

A STUDY OF ROLE OF USG IN PRENATAL DIAGNOSIS

Desmond David Joachim Dcruz¹

¹Assistant Professor, Department of Radiodiagnosis and Imaging, Kanachur Institute of Medical Sciences, Mangalore.

ABSTRACT

BACKGROUND

Genetic diseases are often perceived as so rare that the average practitioner will seldom encounter them. However, our increasing knowledge and technologic advances in prenatal diagnosis have demonstrated that this is far from the case. The availability of prenatal diagnosis for a wide range of disorders continues to increase with advances in other areas of genetics. In addition, progress has been made in population screening tests to identify couples who carry a genetic disorder. These improvements in prenatal screening and diagnosis mean that many more at-risk couples are able to have unaffected children. In addition to reproductive choice, carrier screening and foetal diagnostic testing afford the important opportunity for preparation of the family and the delivery site for the birth of a foetus with a known genetic disorder. Ultrasound plays a central role in the provision of prenatal screening and diagnosis. Not only is ultrasound key to guiding prenatal diagnostic procedures, but integration of a genetics-based prenatal diagnosis program has been shown to increase the accuracy of diagnosis when compared to ultrasound alone. This study includes a discussion of prenatal diagnosis by sonography and its contribution to the provision of accurate and precise prenatal diagnosis.

MATERIALS AND METHODS

Seventy patients who came in for the routine anomaly scan were made to undergo USG scanning and the results are reported. This study is done in the Department of Radiodiagnosis and Imaging in Kanachur Institute of Medical Sciences, Deralakatte, Mangalore.

RESULTS

There was no significant correlation between nuchal translucency with other abnormalities in the first trimester and none of the malformations found were interrelated significantly with each other as the test for significance for interrelation came to be insignificant in the second trimester.

CONCLUSION

Indications for the sonography, the actual gestational age, the population which are under examination and experience of the examiner are all the factors that has to be looked before coming to a final diagnosis.

KEYWORDS

Ultrasound, Non-Invasive, Prenatal, Diagnosis, Role.

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BACKGROUND

Over the past years with the emergence of sophisticated and high-resolution ultrasonography and a greater proportion of the maternal population achieving pregnancies at an advanced maternal age, the ability to screen for foetal aneuploidy and other foetal abnormalities has achieved monumental importance in the management of obstetric patients. This task can be accomplished through various testing modalities in the second trimester, such as biochemical serum marker screening as previously discussed, detailed ultrasonography, and if indicated, invasive testing. Invasive forms of testing, such as

amniocentesis, chorionic villus sampling and cordocentesis are diagnostic tests that provide almost a 100% diagnostic accuracy of the presence or absence of aneuploidy. Genetic amniocentesis testing has traditionally been offered to patients who are considered to be at high risk for foetal Down syndrome. These are women whose age at the time of delivery is at least 35 years of age have an abnormal serum marker screen or both. Biochemical screening and ultrasonography for the purpose of aneuploidy detection are screening tests associated with a high number of false-positive results. Nevertheless, owing to the potential significant risks of invasive testing such as pregnancy loss, rupture of membranes, bleeding and infection, many patients choose to undergo screening surveillance initially and then decide upon further, more invasive forms of diagnosis, if necessary.

According to most studies, 2% to 3% of living newborns have a congenital malformation.^{1,2} When considering birth defects noted in the first years of life, this incidence is nearly doubled. With the decline in infant mortality in the United States from infection and malnutrition, congenital

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Corresponding Author:
 Dr. Desmond David Joachim Dcruz,
 Assistant Professor, Department of Radiodiagnosis and Imaging,
 Kanachur Institute of Medical Sciences, Mangalore.
 E-mail: desmonddcruz@yahoo.com
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malformations are now a leading cause of infant mortality and responsible for greater intensive care nursery admissions.³ Congenital defects range from enzyme deficiencies caused by single gene defects to complex associations of structural defects. The continuum between purely biochemical abnormalities and structural birth defects includes disorders of structure, function, metabolism and behavior. Birth defects result from the interaction between the genetic makeup of the embryo and the environment in which it develops. The basic developmental information is encoded in genes, but the genotype is subjected to environmental influences that can impact the observed phenotype. In some cases, the genetic information is expressed regardless of environment, whereas in others, environmental causes interfere with normal development despite a normal genotype. Although, some processes are primarily environmental and others primarily genetic, the distinctions between the two are not perfect. Despite considerable advances and research over past several decades, the cause of more than half of human congenital abnormalities remains unknown. Of those with a recognised cause, approximately 15% to 20% are autosomal genetic diseases and 20% are cytogenetic in origin. Less than 1% of anomalies are thought to occur owing to teratogenic medications.⁴ Some of the remaining defects are associated with other environmental exposures during pregnancy including infectious agents (3%), maternal disease states (4%), mechanical problems (1% to 2%), irradiation and unknown environmental causes. The remainder are of unknown or complex aetiology (multifactorial, polygenic, spontaneous errors of development and synergistic interactions of teratogens).⁵

