

## Introducing the “Tick Sign” and its Role in Diagnosing Outflow Tract Anomalies at 11 -14 Weeks Scan

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### Abstract

**Objectives:** To evaluate the normal tick shaped orientation of the arches in first trimester fetuses and to propose the use of this sign, the alteration of which has a significant role in diagnosing cardiac anomalies especially the transposition of great arteries in the first trimester.

**Methods:** This was a retrospective study from November 2010 to April 2013 conducted in fetal medicine unit, Mediscan systems, Chennai, Tamil Nadu, India. All the fetuses who had first trimester scan followed by target scan in our center were included in our study. Fetal cardiac examination was standardized by including the Color four chamber and the “tick sign” as a part of our mandatory anatomy. The operators were trained adequately before they start independent imaging.

**Results:** A total of 178 normal fetuses were reviewed, the peculiar “tick” shaped arches were seen in 58 (32%) of the fetuses. Out of these, 3 (5%) were 11 - 12 weeks, 33 (56%) were 12 - 13 weeks, and 22 (37%) were 13 - 14 weeks. All the fetuses with normal “tick sign” had normal echocardiography at target scan. Two fetuses who were diagnosed with transposition of great arteries at target scan, when we retrospectively reviewed the images at 11 - 14 weeks scan, the “arches view” showed abnormal orientation of the two arches. Including the tick sign as part of mandatory anatomy in first trimester, a case of transposition of great arteries was picked in the first trimester.

**Conclusion:** The “tick sign” is consistently reproducible in normal fetuses in 11 - 14 weeks scan especially between 12 - 14 weeks. Alteration of this normal orientation is useful to suspect and diagnose cardiac anomalies especially outflow tract anomalies even in first trimester. We recommend inclusion of arches view (“Tick sign”) as part of mandatory anatomy in first trimester scan.

**Keywords:** Fetus; Ultrasound; First Trimester Screening; Echocardiography; “Tick Sign”

### Abbreviations

AAo: Ascending Aortic Arch; ALARA: As Low as Reasonably Achievable; ASD: Atria Septal Defect; AVSD: Atrioventricular Septal Defect; AO: Aorta; C TGA: Corrected Transposition of Great Arteries; CHD: Congenital Heart Disease; DORV: Double Outlet Right Ventricle; DA: Ductal Arch; AA: Aortic Arch; Dao: Descending Aortic Arch

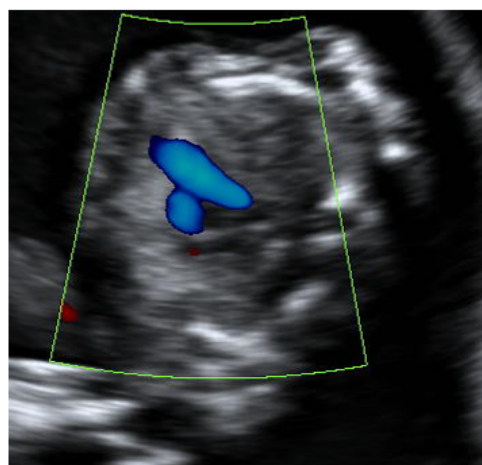
## Introduction

Prior to 11 weeks the fetal heart is seen as a three chamber structure with four chamber being visible in later gestation [1]. The fetal heart is the organ with the highest probability of major anomalies. Prenatal diagnosis of congenital heart diseases is always a difficult task in second trimester and owing to the small size of the fetal heart, imaging is even more challenging at the 11 - 14 weeks scan. First trimester scan not only allows us to screen for aneuploidy by nuchal translucency but also gives us an opportunity for early diagnosis of major anomalies.

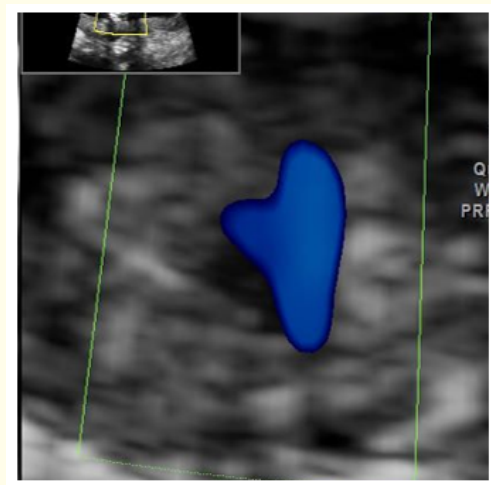
There are reports highlighting the value of fetal echocardiography in cases of increased risk in view of increased nuchal translucency [2,3]. However, significant number of major cardiac malformation may be found in fetuses with normal NT. Fetal heart scanning by the four chamber alone [4,5] is an excellent screening method but as seen in the second trimester we may miss cardiac anomalies involving the outflow tracts if only four chamber view is used at the 11 - 14 weeks of gestation. The three vessel view as suggested by Yoo., *et al.* [6,7] in second trimester cardiac imaging, is a transverse view of the upper mediastinum, which demonstrates the main pulmonary artery (PA) ascending aorta (AO) and the superior vena cava (SVC) from left to right in a straight line. Though it is possible to image the three vessel view at 11 - 14 weeks scan, but unlike the second trimester, it is not feasible to include the PAS view as a part of protocol in first trimester in low risk population in view of technical difficulties associated with it. However, the three vessel trachea view [8-10] which adds information on great vessels can be used, especially with the application of color Doppler. Color Doppler imaging of the fetal heart including the standard four chamber view and the three vessel trachea view proves to be easier and more reliable [11] at 11 - 14 weeks scan.

We are introducing a novel ultrasound marker the “tick sign” in cardiac imaging at 11 - 14 weeks of gestation. Under normal circumstances aorta arises from left ventricle and is directed slightly towards the right-side. The ascending aorta curves to the left and forms the cranial aortic arch. In contrast, the pulmonary artery forms the right outflow tract and crosses the aorta perpendicularly and comes to lie on the left side. It follows a straight course, giving off right and left pulmonary artery and forms the caudal ductal arch.

