Original Article

Prevalence and Outcome of Increased Nuchal Translucency in Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria: A Cohort Study

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Received: 05-Apr-2019;
Revision: 05-Aug-2019;
Accepted: 28-Mar-2020;
Published: 11-Jun-2020

ABSTRACT

Background: An important component of the first-trimester scan is nuchal translucency thickness at 11 weeks to 13 weeks 6 days of gestation. A nuchal translucency ≥3.3 mm is a significant early pregnancy scan finding associated with Trisomies 13, 18, and 21 and congenital heart diseases. **Aims:** To determine the prevalence and outcome of increased fetal nuchal translucency among pregnant women. **Subjects and Methods:** A prospective cohort study at the Obstetrics and Gynaecology Department of Usmanu Danfodiyo University Teaching Hospital Sokoto. This was a prospective study of 265 consecutively recruited women in the first trimester of pregnancy who presented to antenatal clinics over a 20-week period. An NT scan was conducted at 11 weeks to 13 weeks 6 days followed by an anomaly scan at 18–22 weeks. Patients were followed up to delivery and 6-week post-partum. The neonates were examined at delivery and at 6-week postnatal life. Data entry and analysis was done with IBM SPSS version 20. The level of significance was set at less than 0.05. Frequency distribution; student *t*-test and Chi-squared test. **Results:** The 95th percentile NT was 3.3 mm and the prevalence of increased NT above 3.3 mm was 3%. The mean maternal age of the participants was 28.1 ± 5.1 years and the modal parity was Para 0. The most common anomalies associated with increased NT were ventricular septal defect and spina bifida. A congenital anomaly was significantly associated with increased NT ($P < 0.001$). **Conclusions:** The prevalence of increased fetal nuchal translucency is relatively high in our environment and is associated with congenital fetal defects. Routine screening with first-trimester ultrasound will help detect congenital anomalies early.

Keywords: *Nuchal translucency, Anomalies, Obstetrics, Nigeria*

Introduction

The first-trimester scan was introduced initially with the aim of measuring the fetal crown-rump length to achieve accurate pregnancy dating, especially where the last menstrual period is unknown.[1] However, during the last few years, improvement in the resolution of ultrasonography machines has made it possible to describe the normal anatomy of the fetus and diagnose or suspect the presence of a wide range of fetal defects in the first trimester of pregnancy.[1,2] The anatomical survey of a fetus in the first trimester is best done toward the end of the first trimester usually between the 11th to 14th week of gestation.[3] An important component of the 11–13^{+6} week scan is measurement of fetal nuchal translucency thickness, which provides effective

Access this article online

Quick Response Code:

Website: www.njcponline.com

DOI: 10.4103/njcp.njcp_191_19

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How to cite this article: Sulaiman B, Shehu CE, Panti AA, Saidu SA, Onankpa B, Ekele BA. Prevalence and outcome of increased nuchal translucency in usmanu danfodiyo university teaching hospital, Sokoto, Nigeria: A cohort study. Niger J Clin Pract 2020;23:864-9.

screening for chromosomal abnormalities, major defects of the heart and great arteries, and a wide range of skeletal dysplasia and genetic syndromes.[1]

The optimal gestational age for performing nuchal translucency measurement has evolved over the years. When it was first introduced in the early 1990s, crown-rump length (CRL) of 36 mm (10^{+3} weeks) was chosen as the lower limit in order to provide the patient with information about the risk of fetal abnormalities as early as possible.[4]

However, it soon became apparent that the first-trimester scan can provide much more information about the fetus than simply a crown-rump length and nuchal translucency measurements. Waiting until the pregnancy reaches 11 weeks' gestation (CRL of 45 mm) allows for a more complete fetal examination without sacrificing screening efficiency and without causing an unreasonable delay.[4]

The enormous value of first-trimester screening is that it provides a way to document both visually through ultrasound and physiologically through chemistry that a pregnancy is developing normally.[5] Measurement of fetal nuchal translucency thickness at $11–13^{+6}$ weeks provides an effective method of screening for chromosomal defects, major cardiac defects, and a wide range of fetal malformations and genetic syndromes.[6] It has also been shown to be a predictor of some medical disorders of pregnancy like gestational diabetes mellitus.[7]

In our environment and some other parts of Nigeria, ultrasound in the first-trimester is carried out mainly to confirm pregnancy, viability, number of fetus (es), and dating of the pregnancy. The aim of this study was to determine the prevalence and outcome of increased nuchal translucency among pregnant women in our environment.

