European Journal of Molecular & Clinical Medicine

ISSN 2515-826 Volume 09, Issue 03, 2022

Study of Nuchal Translucency (NT) at 11-13^{+6} Weeks of Gestation as a Screening Tool to Identify Fetal Abnormalities

Nilofer[1], Sunitha Ch[1], Medabalini Haritha[1], K.S.S. Bhavana[2]

[1]Assistant Professors, Department of Obstetrics & Gynecology, DR PSIMS & RF, Vijayawada, AP, India.

[2]Final Year Postgraduates, Department of Obstetrics & Gynecology, DR PSIMS & RF, Vijayawada, AP, India.

ABSTRACT

Background: The accuracy of diagnosis reported in multiple large series has pushed both screening and diagnostic testing for chromosomal disorders to the window now refe (nuchal translucency scan).11-13+6 weeks scan shows normal foetal anatomy and identifies severe structural problems. Early detection of these problems allows for safer and easier pregnancy termination. Tests include chorionic villous sampling and amniocentesis carry a 1% foetal loss risk. So non- invasive screening tests are required.first trimester screening is a new non-invasive technique that combines maternal blood screening and foetal screening to discover chromosomal abnormalities (including trisomy 21).Because there are few studies in this field, the current study aims to investigate the utility of high resolution ultrasound as a screening test for aneuploidy risk in late first trimester foetuses. Objectives :1. Assess the utility of ultrasound as a screening tool for foetal first trimester aneuploidies.2. Ultrasound to identify aneuploidy- prone foetuses.3. To establish the use of ultrasonography in regular first trimester screening.

Materials and Methods: This research performed at Vydehi Institute of Medical Sciences Hospital and Research Centre studied 220 pregnant ladies. Present study investigated increased nuchal translucency and foetal abnormalities.

Results: Present investigation found that foetal nuchal translucency increased with abnormalities. This study has shown that foetal nuchal translucency can be used to test for chromosomal abnormalities, heart problems, and morphological malformations at 11-13+6 weeks gestation. The earlier the foetal anomalies are detected, the more acceptable and less traumatic the pregnancy is for the expectant moms.

Keywords: Nuchal Translucency; Chorion Villus Sampling; Cordocentesis; Amniocentesis; Down's syndrome; Aneuploidy; Fetal Abnormalities; Cardiac defects.

Corresponding Author: Dr. Nilofer, Assistant Professors, Department of Obstetrics & Gynecology, DR PSIMS & RF, Vijayawada, AP, India.

INTRODUCTION

Prenatal testing for chromosomal abnormalities is intended to accurately determine a patient's risk of having a chromosomally abnormal foetus. There are numerous prenatal screening and diagnostic tests available, each with unique benefits and drawbacks. No one screening test is superior in all situations, necessitating nuanced, patient-centered counselling from obstetric care professionals and complex decision-making by patients. During each pregnancy, patients should be educated about alternatives to foetal chromosomal abnormality testing. Obstetricians should be prepared to discuss the risks of foetal chromosomal disorders as well as the benefits and limitations of existing screening and diagnostic techniques. When given appropriate and reliable information, patients can make well-informed decisions about their own health care. Patients should be offered both screening and diagnostic tests, with the option to decline during counseling. At 11–13 weeks of gestation, increased foetal nuchal translucency thickness (NT) is related to chromosomal abnormalities and severe malformations.[1] High NT is associated with a higher risk of foetal death in chromosomally normal foetuses with no evident abnormalities, ranging from 1% to 5% in those with NT between the 95th and 99th percentiles. The 11–13-week scan is also useful in detecting multiple pregnancy and determining chorionicity and amnionicity, which are

