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Original Research Article

First trimester diagnosis of fetal cardiac anomalies: a sonopathological correlation study

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ABSTRACT

Background: Accurate diagnosis of structural cardiac anomalies in the first trimester is critical due to its impact on anxiety and pregnancy management. This study aims to evaluate the correlation between first-trimester ultrasound (USG) findings of cardiac anomalies and perinatal pathological evaluations.
Methods: This retrospective study was conducted at Mediscan systems, a tertiary care fetal medicine center in South India, analyzing first-trimester scans from January 2012 to December 2017. Singleton pregnancies with detected cardiac anomalies were identified from the sonocare database. Only those cases with subsequent perinatal autopsy were included in the study cohort.
Results: In the study cohort, the mean maternal age was 26.6 years (range 19-44), mean BMI was 26.1 (range 17.5-42.8), and mean crown-rump length was 65 mm (range 48-82 mm). Ultrasound findings and autopsy results were in complete agreement in 62% of cases. Autopsies provided additional information in 28% of cases, while 10% of cases had discordant findings. Notably, the accuracy improved in the second cohort, with complete agreement rising from 49% to 76% and mismatches reducing from 21% to zero.
Conclusions: The study highlights that a systematic checklist enhances the accuracy of first-trimester cardiac assessments, achieving correct diagnoses in 90% of cases. The improvement over time underscores the effectiveness of refined diagnostic protocols. Despite these advances, challenges in differentiating certain anomalies persist, but no prenatally diagnosed anomalies were found normal on autopsy, reinforcing the reliability of early diagnoses and the ability to provide confident counselling.

Keywords: First trimester, Cardiac anomalies, Ultrasound, Perinatal autopsy, Diagnostic accuracy

INTRODUCTION

The imaging of the fetal heart has undergone significant advancements since the first ultrasonographic visualization in the early 1970s.[1] The origins of fetal echocardiography can be traced to 1972, with early studies focused on real-time heart tracing and fetal cardiac output calculations using M-mode tracings.[2] In 1980, the field progressed with Allen et al performing fetal echocardiography using eight scan planes for anatomical evaluation, and Sahn et al utilizing ultrasound to reproduce cross-sectional views of the fetal heart, adapted from pediatric echocardiography.[3,4]

Over the past 35 years, technological advancements, including higher imaging resolution and the introduction of color Doppler, have revolutionized fetal cardiac imaging. What began with detecting heart movement through pulsed ultrasound has now evolved to include comprehensive structural and functional assessments, with tools like Doppler and fetal intelligent navigation echocardiography (FINE) enabling 4D imaging.[5] The international society of ultrasound in obstetrics and gynecology (ISUOG) now recommends fetal echocardiography between 18-22 weeks for high-risk pregnancies to detect cardiac anomalies.[6]

Increasing numbers of patients are being identified as high-risk for congenital heart disease at earlier gestational ages due to nuchal translucency screening. Early detection, whether in high-/low-risk groups, allows for more detailed investigation into family histories of genetic syndromes or anomalies and enables safer, earlier options for pregnancy termination in cases of major cardiac anomalies.[7]

Although fetal anomaly screening is traditionally performed in the second trimester, many structural abnormalities can be reliably detected as early as 11-14 weeks.[8-10] First-trimester cardiac evaluation success rates range from 43-95%, depending on operator experience, equipment, and patient population.[11-13] Improved detection rates have been reported with the increasing use of transvaginal scanning.[14]

In our practice, all fetuses undergoing nuchal translucency scans at 11-14 weeks also receive a cardiac evaluation, with transvaginal scans used when transabdominal scans are insufficient.[15] While ultrasound offers high diagnostic accuracy, it still has limitations, and fetal autopsy remains the gold standard for confirming ultrasound findings.[16] Given the potential anxiety and pregnancy management implications of diagnosing a structural cardiac anomaly at 11-14 weeks, it is crucial to understand the accuracy of ultrasound at this early stage.

Aims and objectives

Aim and objectives were to determine correlation of cardiac anomalies detected at 1st trimester USG with perinatal pathological evaluation and to determine factors impacting detection of cardiac anomalies at 1st trimester USG.

METHODS

This was a retrospective study carried out at Mediscan systems. This is a tertiary care fetal medicine centre in South India. First trimester scans performed between January 2012 to December 2017 were taken as part of study. All the singleton pregnancies with fetuses detected with cardiac anomaly at first trimester scan were searched for in the sonocare database. Cases wherein perinatal autopsy was performed were sub-grouped and only formed the study cohort. In the cases retrieved, data on other parameters like maternal BMI at time of scan, fetal crown rump length (CRL) and presence of aneuploidy marker or multisystem anomaly, if any, were analysed.

Inclusion criteria

Foetuses with CRL of 45-84 mm at time of scan, fetal autopsy done at Mediscan, perinatal pathology unit were included.

