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Evaluating the Diagnostic Significance of Major Cardiac Anomalies via First Trimester Ultrasound and Their Association with Elevated Nuchal Translucency, Tricuspid Regurgitation, and Irregular Ductus Venosus Flow

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Abstract

Background: Congenital heart defects (CHDs) are a major cause of death and illness in newborns. Early detection is vital for prompt treatment and better outcomes. This study explored the effectiveness of first-trimester ultrasound in identifying CHDs and its association with increased nuchal translucency (NT), tricuspid regurgitation (TR), and abnormal ductus venosus (DV) flow.

Methods: This cross-sectional study involved all pregnant women who had first-trimester screening ultrasounds performed by an obstetrician or radiologist at Forghani Hospital between 2017 and 2024. These women were subsequently referred for fetal echocardiography at 16-18 weeks of gestation at Hazrat Masoumeh Hospital in Qom, Iran. Postnatal neonatal echocardiography was conducted for all cases. The study calculated the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of increased nuchal translucency (NT), tricuspid regurgitation (TR), and abnormal ductus venosus (DV) flow in detecting congenital heart defects (CHDs).

Results: The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of increased nuchal translucency (NT) for detecting congenital heart defects (CHDs) were 74.7%, 98.3%, 90.9%, and 94.7%, respectively. For tricuspid regurgitation (TR), these values were 71.9%, 97.7%, 87.5%, and 94.1%, respectively. Regarding abnormal ductus venosus (DV) flow, the values were 82.2%, 95.1%, 78.5%, and 96.1%, respectively. The diagnostic accuracy for detecting CHDs using NT, TR, and abnormal DV flow was 94.1%, 93.1%, and 92.8%, respectively.

Conclusion: Targeted fetal ultrasound in the first trimester is a valuable diagnostic tool for detecting CHDs. Early detection can contribute to improved neonatal outcomes.

Keywords: Congenital heart disease, Nuchal translucency, Tricuspid regurgitation, Ductus venosus flow

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Introduction

Congenital heart disease (CHD) is the most prevalent severe congenital anomaly, with an average prevalence of approximately 22.8 per 1000 live births. This prevalence has increased by 10% every five years (1). Fetal ultrasound examination between 11 and 13 weeks of gestation can detect a wide range of non-chromosomal fetal anomalies (2-4). In first-trimester screening, non-chromosomal fetal anomalies can be academically categorized into three groups (4). The first group comprises anomalies directly assessable and diagnosable. The second group includes cardiac defects indirectly detectable via markers assessed during screening. These involve increased nuchal translucency (NT), tricuspid valve regurgitation, and abnormal ductus venosus flow (5-8). The third group encompasses anomalies that either develop later in gestation or exhibit phenotypic expression postnatally, thus remaining undetectable in the first trimester (9-11). The diagnostic value of first-trimester ultrasound in identifying major cardiac defects is a critical aspect of fetal imaging and the study of congenital heart disease. Ultrasound at this stage can identify major cardiac

structural abnormalities, impaired cardiac function, and abnormal venous flow (12). Increased nuchal translucency (NT) thickness in the fetus may indicate an increased risk of chromosomal and cardiac abnormalities. Numerous studies have investigated increased NT as a risk marker for both cardiac defects and genetic disorders (13, 14). Tricuspid valve regurgitation (TVR): This condition can disrupt blood flow and cardiac function. On echocardiography, TVR may manifest as abnormal blood flow patterns within the heart. Early diagnosis is crucial due to the potential for serious consequences for the fetus (15). Ultrasound can detect abnormal flow in venous channels. Such abnormal flow typically indicates cardiac anomalies or dysfunction in other organs (16). This study was designed to investigate further the relationship between other major fetal cardiac anomalies and elevated nuchal translucency (NT), tricuspid regurgitation abnormalities of the ductus venosus at first trimester 11-13 weeks screening in singleton pregnancies treated with fetal echocardiography.

Methods

This study was conducted as a cross-sectional analytical investigation. The research population consisted of all pregnant women referred to the fetal echocardiography department of Hazrat Masoumeh Hospital in Qom for fetal echocardiography between 2017 and 2024. Sampling was performed using a convenience sampling method. The sample size was determined using a formula that accounts for a 5% Type I error rate, a sensitivity of 29.9% for NT measurement in detecting CHD, a detectable difference (d) of 5%, and a prevalence (p) of 50%. Based on a similar study (10), the estimated sample size was 580 participants. To account for potential attrition, 600 pregnant women were ultimately enrolled.