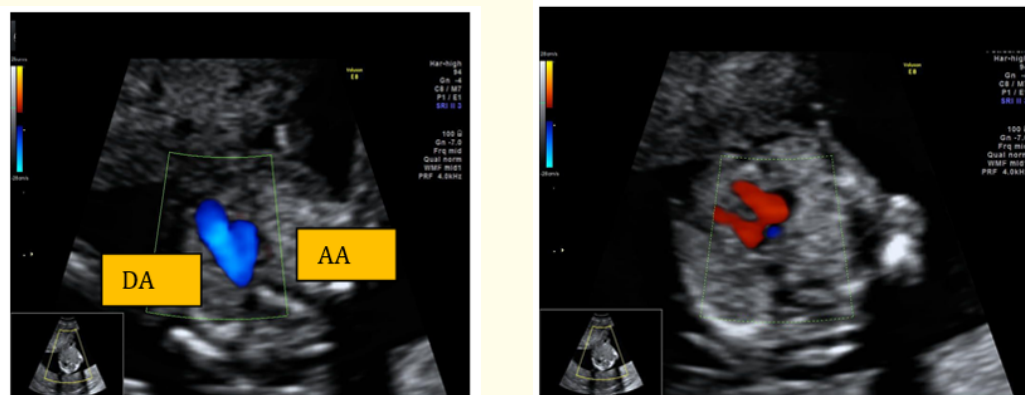
“Tick sign” is obtained by using color doppler with cephalic tilt from four chamber view at the level of the Three Vessels and trachea view. The long arm seen on the left, represents the ductal arch and the right sided short arm represents the aortic arch.



**Figure 1:** PAS view in first trimester.



**Figure 2:** The three vessels trachea view in first trimester.



**Figure 3:** The “tick sign” and four chamber view.

## Material and Methods

The total cases were divided in to two groups:

- **Group A:** It was a retrospective analysis (from September 2012 till April 2013) of Color images of fetal heart archived at 11- 14 weeks of gestation (CRL of 45 - 84 mm) done at first trimester department, Mediscan Systems, Chennai. A mixed population of both low and high risk cases who had a normal first trimester scan with us were included in the study. All the cases seen in our first trimester unit were examined by a single operator.

- **Group B:** A retrospective study was conducted over a period of 2 year and 6 months from 1<sup>st</sup> November 2010 to 30<sup>th</sup> April 2013 in first trimester unit of Mediscan systems. This group was sub divided in to - the cases before and after the introduction of the “tick sign” (1 Sept 2012). All the cases with first trimester cardiac anomaly with CRL between 45 - 84 mm were included. The analysis was done by two experienced operators independently.

### Exclusion criterion

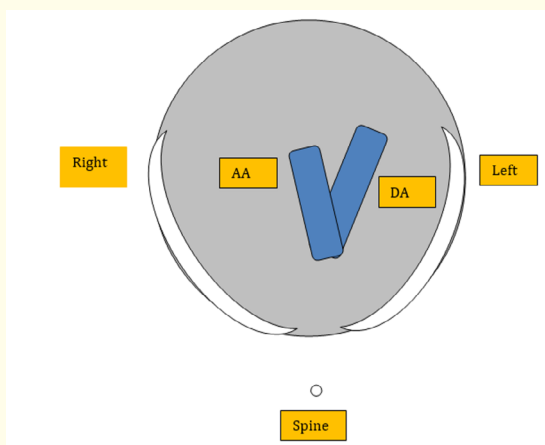
Multiple order gestation was excluded from the study.

Data’s were retrieved from “SONOCARE” (MEDISCAN) and were analyzed using Microsoft Excel and Chi square test was used for statistical analysis.

Fetal cardiac examination was standardized by including the Color four chamber and the “tick sign” as a part of our mandatory anatomy. The operators were trained adequately before they start independent imaging.

Ultrasonography was performed using Voluson S8, E6, E8, Aloka, Logic 730 expert. Examinations were performed transabdominally or transvaginally if necessitated. We used Transabdominal 5 MHz and trans vaginal 9 MHz transducers.

The “tick sign” was obtained by using color doppler with cephalic tilt from four chamber view at the level of three vessel and trachea view. The long arm seen on the left, represents the ductal arch and the right sided short arm represents the aortic arch.

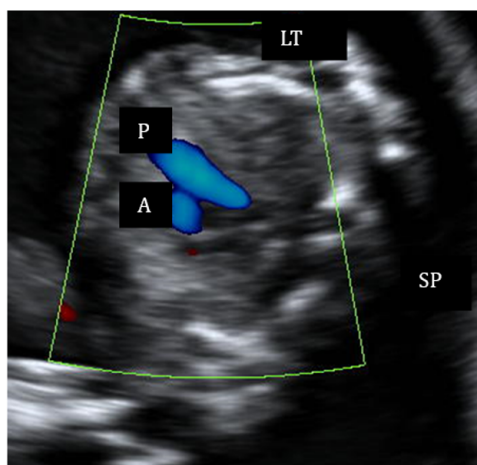


**Figure 4:** Line diagram of the three vessels trachea view (“Tick sign”).

### Prerequisite for cardiac imaging in first trimester:

1. Use cardiac setup.
2. Appropriately zoom the image.
3. The PRF, the color gain and B mode gain needs to be adjusted according to the gestational age, maternal habitus and fetal position.

We should be able to demonstrate two separate inflows and then from there a cephalic tilt will give us “tick sign”. The ideal position of the fetus for cardiac imaging would be posterior spine at 6 ‘O’clock position. However it is possible to get the “tick sign” in other positions with manipulation of the probe. If the fetal position is not conducive then we should finish the rest of the sonography and then revisit the fetal heart. At times despite of all the measures it is not possible to get “tick sign” especially with anterior spine trans abdominally than we can perform a transvaginal scan. The Color four chamber view was a part of mandatory anatomy at 11 - 14 weeks scan in our unit. But from 1 September 2012 we have made the “arch view” - the “tick sign” as a part of our mandatory cardiac imaging. In our FTS protocol the three vessel view (PAS view) is accepted in cases where imaging of Tick becomes difficult.



**Figure 5:** PAS view in first trimester scan.

It is very important to keep in mind the ALARA principle in first trimester cardiac imaging.

Use of color doppler and pulse wave doppler in the first trimester should be kept as minimum as possible. Therefore fetal echocardiography should be reserved only in cases with anomalies suspected on the initial cardiac screening.

### Interpretation of the “Tick sign”

1. Number of arms: We should be able to see two arms of the tick.
2. The orientation of the great vessels: Ductal arch on the left of the aortic arch.
3. Length: Ductal arch being longer than aortic arch.
4. Direction and color flow: Ductal arch being straight and the aortic arch being oblique. Both the arches should have blood flow towards the spine.

Any deviation from the above indicates outflow tract anomaly and needs detailed fetal echocardiography.