At present, the ideal time to scan for foetal malformation is during the first trimester. This is a marked change in screening policy due to the significant advances, which have been made in antenatal screening for foetal chromosomal abnormalities over the past 20 years.⁶ In the past, invasive prenatal diagnosis for Down syndrome with amniocentesis or Chorionic Villus Sampling (CVS) was offered only to women of advanced maternal age or those who previously had an affected child.⁷⁻¹² In a recent survey of perinatologists in the United States, 4600 used nuchal translucency sonography and 27% used the serum markers PAPP-A and human chorionic gonadotropin during the first trimester to screen for Down syndrome.¹³ With the starting of national training programs for nuchal translucency sonography, it is likely that first trimester based screening programs for Down syndrome will become dominant.¹³⁻¹⁵

In India also, similar standards are now being accepted and the present study puts in a sincere effort to find the most common USG markers that is helpful in the prenatal diagnosis.

Aims and Objectives

To find the incidence of USG markers that is helpful in the prenatal diagnosis.

MATERIALS AND METHODS

This study was done in the Department of Radiology at Kanachur Institute of Medical Sciences at Deralakatte, Mangalore.

The study was conducted in 70 patients from August to November 2017.

The patients were routinely scanned in the first trimester and then in the second trimester. In the first trimester, the foetal nuchal translucency, the nasal bone, Doppler sonographic evaluation of ductus venosus blood flow and abnormal tricuspid regurgitation were checked. Enlarged nuchal translucency was noted. In the second trimester nuchal fold thickening, echogenic intracardiac focus, shortened long bones, hyperechoic bowel, renal pyelectasis, Choroid Plexus Cysts (CPCS), clinodactyly and hypoplastic or absent nasal bone were noted.

The image should be adequately magnified so that only the foetal head, neck and upper thorax could be viewed in the viewing area. The foetal neck should be neutral and the measurements should not be taken in the hyperflexed or hyperextended positions. The skin at the foetal back should be clearly differentiated from the underlying amniotic membrane. Measurement calipers should be placed on the inner borders of the echolucent space and should be perpendicular to the long axis of the foetus.

The nasal bone is also observed in the mid sagittal plane, and if it is absent, then repeat scan is performed after 3 weeks before proceeding for the other forms of diagnosis.

Patients who showed positivity for the different USG markers were noted and then were referred for triple marker test, which is a Gold standard for detecting the different aneuploidy. The significance of finding two or more markers in the same foetus is calculated.

RESULTS

Total	Mean	Standard Deviation
47	1.29	0.55

Table 1. First Trimester Scan (<2 mm Nuchal Translucency)

Total	Mean	Standard Deviation
23	2.03	0.21

Table 2. >2 mm Nuchal Translucency (NT)

Total	Nasal Bone not Developed	Ductus Venosus Inverse Flow	Abnormal Tricuspid Regurgitation
10	7	2	1

Table 3. The Nasal Bone (N), Doppler Sonographic Evaluation of Ductus Venosus Blood Flow (I) and Abnormal Tricuspid Regurgitation (R)

Nuchal Translucency with Other Abnormalities Found on USG	X Value	P-Value	Significance
9	0.642	0.07	Not significant

Table 4. Correlation between Nuchal Translucency with Other Abnormalities- (Test for Significance)

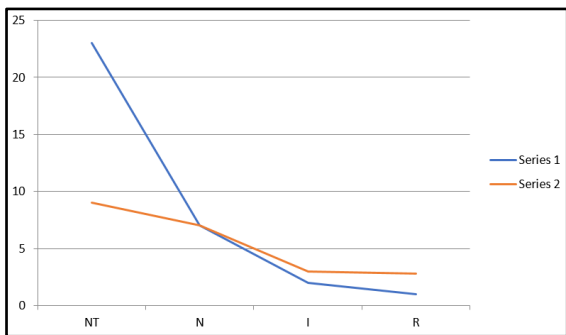


Figure 1. Correlation between Nuchal Translucency with Other Abnormalities- (Test for Significance)



Image 1. USG showing Nuchal Translucency

Total	Positive	Negative
70	21	49

Table 5. Echogenic Intracardiac Focus



Image 2. Echogenic Intracardiac Focus

Echogenic Intracardiac Focus	21
Shortened long bones	4
Hyperechoic bowel	19
Renal pyelectasis	7
Choroid Plexus Cysts (CPCS)	2
Clinodactyly	1
Hypoplastic or absent nasal bone	6

Table 6. Other Malformations Found

None of the malformations found were interrelated significantly with each other as the test for significance for inter-relation came to be insignificant.