The study's inclusion criteria encompassed pregnant women who had undergone first-trimester ultrasound examinations by an obstetrician and fetal echocardiography by a pediatric cardiologist. Exclusion criteria included concurrent anomalies, maternal use of teratogenic drugs, first-trimester ultrasound performed at other centers, incomplete medical records, maternal collagen vascular diseases, and fetal genetic abnormalities. All participants were recruited from Farghani Hospital. First-trimester screening ultrasounds were performed by a single obstetrician, after which participants were referred for echocardiography by a single pediatric cardiologist. All fetal ultrasounds were performed at 13 weeks of gestation, and fetal echocardiograms were conducted between 16 and 18 weeks of gestation. Postnatal follow-up of these infants was also conducted. In the next section, data from pregnant women's medical records, including maternal age, fetal sex, fetal echocardiography findings, and nuchal translucency (NT) measurements from first-trimester ultrasounds, were reviewed and entered into the research study's checklists. A specialist cardiologist had previously performed fetal echocardiograms. All these findings were recorded in the study checklists. Key ultrasound observations—such as increased NT, tricuspid regurgitation, and abnormal ductus venosus flow—were utilized to diagnose major congenital heart defects. These findings were used to calculate sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) using appropriate formulas. The postnatal diagnosis served as the gold standard for assessing the diagnostic accuracy of congenital heart disease.

Results

In this study, after reviewing the medical records, 107 cases (17%) were diagnosed with CHD. Of these, approximately 18 cases were significant CHDs. Nine of these significant CHD cases resulted in stillbirths (fetal death during pregnancy or at delivery). The remaining cases were classified as non-significant CHDs.

This study examined 600 pregnant women between 16 and 18 weeks of gestation. Of these, 107 fetuses (17.8%) were diagnosed with congenital heart disease (CHD), while 493 fetuses (82.2%) were healthy and without CHD Figure 1.

The mean maternal age was 34.6 ± 3.6 years for those with healthy fetuses and 34.7 ± 4.04 years for those with fetuses diagnosed with CHD. Regarding nuchal translucency (NT) findings, 80 of the 107 cases (13.3%) with CHD exhibited increased NT. A statistically significant association was found between increased NT and the presence of CHD ($P=0.001$) (Table 1). Using standard formulas, we determined the sensitivity, specificity, PPV, NPV, and accuracy of NT in diagnosing CHD. Sensitivity was 74.7%, determined by dividing true positives by the total of true positives and false negatives. Specificity was 98.3%, calculated by dividing true negatives by the total of true negatives and false positives.

The PPV, calculated as true positives divided by the sum of true positives and false positives, was 90.9%. The NPV, calculated as true negatives divided by the sum of true negatives and false negatives, was 94.7%. Finally, the overall diagnostic accuracy of NT was 94.1%. Of the 107 cases (17.8%) diagnosed with CHD, 77 (12.8%) presented with tricuspid regurgitation (TR). A statistically significant association ($P=0.001$) was found between TR and the presence of CHD.

The calculated sensitivity, specificity, PPV, NPV, and diagnostic accuracy for TR are 71.9%, 97.7%, 87.5%, 94.1%, and 93.1%, respectively (Table 1). Of the 107 cases (17.8%) diagnosed with CHD, 88 cases (14.7%) exhibited abnormal ductus venosus (DV) flow. A statistically significant association ($P=0.001$) was found between abnormal DV A-wave and the presence of CHD (Table 1). Abnormal DV flow demonstrated a sensitivity of 82.2%, specificity of 95.1%, PPV of 78.5%, NPV of 96.1%, and an

Table 1. Distribution of Fetal Sonographic Findings in Pregnant Women with and without Congenital Heart Disease (CHD)

Variable	Group	CHD n (%)	Non-CHD n (%)	Total n (%)	*P* value
Nuchal Translucency (NT)	Normal (≤95th percentile)	27 (4.5)	485 (80.8)	512 (85.3)	**<0.001***
	Increased (>95th percentile)	80 (13.3)	8 (1.3)	88 (14.7)	
Tricuspid Regurgitation (TR)	Present	77 (12.8)	11 (1.8)	88 (14.7)	**<0.001***
	Absent	30 (5.0)	482 (80.3)	512 (85.3)	
Ductus Venosus (DV) Flow	Abnormal[‡]	88 (14.7)	24 (4.0)	112 (18.7)	**<0.001***
	Normal	19 (3.2)	469 (78.2)	488 (81.3)	
Total		107 (17.8)	493 (82.2)	600 (100)	