important predictors of outcome in such pregnancies.[2] Many nations worldwide offer prenatal screening for Down syndrome (trisomy 21) and other chromosomal abnormalities such as trisomy 13 and 18.[1,2] The risk of DS in a foetus increases with maternal age. DS is associated with intellectual disability as well as other health problems such as congenital heart disease.[3–5] Prospective parents are told about DS, other chromosomal disorders, and prenatal screening and can make an informed decision. Trisomy 21 causes Down Syndrome (DS), which causes congenital and developmental issues in children. Early cytogenetic diagnosis of DS cases is critical for optimal health treatment and reducing the risk of subsequent DS deliveries in mothers.[4] Trisomy 21 affects 1 in 1000 live births, but it varies by ethnicity. According to a National Down Syndrome Society survey, people with DS live to be 55.[2-5] DS is associated with hypotonia, craniofacial abnormality, flat facial profile, excess skin at the nape of the neck, hypotonia, hyperflexibility of joints, pelvic dysplasia, anomalous ears, dysplasia of the mid phalanx of the fifth finger, and a transverse palmer crease (simian crease) in early infancy.[4,5] An upward tilt to the eye, a flat nasal bridge, and a short neck are all frequent traits. White dots on the iris of the eye (called "Brushfield spots") are also common.[6] Most patients have mild to moderate mental retardation. Prenatal diagnosis can prevent DS children in high-risk pregnancies.

However, chorionic villus sampling and amniocentesis have been linked to a 0.5-1 percent increased risk of miscarriage.[7] Ultrasound during 12 to 24 weeks of gestation detects trisomy risk by looking for thin or nonexistent nasal bones, broad nuchal folds, and large ventricles. The gold standard for prenatal diagnosis is cytogenetic analysis. However, quick aneuploidy testing procedures including FISH, QF-PCR, and MLPA are also commonly utilised in prenatal diagnosis laboratories.[5] At 11–13 weeks of gestation, increased nuchal translucency thickness is related to chromosomal abnormalities and severe malformations. Fetal death risk is increased by 1% in those with NT between the 95^{th} and 99^{th} percentiles and by 5% in those with NT > 99th percentiles in chromosomally normal fetuses with no apparent abnormalities. 5, 6. The 11–13-week scan can also be used to diagnose multiple pregnancies and assess chorionicity and amnionicity, two key factors in the fate of such pregnancies.[6] However, according to Nicolaides in 1992, only the invention of ultrasound scanning permitted physicians to detect the nuchal edema shown by some foetuses. Nuchal translucency (NT) is an ultrasound sign that has been shown to be useful in screening for aneuploidy during the first trimester. Increased NT has also been linked to pathologic diseases such as structural foetal abnormalities, heart deformities, miscarriage risk, and intrauterine death. However, case-series studies have shown that many foetuses with high NT in the first trimester have normal neonatal outcomes.[7] Early diagnosis of structural abnormalities is now possible be grateful to technological advances and the introduction of high-resolution equipment. Furthermore, measuring foetal nuchal translucency thickness at $11\text{-}13^{+6}$ weeks has been shown to be an effective method of screening for chromosomal abnormalities.[8-10]

A complete foetal anatomical survey in the first trimester can help to identify foetuses with structural abnormalities earlier in the course of pregnancy and can help to offer options pertaining to counselling, prenatal tests for karyotype, and possible termination of pregnancy at an earlier stage, if needed. This is critical in a country like India, where karyotype and biochemical tests are expensive and difficult to obtain.

Aims and Objectives

- To evaluate the use of ultrasound as a screening tool for detection of fetal aneuploidies in first trimester.
- To identify the fetuses at risk for aneuploidy by ultrasound.
- To establish the need of use of ultrasound in first trimester screening as a routine

MATERIALS & METHODS

Design

This study was conducted at DR PSIMS & RF, Vijayawada, AP, India., which is a teaching institution. This prospective study has been conducted on 220 pregnant women, between 11-13weeks and 6 days of gestation with reliable LMP details attending antenatal clinic at, DR PSIMS & RF during a period of one and half years from 2018-2020.

Method

The patient's detailed history was taken and any risk factors of having fetal abnormality noted. A thorough clinical examination was made at booking. Blood pressure, pulse rate, presence of pallor/edema/Icterus noted. A detailed systemic examination and obstetric examination was made. All preliminary investigations as outlined in the proforma carried out.