Subjects and Methods

The study was a prospective cohort study conducted at the Department of Obstetrics and Gynaecology of Usmanu Danfodiyo University Teaching Hospital. It was approved by the Health Research and Ethics Committee of Usmanu Danfodiyo University Teaching Hospital (UDUTH/HREC/2014/No. 317). Pregnant women at $11–13^{+6}$ weeks gestation who presented to booking clinic were recruited consecutively using convenient sampling method, after obtaining their informed consent. Inclusion criteria were gestational age of $11–13^{+6}$ weeks, live, and singleton pregnancy. Exclusion criteria were multiple pregnancy and patients at or beyond 14 weeks gestational age. The minimum sample size was determined using standard formula for cohort study.

$n = z^2pq/d^2$[8]

where:

n = minimum sample size required

z = standard normal deviate at 95% confidence level (1.96)

p = estimated proportion of variable of interest in the population = 3.3%[9] (i.e., 0.033)

d = tolerable alpha error or precision = 0.05

q = complementary probability of p (q = 1 – p)

The calculated sample size was 49 subjects.

Adjustment for expected response rate: To accommodate for attrition, the estimated sample size, n, was divided by 0.9 (with the anticipation of a 90% response rate, R).[8] Thus, $n_s = n/R = 49/0.9 = 54.4$ approximately 54 subjects.

Adjustment for the expected proportion of women eligible (because of the inclusion criteria of gestational age 11–14 weeks), those eligible might be low (like 20%).[8]

If the expected percentage of pregnant women eligible was 20%, then sample size = 54/0.2 = 270 subjects.

At least 10 subjects were recruited per week for a period of 20 weeks (April 2015–August, 2015). A structured interviewer administered questionnaire was completed for all the participants to obtain information on sociodemographic data, index pregnancy and previous pregnancy, family, and medical history. Routine investigations for booking were requested; nuchal translucency (as described by Nicolaides *et al*.[1]) and anomaly ultrasound scans were carried out at $11–13^{+6}$ weeks and 18–22 weeks, respectively. To minimize intra and inter observer errors, the ultrasound scans on each woman were carried out by at least two researchers and the average NT was used.

In the assessment of fetal NT, GE Voluson 730 PRO with 3.5–6.5 MHz curvilinear probe was used. It has a high resolution with a video-loop function and calipers that provided measurements to one decimal point. Fetal NT was measured by transabdominal sonography. Only the fetal head and upper thorax were included in the image for measurement of NT. The magnification was as large as possible and always such that each slight movement of the caliper produced only a 0.1 mm change in the measurement. In magnifying the image, either pre or post freeze zoom, the gain was turned down. This was

to avoid the mistake of placing the caliper on the fuzzy edge of the line which could cause an underestimation of the nuchal measurement. A good sagittal section of the fetus, as for measurement of fetal crown-rump length, was obtained and the nuchal translucency was measured with the fetus in the neutral position. Measurement was not taken when the fetal neck was hyperextended. Care was taken to distinguish between fetal skin and amnion and this was achieved by waiting for spontaneous fetal movement away from the amniotic membrane. Alternatively, the fetus was bounced off the amnion by asking the mother to cough and/or by tapping the maternal abdomen. The maximum thickness of the subcutaneous translucency between the skin and the soft tissue overlying the cervical spine was measured. The caliper was placed on the lines that define the NT thickness—the crossbar of the caliper was such that it was hardly visible as it merged with the white line of the border and not in the nuchal fluid. During the scan, three measurements were taken and the maximum one was recorded. All the participants were followed up with an anomaly scan to identify fetuses (with normal and abnormal NT measurement) that developed detectable congenital anomaly.

All the women were also followed up till delivery and the neonates were examined for clinical features of chromosomal or congenital disorder at delivery and at 6 weeks by a Neonatologist. Data obtained was recorded and analyzed using IBM Statistical Package for Social Sciences (SPSS) Version 20. Simple tables were used to display frequencies and percentages. NT value ≥the 95th percentile was assigned as increased NT. The fetuses were categorized into normal and increased NT. Chi-squared and Fisher's exact tests were used for categorical variables while student *t*-test was used for continuous variable.

Results

Two hundred and seventy women were recruited into the study. Of these, 3 voluntarily withdrew following the first-trimester scan while 2 were lost to follow-up. Data analysis was done for the 265 women who fully participated in the study.

The age of the mothers ranged between 18 and 40 years with a mean age of 28.1 (5.1) years. While most of the women were para 1–4 (55.9%), modal parity was para 0 [Table 1].

