Fetal cardiac screening; why bother?

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Introduction

Cardiac abnormalities are the commonest form of congenital malformation, with moderate and severe forms affecting about 0.6% of live births1. Although congenital heart disease remains an important cause of death in infancy, not all forms of major congenital heart disease will be evident at birth or in the early neonatal period 2,3. Reports indicate that approximately 25% of babies with severe forms of congenital heart disease are still discharged from hospital undiagnosed and in some cases the cardiac lesion is not recognized during life 2,4,. Early diagnosis of such babies would improve survival, as well as reducing the morbidity associated with circulatory collapse prior to recognition of a problem and administration of appropriate treatment. Recent studies have assessed pulse oximetry as a form of screening for serious forms of congenital heart disease in the neonatal period, with results suggesting that this, used in conjunction with clinical examination prior to discharge, improves the detection rate of duct dependent lesions 5,6. Although this has been advocated, it is not current practice in the UK and some lesions would still be overlooked using these methods. Antenatal screening could potentially detect many of the major life threatening forms of congenital heart disease, though this is dependent on adequate resources being available for appropriate teaching and training, as well as other issues, such as sufficient time being allocated for obstetric ultrasound scans and the use of adequate ultrasound equipment.

Antenatal diagnosis of congenital heart disease

Antenatal diagnosis of congenital heart disease has become well established over the last 25 years and a high degree of diagnostic accuracy is available and expected in tertiary centres dealing with diagnosis and management of fetal cardiac abnormalities. Virtually all major forms of congenital heart disease, as well as some of the minor forms can be detected in the fetus, in experienced centres 7,8. There are, however, some lesions that cannot be predicted from fetal life, even in experienced hands, and this should be acknowledged. These include a secundum type of atrial septal defect and a persistent arterial duc, as all fetuses should have a patent foramen ovale and an arterial duct. In addition, some types of ventricular septal defect may be difficult to detect, either because of their size or position. The milder forms of obstructive lesions of the aorta and pulmonary artery can develop later in life with no signs of obstruction during fetal life. One of the main reasons for making an antenatal diagnosis is to detect major forms of cardiac abnormality early. Diagnosis during pregnancy, of anomalies associated with significant morbidity and mortality, allows parents to consider all options, including interruption of pregnancy. Prenatal diagnosis also gives time to prepare families for the likely course of events after delivery and to optimise care for the baby at birth. Where appropriate, delivery can be planned at or near a centre with paediatric cardiology and paediatric cardiac surgical facilities. Whilst treatment for the vast majority of cases will take place after birth, prenatal treatment may be considered in a few select cases. Additionally, the value of confirming normality and providing reassurance to anxious parents, particularly if they have already had an affected child, should not be underestimated.

Does prenatal diagnosis make a difference to outcome?

Whether prenatal detection actually improves outcome in all cases is not easy to prove. One of the difficulties about making a comparison between outcome following prenatal diagnosis and cases diagnosed after birth, is that prenatal diagnosis allows assessment of outcome from diagnosis in fetal life, including spontaneous intrauterine death and early neonatal death prior to surgery. In contrast, babies with a postnatal diagnosis are those that have survived fetal life and often the early neonatal period to reach a tertiary centre for treatment. Thus the comparison has not always been like for like, as those babies presenting to a tertiary centre in