Exclusion criteria

Autopsy carried out after 16 weeks of pregnancy and autolysed specimen at the time of autopsy were excluded.

Ultrasound protocol

Cardiac assessment was done for all patients as part of the routine first trimester scan, irrespective of whether they were low or high risk based on medical or prior obstetric history. All ultrasounds were performed using a GE Voluson E6/ E8 machine using 1.5-4.6 MHz convex transducer and a 2-7 MHz volume transducer. Both colour and power Doppler were used alternatively to achieve appropriate images. Cardiac anatomy was evaluated by trans-abdominal route for all. Transvaginal scans were performed using 4-9 MHz probe, if there was a failure to achieve adequate sections or a suspicion of an abnormal finding using trans-abdominal imaging.

The standard checklist for cardiac imaging

Cardiac and visceral situs. The inflows across the atrioventricular valve in four chamber view. Flow through the arches (ductal and aortic) in colour at the level of 3 vessel trachea view. Evaluation times and machine output standards were assigned confirming to ALARA principles (Figure 1 D), considering that we were evaluating fetuses <14 weeks of gestation.

If an anomaly was detected in any one or more of these views in the fetus then the same was reported by the sequential segmental analysis approach. However, considering the smallness of the heart at this juncture, limitations to ascertaining and reporting certain sections of the cardiac anatomy, (e.g. Atrial situs, pulmonary venous anatomy, altered systemic venous anatomy) exist.

Cardiac anomalies per se, especially those identified at first trimester fall under the group of major malformations, even if isolated.

Technique of perinatal pathology

Fetuses were preserved in 10% formalin, and given the small size of the heart, autopsies were conducted using magnifying glasses, operating microscopes, and delicate instruments (Figure 2 A and B). The "flow of blood" technique was applied during cardiac autopsies, following the standard protocol used for any trimester. Initially, a complete external heart assessment was conducted in situ (Figure 3 C), noting the following: Heart situs, size, axis, and apex, Superior and inferior vena cava (side and number), atrial appendages (presence and situs)- Position of anterior and posterior interventricular grooves, outflows (presence, relationship, size), aortic arch (sidedness, branches), pulmonary artery branches (size), and ductus arteriosus (side and size).

The heart was then dissected, beginning with the right atrium (Figure 3 D-E) and progressing through the right ventricle and outflow tract. This included inspecting the tricuspid valve, pulmonary valve, and pulmonary artery.

The left side was similarly opened, with examination of left atrium, mitral valve, left ventricle, and aortic valve. Throughout, chordae, papillary muscles, and interventricular septum were checked for defects.

Photographs were taken at each stage for documentation and review.

