First Trimester Ultrasound Screening for Congenital Abnormalities

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Abstract

Background: Congenital abnormalities are one of the important contributors to perinatal morbidity and mortality worldwide. The prenatal screening for these conditions is one of the major aims of a good antenatal unit. Over the years there has been a gradual change in the approach used, especially with the introduction of first trimester ultrasound as a reliable screening method.

Objective: To give a comprehensive review of the basis for first trimester ultrasound screening for congenital abnormalities, it's utilization in the prenatal screening for chromosomal, structural and genetic abnormalities as well as its limitations.

Source: An electronic database search and review of relevant literatures with the use of the following keywords: first trimester screening, ultrasound scan, nuchal translucency and prenatal screening. Manual search was also conducted for recent issues of key journals and current texts.

Conclusion: The first trimester scan has been proven to be an equally effective method of prenatal screening for congenital abnormalities compared to older methods of screening. It is recommended for implementation in antenatal units especially in developing countries. There is however, the need for proper training and regular auditing of results to achieve the best result.

Key words: First trimesters scan, Nuchal Translucency (NT), Prenatal screening, Congenital abnormalities.

Introduction

Ultrasound scan is the main tool in the prenatal detection of congenital abnormalities. It allows the examination of internal and external anatomy of the fetus and the detection of not only major defects but also subtle markers for chromosomal abnormalities[1]. In addition the ultrasound scan has found a vital use in the study of the blood flow patterns in both the uteroplacental and fetoplacental circulations, which are referred to as the doppler. Modern antenatal care worldwide offers ultrasound scan as part of screening service for both maternal and fetal disorders. Traditionally however, the terminology “prenatal screening” refers to screening for fetal abnormality[2].

There are numerous reports on the value of ultrasound prenatal screening at 18-23 weeks commonly referred to as anomaly scan. This is the routine in most antenatal care units, partly because available scans can only produce satisfactory images at about that gestational age using the transabodominal probes. With improved technology, in particular the development of the transvaginal ultrasound probes, it has become possible to examine the fetal anatomy in details in the first trimester[3]. The potential advantages of such early screening are numerous and include the early detection of non-viable fetus, major fetal abnormalities, plural pregnancies and their chorionicity [3, 4, 5.] Ultrasound at this stage can be used either for primary diagnosis or secondary diagnosis (as a guide to invasive procedures). Studies have shown that pregnant woman prefer first trimester rather than second trimester

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screening[6]. There has also been a rising interest in the use of the ultrasound to screen for congenital malformation by researchers in recent times. Literatures on such researches are however scanty and are not usually available to many practitioners.

The paper will review the available literatures on first trimester ultrasound screening, the scientific basis and scope of diagnosis as its limitations. It shall also review its advantages and disadvantages as well as application in special circumstances.

Basis for First Trimester Screening

A lot of literature is available that report on common methods of screening for congenital malformations in pregnancy. Most of the methods are done in the second trimester of pregnancy.

Screenings for structural anomalies are usually achieved with the scan performed at about the 18-23 weeks of pregnancy or through the determination of certain biochemical markers such as alpha-fetoprotein. In the best of centers, about 1% of report structural abnormalities are detected by antenatal sonography[7]. In most developing countries most pregnant women book late and may be able to have scan done only toward delivery date[8].

Screening for chromosomal anomalies is usually done through combination of maternal serum biochemistry and maternal age [9, 10]. The earliest gestation at which the screening can be performed is 15th week. Screen positive women are then subjected to invasive procedures, for the final diagnosis. This whole process may be taken up to 2-3weeks and by which period the decision to abort an affected fetus is associated with more hazards[11].

The first trimester screening for congenital abnormalities by ultrasonography scan affords an opportunity for early diagnosis or confirmation, with bonus affects which include the fact that the natural history of certain conditions can be assessed, interventional fetal therapy can be employed where feasible and post natal treatments planned for in advance[7]. In a few women, early prenatal screening allows them to adjust to the birth of an affected child that they would not abort.