postnatal life have already demonstrated some survival advantage. In addition, the fetal spectrum of heart abnormalities has been weighted towards complex lesions and those associated with extra-cardiac and chromosomal anomalies. Thus, the overall outcome in unselected series has been poorer than expected than from postnatal series. There has, however, been a notable change in the proportion with other abnormalities, for example, in our unit at Evelina Children's Hospital, the number of cases of fetal congenital heart disease with confirmed associated chromosomal anomalies has fallen from 19% in 2000 to 11% in 2008. This is partly related to improvement in obstetric screening, so that more isolated cardiac abnormalities are detected, and is partly attributable to the introduction of the nuchal translucency measurement in the irst trimester for the detection of chromosomal abnormalities 9,10. This latter method has led to the detection of trisomies earlier in pregnancy and although a significant number of these may be associated with heart disease, many may no longer be referred for detailed evaluation of the fetal heart. It should also be noted that the detection of some cardiac lesions can lead to the diagnosis of a chromosomal abnormality. Some lesions, such as atrioventricular septal defect, have a high association with chromosomal anomalies whereas as others, such as transposition of the great arteries, are rarely associated. Any improvement in survival as a result of fetal diagnosis would be expected to be seen in isolated cardiac lesions that are duct dependent for either the systemic or pulmonary circulation. Some studies, indeed, have suggested an improved outcome for these types of lesions. A French study looking at transposition of the great arteries, compared outcome of babies between antenatally and postnatally diagnosed cases. This study reported significantly lower preoperative and postoperative mortality for antenatally diagnosed babies, although there was no evidence of difference in postoperative morbidity11. In another French study 12, detection rates and mortality for babies with transposition of the great arteries were compared between three time periods. Between 1983 and 1988, 12.5% were antenatally diagnosed and the mortality for transposition was 23.5%; between 1989 and 1994 48.1% were antenatally diagnosed and mortality was 12.0%; and between 1995 and 2000 72.5% were antenatally diagnosed and the mortality was 5%. Although there may be several reasons for the difference, this data suggests that antenatal diagnosis of transposition is associated with a lower mortality. There are further studies that have suggested improved outcomes for hypoplastic left heart syndrome and coarctation of the aorta 13,14. Others, however, have not demonstrated a benefit in terms of survival, but have shown, for example in cases of hypoplastic left heart syndrome, that the baby is in a better pre-operative state15. Thus prenatal diagnosis could have a beneficial effect in terms of morbidity in some cases. Overall, however, prenatal screening should not be advocated on a survival advantage alone. Antenatal detection does give parents choice, even though the choices may be difficult and not always welcome. Clearly great distress can be caused by an antenatal diagnosis and the decision making that follows. However, extra distress can be limited if the parents are given all the support and information that they need in order to make the right decision for them16. Following the diagnosis of major congenital heart disease the parents are given information regarding the abnormality including the management and likely outcome. Based on this they may, in some cases, elect to interrupt the pregnancy. In the early days of prenatal diagnosis, the termination rate was high, but in latter years the overall proportion electing to stop the pregnancy is in the region of 25%. However, this figure is higher for complex lesions and those that will result in single ventricle palliation. Although decision making regarding termination of pregnancy is a complex process, there are some consistent themes. Influencing factors include the perceived severity of the condition, the predicted quality of life for the child and the impact on the family. Additional factors are chosen lifestyles and financial situation as well as cultural and religious beliefs 16. Parents that choose to proceed with the pregnancy make an active choice to do so and in a sense have self selected to cope with what lies ahead. This is particularly significant in cases where single ventricle palliation is the treatment strategy. Although there have been concerns about the anxiety caused by prenatal diagnosis, in most cases parents, who are aware of a problem before birth and have been appropriately counselled, will be better informed and prepared at the time of initial surgical or interventional treatment after birth 17.

Should antenatal screening for congenital heart defects take place?

An effective antenatal screening programme could help to improve the prenatal detection and hence early diagnosis of life threatening congenital heart disease. Improved morbidity and mortality could then be facilitated by planning peri-natal care to optimise the management of a baby known to have a cardiac lesion. Such a model has already been started in some units in regions where antenatal detection is significant. Of referrals to the cardiac unit at Evelina Children's Hospital born in 2006, there were 220 babies with significant (defined as that requiring surgery or catheter intervention under a year of age) congenital heart disease. Of these liveborns, 51% had had a prenatal diagnosis. Wilson and Jungner 18 defined the criteria to assess the

validity of any screening programme. Although antenatal screening for congenital heart defects requires resources for on-going training and skill maintenance, it can potentially fit many of the criteria. The criteria are that:
1. Disorders to be screened for should be clinically well defined - congenital heart defects are well defined
2. The incidence of the conditions should be known - the incidence of congenital heart disease is known
3. Disorders to be screened for should be associated with significant morbidity or mortality -this applies to the major forms of congenital heart defects
4. Effective treatment should be available - in the instance of antenatal diagnosis, this would include interruption of pregnancy, peri-natal care managed in a specialist centre, or rarely intrauterine treatment
5. There should be a period before onset of the disorder during which intervention is possible to improve outcome or allow informed choice - this applies to antenatal diagnosis
6. There should be an ethical, safe, simple and robust screening test - ultrasound screening is thought to be safe, ethical and acceptable
7. Screening should be cost-effective - the cost effectiveness of antenatal screening will be influenced by the skill of the sonographer in detecting anomalies and the time taken to perform the scan 19.