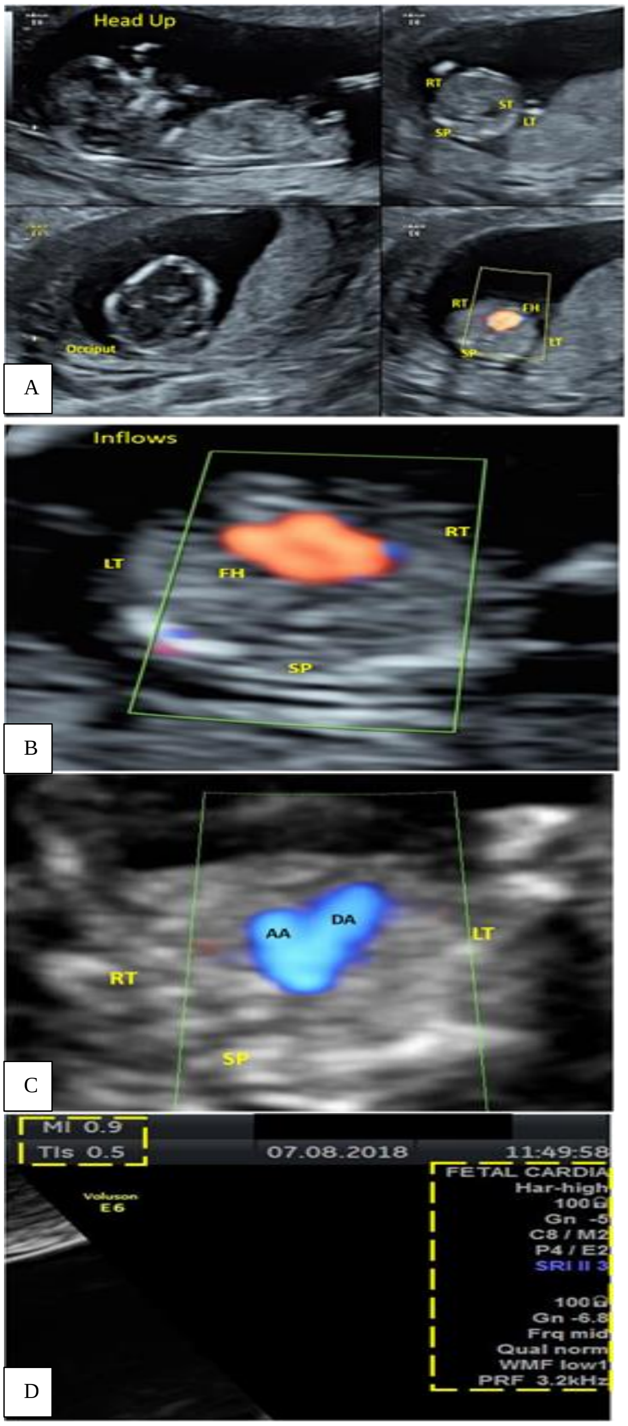

Figure 1 (A-D): Standard checklist for cardiac imaging. Normal cardiac and visceral situs, flow across trioventricular valves in color and flow across arches (Ductal and aortic) in color. Machine settings for cardiac imaging.

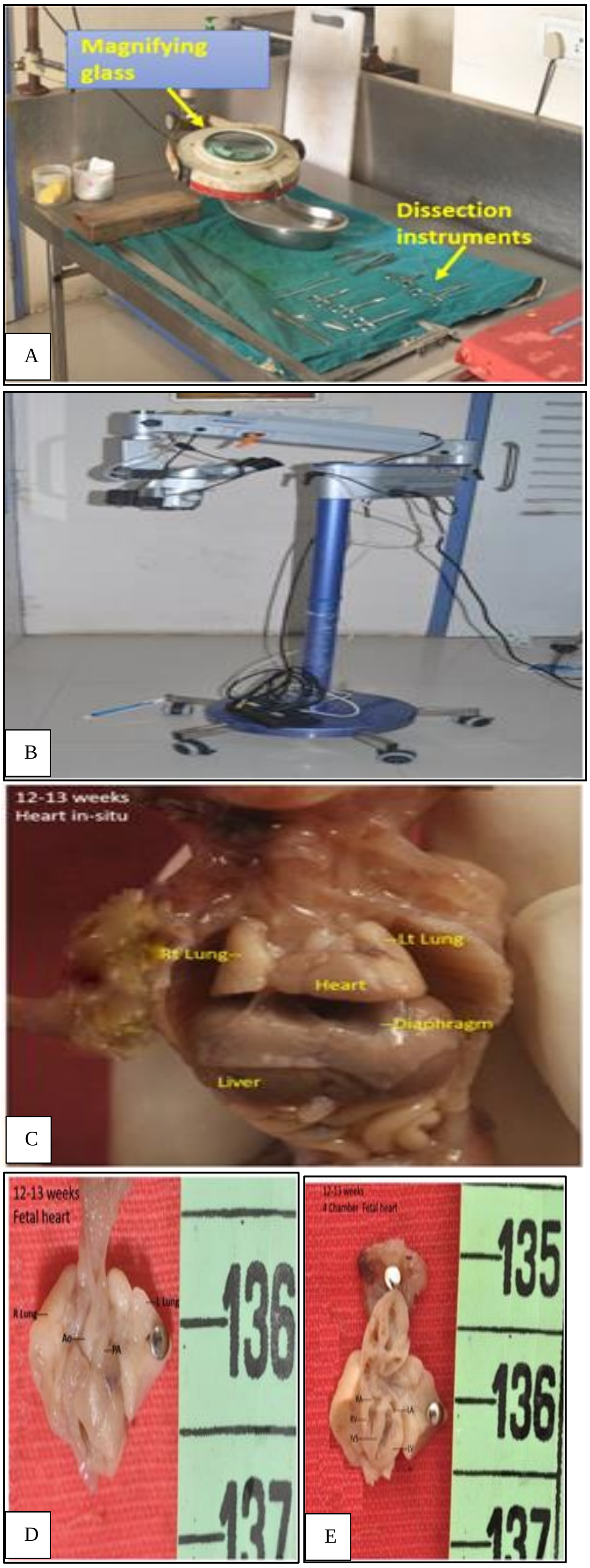

Figure 2 (A-E): Perinatal autopsy-instruments and autopsy images. Instruments for perinatal autopsy, operating microscope, *In-situ* heart at 1st trimester autopsy, 1st trimester fetal heart-undissected and 1st trimester fetal heart-dissected.

