Original Article

Nuchal Translucency in Pregnant Women Beyond 35 Years and its Relation to Congenital Cardiac Abnormalities: A Cross-Section Study

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ABSTRACT

Objective: To evaluate the relation between elevated Nuchal Translucency (NT) and fetal cardiac anomalies.

Patients and Methods: Referred patients to fetal medicine units of three centers in Egypt in the first trimester due to elevated NT were involved for reassessment and counseling. Chromosomally abnormal fetuses were excluded. Fetal echocardiography was done at 18-22 weeks of gestation to evaluate fetal heart abnormalities. Follow up or termination was done according to results obtained from echocardiography. Obstetrical and neonatal outcomes were reported.

Results: Nine cases (25.7%) had normal NT while 26 (74.3%) had increased NT. The mean age was 39.1 ± 2.2 years, with positive consanguinity in 8 (22.9%) of cases. There were 5 cases with abnormal karyotyping that were excluded. Echocardiography was normal in 15 (71.4%) cases while abnormalities were found in 6 (28.6%) cases. Obstetrical and neonatal outcomes were better in cases with normal than cases with abnormal echocardiography.

Conclusion: Better obstetrical and neonatal outcomes were found in cases with increased NT with normal echocardiography while poor outcomes were found in the abnormal findings and early termination of such cases is recommended.

Key Words: Congenital heart disease, fetal anomalies, karyotyping, nuchal Translucency.

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INTRODUCTION

Between 10 and 14 weeks of human gestation, ultrasound examination of fetal nuchal translucency (NT) is an essential consideration of first-trimester screening for trisomy 18, trisomy 13, and trisomy 21[1].

Elevated NT has been linked to a variety of pathologic diseases, involving structural fetal anomalies, cardiac anomalies, an increased incidence of miscarriage, and intrauterine mortality. Case-series studies, on the other hand, have shown that a significant majority of fetuses with elevated NT during the first trimester had no abnormalities and excellent neonatal outcomes[2,3].

Elevated nuchal translucency (NT) in fetuses with a typical karyotype is related with a higher risk of fetal structural malformations, most often congenital heart defects (CHDs)[4], and the risk of CHD rises dramatically with rising NT[5,6].

The widespread use of NT screening has led to a deeper examination of first- trimester cardiac structure in screening populations, allowing for the discovery of significant CHDs earlier. Furthermore, the present study aims to assess the relation between increased NT in pregnant women beyond 35 years carrying chromosomally normal fetuses and detect any correlation between increased NT and CHD.

PATIENTS AND METHODS

Study design and setting

This study is a cross-sectional multicenter study. The study was performed at fetal medicine units of Obstetrics and Gynecology departments of Tanta and Benha Universities, and at Alnamoury fetal center. The study was performed in the period from June 1, 2021 to December 31, 2022.

Patients

Referred patients (n=35) to the three fetal medicine units had increased NT for first-trimester reassessment and counseling. Participants were selected in accordance with inclusion and exclusion criteria. The inclusion criteria are:

i. age ≥35 years,

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ii. gestational age of 11-13 weeks,

iii. no history of previous malformed baby or chromosomal abnormality. The exclusion criteria were: (i) chromosomally abnormal fetuses (ii) patients with diabetes mellitus, liver or cardiac disease, (iii) Twins or higher older pregnancies (iv) patients declined to participate in the study.

Intervention

We used 3 high resolution devices in our study according to operator preference and availability of machines. We DC-70 EXP, Mindray, Sonoscape P30pro and Voluson P8 in examination of included patients in the current study. Trans-abdominal scans were done to measure the CRL and the NT at 11-13+6 weeks. The maximum thickness of the sonolucent zone (fluid accumulation) between the inner aspect of the fetal skin and the outer aspect of the soft tissue overlaying the cervical spine or the occipital bone was assessed to determine nuchal translucency. Measurements must be done from inner border of the horizontal line placed on defining lines of NT thickness. The caliper should be merged with the white line of NT border, not inside the nuchal fluid. NT is taken at 95 percentiles. Patients with normal NT were discharged and provided routine antenatal care with no further testing. The patients with increased NT underwent amniocentesis at 15 weeks for karyotyping. Further fetal echocardiography was done at 18-22 weeks.