DISCUSSION

The most powerful marker available today for differentiating Down syndrome from other euploid pregnancies is the first trimester USG measurement of the foetal nuchal translucency measurement. It is the normal subcutaneous fluid-filled space between the back of the foetal neck and the skin, which covers it. Normally, this space is small and insignificant, but in many foetuses with Down syndrome, this space can be significantly increased. In majority of the case, it will be more than 2 cm. There is a direct significant correlation between increasing nuchal translucency measurement and risk for Down syndrome and other malformations.⁷ It may be due to cardiac failure, extracellular matrix diseases and also the lymphatic malformations.⁷ This finding has been described as septated cystic hygroma and is present when the nuchal translucency space is enlarged extending along the entire length of the foetus and in which septations are clearly visible.¹² Isolated cystic hygroma is seen in more than one in 300 first trimester pregnancies. In a recent prospective study of routine first trimester sonographic screening, septated cystic hygroma was shown to have a 50% chance of being associated with foetal aneuploidy with most cases being Down syndrome as well as cases of Turner syndrome and Trisomy 18.¹²

The practical benefit of being able to counsel patients in the first trimester following the identification of septated cystic hygroma is that there is no need to delay decision making, while awaiting serum marker results or using computerised risk calculation algorithms. When faced with a chance of foetal aneuploidy, it is reasonable to offer such patients, the immediate option of CVS, and if foetal aneuploidy has been excluded, a detailed foetal anatomic evaluation, including foetal echocardiography should be performed at 18 to 20 weeks' gestation.¹²

Nasal bone sonography in the first trimester appears to be a clear association between the absence of the foetal nasal bones on first trimester ultrasound examination and Down syndrome. In a study conducted by Cicero et al,¹⁵ 701 foetuses with increased nuchal translucency were evaluated for the presence or absence of the nose bones during first trimester ultrasonography. The foetal nasal bones could not be visualised in 73% of Down syndrome foetuses (43 of 59) and in only 0.5% of unaffected foetuses (3 of 603). The authors also felt that the absence of the foetal nose bone was not related to nuchal translucency thickness and therefore could be combined into a single ultrasound screening modality with a predicted sensitivity of 85% for a 1% false-positive rate.¹⁵ This study was subsequently expanded to a larger series of 3829 high risk.

First trimester Doppler sonographic evaluation of ductus venosus blood flow has been described as an adjunctive test for foetal aneuploidy screening. Forward triphasic pulsatile ductus venosus flow, whereas reversed flow at the time of the atrial contraction has been associated with aneuploidy and foetal cardiac malformations.⁸

An association has been suggested between foetal aneuploidy and abnormal tricuspid regurgitation noted during 1st trimester sonography.¹⁶

Although, these data are encouraging regarding an association between first trimester tricuspid regurgitation and chromosomal abnormalities like ductus venosus assessment, it is unclear whether this form of screening will have any role in general population screening.

The "genetic sonogram," which evaluates for structural malformations and a range of second trimester soft markers for aneuploidy, such as short femurs, echogenic bowel, echogenic intracardiac foci and increased nuchal fold has gained widespread acceptability.

All pregnancies are theoretically at risk for foetal malformations. Other risk factors include increasing maternal age particularly after 35 years due to higher risk of nondisjunction, abnormal biochemical screening results are also quite common, history of previous foetal aneuploidy, known balanced translocation, which are run in family or other structural rearrangements in one or in isolated cases where both parents are involved and abnormalities visualised on prenatal ultrasound. In aneuploid foetuses, sonography may reveal gross structural abnormalities, other findings like growth retardation and also aneuploidy markers. "Soft" USG markers are variations in normal anatomy that except for their relationship to aneuploidy (especially trisomy 21) are unlikely to be clinically significant. Some of the most common sonographic markers seen in the second trimester include, echogenic intracardiac focus, shortened limb bones, hyperechoic bowel, which may be isolated or multi-focal, renal pyelectasis, choroid plexus cysts, clinodactyly and absent or deformed nasal bone. Structural or major anomalies, which include central nervous system anomalies, facial abnormalities, cystic hygroma, diaphragmatic hernia, cardiac defects, gastrointestinal abnormalities, genitourinary anomalies, non-immune hydrops and extremity abnormalities. Many foetuses with trisomies 18 and 13 have multiple major structural anomalies, which include CVS and CNS anomalies; however, this may not necessarily apply to Down syndrome cases. Only 25% of second trimester foetuses with Down syndrome have ultrasonographically detectable major congenital anomalies⁶ before 20 weeks, structural anomalies were detected by sonography in only 16% to 17% of trisomy 21 foetuses.¹⁷

CONCLUSION

The best way to understand and give the benefit at a proper time to the patient is the need of the hour. The patient would be anxious and this study proves that the fact that USG is the best way to screen and those high-risk cases can be subjected to chromosomal studies, which is still the gold standard for pin pointing the diagnosis.

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