All 220 pregnant women between 11-13 weeks 6 days of gestation were offered counselling before the screening. In the counselling the patients were made aware of the uses of ultrasound at 11-13 weeks and 6 days of gestation (such as to date the pregnancy accurately, to diagnose multiple pregnancy, to diagnose the viability of the fetus, to assess the chance of Down's syndrome and other chromosomal abnormalities/fetal abnormalities by measuring fetal nuchal translucency).The women were counselled about the interpretation of the results of the screening procedure and the possibility of an invasive procedure for fetal tissue sampling for karyotyping such as Chorion Villus sampling or amniocentesis if the patient turns out to be at high risk for Down’s syndrome or other fetal abnormalities.

The women were counseled about the risks of pregnancy loss associated with the invasive procedures. If the woman refuses invasive procedure, at the end of the counselling, she was not offered a diagnostic test. After counselling, pregnant women were offered ultrasonography. The scans were carried out by the trained sonographers. During the 11-13weeks and 6 days scan, the fetal CRL, Nuchal translucency, any structural abnormalities in the fetus, uterine anomaly, adnexa, cervix length were noted. After the scan, the estimated chance for having Down's syndrome or other fetal abnormalities was discussed with the pregnant woman and her family. If the woman was at high risk, she was offered triple test or quad test or an invasive test to determine the karyotype of the fetus by either Chorion Villus Sampling /Amniocentesis/Cordocentesis.Our institution is registered under PNDT Act and will follow the rules and regulations according to the act.

Inclusion criteria

- All the pregnant women in 11-13 weeks and 6 days of gestation calculated by last menstrual period or by previous ultrasound study.

Exclusion Criteria

- Pregnant women less than 11 weeks and more than 13 weeks 6 days of gestation Results are documented as follows:

If NT >3 mm or > 95th percentile for that gestational age, the women were considered to be at high risk (screen positive) of having Down's syndrome/other chromosomal abnormalities/cardiac defects/other structural defects and hence these women were subjected to invasive procedures such as CVS/amniocentesis/cordocentesis in order to determine the karyotype of the fetus.

Interpretation and action

If karyotyping normal, then follow up was done with an anomaly scan at 18-20 weeks of gestation. If lethal anomaly detected at anomaly scan, pregnancy was terminated. If no congenital anomalies picked up, fetal echocardiography done to detect any congenital cardiac defect. If no congenital cardiac defect detected, pregnancy was continued followed by term scan. After delivery, the baby was evaluated by the paediatrician for anomalies.

Endpoints to assess outcome of pregnancy:

- Pregnancy loss - Spontaneous abortions
- Fetal aneuploidy (Trisomy 21, 13, 18 Turner's syndrome)
- Cardiac Defects/Pulmonary defects/Abdominal wall defects/Skeletal defects/Genetic Syndrome
- Perinatal morbidity
- Perinatal mortality

Statistical Methods: Chi square test have been used to test the significance of fetal abnormalities in relation to the NT and Diagnostic statistics were used to find the diagnostic value of NT in relation to fetal abnormalities.

Statistical software: The Statistical software namely SPSS 11.0 and Systat 8.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc

RESULTS

Table 1: Age Incidence

Age in Years	Number	%
<= 20	35	15.9
21-25	86	39.09
26-30	82	37.72
31-35	14	6.36
>35	2	0.9
Total	220	100

Majority of the pregnant women were between 21-25 years(40.5%), 38.5% were 26-30 years, 15.5% were<=20 years, 5% between 31-35 years and 0.5% more than 35 years.

Table 2: Gravida

Gravida	Number	%
Primigravida	106	48.18
Multigravida	114	51.81
Total	220	100

Majority are multigravida 51% followed by primigravida 49%

Table 3: Gestational Age

Gestational age in Weeks	Number (n=100)	%
11-12	66	30
12.1-13	95	43.18
13.1-13.6	59	26.8
Total	220	100

Most of the pregnant women were scanned between 12.1-13 weeks (43.18%) 26.8% between 13.1-13.6 weeks, 30 % between 11.1-12 weeks.