Patients' allocation

Patients were allocated into two cohorts; the first group involved cases with normal fetal echocardiography and the second group involved cases with abnormal fetal echocardiography.

Study parameters

Maternal demographic characteristics, sonographic reassessment at 11-14 weeks, abnormal fetal echocardiography were recorded. Follow up of all patients until delivery and pregnancy outcomes were recorded. Any adverse outcomes such as termination of pregnancy (TOP), preterm birth or delivery of a child with anatomical abnormalities were recorded. Neonatal morbidity and mortality were recorded.

Ethical approval and study registration

This research was approved by the ethical committee of Tanta University and obtaining an informed consent from all of the participants.

Statistical methods

Data were analyzed using SPSS version, 18 (USA, Chicago). The tests used were mean, standard deviation, range, number and percentage. Non- parametric tests were utilized. *P-value* of ≤0.05 is regarded significant.

RESULTS

Refereed cases (n=35) to fetal medicine units in both universities and Alnamoury fetal center were reassessed for increased NT. Patients' flow all through the study is shown in (Figure 1).

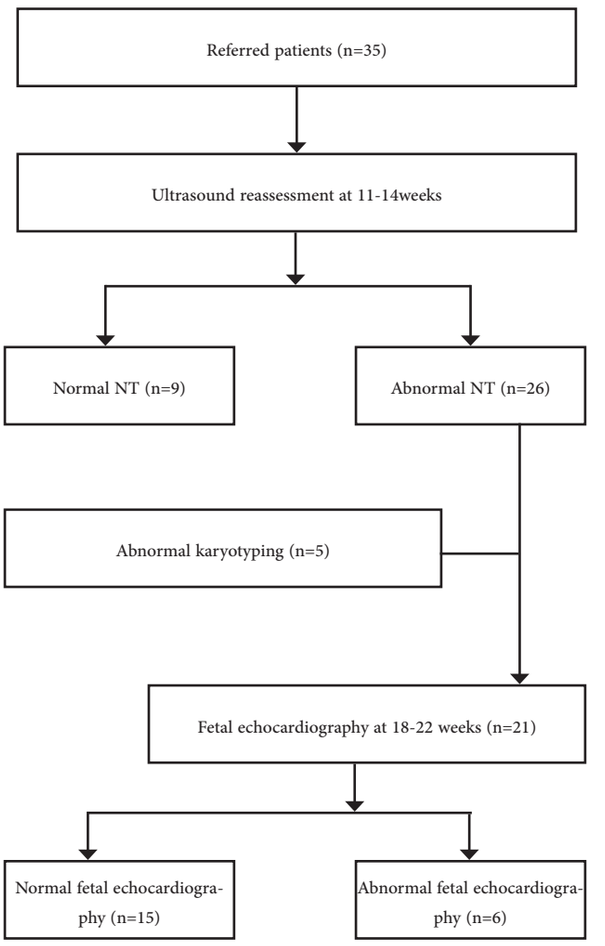

Fig. 1: Flow chart of patients through the study (n=35)

The demographic data of included cases were shown in table 1. The mean age was 39.1 ± 2.2 years, the median parity was 3 (range 2-4), the mean BMI was 24.6 ± 3.1. Consanguinity was present only in 8 (22.9%). The mean of gestational age at first examination was 12.4 ± 0.6 weeks. Data of first ultrasound examination were presented in (Table 1).