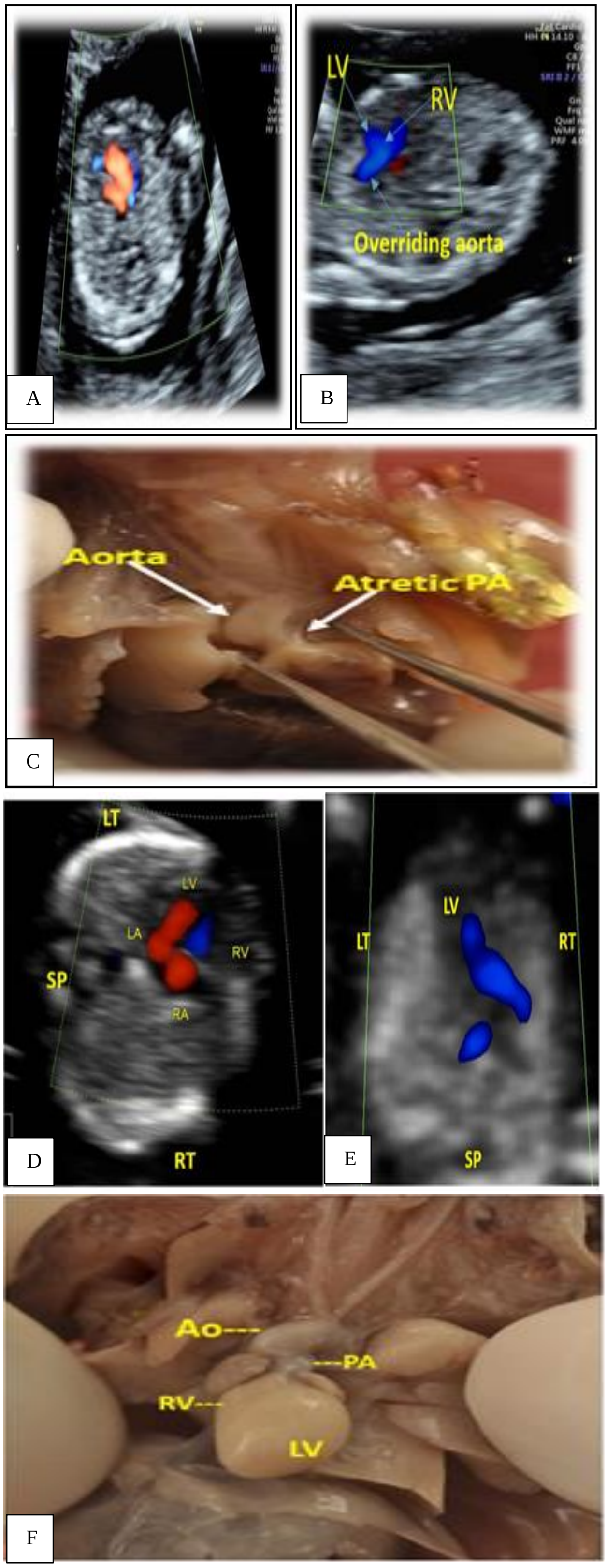

Figure 3 (A-F): Complete agreement-full agreement between ultrasound and autopsy-cases from excel sheet.Two inflows, single outflow tract (Aortic override with pulmonary atresia), tetrology of Fallot with pulmonary hypoplasia. Single inflow across left AV valve, single outflow (Aorta) from left ventricle and hypoplastic right heart syndrome.

