ terminated	4 (2.1%)	7 (3.8%)	

Table 6: First two dimensional ultrasound scan results among the studied group.

Fetal abnormality	Total	Increased NT	1st US scan	2nd US scan	TOP	Missed abortion IUFD	Live birth
Nervous system							
-Occipital encephalocele	1	--	1	0	0	0	1
-Bilateral ventriculomegaly	1	--	0	1	0	0	1
Congenital heart defect							
-VSD	1	--	0	1	0	0	1
Urogenital system							
-Bilateral hydronephrosis	1	--	0	1	0	0	1
Skeletal							
-Mermaid syndrome	1	--	1	0	1	0	0
Multiples -Echogenic kidney with dilated renal pelvis, Bilateral club foot, AVSD (Trisomy 13)	1	1	1	0	0	0	1
Others							
-Cystic hygroma with fetal hydrops	1	1	1	0	0	1	0

TOP: Termination of pregnancy. IUFD: Intrauterine fetal death

The present results demonstrated a significant increase in age among abnormal US in comparison with the normal US (P value>0.001). The results also demonstrated a significant increase in positive consanguinity among the abnormal US in comparison with the normal US as illustrated in Table 7.

Table 7: Association between abnormal US / terminated and demographic data.

Demographic data	Normal US (n=179)	Normal US (n=179)	p value
Maternal age			
20-25 y	61 (34.1%)	2 (28.6%)	
>25-30 y	80 (44.7%)	0 (0%)	0.001*
>30-35 y	34 (19.0%)	3 (42.9%)	
>35-40 y	4 (2.2%)	2 (28.6%)	
Residence			
Urban	60 (33.5%)	3 (42.9%)	0.609
Rural	119 (66.5%)	4 (57.1%)	
History of Consanguinity			
Positive	50 (27.9%)	5 (71.4%)	0.025*
Negative	129 (72.1%)	2 (28.6%)	

P-value< 0.001: highly significant, P-value <0.05: significant, P-value >0.05: Non-significant.

The present results demonstrated a statistically significant increase in CRL among the abnormal US group in comparison with the normal US group as illustrated in Table 8.

Table 8: Association between abnormal US / terminated and CRL.

	Normal US (n=179)	Abnormal US/terminated (n=7)	p value
CRL Mean ± SD	68.25±12.62	79.28±9.12	0.023*

DISCUSSION

Fetal structural anomalies complicate 2-3% of all pregnancies. Screening for fetal abnormalities at 11 to 13 weeks' gestation can provide a detailed fetal anatomic evaluation, with the aim of identifying fetuses with major structural anomalies early in pregnancy. (7)

Screening for structural abnormalities is routinely performed by ultrasound between 18–22 weeks of gestation. However, increasing evidence has suggested that about half of fetal structural abnormalities can be detected during the first trimester of pregnancy with low false-positive rates. (8)

Regarding the demographic characteristics of the studied cases, our results indicated that the mean age was 27.67±4.21 years old. Our result revealed that 30.3% of the cases were positive consanguinity. Regarding the anthropometric measurements among the studied group, our results revealed that the mean weight, height and BMI of the studied were 78.41± 8.75 kg, 166.78± 4.95 cm and 28.19± 2.70 respectively.

Such findings are in agreement with Snaifer et al. (9) in Lebanon that indicated that the patients' mean age was 27.5 ± 8.5 years with a 35% consanguinity rate that lead to increased anatomical and chromosomal fetal anomalies. Additionally, Aloui et al. (10) study in Tunisia indicated a marked association of parental consanguinity with increased congenital anomalies rates. Syngelaki et al. (11) studied the diagnosis of fetal non-chromosomal abnormalities on routine ultrasound examination at 11–13 weeks' gestation and indicated that median maternal age was 31.0 years old and median maternal weight was 67.5 kg.