This study investigates the feasibility of including the “tick sign” in the first trimester protocol and its diagnostic value for the detection of outflow tract anomalies. There is a need to shift the target scan done at 20 weeks to early gestations as the physiological and psychological impacts of a termination of pregnancy increase with increasing gestational age which can lead to ethical issues in the second half

of pregnancy that to in cases of viable fetuses with serious handicaps. It is a right of the pregnant women to decide against continuing a pregnancy with a severe anomaly which is the main aim of prenatal diagnosis to provide as much relevant information as possible to her as early as possible [15].

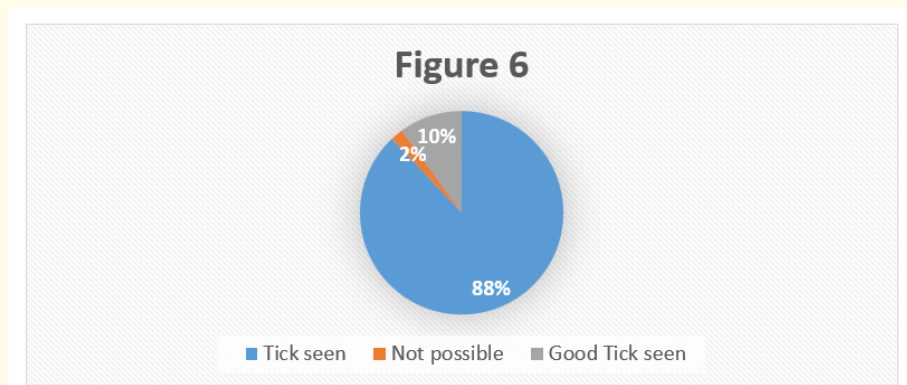
## Results

### Group A

The achieved images were analyzed for color four chamber and the presence of the “tick sign”. They were divided in to three groups: Cases with good tick, difficult to get tick and not good tick. The tick was said to be good if there was documentation of the left side of the fetus by the position of the apex of the heart (with or without color) followed by the image of the three vessel trachea view in color (“Tick sign”). Only those were the criterion of “tick sign” were met, were included in the good tick group. In cases where there was documentation of three vessel view (PAS view) in B Mode or in color without “tick sign” were included in difficult to image tick.

S.no	Tick Sign	Number of cases (%) n = 1996
1.	Good Tick	1752(88%)
2.	Not possible/difficult	45(2%)
3.	Not good	199(10%)

**Table 1:** Distribution of cases with respect to the tick sign.



**Figure 6:** “The tick sign” in cases with normal first trimester scan.

Of the total 1752 cases, 1685 (97%) had trans abdominal scan and the remaining 67 (4%) had trans vaginal scan. Maximum number of cases - 1003 (57%) were at 12 - 13 weeks of gestation (Table 2).

S.no	GA (weeks)	Number of cases (%)
1	11 - 12	167 (9.5%)
2	12 - 13	1003 (57%)
3	13 - 14	554 (31%)
4	14	28 (2%)

**Table 2:** Distribution of cases with good “tick sign” according to gestational age.

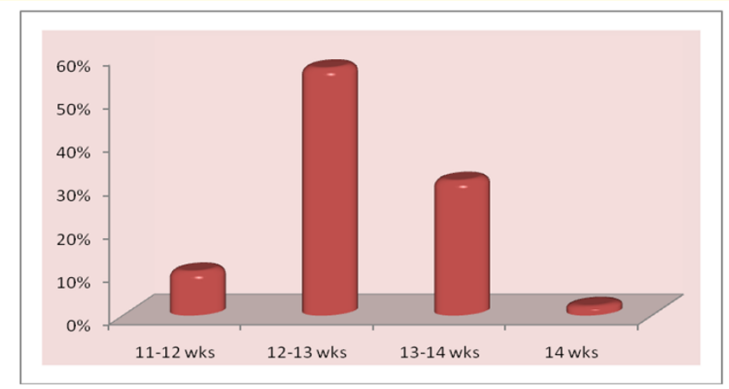


Figure 7: Gestational age split up for fetuses with good tick sign.

S.no	Follow up	Number of cases
1.	Normal second trimester scan	1079
2.	Abnormal second trimester scan	1
3.	IUD at 17 weeks, autopsy revealed structurally normal fetus	1
4.	No follow up	671

Table 3: Distribution of cases on the basis of available follow up.

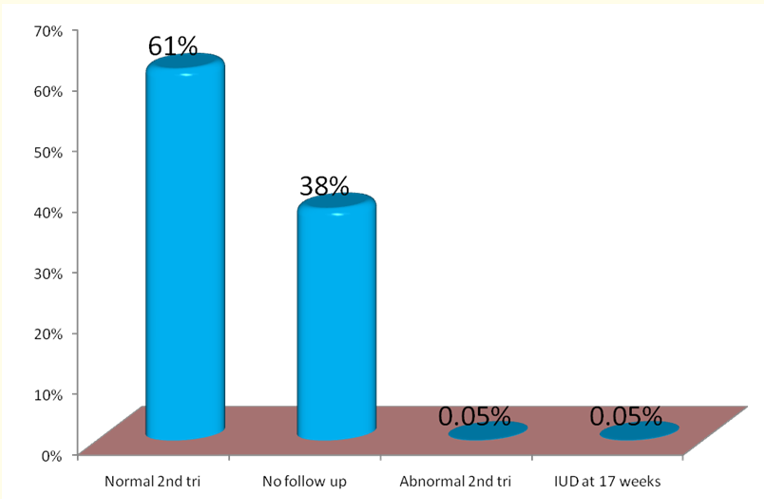
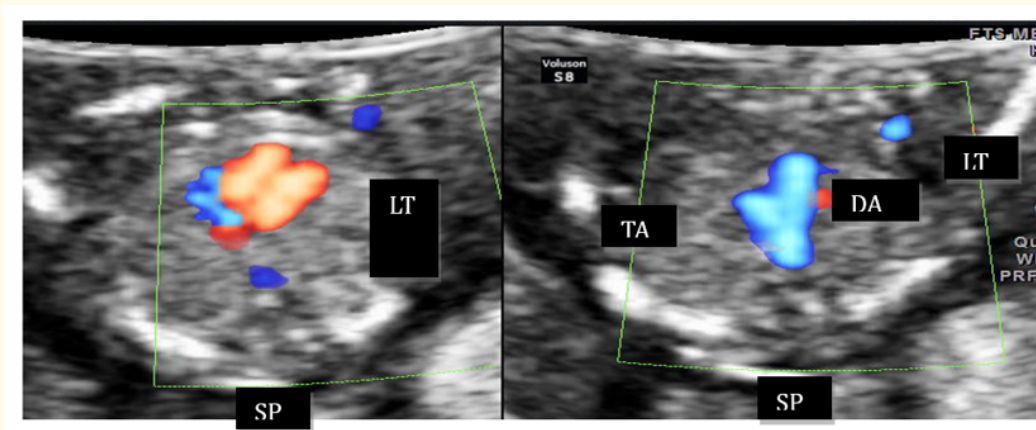


Figure 8: Distribution of cases depending upon the follow up scan.

