ECRONICON OPEN ACCESS

EC GYNAECOLOGY
Research Article

High Nuchal Translucency (NT) with a Normal Karyotype-The Clinical Implications

R Elmidany*, M Zidan, A Al Ibrahim, S Al Obaidly, M Al-Baloushi, N Al Janahi, N Khenyab and Z Al Mansoori

Obstetrics and Gynecology, Women Wellness and Research Centre, Hamad Medical Corporation, Qatar

***Corresponding Author:** R Elmidany, Obstetrics and Gynecology, Women Wellness and Research Centre, Hamad Medical Corporation, Qatar.

Received: June 20, 2019; **Published:** July 12, 2019

Abstract

Objectives: To study the Prevalence of structural and biometry anomalies in those fetuses with High NT and normal karyotype and their outcome.

Methodology: Retrospective research of All the patients seen in Fetal Maternal Unit with High NT and normal Karyotype over five years period from January 2011. The data was collected from the ultrasound software for ultrasound reports, maternal records for maternal biodata and pregnancy progress, and the neonatal records for the neonatal outcomes.

Two groups were created taking the median NT as a cut off (3.4 mm). Data was kept in password-protected Excel sheet. Data analysis was done using the appropriate statistical software with p values of 0.05.

Results: Total of 56 patients with high Nuchal Translucency with normal karyotype. Mean maternal age 31.6 ± 1.6 years. No correlation between maternal age and NT (r -0,02 and p value 0,87). Among the two groups (NT < or > 3.4 mm) there was a significant deference in the rate of associated anomalies at 2nd trimester scan (0 and 27% for NT < 3.4 mm group and NT > 3.4 group; respectively [p value f 0.017]. No significant deference in the rate of miscarriage (0 and 9.4%[p 0.18]), IUGR (8.3 and 13.8% [p 0.57]), preterm labour (4.2% and 10.3% [p 0.75]), gestational age at delivery (38.7 ± 0.6 weeks and 38.2 ± 0.8 weeks [p 0.39]), birth weight (3311.7 ± 249 grams and 3041.4 ± 253 [p 0.13]), NICU admission (4.2% and 20.% [p 0.19]) or neonatal death (0 and 6.9% [p 0.2]). Out of the cohort, 70% had favourable foetal and neonatal outcome.

Conclusion: A significant number of the patients with high NT and Normal karyotype are ending up having an unfavorable foetal/neonatal outcome; hence a comprehensive counselling, detailed morphology scan, echocardiography as well as growth follow are essential.

Keywords: *Nuchal Translucency (NT); Karyotype*

Introduction

The association between increased nuchal translucency (NT) in the first trimester and chromosomal aberrations is well documented [1,2]. However, NT is increased in 4.4% of euploid fetuses [3].

These fetuses have been reported to be at increased risk of adverse pregnancy outcome, e.g. structural abnormalities, particularly cardiac defects, genetic syndromes, and fetal loss [4,5].

The underlying cause of an enlarged nuchal translucency is unknown. A lot of pathological mechanisms have been advocated, but, for the most part, the fetuses are perfectly normal. Therefore, if the cause which determines the enlarged nuchal translucency is different in normal and abnormal karyotype fetuses, some differences may be manifested in the drainage of the nuchal fluid in the first trimester. Any differences in this respect could help to differentiate normal from abnormal fetuses and would have an effect on the nuchal translucency screening for chromosomopathies and in counseling before prenatal invasive diagnosis [6].

If conventional karyotyping is normal, increased NT is a predictive value of adverse pregnancy outcome, because it is associated with several fetal malformations, congenital heart defects, genetic syndromes, intrauterine death and miscarriages [7].

By definition, 5% of fetuses screened at 11 to 14 weeks have an NT measurement greater than the 95th percentile. Because an increase in the amount of this fluid is associated with a number of apparently unrelated fetal problems, it is safe to assume there are multiple mechanisms underlying the increased thickness. It is also likely that more than one mechanism is involved in some circumstances. These include cardiac dysfunction, abnormalities of the heart and great arteries, venous congestion of the head and neck, altered composition of the extracellular matrix, failure of lymphatic drainage due to abnormal or delayed development of the lymphatic system or impaired fetal movements, fetal anemia, and congenital infection [8].

Souka and colleagues looked at pregnancy outcome in 1320 chromosomally normal fetuses with NT thickness greater than 3.5 mm in the first trimester. The chance of alive birth and no structural defects was 86% when the NT thickness was 3.5 to 4.4 mm, 77% when the NT thickness was 4.5 to 5.4 mm, 67% when the NT thickness was 5.5 to 6.4 mm, and 31% when the NT thickness was greater than 6.5 mm [9].

In this research we present our experience with High NT and normal karyotype and their outcome in an attempt to introduce more efficient antenatal evaluation and aid the counseling.

