Original research article

Nuchal Translucency as an Indispensable Screening Tool for Predicting Congenital Heart Diseases

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Abstract

The aim of this study was to investigate the accuracy of the Nuchal translucency (NT) measurement between 11 and 13 weeks and 6 days of gestation as a marker to screen for congenital heart defects (CHD). 100 pregnant female patients who had come for routine antenatal scan were studied in a time period of 6 months in their later first trimester (12 to 14 weeks) and the nuchal translucency was measured. NT measurement was performed using philips affinity 70g machine in the first trimester examination. The cases were followed up to one month postpartum to assess the presence of CHD.A progressive increase in the prevalence of CHD according to the NT values obtained in the examination was observed. The relationship between NT size and major cardiac defects was analyzed, and it was found that the incidence of cardiac defects increased along with NT size. In sample, the use of NT as a screening method for CHD showed a low sensitivity –of 20% when the 95th percentile was used as the cut-off point. However, the specificity of the method was high - 99.4% for the 4.0 mm cut-off point. The negative predictive value was always above 99% at the different cut-off points. Evaluation of the nuchal translucency should be considered during the first trimester ultrasound as increased NT is associated with a spectrum of fetal abnormalities and chromosomal defects.

Key words : Nuchal translucency, Congenital Heart Diseases, Screening Tool

Introduction

The nuchal translucency is defined as a transient subcutaneous collection of fluid behind the fetal neck seen on ultrasonography at 11-14 weeks of gestation [1]. The 95th percentile for NT measurement increases with gestational age between week 11-14 of gestation and is around 2.5 mm depending on crown rump length, whereas the 99th percentile is 3.5 mm, and decreases after week 14 of gestation along with the reduction of the placental resistance and the beginning of the renal function [2,3]. Fetal cardiology it is a specialty that continues to evolve rapidly for pediatric cardiologists and fetal medicine specialists. In this current overview it was observed the relationship between increased nuchal translucency (NT) and fetal heart structure and function in chromosomally normal fetuses. Fetuses with an increases NT have an increased risk for congenital heart disease (CHD), and this risk increases with increasing NT measurement. The combination between an increases NT, tricuspid regurgitation (TR) and an

abnormal ductus venosus (DV) Doppler flow profile is a strong marker for CHD and should be followed by a fetal echocardiogram at 20 weeks of gestation in fetuses with an Nt > 95th percentile, and also if it is found an increased Nt associated with a tricuspid regurgitation or an abnormal DV flow pattern, or when the Nt measurement is over 99th percentile, it is indicated an earlier echocardiogram and a repeat scan around 20 weeks of gestation. An increased NT is not only a marker for chromosomal anomalies but also a nonspecific one for disturbance in normal early development. CHD are the most common structural and genetic disorders observed in normal karyotype fetuses with an enlarged NT [4,5,6]. Cardiac malformations are among the most common congenital abnormalities. They account for most deaths from congenital defects in childhood. The prevalence is 4 – 8 per 1000 live births [7-10]. Lethal cardiac defects and those requiring intervention within the first year of life are usually classified as major [11]. The estimated prevalence of major congenital heart malformations is 4 per 1000 live births . Prenatal detection of congenital heart malformations is currently based on examination of the four-chamber view of the heart at a second trimester routine ultrasound examination. Measurement of fetal nuchal translucency thickness (NT) in the late first trimester has become an established method of identifying fetuses at risk of aneuploidy [12,13]. Increased NT may also be associated with structural fetal malformations, among them congenital cardiac malformations [14,15] . It has even been suggested that NT measurement can be used as a screening tool for fetal cardiac defects . The aim of this study was to investigate the accuracy of the nuchal translucency (NT) measurement between 11 and 13 weeks and 6 days of gestation as a marker to screen for congenital heart defects (CHD).