This important factor is probably now the big issue. Ultrasound is now widely used for anomaly screening antenatally, with 97% of units in England offering second trimester anomaly scans to all pregnant women20. Appropriate and adequate information must be available to all pregnant women before undergoing any screening tests including obstetric ultrasound. If anomaly scans are performed to look for structural abnormalities, then the heart must be included in the examination. In recent years, both the Royal College of Obstetrics and Gynaecology (RCOG) and the National Institute of Clinical Excellence (NICE) have endorsed that antenatal anomaly screening should be adopted and have issued guidelines stating what should be included as part of the fetal anomaly scan 21,22. In terms of the fetal heart, both of these national guidelines recommend that outflow tract views of the fetal heart, as well as the four chamber view should be included. NICE has used the model of transposition of the great arteries to calculate that there is cost benefit of including views of the outflow tracts of the heart, as opposed to just the four chamber view. In reality, however, not all units have been able to implement this policy. Data from the National Screening Committee (NSC)20, who conducted a survey of all maternity units in the 9 regions of England shows that, in the calendar year beginning 1st January 2002, 97.5% of units reported that four chamber view was examined, but the outflow tracts were only visualised in 57%. This varied between the 9 regions from 25%-84%. Although over 97% of units report examination of the four chamber view, there are still many babies that have a cardiac lesion associated with an abnormal four-chamber view, that are not detected antenatally, even in regions with high detection rates. Data from the Evelina Children's Hospital shows that for babies referred to the children's heart unit in 2006, the proportion of antenatal diagnosis was 81% for hypoplastic left heart syndrome and 52% for atrioventricular septal defect. Detection rates for great artery abnormalities associated with a normal four chamber view remain lower, with 25% of transposition of the great arteries having an antenatal diagnosis.

Status of antenatal screening for congenital heart disease
There remains a two tier system for examining the fetal heart in pregnancy. High risk pregnancies (Table 1) are generally referred to tertiary centres for detailed fetal echocardiography, though the expected rate of cardiac abnormality is relatively low in these groups.

Table 1: High risk groups
1) *Maternal factors identified at booking*
(i) Family history of congenital heart disease.
a) Sibling
- one affected child recurrence risk 2-3%
- two affected children recurrence risk 10%
- three affected children recurrence risk 50%
b) Parent - either parent affected risk in the baby between 2-5%
(ii) Maternal diabetes - risk 2-3% - good diabetic control in early pregnancy may diminish this risk
(iii) Exposure to teratogens in early pregnancy such as lithium, phenytoin or steroids - risk 2%
2) *Fetal high risk factors*

(i) Extra-cardiac fetal anomaly present on ultrasound - many types of abnormality, for example exomphalos or diaphragmatic hernia, may be associated with congenital heart disease - abnormalities in more than one system in the fetus should arouse the suspicion of a chromosome defect
(ii) Fetal arrhythmias can be associated with structural heart disease
(iii) Non-immune fetal hydrops - may be caused by structural heart disease or fetal arrhythmia
(iv) Increased nuchal translucency in the first trimester - 6-7% risk even when the fetal karyotype normal