*Chi-square test

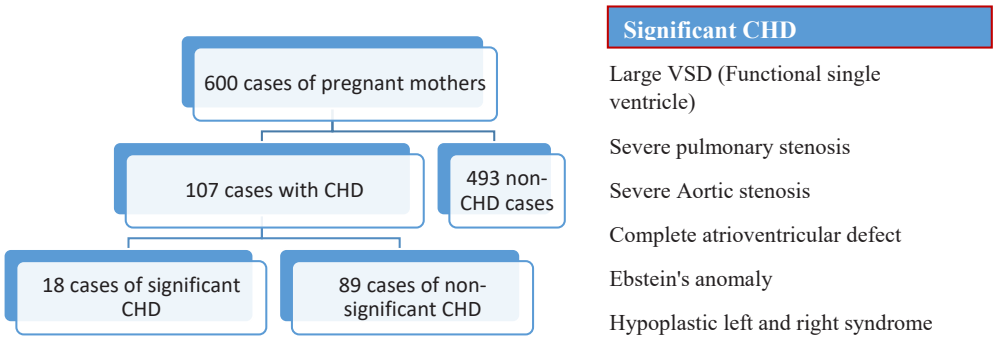

Figure 1. How patients are included in the study

overall diagnostic accuracy of 92.8%.

Discussion

Ultrasound examinations during the first trimester are crucial for the early detection and diagnosis of severe congenital heart defects and other abnormalities.

The correlation between increased nuchal translucency (NT), tricuspid regurgitation, and abnormal ductus venosus flow can serve as a strong predictor for managing significant fetal cardiac issues. Therefore, incorporating these parameters into first-trimester ultrasound assessments can lead to improved outcomes and enhanced quality of care for both mother and fetus. Our study demonstrated that all three variables, NT size, TR, and abnormal ductus venosus flow, exhibited high sensitivity, specificity, and diagnostic accuracy in predicting congenital heart defects (CHDs) during prenatal screening. This result aligns with the result of previous research; for instance, J.M. Martínez et al (9). Abnormal ductus venosus (DV) flow observed during first-trimester ultrasound is an independent predictor of CHD and should be considered a reason to perform fetal echocardiography. This study found that including DV blood flow assessment improved the early detection rate of CHD by 11% compared to solely using NT measurement. Minnella et al conducted a retrospective study analyzing the association between major fetal cardiac defects and increased nuchal translucency (NT), tricuspid regurgitation, and abnormal ductus venosus flow in a large cohort of singleton pregnancies undergoing ultrasound examinations between 11 and 13 weeks of gestation. The study involved anatomical fetal assessment, NT measurement, and Doppler evaluation of tricuspid and ductus venosus flow. The diagnostic performance of each marker individually and in combination for detecting major congenital heart disease was assessed. The results demonstrated that, between 11 and 13 weeks of gestation, combined assessment of fetal NT, tricuspid flow, and ductus venosus flow can improve the early detection of cardiac defects (17). The results of this study were consistent with the results of our study. The results of Pereira's study showed that if, in addition to screening for major heart defects using fetal NT and DV flow, we also evaluate flow in the tricuspid valve, the screening performance in detecting these defects will improve (11). Borrell et al conducted a study to determine the optimal method for combining fetal nuchal translucency (NT) and ductus venosus (DV) blood flow measurements in detecting major cardiac defects among chromosomally normal fetuses during first-trimester ultrasound screening. Their findings indicated that utilizing combined NT and DV Doppler measurements to select 2.7% of the general pregnant population for further fetal echocardiography would allow for the detection of half of all major fetal cardiac defects in the first trimester (18). Therefore, similar to our study, these findings highlight the importance of using these sonographic parameters in the early detection and management of fetal cardiac defects.