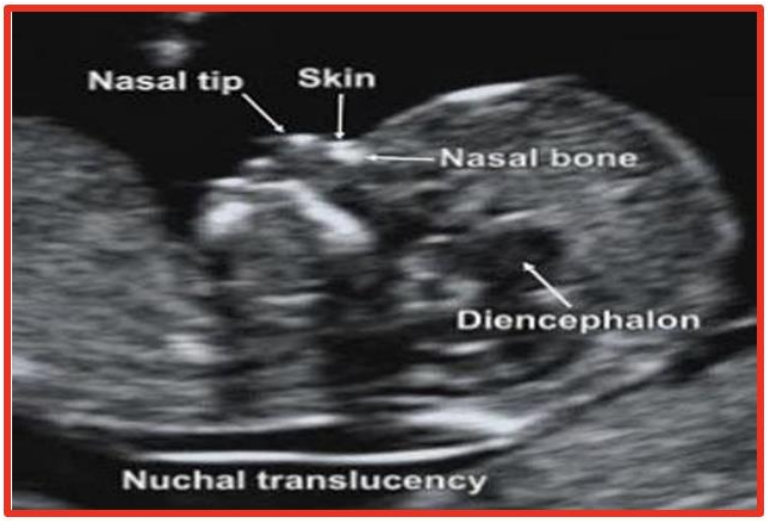

Diagram 1 : Ultrasonogram of 11 week old fetus showing measurement of crown-rump length and fetal nuchal translucency thickness

Material and Methods

100 pregnant female patients who had come for routine antenatal scan were studied in a time period of 6 months in their later first trimester (12 to 14 weeks) and the nuchal translucency was measured. NT measurement was performed using PHILIPS Affinity 70 G machine in the first trimester examination when the fetal crown-rump length (CRL) was between 45 to 84 mm. The cases were followed up to one month postpartum to assess the presence of CHD.

Sonographic criteria to maximize quality of nuchal translucency sonography :

- Gestation should be limited to between 10 weeks 3 days and 13 weeks 6 days.
- Fetus should be examined in a mid-sagittal plane.
- Fetal neck should be in a neutral position.
- Fetal image should occupy at least 75% of the screen.

- Calipers should be placed on the inner borders of the nuchal fold, perpendicular to the long axis of the fetal body.
- At least three nuchal translucency measurements should be obtained, with the mean value to be used.

Results

A progressive increase in the prevalence of CHD according to the NT values obtained in the examination was observed. The relationship between NT size and major cardiac defects was analyzed, and it was found that the incidence of cardiac defects increased along with NT size; the prevalence was negligible with a normal NT, it increased to 1 per 50 with an NT of 4.5 to 5.4 mm, and 2 per 50 with an NT 5.5 mm. Cardiovascular anomalies are the most frequently encountered defects in chromosomally normal fetuses with increased NT. Early fetal echocardiography and anomaly scan should be considered in these fetuses.

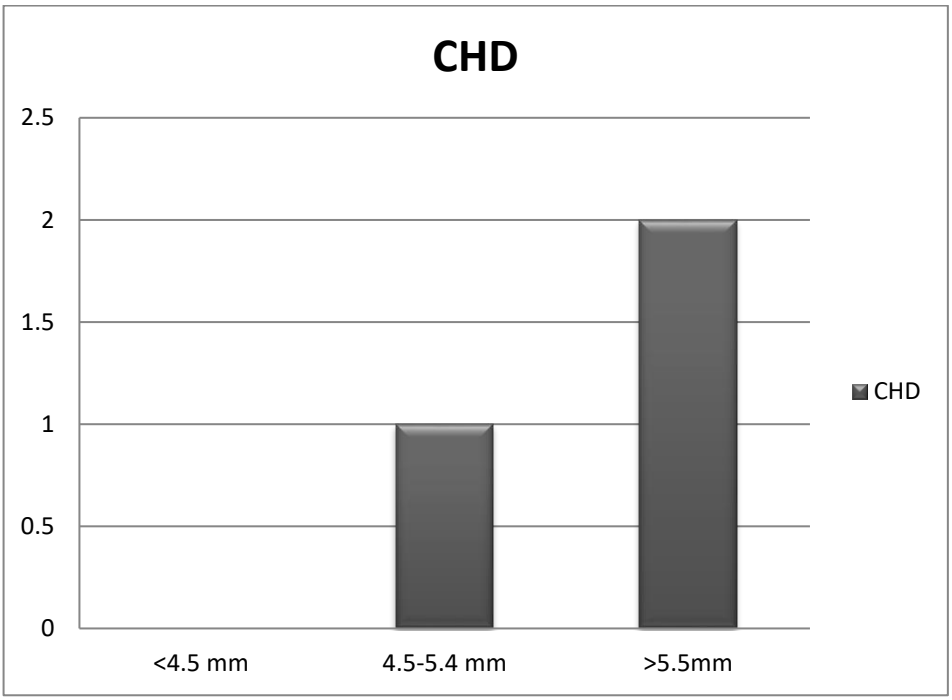

Fig 1 : CHD cases per 100 patients according to NT measurement

The above Figure shows that incidence of CHD increases with increasing Nuchal translucency.