Table 4: Past Obstetric History

Past Obstetric History	**Number**	**%**
Nil	172	78.0
Previous History of Unexplained 1st Trimester Pregnancy Loss	34	15.45
Previous History of IUD	5	2.2
Previous History of Anencephaly Baby	3	1.36
Previous History of Baby having Anomalies	1	0.45
Previous History of Still Birth	2	0.9
Previous History of Molar Pregnancy	2	0.9
Previous History of Pre-term Delivery	1	0.45
Total	220	100

78 % of pregnant women had no significant risk factors in the past obstetric history 15.45 % of pregnant women had previous history of unexplained Ist trimester pregnancy losses 2.2 % of pregnant women had previous history of IUD 1.36% of pregnant women had previous history of anencephaly baby 0.45 % of pregnant women had previous history of baby having anamolies 0.9% of pregnant women had previous history of still birth 0.9% of pregnant women had previous history of molar pregnancy 0.45% of pregnant women had previous history of Pre-term delivery.

Table 5: Risk factors in the present pregnancy identified identified at the time of NT scan

Risk factors in the present pregnancy	**Number**	**%**
Nil	186	84.54
Overt Diabetic	6	2.72
Previous LSCS	25	11.36
Elderly Primi	3	2.36
Total	220	100

84.54% women had no risk factorsat the time of NT scan

11.36 % were previous LSCS

2.72 % of overt diabetes

2.36 % of elderly primi

Table 6: Risk Factors in the Present Pregnancy

Risk factors in the present pregnancy	Number	%
Nil	180	81.81
GDM	11	5
PIH	4	1.81
Decreased liquor	2	0.90
Breech presentation	3	1.36
PROM	3	1.36
PPROM	2	0.9
Polyhydramnios	2	0.9
Placenta previa	7	3.18
Total	220	100

81.81 % had no risk factors in the present pregnancy 5 % had GDM

1.81 % had placenta previa and PIH

1.36 % had PROM

1.36 % had breech presentation, 0.9 % had polyhydramnios and PPROM

Table 7: Nuchal Translucency

NT	Number	%
<=3mm	209	95
>3mm	11	5
Total	220	100

95% 0f pregnant women had NT <=3mm

5% of pregnant women had NT>3MM

Table 8: Fetal Abnormalities

Fetal Abnormalities	Increased NT
Trisomy 21*	3
Trisomy 18	0
Trisomy 13	0
Cardiac defects*	2
Pulmonary defects	3
Abdominal wall defects	0
Genetic syndromes	0
Polydactyly*	1
Cleft palate	2
Anencephaly	1
Spinal abnormalities	3
Head and neck	1

out of 12 patients with increased nuchal translucency

20% had cardiac defects and trisomy 21, 20% had pulmonary defects 20% had spinal abnormalities (sacral agenesis and spina bifida)

10% had polydactyly

10% had anencephaly

10 % had head and neck deformities

*same foetus with more than one abnormality

Table 9: Mode of Delivery

Mode	Number	%
Cesearean	56	25.46
Vaginal	164	74.54
Total	220	100

74.54% had vaginal deliveries

25.46 % had caesearean

Table 10: Birth Weight

Birth Weight (in Kgs)	Number	%
<=2.0	26	11.82
2.1-2.5	27	12.27
2.6-3.0	84	38.18
3.1-3.5	75	34.09
>3.5	13	0.59
Total	220	100

Table 11: NICU Admission

NICU Admission	Number	%
IUGR	3	12
Septicemia	2	8
MAS	6	12
Preterm	15	64
Total	25	100

Table 12: Diagnostic Value of Increased NT Concerning Fetal Abnormalities

Diagnostic Value of NT	Number
True Positives	7
True Negative	192
False Positive	3.5
False Negative	4
Sensitivity (%)	62.6
Specifity (%)	97.2
PPV (%)	72.0

Table 13: Diagnostic Value of Increased NT in Relation to Cardiac Defects

Diagnostic value of increased NT	Number
Total Positive	2
Total Negative	182
False Negative	7
False Positive	2
Sensitivity (%)	19.2
Specificity (%)	98.6
PPV (%)	66.7

DISCUSSION

One of the major objective of prenatal screening for foetal nuchal translucency at 11-13 weeks 6 days of gestation is to detect foetal defects early. There are several methods for identifying an abnormal foetus, including maternal serum markers, second trimester anomaly scans, and invasive tests such as CVS/amniocentesis/cordocentesis (for foetal karyotyping), but the ideal method is one that is non-invasive, less expensive, and provides reliable information quickly, so that affected women can be offered an early termination option. Nuchal translucency satisfies all of the above requirements of an excellent screening test.