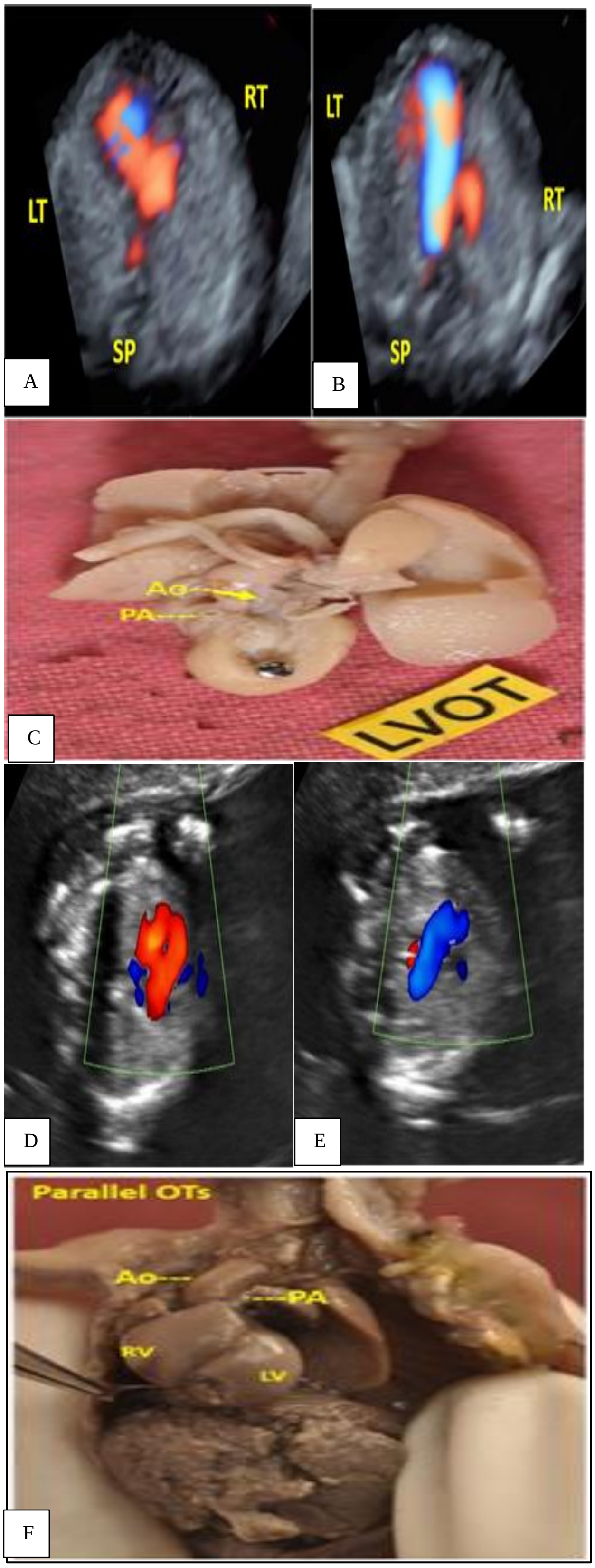

Figure 4 (A-F): Partial agreement-autopsy confirmed ultrasound findings but provided additional information cases from excel sheet. Single inflow, single outflow, hypoplastic right heart syndrome. two inflows, single outflow tract, parallel outflow tract – transposition of great vessels.

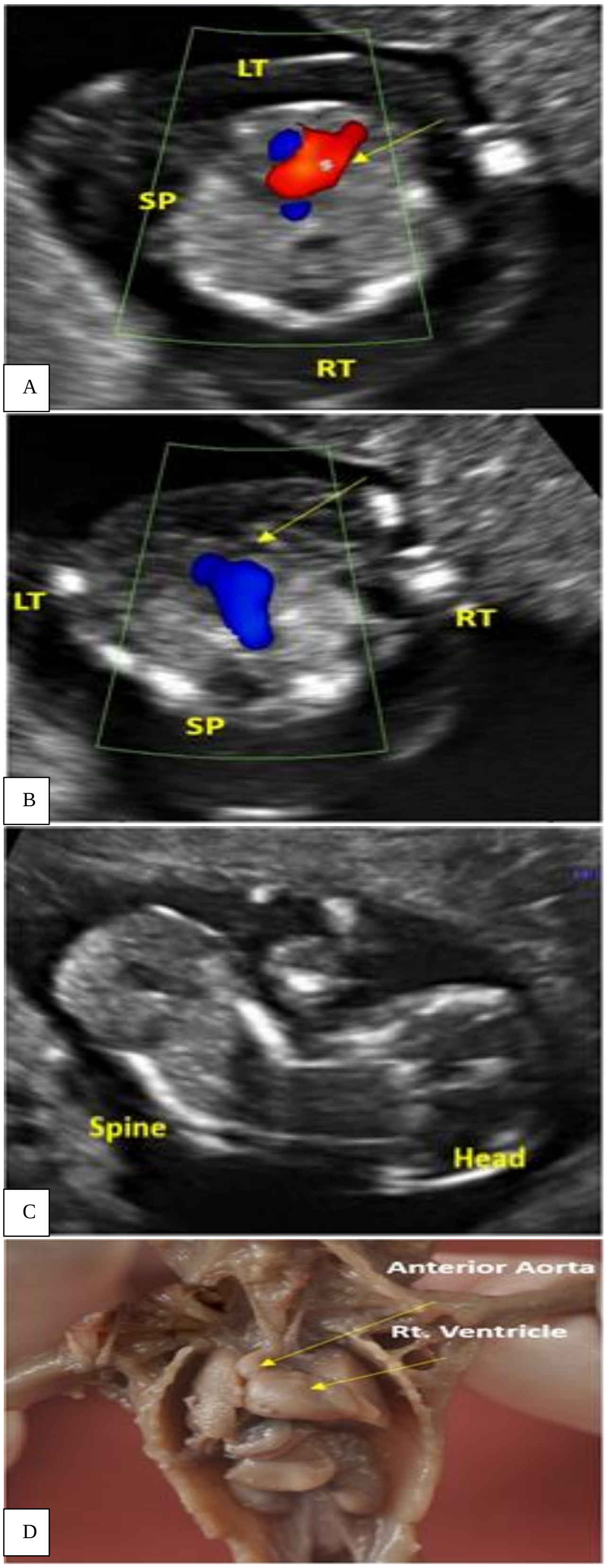

Figure 5 (A-D): Disagreement (mismatch) ultrasound and autopsy did not correlate-case from excel sheet. Single central inflow, single outflow, angulated spine and mitral atresia with double outlet right ventricle (DORV).