The majority of cases of congenital heart disease will occur in low risk groups and these will only be detected antenatally if examination of the fetal heart is incorporated as part of routine obstetric ultrasound screening. Approximately 200 cardiac abnormalities are detected annually at the Evelina Children's Hospital, of whom between 130 and 150 have been identified in low risk groups by sonographers performing routine anomaly scans. The concept of antenatal screening for congenital heart defects in low risk groups by teaching obstetric sonographers to incorporate the four chamber view of the fetal heart at the time of the routine obstetric anomaly scan, was introduced in the UK in 198623. Subsequently, from 1988-1991, an intensified four chamber view training programme was conducted in what was then called the South East Thames Region24. Following a period of intensive teaching and training, there was significant improvement in the antenatal detection rates for congenital heart disease in the obstetric ultrasound units participating in the study. Detection rates for four chamber abnormalities as a result of screening increased from 3% to 67%, in the these units. What has been learnt from this study and subsequent studies is that obstetric sonographers can learn to obtain and correctly interpret certain views of the heart, such as the four chamber view, but this requires ongoing commitment and effort from those performing the scans and from those teaching them 24-26. Thus, whilst screening the fetal heart can be effective, there is a huge variation in detection rates, with overall detection rates remaining relatively low. In the mid 1990's, Bull27 reported that the detection rate of significant CHD (defined as that requiring surgery or catheter intervention under a year of age) varied widely around the country. In the 15 postal districts with detection rates significantly above average, the prenatal detection rate was 54%. Informal data collected on behalf of the British Congenital Cardiac Association in 2007, suggests that prenatal detection of cardiac abnomalities is still weighted towards London and the South East. The proportion of babies with significant congenital heart disease diagnosed antenatally is 50-55% in London paediatric cardiology centres and is 20-30% in the centres outside London. Studies from other countries also suggest huge variations in detection rates28,29. Data collected by NICE when reviewing studies looking at the fetal heart in low risk populations, indicate that the overall sensitivity of detecting cardiac anomalies ranged from 4.5% to 86.1% with a specificity of 99.9% 22. Four chamber view examination is an effective method of detecting some of the severe forms of cardiac malformation before birth. However, some major lesions, such as transposition of the great vessels and Tetralogy of Fallot, are often associated with a normal four chamber view. Thus, including examination of the arterial outflow tracts would greatly improve the prenatal detection rates of major life threatening forms of congenital heart disease30,31. Although some obstetric ultrasound centres have managed to successfully incorporate views of the arterial connections as well as the four chamber view, many have not managed this step as yet.

What is being detected prenatally?
The diagnoses in large fetal cardiac series are skewed towards the severe end of the spectrum of cardiac abnormality, with the majority of abnormalities being associated with an abnormal four chamber view7. This bias is a reflection of four chamber view screening which has been used in routine obstetric anomaly scanning for over 20 years. As a result there has been a predisposition towards lesions that will result in single ventricle palliation rather than a corrective procedure. However, over the last 10 years there has been some improvement in the proportion of great artery abnormalities being detected by screening. Of the fetal cardiac abnormalities referred to Evelina Children's Hospital from sonographers screening low risk groups, approximately 18% had great artery abnormalities in 1998 and 29% in 2008. It has been argued that the antenatal detection of lesions that may be overlooked by pulse oximetry and clinical examination, such as coarctation of the aorta and other left heart obstructive lesions, is poor32. Perhaps not all of these would be easily identified by antenatal screening but many may have signs on the antenatal scan that an experienced sonographer can be taught to notice. In 2008, there were 16 fetuses with a coarctation of the aorta diagnosed in the fetal cardiology unit at Evelina Children's Hospital. Of these, 11 cases were referred because of a suspected cardiac problem at the time of the routine obstetric anomaly scan, demonstrating that such lesions can be picked up by screening.

Factors influencing antenatal screening for heart defects

Antenatal screening for major forms of heart abnormality is possible though there are many issues relating to its success. There is a general tendency to conclude that antenatal screening is poor at detecting heart abnormalities, though the reasons for this warrant further address. Detection of cardiac abnormalities is dependent on the skill of sonographers performing routine obstetric ultrasound scans. A formal programme for education and training regarding the fetal heart is necessary to ensure that sonographers are taught the skills of fetal heart examination and that they can maintain those skills. The survey conducted by the NSC20 showed that although 94% of units provided access for continuous education, only 66% could release the staff to attend courses because of staff shortages. There also did not seem to be a single source of funding for education and training. In order to detect anomalies, units need to have appropriate ultrasound equipment. The NSC survey suggests that only 65% of units in England reported they have sufficient needs for their workload and 61% provided adequate image quality. The revised antenatal guidelines from NICE22 have recommended that fetal anomaly scans should be performed with equipment of adequate standard, as approved by the NSC. If this is implemented, there should be some improvement in antenatal detection rates. The time allowed for the obstetric anomaly scan will also influence how long can be spent examining the fetal heart and thus, the detection rates of abnormalities. Results of the NSC survey showed that the majority of units (58%) allow 15-20 minutes, with a further 33% allowing 20-30 minutes. However, there were 9% of units that only allow 10-15 minutes, which would make examination of the heart less feasible. The time required to examine the fetal heart should decrease as sonographers gain more experience and confidence19. But it should also be remembered that obstetric ultrasound is only one modality offered by ultrasound units, with an increase in workload in one area having potential impact on other parts of the service. Thus, some units may not have set a high priority for antenatal screening of the fetal heart. A very important aspect of antenatal screening is audit of activity and monitoring and feedback of both false positive and false negative cases, as well as the true positives. This currently seems to be a weak link. The NSC report suggests that 80% of units screening for fetal anomalies were not able to provide detection rates for various abnormalities, although 60% reported they audited detection rates. Audit of activity is vital in a screening programme, both to monitor the efficacy of screening but also to encourage and motivate the staff performing the scans. NICE has strongly recommended that all units should participate in regional congenital anomaly registers and/or UK NSC approved audit systems to facilitate the audit of detection rates.