The nuchal translucency measurements ranged between 0.4 and 5.0 mm with a mean NT of 1.8 (0.8) mm. Only 8 (3.0%) fetuses had NT ≥3.3 mm which was the 95th percentile in this study. In 106 (40%) of the women, the NT scan was performed at a gestational age of 12 weeks, while 4 (1.5%) of the women were scanned at 11 weeks. Increased NT was not associated with 11–13 weeks 6 days gestational age (P = 0.80) [Table 2].

The majority 255 (96.2%) conceived the pregnancy spontaneously, 8 (3.0%) conceived following ovulation induction with clomiphene citrate, and 2 (0.8%) had *in vitro* fertilization and embryo transfer. When the increased NT was compared with the mode of conception, there was no statistically significant relationship between the two (P = 0.35, 95% C1 = 0.22–0.51). Mean NT in males and females was 2.2 (0.2) mm and 2.1 (0.1) mm. There was no significant difference between the NT of the sexes (P = 0.85, 95% CI = 0.66–0.95).

The majority of the patients 254 (94.3%) at the time of presentation for the NT scan had no complaint. However, 11 (4.2%) complained of vaginal bleeding and of these 4 (1.5%) showed increased NT. There was a statistically significant relationship between vaginal bleeding and increased NT (P < 0.001, 95% CI = -0.002–0.003).

Anomaly scan was done for 263 mothers. Two women had missed miscarriages at 15 and 18 weeks, respectively. The anomaly scan revealed 5 (1.9%) cases of congenital anomalies [Table 3]. 2 (0.8%) babies had ventriculomegaly and polycystic kidney, respectively, while 3 (1.1%) had multiple congenital anomalies. The anomalies seen were spina bifida, anencephaly, and ventricular septal defect in two babies, while 1 baby had spina bifida, ventricular septal defect, and duodenal

Table 1: Sociodemographic characteristics of the participants

Sociodemographic characteristics	Frequency	Percentage
Age		
15-19	10	3.8
20-24	59	22.3
25-29	86	32.4
30-34	76	28.7
35-39	31	11.7
40-44	3	1.1
PARITY		
0	81	30.6
1-4	147	55.5
≥5	37	13.9
Total	265	100

Table 2: Gestational age at NT scan

Gestational age (weeks)	NT <3.3	≥3.3	*P*	CI
11^{+0}-11^{+6}	80 (30.2%)	4 (1.5%)	0.80	0.55-0.91
12^{+0}-12^{+6}	103 (38.9%)	3 (1.1%)		
13^{+0}-13^{+6}	74 (27.9%)	1 (0.4%)		
Total	257 (97.0%)	8 (3.0%)		

Table 3: Fetal outcome

System	Anomaly at scan	Frequency	Outcome	Anomaly after birth	NT (mm)
Cardiovascular	Ventricular septal defect	3	TOP*	TOP*	4.6
Gastrointestinal	Duodenal atresia	1	Delivery, Early neonatal death		3.8
CNS	Ventriculomegaly	2	TOP*	Hydrocephalus	4.1
	Anencephaly	1			
	Spina bifida	3			
Skeletal		1	Delivery	Polydactyl	2.3
Renal	Polycystic Kidney	1	Delivery	Polycystic kidney	4.8

*Termination of Pregnancy

atresia. There was a statistically significant association between the congenital anomalies and increased NT ≥3.3 mm ($P < 0.001$, 95% CI = - 0.000 – 0.006). It is worthy to note that all the fetuses that had congenital anomalies showed NT measurement greater than 3.3 mm.

The 2 babies with spina bifida, anencephaly, and ventricular septal defect had early fetal demise and the pregnancies were terminated while the two fetuses with ventriculomegaly and polycystic kidney were delivered with congenital hydrocephalus and polycystic kidney disease at birth, respectively, and 1 baby with a normal NT measurement had only polydactyl. The baby with duodenal atresia was delivered at term, however, died 5 days post-delivery. Of the eight babies with increased NT >3.3 mm, 3 (1.1%) of them were delivered grossly normal.