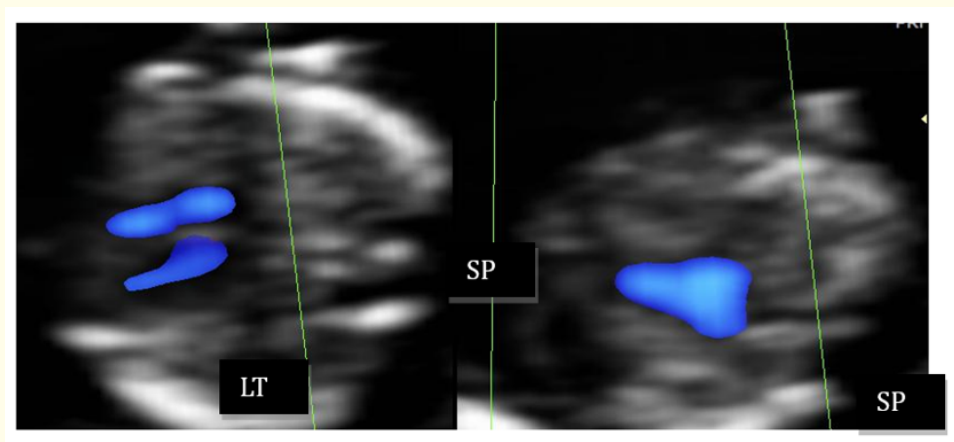
We retrospectively analyzed the position of the fetal spine in all the cases with good tick sign. It was observed that maximum 222 (50%) of the cases, the spine was at 6 ‘o’ clock position.



**Figure 9:** “Tick sign” with fetal spine at 6’O’ clock position.

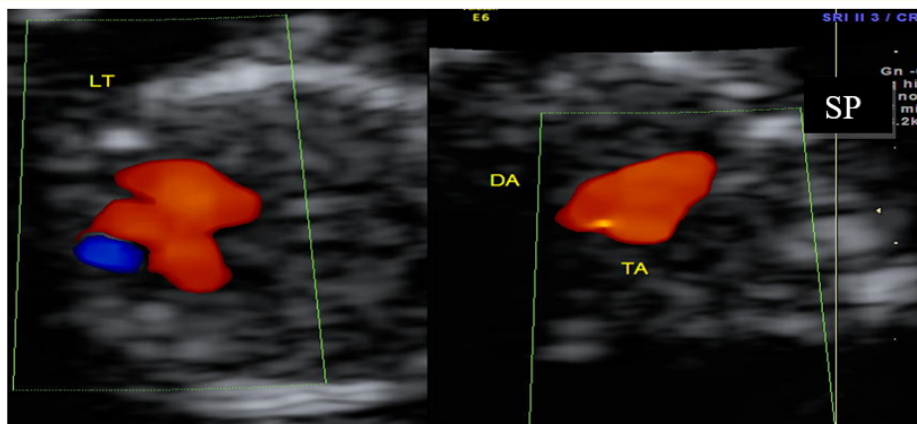
Next in order was 4, 7 and 2 ‘o’ clock followed by 5 and 8 ‘o’ clock position. The least common was 10,12,1 and 3 ‘o’ clock position.

We have observed that it is easy to get the tick sign when the apex of the heart is anterior with the spine at 6, 4 and 7 ‘O’ clock position and is difficult to get the same when the spine is anterior. It is judicious to finish rest of the scan when the fetal spine is anterior and then image the heart when the fetus changes the position.

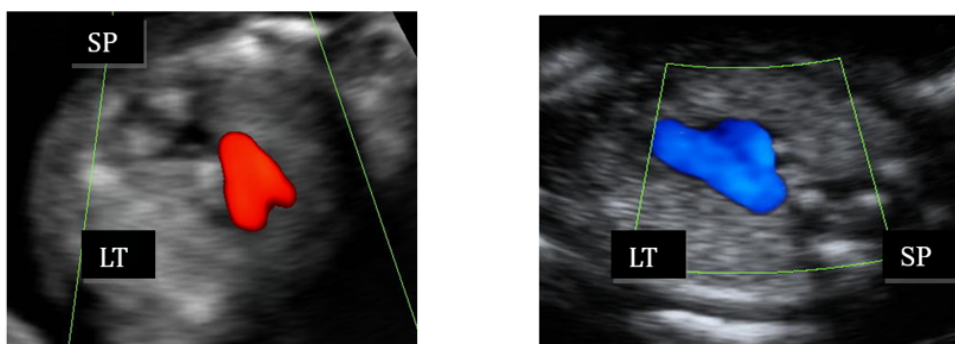


**Figure 10:** “The tick sign” with fetal spine at 4’O’ clock position.





**Figure 11:** “The tick sign” with fetal spine at 2 ‘O’ clock position.



**Figure 12:** “The tick sign” with fetal spine at 11 ‘O’ clock and 5 ‘O’clock position.

### Group B

We had a total of 109 cases of cardiac anomalies in the first trimester over a period of two year and 5 months.

In these 109 cases, 4 chamber was found to be abnormal in 87 and normal four chamber in 20 cases. In remaining 2, it was difficult to determine the normalcy. Outflow tract anomalies were seen in 81 cases.

63 fetuses had both abnormal four chamber and outflow tracts and 18 had normal four chamber and abnormal outflow tracts. In the outflow tract anomalies (81), the tick sign was not seen in 69 fetuses, seen in 2 and cannot be commented in 10.