Study categories

To assess correlation between ultrasound and autopsy findings, cases were divided into three categories:

Category 1: Complete agreement: Full concordance between ultrasound and autopsy findings (Figure 3 ultrasound and autopsy images of two cases from excel of complete agreement-case no. 13 and 42).

Category 2: Partial agreement: Autopsy confirmed ultrasound findings but provided additional anatomical details (Figure 4-ultrasound and autopsy images of two cases from excel of partial agreement-case no. 13 and 15).

Category 3: Disagreement: Ultrasound and autopsy findings were entirely mismatched (Figure 5 ultrasound and autopsy images of one case from excel of disagreement-case no 5).

Minor anomalies, such as a persistent left superior vena cava or aberrant right subclavian artery, were excluded from the correlation analysis as they were not part of standard first-trimester ultrasound protocols.

Study period

The study was divided into two cohorts (2012-2014 and 2015-2017), with both cohorts following the same assessment protocol, ensuring comparability between the two periods.

RESULTS

Study cohort

Out of the total 33432 scans performed in the first trimester during the study period, there were 479 fetuses with cardiac anomaly, either isolated or as a part of multisystem anomaly. Of these, 89 fetuses were given for autopsy. Nine fetuses were damaged or autolysed making the autopsy findings difficult and hence were excluded. So, the final number of fetuses in the study was 80.

Mean maternal age in the study cohort was 26.6 years (19-44 years) mean maternal BMI was 26.1 (17.5- 42.8) whereas the mean CRL was 65 mm (48-82 mm).

Degree of correlation

Referring to the definitive reporting, in 50/80 (62%) cases there was complete agreement between the ultrasound and the autopsy (category 1).

In 22/80 (28%) cases there was a partial match as autopsy provided additional information besides confirming the ultrasound findings (category 2), while in remaining 8/80 (10%) cases the autopsy findings did not correlate to the scan findings (category 3) (Table 1).

Partial agreement analysis

On further subgroup analysis of 22 cases of the partial agreement category, it was noted that in upto three fourth of the cases, (73%) the additional information was provided in form of nature of anatomical description and origin of the outflow tracts. In remaining quarter of the cases, additional information was obtained in the inflows/four chamber view of the heart (Table 1).

Disagreement (mismatch) analysis

Similarly on further subgroup analysis of mismatch cases, it was noted that in seven out of eight cases cardiac anomaly was a part of cystic hygroma or multisystem anomaly (Table 2).

Table 1: Degree of correlation.

Variables	N	Percentage (%)
Partial agreement analysis, (n=80)		
Complete agreement	50	62
Partial agreement	22	28
Disagreement	8	10
Subgroup of partial agreement, (n=22)		
Situs	0	0
Inflows	6	27
Arches	16	73

Table 2: Subgroup analysis of disagreement cases.

USG findings	Autopsy findings	Additional findings/ comments
Outflows not well seen	Normal outflow tracts balanced AVSD	Cystic hygroma
AV, VA concordance, cross over +	Transposition of great vessels	Multisystem anomaly
Single OT, truncus arteriosus	Aortopulmonary window defect	-
Aorta seen, pulmonary artery not seen	Interrupted aortic arch	Cystic hygroma
AVSD, single inflow and outflow	Mitral atresia with DORV	Angulation of spine
AVSD with single OT	DORV with pulmonary artery hypoplasia	Meckel Gruber syndrome
Double outlet right ventricle	Hypoplastic left heart syndrome	Cystic hygroma
Situs ambiguous, OT anomaly	DORV with pulmonary artery hypoplasia	Multisystem anomaly

AVSD-Atrioventricular septal defect, OT-outflow tract, DORV-double outlet right ventricle, AV-VA concordance- atrioventricular, ventriculoarterial concordance.

Comparison between two cohorts

When the correlation between the two cohorts in terms of diagnosis accuracy was studied, we found that the imaging accuracy has significantly become better in the second (2015-2017).

There has been a significant increase in the number of cases with complete agreement in second cohort from 49% to 76%. Besides this there has been a significant drop in the number of disagreements (mismatches) in the second cohort with percentage dropping down from 21% to nil (Figure 6).