First trimester screening implies ultra sonography conducted between 11 and 13^{+6} weeks of pregnancy. Eleventh week is recommended as the earliest gestation for conducting prenatal ultrasound screening for two reasons. Firstly the follow up diagnostic test, chorionic villus sampling (CVS) is not advised to be done at an earlier gestation because of the higher risk of oromandibulofacial deformities (OFMD), transverse limb deformities and abortion [9, 11]. Secondly, some fetal structures could not be differentiated before this gestation. For example, the four-chamber heart view is only demonstrable after 10 weeks, while the fetal bladder can be visualized in 80% of cases at 11 weeks and 100% by 12 weeks.

Selecting an upper limited of 13^{+6} weeks also has well deserved reasons. First, it is thought that one of the options utilized in an affected situation is pregnancy termination. Studies have shown that most women would terminate an affected pregnancy following prenatal diagnosis[12]. An early or first trimester termination is less hazardous. Secondly, the optimum time for measuring the nuchal translucency is 10-13 weeks, being 98-100% and falls to 90% after 14 weeks[9]. In conditions where, the ultrasound serves as a secondary diagnostic tool such as ultrasound guided chorionic villus sampling, the success of the aspiration in terms of ease of tissue yield and abortion rate seems better when the procedure is performed at about 11-14weeks[11].

Chromosomal Abnormalities

Down's syndrome (DS) is the commonest form of chromosomal observed in clinical practice. The prenatal screening for DS in the second trimester using maternal serum biochemical markers has been established part of obstetric practice in may countries over the past decade[13].

Multicentre studies have reported that ultrasound scan can identify and measure the fluid collection in the subcutaneous tissue overlying the cervical spine of the fetus [9, 14, 15]. This fluid collection is represented by a hypo echoic

zone, referred to as the nuchal translucency (NT). The introduction of the NT measurement, has now replaced the second trimester maternal serum biochemistry (MSB) in many centers in developed countries.

For the NT measurement to be acceptable, the following minimum expectations must be met (i) the CRL should be between 45mm and 84mm. which correspond to a gestation between 11 and 14 weeks calculated from the last menstrual period, (ii) the maximum thickness should be obtained in the mid sagittal section of the fetuses, using the on-to-on rule [6,7,15,16]. Several reports on the NT measurement in the early 1990s demonstrated an association between increased NT and a wide range of chromosomal abnormalities (Table i) [17,18,19,20]. The mean prevalence of chromosomal abnormalities in fetuses with increased NT was 28.7% and the range was from 11% to 88%[6]. This variation presumably reflects the difference in the maternal age distribution and the definition of the minimum abnormalities NT, which ranged from 2mm to 10mm [3,6].

Subsequent studies in the mid 90s sought to clarify the association between maternal age, NT measurement and risk of chromosomal abnormalities. The conclusions were that (i) the risk of chromosomal abnormalities increase with both maternal age and fetal NT thickness and (ii) in pregnancies with low fetal NT, the maternal age related risk is reduced [6, 17, 21]. Other prospective Multicentre studies also established that (i) in normal pregnancies, fetal NT thickness increases with gestation and (ii) that in trisomies

Table 1: Early Reports on the Association Between Increased NT Thickness and Chromosomal Abnormalities

			Abnormal Karyotype (n)				
Study/Year	NT thickness (mm)	Total	Trisomy 21	Trisomy 18	Trimsomy 13	45X	Others
Johnson et al/1993	≥2.0	68 41 (60.3%)	16	9	2	9	5
Hewitt/1993	≥2.0	29 12 (41.4%)	5	3	1	2	1
Shulman et al/1992	≥2.5	32 15 (46.9%)	4	4	3	4	-
Nicolaides et al/1992	≥3.0	88 33 (37.5%)	21	8	2	-	2
Ville et al/1992	≥3.0	29 8 (27.6%)	4	3	1	-	-
Wilson et al/1992	≥3.0	14 3 (21.4%)	-	-	-	1	2
Trauffer et al/1994	≥3.0	43 21 (48.8%)	9	4	1	4	3
Brambati et al/1995	≥3.0	70 8 (11.45%)	?	?	?	?	?
Comas et al/1995	≥3.0	51 9(17.6%)	4	4	-	-	1
Pandya et al/1995	≥3.0	1,015 194 (17.6%)	101	51	13	14	15
Szabo et al/1995	≥3.0	96 4 (44.8%)	28	10	-	2	3
Shute-Valentin and Schindler/1992	≥4.0	8 7 (87.5%)	7	-	-	-	-
Van Zalen-sprock et al/1992	≥4.0	18 6 (33.3%)	3	1	-	1	1
Nadel et al/1993	≥4.0	63 43 (68.3%)	15	15	1	10	2
Savoidelli et al/1993	≥4.0	24 19 (79.2%)	15	2	1	1	-
Cullen et al /1990	≥6.0	29 15 (51.7%)	6	2	-	4	3
Suchet et al/1992	≥10.0	13 8 (61.5%)	-	-	-	7	1
Total		1,690, 485(28.7%)	238	116	25	59	39