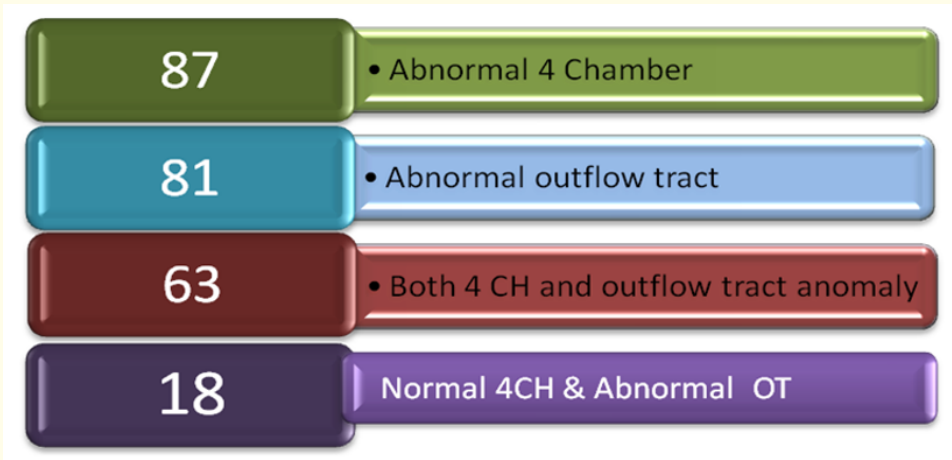


Figure A

S.no	GA (weeks)	Number of cases (%) n = 109
1	11 - 12	11 (10%)
2	12 - 13	34 (31%)
3	13 - 14	62 (57%)
4	14	2 (2%)

Table 4: Distribution of cases with cardiac anomaly based on gestational age.

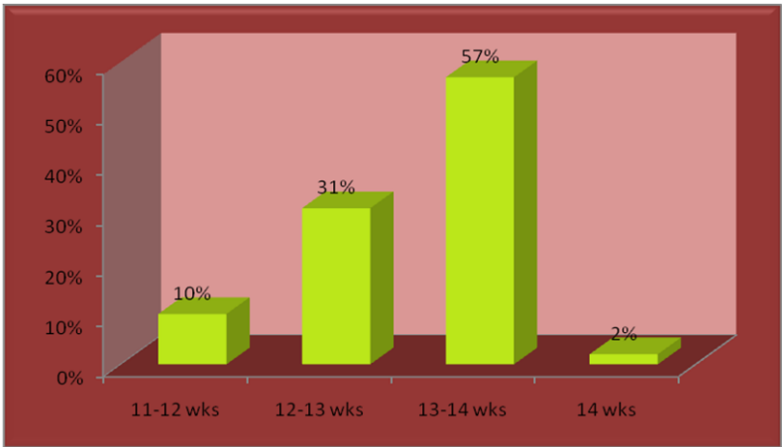


Figure 13: Distribution of cases with cardiac anomaly based on gestational age.

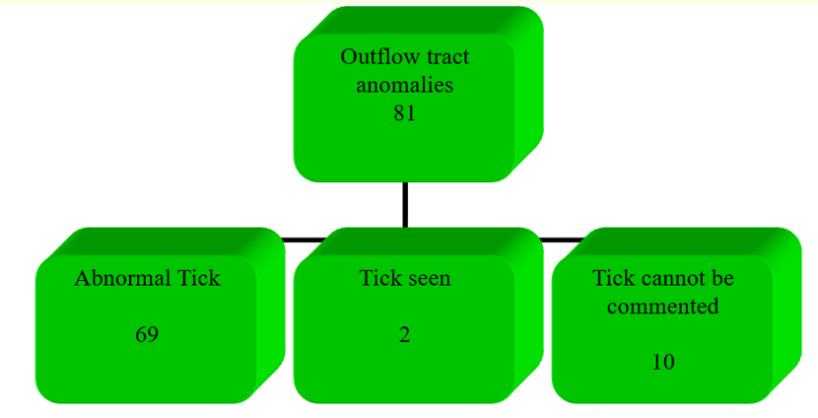


Figure B

We have included in the study period the time when the tick sign was not a part of our mandatory anatomy in first trimester hence it was difficult to comment on the tick sign in ten fetuses.

S. no	NT	Number of patients
1	Normal	47 (45%)
2	Increased	55 (52%)
3	Not possible	31 (3%)

Table 5: Nuchal translucency in all cardiac anomalies.

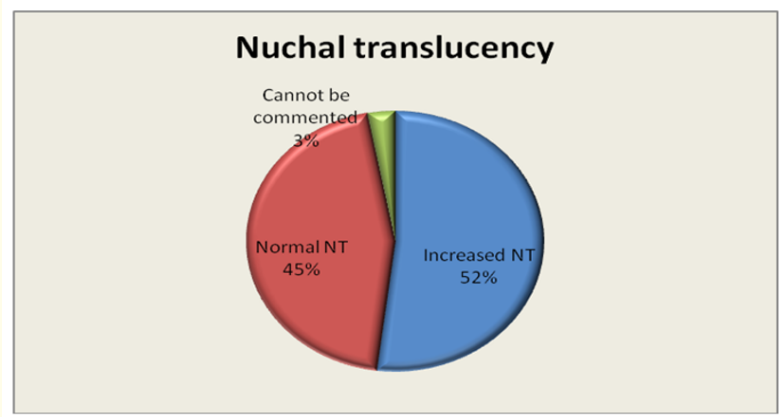


Figure 14: Split up of cardiac anomalies with respect to nuchal translucency.

Karyotyping was done in 16 cases and was normal in 10, abnormal in 5 and one case had culture failure.

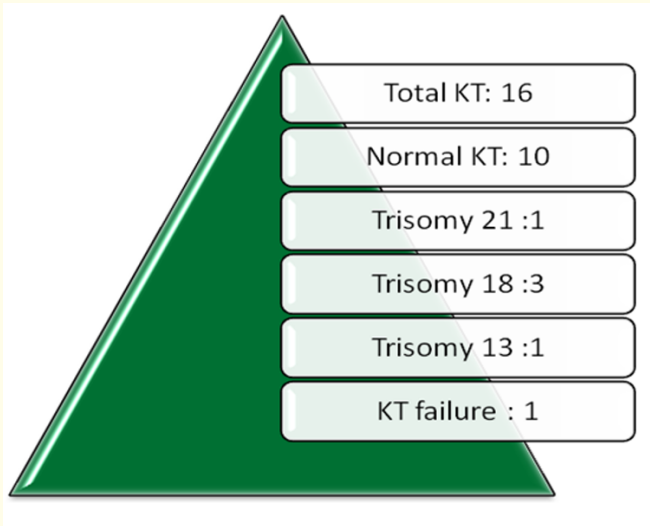


Figure 15: Results of karyotype in fetuses with abnormal heart.