Most women in this study were between the ages of 21 and 25, were multigravida, followed by primigravida, and were screened between 13 weeks 6 days of gestation. (43.18% between

and 13 weeks, 26.8% between 13.1 and 14 weeks) Approximately 20.8 percent) of pregnant women had substantial risk factors in their previous obstetric history (e.g.; previous history of foetal anomalies, previous history of Anencephaly, previous history of unexplained foetal loss). 95% of pregnant women had normal nuchal translucency (NT3mm), while 5% had enhanced nuchal translucency (NT>3mm). Six pregnant women out of twelve had elevated NT with abnormalities. Three pregnant women with elevated NT had no malformations, while three pregnant women with normal NT had anomalies. Schwärzler et al. conducted a study on 4523 patients, with a sensitivity of 76 percent and a specificity of 95.3 percent, respectively. Snijders et al. conducted a study on 96127 patients, with a sensitivity of 77 percent and a specificity of 91 percent, respectively.[11] In comparison to the previous investigations, the current study enrolled 220 patients and achieved a sensitivity of 59.8% and a specificity of 97.2 percent.Increased nuchal translucency thickness indicates a group at risk for not only chromosomal abnormalities, but also for all major heart problems, structural malformations. Our study demonstrates that 20% of significant cardiac and great artery anomalies are connected with increased nuchal translucency thickness during 11-13 weeks+6 days of gestation. This screening procedure outperformed the previously reported sensitivity of 26% utilising the four-chamber image of the heart at 16-22 weeks gestation. Our data suggest that greater nuchal translucency thickness is a clinical indicator for foetal echocardiography. Pregnancies identified as having a high risk of heart abnormalities using nuchal translucency scanning do not need to wait until 20 weeks for specialised echocardiography.[12-14] Due to advancements in the resolution of ultrasound scanners, comprehensive heart screening may now be performed during the first trimester of pregnancy. Two aneuiploidies were identified in this investigation. Additionally, it was discovered that higher nuchal translucency was associated with 10% cardiac problems (Ventricular septal defects), 21% spinal abnormalities, 10% polydactyly, 10% anencephaly, 10% head and neck anomalies, 10% cleft palate, and 11% esophageal atresia.[15]

One patient had normal nuchal translucency in the presence of a heart problem. Additionally, first trimester ultrasound examinations are used to confirm foetal viability, accurately date pregnancy, discover multiple pregnancies early, and assess the uterus, adnexa, and cervical length for severe defects.

CONCLUSION

Fetal nuchal translucency measurement at 11-13weeks+6 days of gestation, which has traditionally been used to identify foetuses at high risk of aneuploidy, also identifies the majority of pregnancies with major cardiac defects and structural defects. As a result, foetal NT can be used as an early screening tool to detect foetal abnormalities. Nuchal translucency measurement is a non-invasive, reliable early screening tool for identifying foetuses at risk for foetal aneuploidies/structural defects/genetic syndromes. Prenatal screening for foetal anomalies has been pushed into the first trimester thanks to nuchal translucency ultrasound. When maternal serum free (3HCG and PAPP-A at 11-13weeks+6 days of gestation were also taken into account, the detection rate of chromosomal defects increased upto 85-90 percent, when absent nasal bone is also included with the first trimester nuchal translucency and serum biochemistry detection rate increased to more than 95 percent. Other advantages of an 11-13weeks+6days scan include confirmation of foetal viability, accurate pregnancy dating, early detection of major foetal abnormalities, detection of multiple pregnancies, the condition of the uterus, adnexa, and cervical length. Normal foetal nuchal translucency measured between 11-13weeks +6days of gestation reassures the woman that her foetus is not at risk of chromosomal abnormalities. The measurement of normal nuchal translucency reduces the number of invasive procedures such as CVS/amniocentesis/cordocentesis, all of which have an abortion risk. The measurement of increased foetal nuchal translucency gives women with affected foetuses the option of terminating their pregnancy early. There were 220 pregnant women in this study. To develop a definitive protocol, the study should be expanded to include a larger number of patients.