Other forms of antenatal screening for heart defects

Another method for increasing the yield of fetal detection of congenital heart abnormalities that has been proposed is first trimester nuchal translucency screening. Initial studies showed that detailed fetal echocardiography confirmed major structural heart disease in 6-7 % of fetuses, when the first trimester nuchal translucency was above the 99% confidence limits and in whom the karyotype results were normal9. Of all the fetal cardiac abnormalities seen at the Evelina Children's hospital in 2008, 7.5% were referred because of a raised nuchal translucency measurement with 15% overall having a raised measurement. However, the proportion of units offering nuchal translucency screening is low, with 16% of units in England offering this to all women and 27% offering it to some20. This form of screening is region dependent and most common in London and the South

East. The updated NICE guidelines22 do not currently recommend routine screening for cardiac defects using nuchal translucency screening.

Summary

Ultrasound screening for fetal anomalies, including abnormalities of the fetal heart is recommended by both NICE and RCOG. Antenatal detection allows parental choice regarding interruption of pregnancy, time for parental preparation and planning of delivery to optimise care and outcome for the baby. However, there is a dramatic variation between regions in the uptake of antenatal cardiac screening. The national challenge now faced regarding examination of the fetal heart, is how to successfully implement incorporation of the outflow tract views in addition to maximising the efficacy of four chamber view screening. The future must also be a prospective national fetal cardiac database or registry auditing what is detected and what is missed. All of us involved in fetal cardiac diagnosis have a duty to take this challenge forward.

References

1. Hoffman JI, Kaplan S. The incidence of congenital heart disease. *J Am Coll Cardiol* 2002;**39**:1890-900.

2. Abu-Harb M, Hey E, Wren C. Death in infancy from unrecognized congenital heart disease. *Arch Dis Child* 1994; **71**: 3–7.

3. Richmond S, Wren C. Early diagnosis of congenital heart disease. *Semin Neonatol* 2001; **6**: 27–35.

4. Wren C, Reinhardt Z, Khawaja K. Twenty-year trends in diagnosis of life threatening neonatal cardiovascular malformations *Arch Dis Child - Fetal and Neonatal Edition* 2008;**93**:F33-F35

5. Griebsch I, Knowles RL, Brown J *et al,.*Comparing the clinical and economic effects of clinical examination, pulse oximetry, and echocardiography in newborn screening for congenital heart defects: a probabilistic cost-effectiveness model and value of information analysis. *Int J Technol Assess Health Care.*2007 ;**23**:192-204.

6. Granelli A deW, Wennergren M, Sandberg K et al *et al,.* Impact of pulse oximetry screening on the detection on duct dependent congenital heart disease: a Swedish prospective screening study in 39,821 newborns. *BMJ* 2009;**338**:145-149

7 Allan, L.D., Sharland, G.K., Milburn, *et al,.* Prospective diagnosis of 1,006 consecutive cases of congenital heart disease in the fetus. *J Am Coll Cardiol,* 1994; ***23*****,** 1452-1458.

8. Allan, L., Hornberger, L., Sharland, G. *Textbook of Fetal Cardiology.* Greenwich Medical Media Limited, London 2000.

9. Hyett, J, Perdu, M, Sharland, G, *et al,.* Using fetal nuchal translucency to screen for major congenital cardiac defects at 10-14 weeks of gestation: population based cohort study. *Br Med J* 1999;**318**:81-85.

10. Pandya PP, Snijders RJM, Johnson S., *et al,* Screening for fetal trisomies by maternal age and fetal nuchal translucency thickness at 10-14 weeks of gestation. *Br J Obstet Gynaecol* 1995;**102**:957-962.