Discussion

The mean maternal age from this study was 28.1 (5.1) years while the majority (32.4%) of the patients were within the reproductive age group of 25–29 years. When compared to the study from Lagos, Nigeria, the proportion of women above the age of 34 years in this study is 12.9% while it is far more than the 4.9% recorded from Lagos.[9] This could be due to different socioeconomic background of the study areas. Although every woman is at risk of chromosomal abnormalities, the risk is high with increasing maternal age.[10] Multiparous women made up 55.4% of the study participants. This is not surprising because the previous obstetric experience has been shown to be a factor that may make a woman more willing than one without prior exposure, to present herself for scanning.[11]

The prevalence of increased nuchal translucency above the 95th percentile (3.3 mm) in this study was 3%. This is similar to the prevalence of 3.3% reported by Oluyede *et al*. at Lagos, Nigeria,[9] though at 2.5 mm as the 95th percentile. Tahmasebpour *et al*. also had similar findings of 3.4 mm as the 95th percentile.[12] Cardiac and extracardiac defects have been found in karyotypically normal fetuses with NT >3.3 mm.[13] All the fetuses with congenital anomalies found in this study have NT greater than 95th percentile. Screening using NT scan can identify significant number of fetuses with congenital anomalies.

The majority (96.2%) of the women in this study achieved pregnancy spontaneously. The mode of conception has not been found to be related to NT measurement in this study. This is in contrast to findings by Maymon *et al*., where they found a small but significant increase in nuchal translucency among women who had assisted conception.[14] The difference may be explained by the small sample size in this study as only 2 (0.8%) had assisted conception. There was a mild but insignificant increase in NT measurements in males when compared to females in this study. This was similar to findings by Douke *et al*.[15] and Ajayi,[16] though it has been shown that the mild increase may be normal in males but abnormal in female fetuses.

5 (1.9%) cases of anomalies were detected during the anomaly scan and all had increased NT scan >3.3 mm. The increased NT is found to be significantly associated with congenital anomalies in this study. Extensive studies from different regions have clearly shown a significant relationship between increased NT and congenital anomalies. The prevalence of fetal defects increases exponentially with increase in NT measurements.[1,6] Congenital cardiac and great arteries defect are among the most common anomalies seen on ultrasonography.[1] In this study, cardiac anomaly and spina bifida were the most common anomaly detected with a prevalence of one point one percent or 11/1000. However, this may be an underestimate since fetal echocardiography was not offered to other women with increased fetal nuchal translucency without anomaly. Higher prevalence rate 2.6/1000[17] and 3.5/1000[18] were reported by Bahado-Singh *et al*. and Mavrides *et al*., respectively, while a lower rate 0.6/1000 was reported from Tehran.[12] Furthermore, the prevalence in this study was lower than 19.1/1000[6] and 17/1000[19] by Atzei *et al*. and Hyett *et al*. respectively. The difference

in prevalence may be due to different environmental and genetic factors. Sample size may have also had an effect on the prevalence in this study as the other studies used a larger sample size over a longer time period. The study from Lagos, Nigeria did not include congenital anomalies as variables.

There were 13 (4.9%) cases of miscarriages; 2 (0.8%) were missed miscarriage which occurred in fetuses with normal NT measurements. There was no statistically significant difference between a miscarriage and increased NT in this study. This is contrary to findings by Cheng *et al*.[20]

Among the babies with anomalies, three of the pregnancies were terminated in 2nd trimester due to early fetal demise, while one was delivered by elective CS due to congenital hydrocephalus. There was a significant relationship between increased NT and congenital anomalies at birth but there was no relationship with morbidity after birth. Different studies have highlighted the relationship between NT measurements and congenital anomalies and other neonatal morbidities.[3,6,9,12,13,17-21]

With effective antenatal care, training of professionals, and provision of proper 2D ultrasound scan machine in our environment, NT scan as a screening test for major anomalies or aneuploidies can be feasible in our environment.[21,22] Combined test with nasal bone and tricuspid valve or ductus venosus flow increases the detection rate to up to 96% with a false positive rate of less than 3%.[22] However, combined first-trimester screening and noninvasive prenatal screening have a higher detection rate than NT alone as screening tests for fetal chromosomal anomaly.[22,23]

Conclusion

From our study, the prevalence of increased fetal nuchal translucency is relatively high in our environment and is associated with major congenital fetal defects. The most common congenital defects seen are spinal bifida and ventricular septal defect. Effective antenatal care services will improve maternal uptake of fetal anomaly screening while routine screening with first-trimester ultrasound will help to detect major congenital anomalies early in a resource constraint setting.

Acknowledgment

The authors acknowledge the financial support from the Usmanu Danfodiyo University Teaching Hospital and Zefafi Specialist Women Hospital.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

This Study was partly sponsored by Usmanu Danfodiyo University Teaching Hospital.

Conflicts of interest

There are no conflicts of interest.

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