We received 24 fetuses for autopsy in which there was concordance of sonographic and pathological findings in 20. In 1, the heart was completely autolysed and hence comment not possible and in three cases autopsy revealed additional findings. Among the anomalies diagnosed in the first trimester were atrio ventricular defects, VSD, Left hypo plastic heart (HLHS) and right hypo plastic heart, pulmonary stenosis, transposition of great arteries (TGA), C TGA and tetralogy of fallot (TOF). It was possible to confirm in diagnosis by either a repeat scan at 16 - 20 weeks in 13 cases or by autopsy in 24 cases.

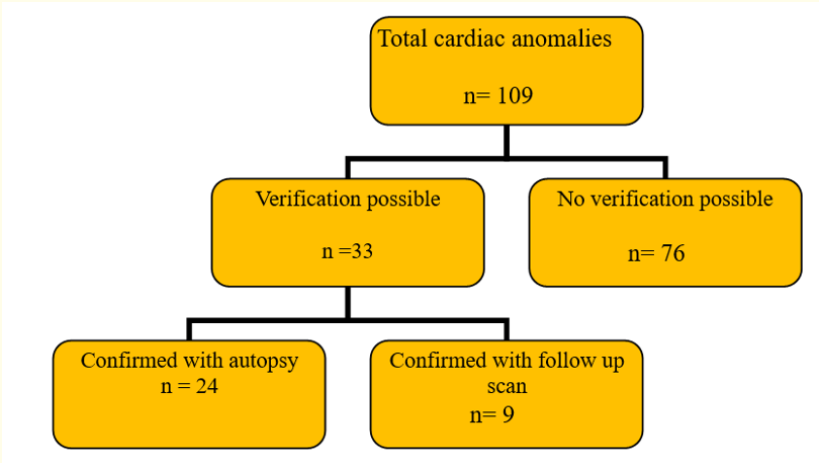


Figure 16: Split of cases where confirmation of diagnosis is available.

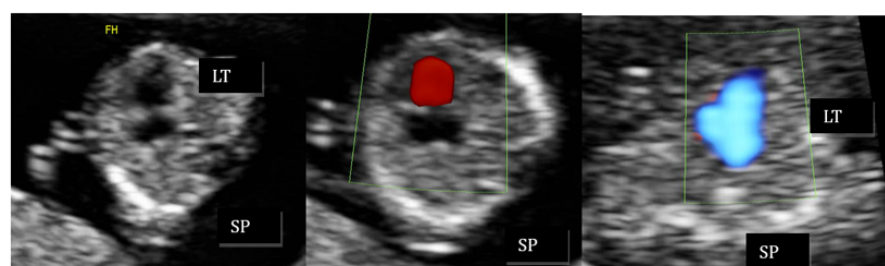
S.no	Scan diagnosis at 11-14 weeks	Karyotype	GA at confirmation	Confirmation Diagnosis	Autopsy findings	Additional comments
1	MR/TR	No KT	16 weeks	Normal study	No autopsy	Lost in follow up
2	VSD with OT anomaly	No KT	17 weeks	C TGA with PA	Same as scan	
3	RT aortic arch	No KT	15 weeks	RT aortic arch with left ducts	No autopsy	No postnatal follow up
4	Suggestive of cardiac anomaly	No KT	16 weeks	HRHS	No autopsy	Termination at 16wks
5	Suggestive of pulmonary stenosis	Normal KT	17 weeks	Pulmonary stenosis	No autopsy	Termination at 17 wks
6	HLHS	No KT	16 weeks	HLHS	No autopsy	Termination at 16 wks
7	TGA	No KT	16 weeks	TGA/DORV	No autopsy	Termination at 22 wks
8	Single outflow tract	No KT	15 weeks	AVSD with single OT	Same as scan	
9	Suggestive of cardiac anomaly	No KT	16 weeks	PA/TA	No autopsy	Termination at 17wks
10	Suggestive of cardiac anomaly	Normal KT	17 weeks	Truncus with subpulmonic VSD	Same as scan	
11	Suggestive of inflow anomaly	No KT	16 weeks	Asymmetry of chambers	No autopsy	
12	TGA with intact IVS	Normal KT	16,20 weeks	TGA with intact IVS	No autopsy	Lost to follow up
13	Suspected OT anomaly	No KT	20 weeks	TOF	No autopsy	

**Table 6:** VSD: Ventricular Septal Defect; AVSD: Atrioventricular Septal Defect; OT: Outflow Tract; KT: Karyotyping; MR: Mitral Regurgitation; TR: Tricuspid Regurgitation; PA: Pulmonary Atresia; TA: Tricuspid Atresia; TGA: Transposition of Great Arteries; C TGA: Corrected Transposition of Great Arteries; DORV: Double Outlet Right Ventricle; HLHS: Hypo Plastic Left Heart Syndrome; HRHS: Hypo Plastic Right Heart Syndrome.

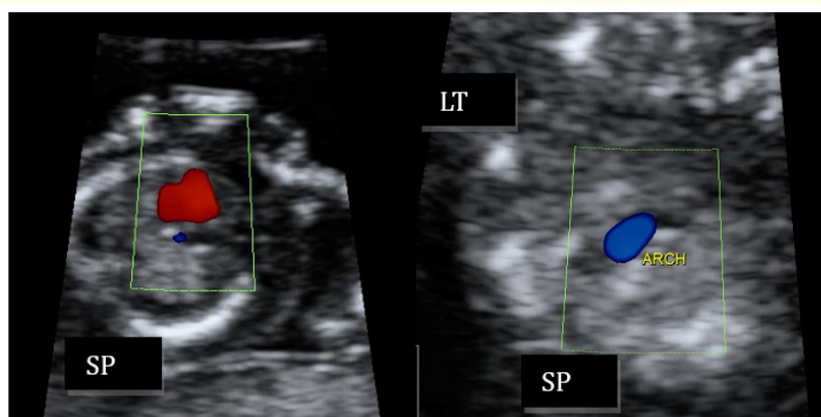
For analyzing the role of “tick sign” in diagnosing outflow tract we grouped the total cardiac anomalies in to before and after the introduction of the “tick sign”. We used chi square test to determine the significance of association between the two groups. We found that the use of the “tick sign” has improved the detection rate of outflow tract anomalies which was found to be statistical significant (p value of  $0.01 < 0.05$ ) and has improved the overall detection rate of proven cases of outflow tract anomalies).