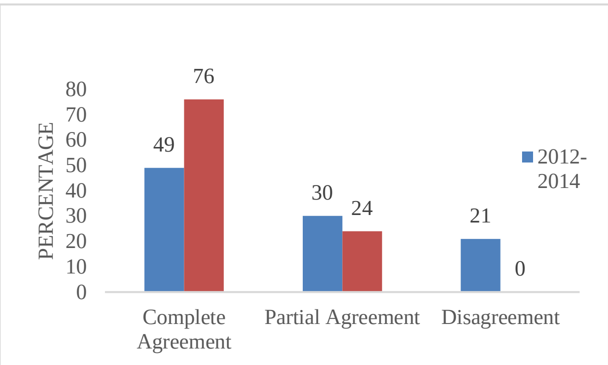

Figure 6: Comparison of correlation amongst various categories of two cohorts.

Sub categorisation of anomaly

Isolated cardiac anomaly was noted in 24/80 (30%) of the cases while in remaining 56/80 (70%) of the cases it was part of a multisystem anomaly or a marker for aneuploidy. In this later group of non-isolated cardiac anomalies only an additional aneuploidy marker was noted in 27/56, (48%) of the cases while multisystem anomaly was detected in remaining 29/56 (52%) of cases (Table 3).

Cytogenetic analysis

Out of 80 fetuses in the group, cytogenetic analysis (karyotyping) was carried out in 26/80 (32.5%) by chorionic villous sampling. In 22/26(27%), the karyotype result was normal while in remaining 4 cases (5%) the karyotyping was abnormal. There were 2 cases of trisomy 18 and one case each of Monosomy X and trisomy 21 (Table 3).

Influence of other factors (variables) on first trimester scan

It was shown in Table 4 below.

BMI and complete sonopathological correlation

When the BMI of the patients was studied, a gradual decline in correlation between the scan and autopsy findings was found. The correlation was only 50% when the BMI was more than 30 (Table 4).

CRL and complete sonopathological correlation

The results did not show statistically significant difference in sonopathological correlation between the cases grouped on basis of CRL as <60 and ≥60 (Table 4).

Table 3: Distribution of anomaly and cytogenetic analysis.

Variables	N	Percentage (%)
Anomaly		
Isolated cardiac anomaly	24	30
multisystem anomaly or marker for aneuploidy	56	70
Cytogenetic analysis (karyotyping)		
Situs	0	0
Inflows	6	27
Arches	16	73

Table 4: Influence of other factors (variables) on first trimester scan.

Factors	Percentage (%)
BMI (kg/m^2)	
<18.5	100
18.5-24.9	73
25-29.9	57
>30	50
CRL	
CRL<60	50
CRL>60	67

DISCUSSIONS

BMI and complete sonopathological correlation

Our result analysis showed that complete correlation decreases with increase in the BMI of the patient. On extensive literature search, there are no direct sonopathological studies on role of maternal BMI on satisfactory first trimester cardiac assessment. Various authors in the recently published studies assessing the feasibility and factors of first trimester cardiac assessment have concluded conflicting results. Votino et al concluded that the maternal BMI was significantly inversely correlated with the ability to visualize some cardiac anatomic structures, although the impact was small (OR=0.9).[17] On the other hand, Persico et al found that there was no difference in the mean maternal BMI between cases with or without a successful transabdominal fetal heart examination.[18]

CRL and complete sonopathological correlation

Similarly, the cases were divided into 2 groups according to the CRL as less than 60 and more than equal to 60 and the extent of correlation was studied. Although a difference in complete correlation was noted between the two groups, the same was not statistically significant. Other recent studies also showed that the fetal crown - rump length measurement does not significantly influence the visualization of the fetal heart or its segments.[17,18] However, this information needs to be interpreted in the light of the fact, that we utilise transvaginal sonography extensively or rather in all patients when we suspect a cardiac anomaly on ultrasound and this indeed has a significant impact on improving the quality of the study performed. Despite this, at CRL <50 mm, anatomical delineation of cardiac structures has significant limitations and hence a using a prudent cut off limit of 60 mm as a limit to ascertain cardiac anatomy in, anomalous fetuses would provide more information.

Defining correlation

Agreement between ultrasound and autopsy findings have been categorized by various authors in different papers by differing methodology.[15,19] Categorization overall in earlier studies of ultrasound and autopsy correlation were as below.[19] a. Complete agreement b. Minor autopsy finding not detected by ultrasound c. Major autopsy finding not detected by ultrasound d. No autopsy findings suspected on ultrasound. e. Minor ultrasound findings not confirmed at autopsy f. Major ultrasound findings not confirmed on autopsy.

We determined that the existing categorization methods were unsuitable for our study, given that all cases involved first-trimester fetuses, where significant limitations arise due to their small size. Additionally, there were no comparable studies with inclusion and exclusion criteria similar to ours to base a categorization on. Some studies have grouped traumatized, macerated, or autolyzed fetuses separately, which can inflate the number of cases where major ultrasound findings were not confirmed at autopsy. To prevent this bias, we excluded autolyzed fetuses from our analysis.