Our results indicated that the prevalence of congenital anomalies in the studied cases during 11-13th pregnancy ultrasound was 2.1% and during second trimester ultrasound was 3.8% and the agreement % between first and second US scan was 83.9%. A previous study by Ding et al. (13) demonstrated that the reason for not all structures being visible in the first trimester is not the failure of the resolution of the ultrasound, but the fact that several structures are not yet formed and therefore, cannot be seen. Therefore, first trimester ultrasound examination could not replace the mid-trimester scan and the 16–20 weeks follow-up examination by conventional second-trimester transabdominal scan should always be performed. Simula et al. (14) indicated that approximately 40% to 66% of fetal anomalies can be identified during the 11−14 week prenatal sonographic examination and all women should be offered a routine complete 11−14 week prenatal sonographic examination.

Two cases were diagnosed with central nervous system anomalies (one case has occipital encephalocele and one case has bilateral ventriculomegaly). One case was diagnosed with ventricular septal defect. One case was diagnosed with bilateral hydronephrosis. One case was diagnosed with mermaid syndrome. One case was diagnosed with Echogenic kidney with dilated renal pelvis, bilateral club foot, atrioventricular septal defect (AVSD, Trisomy 13) and one

case was diagnosed with cystic hygroma with fetal hydrops. Such findings are in agreement with Onyambu and Tharamba, (15) that indicated that the prevalence of congenital anomalies in the sampled population was 3%. The most frequently observed fetal anomalies involved the head (1.6%). Each of the remaining anomalies affected less than 1% of the fetuses and included anomalies of the spine, pulmonary, renal and urinary tract and skeletal systems and majority of the fetuses with anomalies detected on prenatal ultrasound resulted in postnatal mortality within days of delivery. Kenkhuis et al. (16) indicated that the prevalence of early detected anomalies was 0.95% and during 11-13th scan, all particularly severe anomalies were detected (all cases of neural tube defect, omphalocele, megacystis, and multiple severe congenital and severe skeletal anomalies), moreover, the number of false positives and markers is much lower at the early scan, limiting parental anxiety.

Regarding the association between abnormal US / terminated and demographic data, our results indicated a statistically significant increase in abnormal US / terminated among the pregnant women with age group >35-40 years old (42.9%) (P value<0.001) and with positive history of consanguinity (P value=0.025). Such findings are in agreement with Dai et al. (17) that revealed that the kinds of fetal abnormalities, numbers of abortions, and chromosomal abnormality rates increased with increasing maternal age. Additionally, Gul et al. (18) revealed that parental consanguinity is one of the major risk factors for structural, neurological and cardiac anomalies. Similarly, Ozawa et al. (19) indicated that the maternal age, history of miscarriage, and embryonic/fetal size at miscarriage may be independently associated with the frequencies or profiles of cytogenetic abnormalities in early miscarriages.

Regarding the association between abnormal US , terminated pregnancy and obstetric history, our results indicated a significant increase in the history of miscarriage among the abnormal US / terminated group in comparison with the normal US group (P value=0.048). Such findings are in agreement with Visconti et al. (20) that indicated that pregnancies complicated by fetal congenital malformations in patients with two or more pregnancy losses were significantly associated with maternal thrombophilic disease and previous birth defects.

Our results indicated a statistically significant increase in CRL among the abnormal US / terminated group in comparison with the normal US group (P value=0.023). Balsane et al. (21) indicated that at the first transvaginal ultrasound, the mean Z- score for CRL was significantly lower in pregnancies that subsequently aborted compared to pregnancies that remained viable. A recent study by Li et al. (22) indicated that the increased fetal crown-chin length / crown-rump length ratio at 11–14 weeks' gestation is associated with an increased risk of skeletal dysplasia and may be useful in first-trimester screening for this condition. Contrarily, a previous study by Sagi-Dain et al. (23) indicated that low first-trimester CRL might be associated with a significantly increased risk of chromosomal anomalies. Thus, invasive prenatal testing or cell-free DNA screening might be offered in such pregnancies, particularly if dating is certain.

CONCLUSION

This study shows that ultrasound diagnosis at 11–13th week gestational age is possible for some severe anomalies. We recommend the introduction of an 11–13th week scan as first part of the routine anomaly screening in pregnancy, as this enables early identification of severe anomalies.

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