## Discussion

In this study we have introduced the “tick sign” and evaluated its role in diagnosing outflow tract anomalies. In this study we described our experience with the use of color flow doppler imaging of the three vessel trachea view in the prenatal diagnosis of congenital heart disease especially, the outflow tract anomalies at the 11 - 14 weeks of gestation in a mixed low and high risk population. In the first tri-



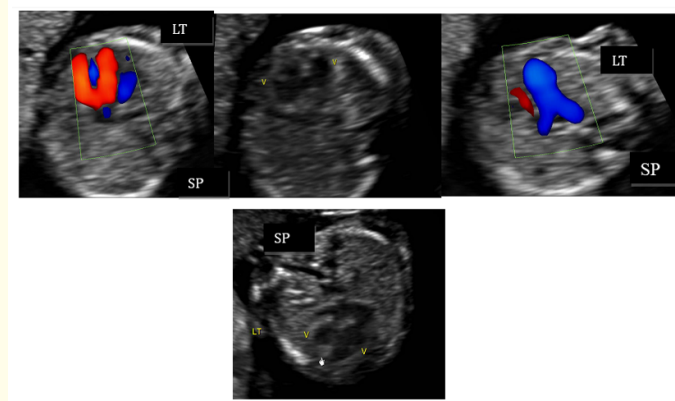
**Figure 17:** AVSD with normal outflow tracts.



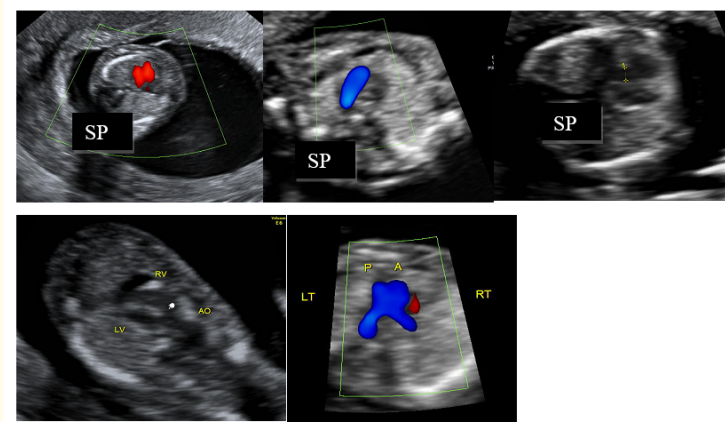
**Figure 18:** Right AV valve regurgitation present. Left ventricular outflow tract and arch seen. Right ventricular outflow tract and arch not seen.



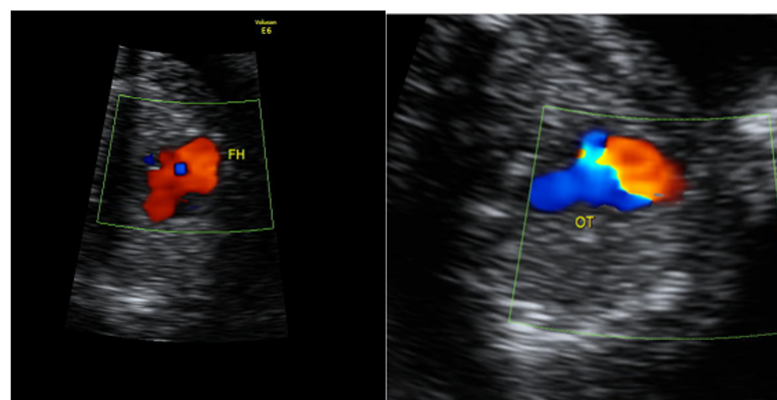
**Figure 19:** Suggestive of critical aortic stenosis. Globular left ventricle with poor contractility (evolving hypoplastic left heart syndrome (HLHS)).



**Figure 20:** Scan at 12 weeks ventricular septal defect with abnormal outflow tracts corrected TGA.



**Figure 21:** Ventricular septal defect. Overriding of aorta. Pulmonary artery stenosis.



**Figure 22:** Scan at 12 weeks showing two inflows with abnormal tick.



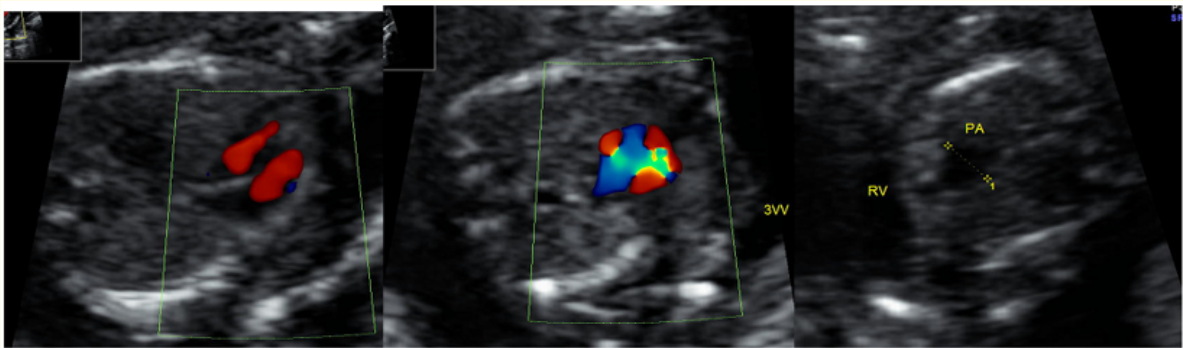


Figure 23: Scan at 16 weeks with normal four chamber with single outflow with swirling of flow.

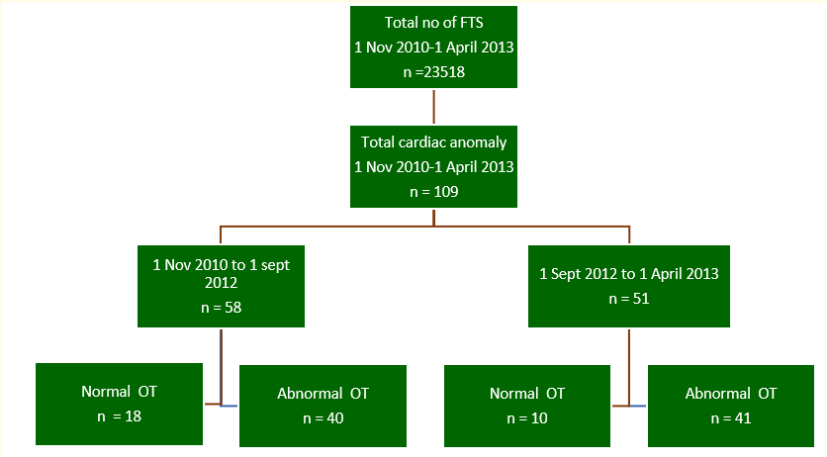


Figure C

mester low risk population, cardiac anomalies like, transposition of great arteries, tetralogy of Fallot, double outlet right ventricle may go undetected if four chamber alone is used [19]. The detection rate of heart malformation can be increased by 30% if we include the ventricular outflow tracts in addition to four chamber view as a part of mandatory cardiac imaging [20,21]. It has been established that most of the malformations of the outflow tracts can be picked up in the three vessel view in the second trimester [5]. In first trimester, B mode imaging of the three vessel view in all cases is challenging, however the use of color Doppler makes it possible to include the three vessel trachea view in the first trimester screening.