Table 1: Demographic data of enrolled patients (n=35)

Age (yrs)	Range	36-45
	Mean ± SD	39.1 ± 2.2
Parity	Range	2-4
	Median	3
BMI (kg/m^2)	Range	18.4-31.3
	Mean ± SD	24.6 ± 3.1
Consanguinity	Yes	8 (22.9%)
	No	27 (77.1%)
Gestational age at first examination	Range	11.2-13.6
	Mean ± SD	12.4 ± 0.6
First trimester US examination	CRL (mm) Range	15-79
	CRL (mm) Mean ± SD	58.7± 13.9
	NT (mm) Range	0.8-36
	NT (mm) Median	3.5
	Normal (n,%)	9 (25.7%)
	Abnormal (n,%)	26 (74.3%)
Amniocentesis (Abnormal karyotyping)		5 (14.3%)
Fetal echocardiography at (18-22) weeks (n=21)	Normal (n,%)	15 (71.4%)
	Abnormal (n,%)	6 (28.6%)

Nine cases (25.7%) had normal NT and received ordinary antenatal care with no further testing while 26 (74.3%) had increased NT as shown in (Figure 2). Furthermore 5 (14.3%) cases had abnormal karyotyping and were excluded. Abnormal fetal echocardiography was detected in 6 (28.6%) of remaining cases. Results of abnormal echocardiography were shown in (Figures 3,4,5).

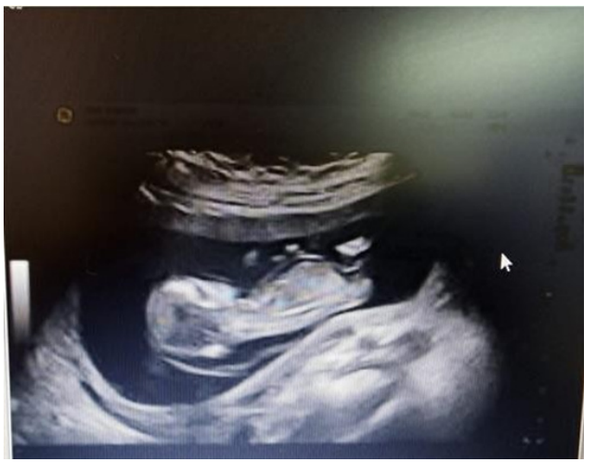

Fig.2: Abnormal NT in 12 weeks embryo.

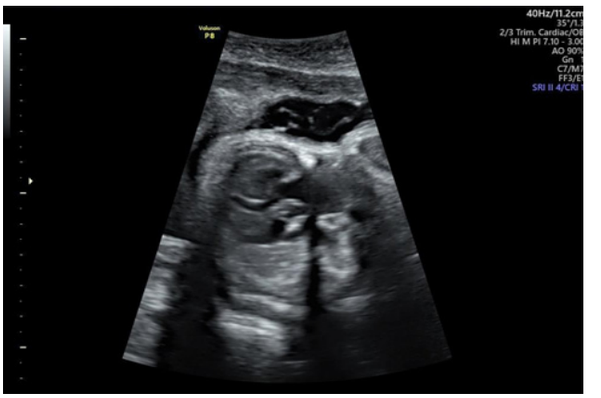

Fig. 3: Results of fetal echocardiography at 18-22 weeks. There is hypertrophic cardiomyopathy (HCM), ultrasound scan shows thickened hypertrophic left and right ventricles with limited contractility.

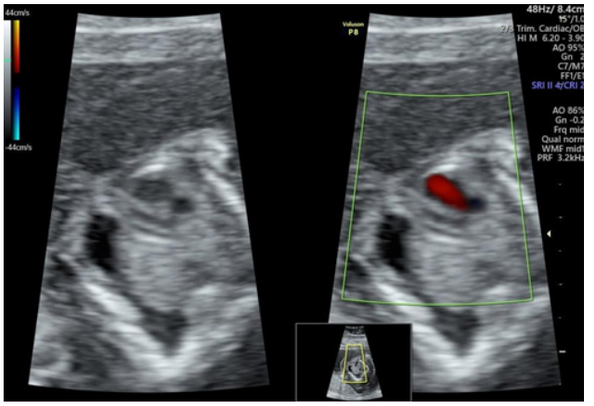

Fig. 4: Results of fetal echocardiography at 18-22 weeks. Ultrasound shows hypoplastic left heart syndrome with ventricular discordance and absent left ventricular filling.