Table 1: Absolute NT values

	n	**Minimum(mm)**	**Maximum(mm)**	**Median(mm)**
With CHD	3	0.9	5.1	3.5
Without CHD	97	0.5	1.3	1
Total	100	0.5	2.1	1.2

Median NT was 3.50 mm for the cases with CHD, and 1.0 for the non-CHD group;this difference was statistically significant.

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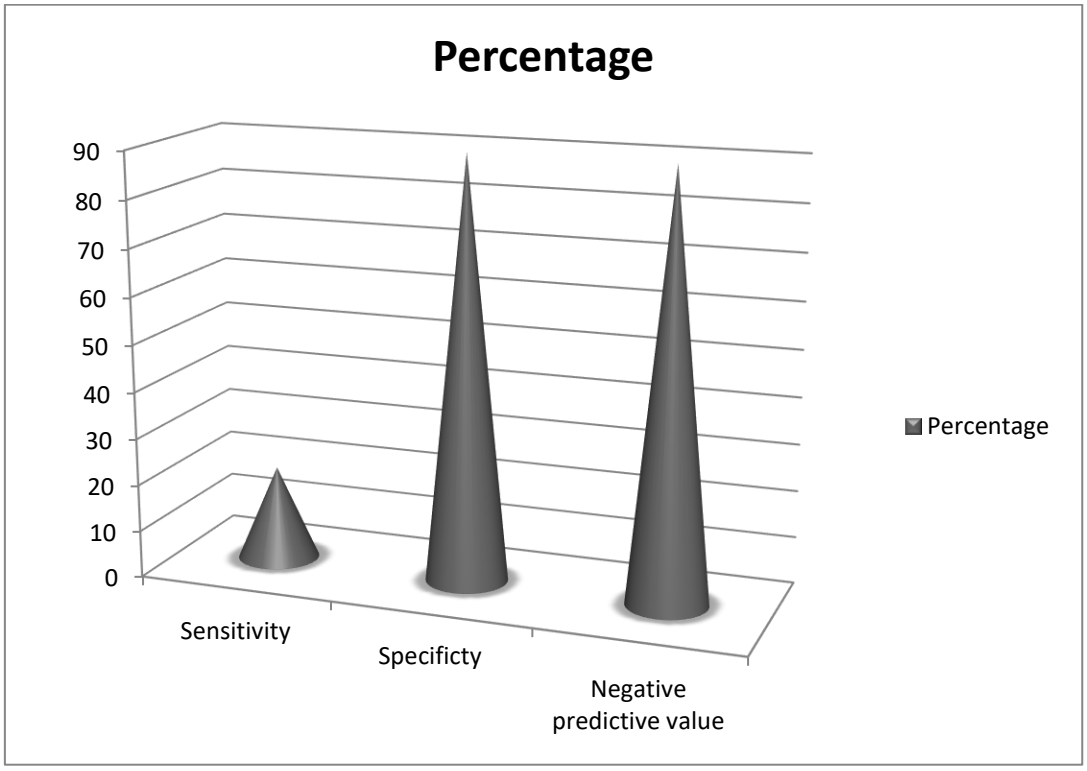

Fig 2 : NT as a screening tool

The above bar graph shows the low sensitivity, high negative predictive value and specificity of NT for screening of CHD.

CHDs are uncommon among the low risk population, with an incidence lower than 1%. Thus, the test would likely have a greater impact for groups at high risk for CHD, such as mothers who already had a child with CHD or for mothers with CHD, whose recurrence risk may reach 5%-10%. In cases in which the CHD is part of a genetic syndrome, the risk of recurrence is equivalent to that attributed to the risk of recurrence of the genetic disease. However, it would not exclude the need for a thorough assessment using fetal echocardiography.

Discussion

Hyett et al. [16] reported that in a cohort of 29154 pregnancies, 56 % of the fetuses with major CHD had an increased NT measurement. It was observed an increased prevalence of CHD associated with increased NT thickness. The NT measurement could be the first screening step in the detection of CHD. NT screening is only a modest efficient strategy for detecting all cHD when is used alone, but may be effective in detecting specific CHD likely to benefit from prenatal diagnosis. In a meta-analysis including 58492 fetuses, Makrydimas et al. [17] found that a NT measurement > 99th percentile had a sensitivity of 31 % and specificity of 98.7 % , with a positive likelihood ratio of 24 for the diagnosis of major CHD. A sensitivity of 37 % and specificity of 96.6 % was found using the 95th percentile cut-off. Simpson et al. [18] found a sensitivity of only 15.4 % using 2.0 multiples of the median (MoM) in a prospective study of

34622 fetuses, but their low detection may be explained by the exclusion of the septated cystic hygroma. If they had included the septated cystic hygroma , their detection of the CHD would have been 35,3 % [19]. The median NT thickness is significantly higher in fetuses with major CHD compared to those with normal hearts [20]. the median age for CHD diagnosis was 16.1 weeks of gestation when Nt was > 3.5 mm compared to 22.1 weeks of gestation when was < 3.5 mm [21]. the frequency of cHD varies from 0.6-5 % when the Nt is between 2.5 – 3.5 mm, to 64 % when the NT measurement is above 8.5 mm [22-24].