Comas Gabriel C, Galindo., *et al.* in 2002 has shown a sensitivity of 80% in detection of congenital malformations by fetal echocardiography in a high risk population. They have not included low risk population and has not routinely used the three vessels trachea view as compared to our study [23]. In another study the great vessels and trachea were recognized with the three vessels and trachea view in all except two of 1363 fetuses [12].



Our unit gets on an average 10500 patients referred for first trimester screening per year. It includes a mixed population. We started the cardiac screening using color four chamber in the first trimester many years ago in our institute. However we have introduced the tick sign in September 2013 and has made color four chamber and “tick sign” as a part of mandatory anatomy in first trimester scan. If we suspect a cardiac problem in the initial screening, than we proceed with detailed fetal echocardiography which is followed with detailed counseling of the couple.

In the first part of the study we analyzed the feasibility of imaging “tick sign” in our unit and found it to be reasonably possible with adequate training similar to that needed for NT certification. Except for one, the remaining patients with good “tick” images who had follow up exams were found to have normal fetal echocardiography at the target scan. All of these patients had normal outflow tracts. The only patient where the target scan showed an abnormal fetal echocardiography had AVSD, but this fetus also had normal outflow tracts. This indicates that the anomaly was missed in the four chamber and not the outflow tract.

The ability to visualize the cardiac anatomy at first trimester using transvaginal sonography is well recognized [2]. However there is still doubt regarding the appropriateness of this approach in routine screening. In high risk cases it is valuable in offering the possibility of exclusion of severe defects and also early diagnosis.

It was possible to obtain satisfactory four chamber views in 70% from 12 weeks onwards trans vaginally in a study conducted by P. Johnson, G, Sharland., *et al.* in 1992 [13]. In our study only 4% of 1996 patients underwent transvaginal examination to screen the fetal heart. This was seen in concordance with the study of I.C. Huggon., *et al.* [18] where transabdominal fetal echocardiography predominated in our study when compared to trans vaginal sonography. We opted for transvaginal imaging only when transabdominal views were sub-optimal due to maternal habitus or fetal position. The B mode imaging of the fetal heart trans vaginally at 11 - 14 weeks of gestation is definitely superior to transabdominal view, still we do not encourage for routine transvaginal imaging in low risk population as it is not feasible in all cases. If the same views are examined using color doppler the normalcy of the fetal heart at 11 - 14 weeks can be reasonably predicted.

Out of 109 cases of cardiac abnormalities, we had scan follow up for only 16 cases as most of the couples opted for termination.

Increased nuchal translucency at 11 - 13 weeks scan is one of the reason to look for cardiac anomalies. However, in our study only 52% of the fetus with cardiac anomaly had increased NT and the remaining 45% had normal NT. We found that the group with increased NT had marginally higher chance of associated cardiac defects when compared with normal NT group. This is not in concordance with the study of Mavrides E., *et al.* in 2010 where they found that though increased NT is associated with congenital heart disease but majority of cardiac anomalies occur in fetuses with normal NT [5,6].

Vinals F., *et al.* in 2006 has described the diagnosis of transposition of the great arteries by sequential segmental transverse views (The four chamber, five chamber, three vessels and the three vessel trachea view) in fetuses from 13 - 32 weeks of gestation. The authors found that clues to the diagnosis were the left outflow tract branching seen at the level of the five chamber view and two vessels seen at the level of the three vessel and trachea view. This study favored the effective use of the three vessel trachea view.

Yoichiro Ishii, Noboru Inamura., *et al.* have proposed the V sign from 16 weeks onwards where in the aortic and ductal arches are seen in a tangential section and form a V-shape, pointing to the posterior thorax on the left side of the spine. To our experience in the first trimester, both the arches do not share the same length. The aortic arch being smaller than the ductal hence resembling a “tick”. We proposed that the Inclusion of “tick sign” in our Unit has improved the detection rate of outflow tract anomaly.

## Limitations of the Study

There were only few follow ups as many couples opted for termination without autopsy prior to confirmatory scan. Our institute is a teaching institute, we have multiple operators in our Unit which keeps on changing periodically. This was the reason of not acquiring the “tick” in few cases. We made two false positive diagnosis where in one we suspected dilated aorta and in another anteriorly placed aorta which in follow up examination were not reproducible. It was difficult to document the “tick sign” even in the presence of normal arches in cases of axis deviation and the interpretation of the color flow is difficult in cases of non-immune hydrops as there is third space accumulation of the fluid and decreased flow in the ductus venosus. This in turn leads to impaired filling of the left sided chambers and outflow tracts. Our study was a pilot study where we have included 8 months of period after the introduction of “tick sign”. We are looking forward to a large prospective study on the usefulness of “tick sign” in outflow tract anomalies.

## Conclusion

Most of the cardiac malformations in high risk population can be detected in the first trimester scan, however a comprehensive fetal echocardiography by a skilled specialist is required. The same is not possible in the low risk group as it may be time consuming and demands special skill and knowledge. It is therefore essential that accurate, quick and easily performed scanning views should be integrated in to routine examination, thus improving the diagnostic potential in everyday low risk clinical practice without interfering in the time spent per case. We believe that the three vessel trachea view is efficient in early prenatal diagnosis of cardiac defects which involves the outflow tracts and aortic arch. It enables early visualization of major cardiac anomalies, early investigations, counseling and decision making. In fetuses with major cardiac defects the early scan can either lead to the correct diagnosis or can at least raise the suspicion so that the follow up scan are carried out. In the contrary, a majority of cardiac defects can be ruled out if the heart is normal in its ultrasound appearance even at an early scan. Our study has shown that it is feasible to image “tick sign” at 11 - 14 weeks scan and the inclusion of “tick sign” can improve the detection rate of outflow tract anomalies. We suggest that the four chamber view in Color and the “Tick Sign” should be considered as an effective screening tool in early prenatal sonographic evaluation, in both low and high risk population.

## Acknowledgments

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## Conflict of Interest

There is no conflict of interest.

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