Adapted from “Nuchal translucency and other first-trimester sonographic markers of chromosomal abnormalities” Kypros H. Nicolaides

21 and other major chromosomal abnormalities, fetal NT is increased [6, 16]. Although these studies were conducted on high-risk population with an already increased risk, the applicability of the conclusion in an unselected or low risk population was confirmed in another series of studies[22].

Generally, there is the consensus that risk for trisomies and other chromosomal abnormalities, can be derived by the multiplication of the a priori maternal age. (Prior risk) and the gestation related likelihood ratio (NT deviation from median for the CRL) [9, 16]. The screening positive group is based on a risk cut off of 1 in 300 pregnancies[6]. Any risk above this cut off is screen positive and above is screen negative.

Another important observation from the numerous studies was the issues of operator variability. This observation justifies the need for appropriate training of sonographers, adherence to standard technique and regular auditing of sonographers and images, if NT scan is to be offered routinely as the main screening test for chromosomal abnormalities [3,6.]

Structural Abnormalities

For more than two decades, ultrasound has proven to be the best technique available for prenatal detection of fetal anatomical defects[10]. The incidence of reported structural or anatomical abnormality detected in a high-risk center by antenatal sonography is 1%[23]. In the non-selected population, there may be a decrease in this figure.

Many centers in the world conduct prenatal ultrasound screening for structural anomalies after the 16th week of the gestation, when it is believed that the fetus is large and an anomaly image is readily obtained [7,24,25,26]. There are however, conflicting reports on the impact of such policy, even though it continues to remain the practice.

In the last few years, many centers are beginning to introduce the early ultrasound examination. They may be linked to the facts that an early recognition of an abnormality allows for an optimum decision on the management of the fetus. The practice may however be associated with a higher incidence of reported abnormalities. A study quoted an incidence of 2-6%. This study also agrees with order studies on the superiority of a transvaginal ultrasound over transabdominal ultrasound[26, 27]. The detection rates of congenital abnormalities is however improved when both the transabdominal and transvaginal ultrasound scan are combined[28].

Another important factor for a better outcome of the first trimester scans is optimum gestational age at which most of the fetal structures can be visualized. Studies have demonstrated that the optimum time is between the 11 and 13+6 weeks of pregnancy [3, 9]. 66%-86% of congenital anatomical defects were not recognized by ultrasound conducted mainly by practitioners. This is a justification for appropriate training of sonographers as recommended by some authors based on series of studies at Kings College hospital, London. Another study from same center demonstrates that the detection rate of congenital abnormalities can be improved to 100% following education and appropriate training of sonographers.

There are differences in the incidence of congenital abnormalities in the various studies. In a review from Olabisi Olabisi University Teaching Hospital (OOUTH) and Lagos University Teaching Hospital (LUTH) both in Nigeria, the commonest abnormalities are those of the gastro intestinal system followed by the central nervous system [29,30]. In another study from America, central nervous system abnormalities constitute 50% of all cases recorded[31].

Generally, abnormalities involving most systems can be suspected and defined accurately at the early scan. There is however reports that suggest that difficulty may be encountered in the prenatal detection of abnormalities in some other system. The system that is commonly examined with much caution is the heart and great vessels. The ultrasound scans of the four chambers have resulted in a better pick up rate of congenital heart defects. While it is correct that the four chambers view, value and outflow tracts can always be demonstrated by the 11-13+6 weeks gestation, the accuracy of second

trimester scan is considerably better as anomalies of the great arteries in particular are often not seen in the first trimester [31,32]. Although, the study suggested that first trimester cardiac scanning should be confined to pregnancies at increased risk and should always be followed by as second trimester scan, other studies however suggest that routine cardiac scan in the first trimester and those with any abnormal features sent to fetal echocardiography unit and while follow up second trimester scan is done for those with normal findings [31, 32, 33].