In our study, out of 600 fetuses, 107 cases (17.8%) were identified with congenital heart disease (CHD). Increased nuchal translucency (NT) was observed in 80 cases (13.3%), tricuspid regurgitation (TR) in 77 cases (12.8%),

and abnormal ductus venosus (DV) flow in 88 cases (14.7%). All these markers demonstrated a statistically significant association with CHD ($P=0.001$). The sensitivity and specificity for NT were 74.7% and 98.3%, respectively; for TR, 71.9% and 97.7%; and for DV, 82.2% and 95.1%. These findings are consistent with a study by G. P. Minnella et al (19), conducted on 93,209 pregnancies, suggesting that screening for NT, TR, and DV in the first trimester of pregnancy can contribute to the early detection of CHD. However, discrepancies in CHD prevalence and marker accuracy between the two studies may be attributable to variations in population demographics and diagnostic methodologies. Combining these markers with more advanced diagnostic modalities, such as fetal echocardiography, may enhance diagnostic accuracy.

Research by Karadzov Orlic et al (20) is consistent with the findings of our study. It was highlighted that adding a basic cardiac scan, which has a sensitivity of 67% and specificity of 98%, to these sonographic markers significantly improves diagnostic accuracy, increasing the Area Under the ROC Curve from 0.838 to 0.915.

The combined use of early markers and cardiac scanning can lead to earlier and more accurate detection of CHD during the first trimester of pregnancy. A meta-analysis found that abnormal DV flow in the first trimester is linked to a higher risk of CHD, especially in euploid fetuses.

The study's findings reveal that abnormal DV flow is linked to a relative risk of 6.9 (95% CI: 3.7–12.6) for CHD. Its diagnostic accuracy in euploid fetuses was assessed as good, with an area under the receiver operating characteristic curve of 0.81 (95% CI: 0.78–0.84). These findings align with the results of our study, as abnormal DV flow was also significantly associated with CHD in our research, demonstrating high sensitivity and specificity in diagnosing CHD. Both studies emphasize that abnormal DV flow can serve as a useful marker for identifying CHD in the first trimester of pregnancy. However, the meta-analysis points out that the diagnostic accuracy of DV is lower in high-risk populations and in populations without screening, which may be due to differences in the characteristics of the studied populations. This highlights the importance of combining DV with other markers, such as NT thickness and TR, which was also emphasized in the present study (21). Contrary to the results of our study, which indicate that the use of combined markers (NT, TR, and DV) can detect CHD with relatively high accuracy, the study by Turan et al (22) indicates that despite the presence of these markers, around 50% of CHD cases go unnoticed. This inconsistency in findings might be attributed to variations in study populations, measurement techniques, or advancements in technology. A review study by Karim et al highlights these issues (23). They also showed that even with the use of combined markers, some cardiac anomalies go undetected. While our study reported higher sensitivity, this discrepancy in findings may be attributed to differences in the study population, measurement methods, or technological advancements. To improve the detection and management of congenital heart disease (CHD) during pregnancy, physicians are recommended to utilize a combination of several ultrasound findings, such as nuchal translucency thickness, the presence of tricuspid regurgitation, and the flow pattern in the inferior vena cava, to enhance diagnostic accuracy. Additionally, conducting training workshops for physicians and midwives on the importance of these indicators and how to interpret ultrasound results can aid in the early identification and better management of these conditions. Furthermore, regular follow-ups and additional evaluations for pregnant women with known risk factors, especially at older ages, are advised to ensure that timely preventive and therapeutic measures are implemented.

Conclusion

The study demonstrated that ultrasonography is effective in accurately identifying significant fetal cardiac defects. Increased NT, TR, and abnormal ductus venosus flow were linked to a heightened risk of major cardiac anomalies. These insights may aid in enhancing screening programs for pregnant women. First-trimester ultrasonography allows pregnant women to be informed about the risk of major cardiac defects, facilitating the planning of suitable interventions and neonatal care. In summary, this study highlighted that first-trimester ultrasonography is a crucial diagnostic tool for detecting major fetal cardiac defects and can lead to better neonatal outcomes.

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Supervision: Enayatollah Noori.
Validation: Mohammad Hosein Arjmandnia.
Visualization: Mohammad Hosein Arjmandnia.
Writing–original draft: Enayatollah Noori.

Competing Interests

The authors declare that they have no conflict of interest.

Ethical Approval

This study was approved by the Ethics Committee of Qom University

of Medical Sciences (ethical code: IR.MUQ.REC.1403.082).

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