A preformed checklist for ultrasound cardiac views guided our systematic examination. Minor anomalies identified at autopsy were excluded from correlation assessments, as they were not part of the basic first-trimester cardiac imaging criteria. This checklist not only ensured a more structured approach but also improved the quality of correlation in our study, leading us to classify fetuses into only three categories.

Comparison between two cohorts

There was significant difference in the rate of complete agreement when comparing the 3-year period of 2015-2017 with the previous period of 2012-2014. The number of cases with complete agreement has increased and at the same time disagreement number has dropped significantly.

Similar findings were noted by Struknes et al who studied the correlation trend over the 30 year time period between the prenatal ultrasound and postnatal findings. They concluded a gradual increase in the rate of full agreement between findings on ultrasound and at autopsy in five year intervals during the 30 year period. Similarly, Isaksen et al in their study of over 10 years period (1985-1994) reported an increase in the complete agreement rate from 48% to 82% from the first time period (1985-1989) to second time period (1990-1994) respectively.[19]

Division into two cohorts

Since January 2015, a weekly perinatal review meeting has been held, during which all autopsy cases, including those with cardiac anomalies, are discussed alongside ultrasound images as part of both training and audit. We believe that our imaging accuracy improved in the second cohort due to lessons learned from the initial autopsy series. These meetings have contributed to enhancing the skill sets of both the sonologists and perinatal pathologists. Additionally, the use of transvaginal ultrasound, particularly in cases where transabdominal imaging failed to provide adequate sections or raised suspicion of an abnormality, likely contributed to improved correlation between ultrasound findings and autopsy results.

However, the discrepancy in complete correlation-62% in our data compared to higher rates in two other referenced studies-should be interpreted with caution, as those studies primarily included second- and third-trimester cases, with few first-trimester anomalies, if any, in their analysis

Partial agreement

Partial agreement was observed in 22 out of 80 cases (28%). Further subgroup analysis revealed that in 73% of these cases, autopsy provided critical information regarding the nature and anatomy of outflow tract anomalies. This discrepancy arose because outflow tracts were imaged in the three-vessel trachea view using color Doppler, rather than at their origin from the ventricles, making it challenging to accurately define the anatomy of anomalous outflow tracts. Evaluating outflow tracts in grayscale or color flow during the first trimester is inherently difficult due to the small size of the fetal heart, which is why it is not included in our first-trimester cardiac assessment checklist. Similar findings were reported by Hutchinson et al who noted that outflow tracts were not visualized in 21% of cases by end of 14 weeks gestation.[21]

In the remaining 27% of partial agreement cases, additional information was related to the inflow across the atrioventricular valves in the four-chamber view. Although the anomaly itself was correctly identified in these cases, the affected side of the heart was either not specified or difficult to distinguish.

Disagreement

The 8/80 (10%) of the cases had disagreement. On further analysis of cases in this group we found that 7 out of 8 cases were associated with cystic hygroma or multisystem anomaly. This in our opinion served as a confounding factor in ultrasound evaluation of the fetus. AVSD was one defect in this group of patients which was reported on scan but turned out to be other cardiac anomaly on autopsy in two cases. As the four chamber view in present study was evaluated through the inflows across atrioventricular valve, the crux anomaly was mis-diagnosed. DORV was the most common anomaly which was misdiagnosed and in 3/8 cases and in 2 cases it was mistaken for hypoplastic left heart.

Autolysis

Autolysis of specimens, is known to happen in fetuses sent for autopsy study, especially if they have not been well preserved and sent. Our study being one of first trimester fetuses, autolysis, renders any evaluation, even gross assessment impossible, and hence despite autolysed fetuses being subcategorized in other studies, we decided to eliminate them from our analysis 9/89 (10%), as this would have significantly skewed our data.

Limitations

The main limitation of this study is its focus on evaluating accuracy and methodology of reporting 1st trimester cardiac abnormalities, rather than assessing overall effectiveness of identifying cardiac issues during this period. Use of the stringent correlation criteria have lowered correlation rates. Had study focused exclusively on detecting outflow/inflow tract anomalies, correlation could have approached 100%. However, this would not have aligned with study's objective of advancing segmental analysis of cardiac abnormalities in the 1st trimester.

CONCLUSION

The study demonstrates that a systematic checklist significantly improves imaging accuracy in first-trimester cardiac assessments. The correct prenatal diagnosis of major cardiac anomalies was achieved in 90% of cases, with autopsies providing additional insights in 28% of cases and no false positives. Diagnostic accuracy significantly improved between 2012-2014 and 2015-2017. While BMI and CRL influenced screening, the impact was not statistically significant. Challenges in distinguishing between DORV and hypoplastic left heart persisted, even in the second trimester. Importantly, no prenatally diagnosed anomalies were found to be normal on autopsy, supporting the reliability of early diagnosis and the potential for confident counselling.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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