Some authors have discussed the reliability of first trimester screening for skeletal abnormalities as well as the interpretation of some transient abnormalities of the renal system such as megacystitis and central nervous disorders such as choroids plexus cyst [34]. It is imperative for sonographers to appreciate these facts in other to reduce the relatively high false negative rate in reports.

There are considerable evidences of an association between the nuchal translucency and structural abnormalities. Studies have demonstrated that increased NT measurement may be a marker for a wide range of underlying pathologies[16]. Structural defects that may be identified in the first trimester include omphalocele, anencephaly, while some others such as cardiac and urinary anomalies can only be identified in the second trimester [16, 17]. It is therefore a justifiable policy to look out in details for any structural abnormality in any fetus with an increase nuchal translucency measurement.

Genetic Disorders

Genetics disorders could occur either as single gene defects such as sickle cell disease or genetic syndromes such as Di george syndromes. The early trimester scan can pick up structural markers for some genetic syndrome such as diaphragmatic hernia, and echogenic kidneys. In the prenatal diagnosis for single gene defects it is used as an adjunct to ultrasound guided procedures such as chorionc villus sampling.

Ethical Issues in Early Trimester Screening

There are few ethnical and practical issues with respect to first trimester USS screening for CM, and are worthy of consideration.

1. *Training and Standardization*

As with all aspects of good clinical practices, operators who perform first trimester scan should be training appropriately and their results should be subjected to external quality assurance[6]. It has been established that satisfactory results are achievable after 80 transabdominal scans and 100 transvaginal scans[6, 9.] Several factors have influence on the quality of results. These include gestational age, fetal position, and scan resolution and route of scan (TA or TV).

2. *Routine versus Indicated Ultrasound Scan*

There remains considerable debate about the place of routine ultrasound scanning in pregnancy. Studies from developing countries show that most pregnant women look after the first trimester [8, 37, 38]. This group could therefore not benefit from the 11-14 weeks scan. Although there is a widespread availability of scan in most in developing countries, the positive finding rate is still low and ultrasound examination was recommended only when there a clear obstetrics reasons is clinically established [39]. It is however observed from the study that congenital malformation was not an important consideration to many physicians in recommending women for scan. Studies have established that most malformations are detected in the postnatal period [29, 30]. This will be a justification for routine early ultrasound screening in pregnancy. In obstetric units in many developed countries, ultrasound screening is the norm as recommended by the Royal College of Obstetrician and Gynecologists and more recently, there is the acceptance of early trimester scan as an invaluable procedure in obstetric practice [40].

Several factors are against the implementation of routine early trimester screening in developing countries. Poor awareness of the value among both physicians and women is a major factor [41.] This coupled with poverty and low literacy level contributed to the poor utilization of a prenatal diagnostic service in Nigeria [12]. Most papers however agreed tat there is the desire and need for early prenatal diagnosis in most par

of the world.[42,43].

3. *Ultrasound Screening in Twin pregnancy*
Early Trimester Scan in Twin pregnancy offers numerous advantages. First the determination of zygocity is achievable and this has effect on the future course of the pregnancy. In dichorionic twin, the NT measurement in each fetus provides effective screening that are useful in the prenatal diagnosis of chromosmalities [6]. In monochorionic twin, the scan can predict early onset of twin-twin transfusion syndrome (TTTS) and for which endoscopic coagulation of the communication vessels can be applied. Increased NT are an early manifestation of TTTS in monochorionic twins [6,9].

The prevalence of structural defects per fetus in dizygotic twins is the same as in singleton, whereas the rate in monozygotic twin is 23 times higher. A major challenge in twin gestation is that of what to do when a diagnosed abnormality is discordant. This depend ultimately on the lethality or otherwise of the condition.

Conclusion

Prenatal Screening of congenital abnormalities has been revolutionized with the increasing sophistication of ultrasound devices and imaging capabilities [2,44]. Campbell in 1975 suggested that ultrasound was the tool of the future for the prenatal abnormally screening [45]. The introduction of the 11-13[+6] weeks scan, which began in the early 90s, has gained tremendous acceptance among practitioners world wide, which suggest that the future is now. The benefits are obvious even though it has its limitations. With appropriate training and reports from centers where it has been implemented, it will definitely take no time before more units embrace this innovation.

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