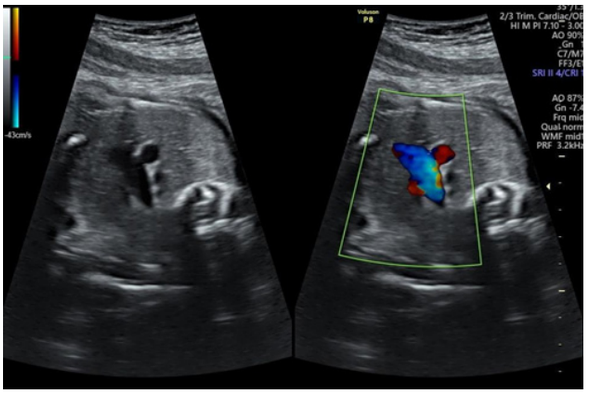

Fig. 5: Results of fetal echocardiography at 18-22 weeks. Ultrasound shows TGA: 3 vessels view show only the aorta as it becomes the more anterior great vessel in TGA cases.

Comparison of obstetrical and neonatal outcomes was shown in (Table 2). Termination of cases with abnormal NT and abnormal echocardiography was noticed in 4 (66.7%) while no cases with normal echocardiography were terminated (p<0.001). The mean gestational age at termination was 28.5±3.2 weeks.

Regarding course of pregnancy, preterm delivery was notice in 7 (46.7%) cases in normal echocardiography group while preterm birth occurred in 2 (33.3%) cases in the abnormal echocardiography group (p=0.584). On the same side, full term birth was present in 8 (53.3%) in normal echocardiography group while no full term cases in the abnormal echocardiography group (p=0.026). The mean gestational age at delivery was 36.5±1.0 weeks in normal echocardiography group while 35.5±0.5 weeks in the abnormal echocardiography group (p=0.032). Delivery mode whether cesarean or vaginal was not significantly different in both groups (p=0.172).

Table 2: Obstetrical and neonatal outcomes of enrolled patients (n=21)

	Normal fetal Echocardiography (n=15)	Abnormal fetal Echocardiograph y (n=6)	Test of significance	*P.value*
Fate of pregnancy Termination				
Continuation of (n,%) pregnancy (n,%)	0 (0.0%) 15 (100%)	4 (66.7%) 2 (33.3%)	11.772	<0.001
Gestational age at termination Mean±SD	----------	28.5±3.2	-------	------
Course of pregnancy				
Preterm (n,%) Full tem (n,%)	7 (46.7%) 8 (53.3%)	2 (33.3%) 0 (0.0%)	0.299 4.918	0.584 0.026
Gest. age at delivery Mean±SD	36.5±1.0	35.5±0.5	-2.311	0.032
Mode of delivery				
Vaginal (n,%) Cesarean (n,%)	5 (33.3%) 10 (66.7%)	4 (66.7%) 2 (33.3%)	1.859	0.172
Neonatal examination				
Healthy Anomalies (n,%)	15 (100%) 0 (0.0%)	0 (0.0%) 6 (100%)	20.00	< 0.001
Neonatal ICU admission (n,%)	9 (60 %)	4 (66.67&)	0.078	0.780
Neonatal mortality	2 (13.3%)	6 (100.0%)	13.013	<0.001

Neonatal outcomes were better in group with normal echocardiography where all cases were healthy with no congenital anomalies while all cases in the abnormal echocardiography group had congenital anomalies. Admission to neonatal ICU was non-significantly different in both groups (p=0.780). Neonatal mortality was almost in all cases in the abnormal echocardiography group while noticed in 2 (13.3%) cases of the normal echocardiography group.