In our sample, the use of NT as a screening method for CHD showed a low sensitivity of 20% when the 95th percentile was used as the cut-off point. However, the specificity of the method was high 99.4% for the 4.0 mm cut-off point. The negative predictive value was always above 99% at the different cut-off points. The association between any form of CHD (isolated or a group that could induce a similar hemodynamic alteration) and increased NT could not be determined. The very high specificity and negative predictive values qualify the examination as an important tool to reassure parents, because the likelihood of heart disease in the presence of a normal NT is very low, less than 1%.

The CHDs described in the literature in fetuses with an increased NT include septal defects and right and left obstructive lesions (both inflow and outflow) and other complex lesions. Isolated totally abnormal pulmonary venous drainage was only found once in the 568 fetuses described with CHDs and an increased NT in these studies. This may purely be due to the low incidence of this defect or, alternatively, it may provide insight to a patho-physiological process linking the increased NT and CHDs. Over the years several hypotheses have been forwarded regarding the underlying mechanism linking the increased NT and CHDs. These include flow disturbances in the neural crest (Harh et al., 1973; Stekelenberg et al., 2003; Sedmera et al., 2005), narrowing of the aortic isthmus causing excessive fluid accumulation in the first trimester (Hyett et al., 1995A), transient cardiac failure (Hyett et al., 1995) and venous congestion together with venous compression (Johnson et al., 1992). Recently, it has been suggested that a delay or disturbance in the development of lymphatic vessels in the neck may explain the excessive nuchal fluid accumulation (Haak et al., 2002). A possible, all inclusive, scenario linking the increased NT and CHDs could be an environmental insult at 6-8 weeks gestation plus the influence of chromosomal and genetic factors causing fluid collection with subsequent disturbances in hemodynamics and lymphoangiogenesis resulting in the increased NT and CHD (Allan, 2006; Haak et al., 2002).

This study has several limitations including a small sample size in comparison to other studies, which can be due to the referral of participants by gynecologists. It might be possible that pregnant women with a sonography indicating an increase in NT thickness do not refer for echocardiography. Another limitation is that due to performing NT sonography by various urologists, NT is reported in different values, which can lead to distortion in decision making and final conclusion. Further studies with larger sample sizes should be selected, and in fetuses with NT greater than the 99th percentile, echocardiography should be performed earlier. In addition, it is recommended that when NT thickness is between 2.5 and 3.5 mm, fetal echocardiography should be repeated during the following weeks.

Conclusion

Evaluation of the nuchal translucency should be considered during the first trimester ultrasound ,as increased NT is associated with a spectrum of fetal abnormalities and chromosomal defects. An NT of 3.5 mm or more should be considered significant and warrants further investigations by serum markers, depending upon the gestational age. Despite the low sensitivity of the test,

increased NT is an important risk factor for CHD, and should be included in the strategy of prenatal screening for these diseases.