REFERENCES

1. Minnella, G. P., Crupano, F. M., Syngelaki, A., Zidere, V., Akolekar, R., & Nicolaides, K. H. (2020). Diagnosis of major heart defects by routine first-trimester ultrasound examination: association with increased nuchal translucency, tricuspid regurgitation and abnormal flow in ductus venosus. Ultrasound in Obstetrics & Gynecology, 55(5), 637-644.
2. American College of Obstetricians and Gynecologists. (2003). Clinical management guidelines for obstetrician-gynecologists. ACOG practice bulletin, 7, 643-648.
3. Zhang, W., Mohammadi, T., Sou, J., & Anis, A. H. (2019). Cost-effectiveness of prenatal screening and diagnostic strategies for Down syndrome: A microsimulation modeling analysis. Plos one, 14(12), e0225281.
4. Jaiswal, S. K., Kumar, A., & Rai, A. K. (2021). Molecular Cytogenetic Classification of Down Syndrome and Screening of Somatic Aneuploidy in Mothers. Cytogenetic and genome research, 161(8-9), 397-405.
5. Asim, A., & Agarwal, S. (2018). Segmental duplication-quantitative fluorescent-polymerase chain reaction: An approach for the diagnosis of Down syndrome in India. Turkish Journal of Obstetrics and Gynecology, 15(1), 18.
6. Cilliers, J. B. F. (2010). Increased nuchal translucency thickness and normal karyotype. South African Journal of Obstetrics and Gynaecology, 16(2), 36-37.

7. Socolov, D., Socolov, R., Gorduza, V. E., Butureanu, T., Stanculescu, R., Carauleanu, A., & Pavaleanu, I. (2017). Increased nuchal translucency in fetuses with a normal karyotype— diagnosis and management: An observational study. Medicine, 96(29), e7521.
8. Cimpoca, B., Syngelaki, A., Litwinska, E., Muzaferovic, A., & Nicolaides, K. H. (2020). Increased nuchal translucency at 11–13 weeks' gestation and outcome in twin pregnancy. Ultrasound in Obstetrics & Gynecology, 55(3), 318-325.
9. Sulaiman, B., Shehu, C. E., Panti, A. A., Saidu, S. A., Onankpa, B., & Ekele, B. A. (2020). Prevalence and outcome of increased nuchal translucency in usmanu danfodiyo university teaching hospital, Sokoto, Nigeria: A cohort study. Nigerian Journal of Clinical Practice, 23(6), 864-869.
10. Miranda, J., Paz y Miño, F., Borobio, V., Badenas, C., Rodriguez-Revenga, L., Pauta, M., & Borrell, A. (2020). Should cell-free DNA testing be used in pregnancy with increased fetal nuchal translucency?. Ultrasound in Obstetrics & Gynecology, 55(5), 645-651.
11. Wilson, R. D., Gagnon, A., Audibert, F., Campagnolo, C., Carroll, J., Brock, J. A., ... & Vallee- Pouliot, K. (2015). Prenatal diagnosis procedures and techniques to obtain a diagnostic fetal specimen or tissue: maternal and fetal risks and benefits. Journal of Obstetrics and Gynaecology Canada, 37(7), 656-668.
12. Phadke, S. R., Puri, R. D., & Ranganath, P. (2017). Prenatal screening for genetic disorders: Suggested guidelines for the Indian Scenario. The Indian Journal of Medical Research, 146(6), 689.
13. Schwärzler, P., Carvalho, J. S., Senat, M. V., Masroor, T., Campbell, S., & Ville, Y. (1999). Screening for fetal aneuploidies and fetal cardiac abnormalities by nuchal translucency thickness measurement at 10–14 weeks of gestation as part of routine antenatal care in an unselected population. BJOG: An International Journal of Obstetrics & Gynaecology, 106(10), 1029-1034.
14. Martínez-Moratalla, J. M., Escribano, D., Gómez-Montes, E., Herraiz, I., & Galindo, A. (2012). Prenatal ultrasound screening for congenital heart defects: current and future strategies. Expert Review of Obstetrics & Gynecology, 7(6), 535-544.
15. Kalousek, D. K., Fitch, N., & Paradice, B. A. (1990). Common Morphologic Defects in Embryos and Fetuses. Pathology of the Human Embryo and Previable Fetus, 63–159.