DISCUSSION

Fetal structural anomalies are present in 3% of pregnant women based on routine scanning and correlation to clinical and demographic characters. Early detection of these anomalies provides parents with perinatal management and give them chance for further screening test and genetic examination. These facilities make obstetrician able to give them an idea about prognosis and management options[7].

Major abnormalities might be easily diagnosed in the first trimester such as hydrocephalus, anencephaly and omphalocele while cardiac anomalies and chromosomal abnormalities need further testing and other diagnostic tests. Usually congenital anomalies are linked to familial psychological upsets, financial and social burdens and the desire to terminate pregnancy do exist in some cases[3,8,9].

In the current study, there was 9 (25.7%) that had normal NT denoting that some cases may had false diagnosis of increased NT and should be reassessed before taking any intervention or proceeding to further testing. This could be done at specific fetal medicine units by highly experienced personnel.

Increased NT is one of the reliable markers of trisomy 21 and other trisomies. Elevated NT is also related to other major abnormalities like heart anomalies omphalocele, diaphragmatic hernia and linked to some syndromes as Noonan syndrome, skeletal dysplasia and spina bifida[10,11].

In the current study we found some anatomical defects associated with the increased NT cases and major cardiac anomalies. The detected lesions were skeletal dysplasia, meningiocele, cystic hygroma and cardiac anomalies.

In the current study we found abnormal echocardiography detecting cardiac anomalies in 28.6% of cases while Grande et al. (2011) reported higher detection of cardiac defects in 57% of cases with raised NT[12]. Another study conducted to evaluate the relation of elevated NT to heart anomalies and they found that cardiac anomalies were found in 9.1% cases at 95th percentile[13].

A recent study conducted by Minnella et al (2020) to assess the relation between raised NT and major cardiac anomalies. They conducted the study on 93 209 pregnancies with no obvious chromosomal defects. They found that 53.6% of cases had major cardiac anomalies. This is greater than the results obtained by the current study due to large sample size in their study[14]. Abnormal left ventricular functions were also noticed in fetuses with increased NT[15].

Regarding the obstetrical and neonatal outcomes, we found that better obstetrical and neonatal outcomes were linked to normal echocardiography while poor outcomes were found in abnormal echocardiography. Petracchi et al. (2019) found poor outcomes with increased rate of termination and miscarriage in cases with increased NT above 4.5 mm[16]. Another study conducted by Tahmasebpour et al. (2012) where poor pregnancy outcomes (abortion and fetal anomalies) were noticed in 25% of cases with increased NT[17].

Lithner et al. (2016) investigated pregnancy outcomes in cases with increased NT ≥3.5mm. They found that the most common defects were cardiac defects and poor pregnancy outcomes were linked to increase NT even with normal chromosomal study[18]. Similar results were obtained by Shakoor et al. (2017)[19], Äyräs et al. (2013)[20].

Another important issue was to give proper counseling for those patients with increased NT. Most cases with normal echocardiography had good obstetrical and neonatal outcomes. On the other hand, cases with abnormal echocardiography should be counseled for termination of pregnancy as obstetrical and neonatal outcomes were very poor and neonatal death was present in all cases. Similar study by Bilardo et al. (2010) stressed on the importance of counseling and assurance of cases with increased NT as the pregnancy outcomes were good with no developmental delay in later years[21].

Limitations of this study were the inter-observer variations in measurement of NT, presence of different devices of ultrasound, small sample size and the high cost of amniocentesis and chromosomal study. The lack of control group in the current study is another weakness point plus loss of some patients as most patients were referred. Data of lost patients were obtained from their referring obstetricians.

CONCLUSIONS

Elevated NT in first trimester is related to heart anomalies and other anomalies. It is better to counsel cases with increased NT and cardiac or other anomalies for termination as early as possible as mortality was found to be inevitable in such cases. On the other hand, we recommend continuation of pregnancy in patients of elevated NT with normal echocardiography and normal anomaly scan as prognosis is good in most cases.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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