References

1. Nicolaides K.H., Azar G., byrne D., Mansur c. & Marks K. (1992). Fetal nuchal translucency: ultrasound screening for chromosomal defects in first trimester of pregnancy. BMJ. 304, 867 – 869
2. Pajkrt E., bilardo c.M., van Lith J.M.M., Mol b.W.J. & bleker O.P. (1995). Nuchal translucency measurement in normal fetuses. Obstet Gynecol. 86, 994 – 997
3. Pandya P.P., Snijders r.J.M., De Johnson S.P., Luordes N.M. & Nicolaides K.H. (1995). Screening for fetal trisomies by maternal age and fetal nuchal translucency thickness at 10-11 weeks of gestation. Br J Obstet Gynaecol. 102, 957 – 962
4. bilardo cM , Muller MA , Pajkrt E , clur SA , van Zalen MM , Bijlsma EK . 2007 . Increased nuchal translucency and normal Karyotype : time for prenatal reassurance . Ultrasound Obstet Gynecol 30 : 11 – 18 .
5. Souka A.P., Von Kaisenberg c.S., Hyett J.A., Snoek J.D. & Nicolaides K.H. (2005). Increased nuchal translucency with normal karyotype. Am J Obstet Gynecol. 192, 1005 – 1021
6. Westin M., Saaltvedt S., bergman G., Almstrom H., Grunewald c. & Valentin L. (2007) . by how much does increased nuchal transluncency increased the risk of adverse outcome in chromosomally normal fetuses? A study of 16Is measurement of nuchal translucency thickness a useful screening tool for heart defects? A study of 16260 fetuses derived from an unselected pregnant population. Ultrasound Obstet Gynecol. 29, 150 – 158
7. Mitchell SC, Korones SB, Berendes HW. Congenital heart disease in 56109 births: Incidence and natural history. Circulation 1971;43:323-32
8. Ferencz C, Rubin JD, McCarter RJ, Brenner JI, Neill CA, Perry LW, Hepner SI, Downing JW. Congenital heart disease: prevalence at livebirth. The Baltimore Washington infant study. Am J Epidemiol 1985;121:31-6
9. Carlgren LE. The incidence of congenital heart disease in Gothenburg. Proc Assoc Eur Pediatr Cardiol 1969;5:2-8.
10. Hoffman JI. Incidence of congenital heart disease: I Postnatal incidence. Pediatr Cardiol 1995;16:103-13
11. Buskens E, Grobbee DE, Frohn-Mulder IM, Stewart PA, Juttmann RE, Wladimiroff JW, Hess J. Efficacy of routine fetal ultrasound screening for congenital heart disease in normal pregnancy. Circulation 1996;94:67-72
12. Pandya PP, Snijders RJ, Johnson SP, De Lourdes Brizot M, Nicolaides KH. Screening for fetal trisomies by maternal age and fetal nuchal translucency thickness at 10-14 weeks of gestation. Br J Obstet Gynaecol 1995;102:957-62
13. Snijders RJ, Noble P, Sebire N, Souka A, Nicolaides KH. UK multicentre project on assessment of risk of trisomi 21 by maternal age and fetal nuchal-translucency thickness at 10-14 weeks of gestation. Fetal Medicine Foundation First Trimester Screening Group. Lancet 1998;352:343-6
14. Souka AP,Von Kaisenberg CS, Hyett JA, Sonek JD, Nicolaides KH. Increased nuchal translucency with normal karotype. Review. Am J Obstet Gynecol 2005;192:1005-1021
15. Hyett J, Perdu M, Sharland G, Snijders R, Nicolaides KH. Using fetal nuchal translucency to screen for major congenital cardiac defects at 10-14 weeks of gestation: population based cohort study. BMJ 1999;318.81-5
16. Hyett J., Perdu M., Sharland G.K., Snijders r. & Nicolaides K.H. (1999). Using fetal nuchal translucency to screen for major congenital cardiac defects at 10-14 weeks of gestation: population based cohort study. BMJ. 318, 81 – 85

17. Makrydimas G., Sotiriadis A. & Ioannidis J.P. (2003). Screening performance of first – trimester nuchal translucency for major cardiac defects: a meta-analysis. Am J Obstet Gynecol. 189, 1330– 1335
18. Simpson L.L., Malone F.D., Saade G.r. & D'Alton M.E. (2007). Nuchal translucency and the risk of congenital heart disease . Obstet Gynecol. 109, 1456 – 1457
19. Hyett J., Snoek J. & Nicolaides K.H. (2007). Nuchal translucency and the risk of congenital heart disease. (Letter to editor). Obstet Gynecol. 109, 1455 – 1456
20. Ghi T., Huggon I.C., Zosmer N. & Nicolaides K.H. (2001). Incidence of major structural cardiac defects associated with increased nuchal translucency but normal karyotype. Ultrasoung Obstet Gynecol. 18, 610 – 614
21. Makrydimas G., Sotiriadis A. & Huggon I.c. et al. (2005). Nuchal translucency and fetal cardiac defects: a pooled analysis of major fetal echocardiography centers. Am J Obstet Gynecol. 192, 89 – 95
22. Hyett J. (2004). Does nuchal translucency have a role in fetal cardiac screening? Prenat Diagn. 24, 1130 – 1135
23. Galindo A., comas c. & Martinez J.M. et al. (2003). cardiac defects in chromosomally normal fetuses with increased nuchal translucency at 10 – 14 weeks gestation. J Matern Fetal Neonatal Med. 13, 163 – 170
24. Clur S.A., Mathijssen I.b. & Pajkrt E. et al. (2008). Structural heart defects associated with an increased nuchal translucency: 9 years' experience in a referral center. Prenat Diagn. 28, 347 – 354