11. Bonnet ., Coltri A, Butera G *et al,.* Fetal detection of transposition of the great arteries reduces morbidity and mortality in newborn infants. *Circulation*, 1999;**99**:916-8

12. Khoshnood B, De VC, Vodovar V, *et al,.*Trends in prenatal diagnosis, pregnancy termination, and perinatal mortality of newborns with congenital heart disease in France, 1983–2000: A population-based evaluation. *Pediatrics* 2005;**115**:95–101.

13. Tworetzky W, McElhinney DB, Reddy MV, *et al,.* Improved surgical outcome after fetal diagnosis of hypoplastic left heart syndrome. *Circulation* 2001; **103**: 1269–73

14. Franklin O, Burch M, Manning N, *et al*. Prenatal diagnosis of coarctation of the aorta improves survival and reduces morbidity. *Heart* 2002; **87**: 67–9

15. Chew C, Stone S, Donath SM, *et al,.* Impact of antenatal screening on the presentation of infants with congenital heart disease to a cardiology unit. *J Paediatr Child Health* 2006;**42**:704-8.

16. Fisher J. Termination of pregnancy for fetal abnormality: the perspective of a parent support organisation. *Reproductive Health Matters* 2008;**16**(31Supplement):57–65

17. Williams IA, Shaw R, Kleinman CS, *et al,.* Parental understanding of neonatal congenital heart disease. *Pediatr Cardiol.* 2008;**29**:1059-65. .

18. Wilson JM, Jungner G. Principles and practice of screening for disease. WHO Chronicle 1968;**22**:473.

19. L Bricker, J Garcia,J Henderson, *et al,.* Health Technology Assessment NHS R&D HTA Programme: Ultrasound screening in pregnancy: a systematic review of the clinical effectiveness,cost-effectiveness and women's views *Health Technology Assessment* 2000; **Vol 4**: No. 16.

20. UK National Screening Committee. Antenatal Ultrasound Screening Ultrasound Survey of England: 2002. April 2005

21. Ultrasound Screening – Supplement to Ultrasound Screening for Fetal Abnormalities RCOG, July 2000

22. National Institute for Clinical Excellence Antenatal care – routine care for the healthy pregnant woman Clinical Guideline March 2008

23. Allan LD, Crawford DC, Chita SK *et al,.* Prenatal screening for congenital heart disease. *Br Med J,* 1986*;**292***:1717-1719.

24. Sharland GK, Allan LD. Screening for congenital heart disease prenatally. Results of a 2 1/2 year study in the South East Thames Region. *Br J Obstet Gynaecol,* 1992*;***9**: 220-225.

25 Tegnander E., Eik-Nes S. The examiner's ultrasound experience has significant impact on the detection rate of congenital heart defects at the second-trimester fetal examination. *Ultrasound Obstet Gynecol* 2006;**28**:8-14

26 Pezard P, Bonnemains L, Boussion F *et al,.* Influence of Utrasonographers training on prental diagnosis of congenital heart disease: a 12 year population –based study. *Prenat Diagn* 2008;**28**:1016-1022.0

27. Bull,C on behalf of British Paediatric Cardiac Association. Current and potential impact of fetal diagnosis on prevalence and spectrum of serious congenital heart disease at term in the UK. *Lancet* 1999;**354**:1242-1247.
28. Khoo NS, Van Essen P, Richardson M, *et al,.*Effectiveness of prenatal diagnosis of congenital heart defects in South Australia: a population analysis 1999-2003. *Aust NZ J ObstetGynaecol* 2008;**48**:559-563
29. Acherman RJ, Evans WN, Luna CF, *et al,.* Prenatal detection of congenital heart disease in southern Nevada: the need for universal fetal cardiac evaluation. *J Ultrasound Med.* 2007;**26**:1715-1719
30. Wigton, TR, Sabbagha, RE, Tamura, RK *et al,.* Sonographic diagnosis of congenital heart disease: comparison between the four-chamber view and multiple cardiac views. *Obstet Gynecol,* 1993;**82***:* 219-224.
31. Kirk JS, Riggs TW, Comstock CH, *et al,.* Prenatal screening for cardiac anomalies: the value of routine addition of the aortic root to the four chamber view. *Obstet Gynecol*, 1994;**84**:427-431.
32 Gandhi A, Patni S. Improving diagnosis of neonatal cardiovascular malformations: a genuine prospect or wishful thinking? *Arch Dis Child*. 2008;**93**:545-6.