Objectives of the Study

The aim of the present study was to study the Prevalence of non-aneuploidy genetic, structural and biometry anomalies in those fetuses with High NT and normal karyotype and their outcome in an attempt to introduce more efficient antenatal evaluation and aid the counselling.

Materials and Methods

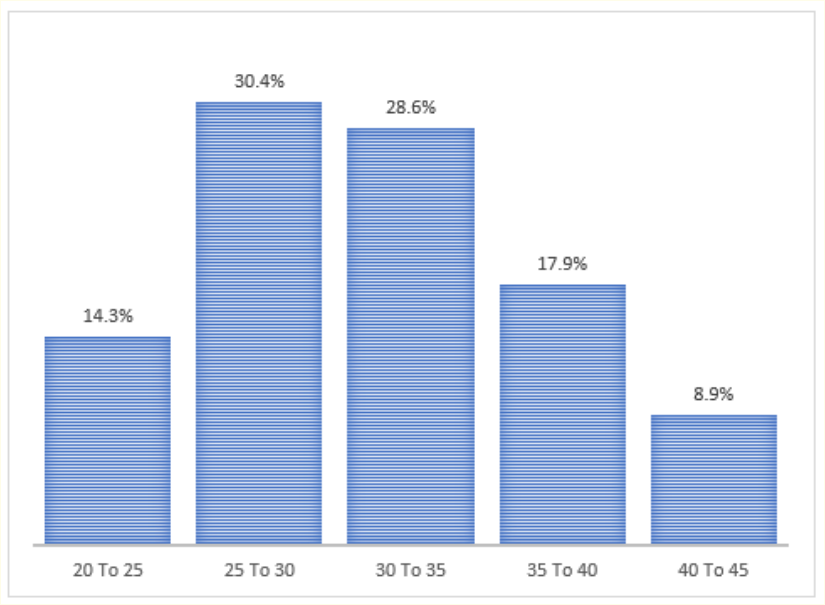
It is a retrospective study, conducted in Feto-Maternal Unit (FMU), Obstetrics and Gynaecology Department, Women's Hospital, Hamad Medical Corporation, Doha, Qatar. We look at the data over five years period from January 2011. We collected the data from the ultrasound software (Astraia Software GmbH Occamstr. 20, 80802 Munich Germany) and maternal records for maternal age, parity, previous significant history, pregnancy progression and mode/time of delivery. Fetal complications include miscarriages, IUGR, IUFD, and preterm labour. Neonatal records with included looking for Birth weight, NICU admission (reasons) and neonatal death (reasons).

We divided our cohorts into two groups taking the median as a cut off (in3.4 mm in our cohort). All of the data mentioned above were compared among the two groups.

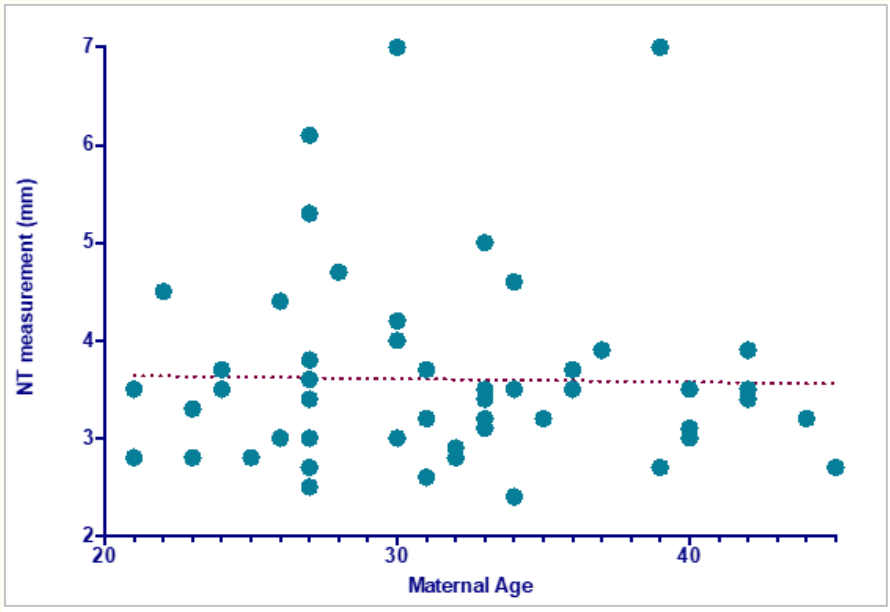
The Data was kept in password protected Excel sheet (© 2010 Microsoft Corporation). The analysis was done using Wizard Statistical Software (version 1.9.13) and GraphPad Prism version 8 macOs, (GraphPad Software, San Diego, California USA, www.graphpad.com) with p values of 0.05.

Results

Total of 56 patients with high Nuchal Translucency with normal karyotype. Mean maternal age 31.6 ± 1.6 years.



Graph 1: *Patients' age groups.*



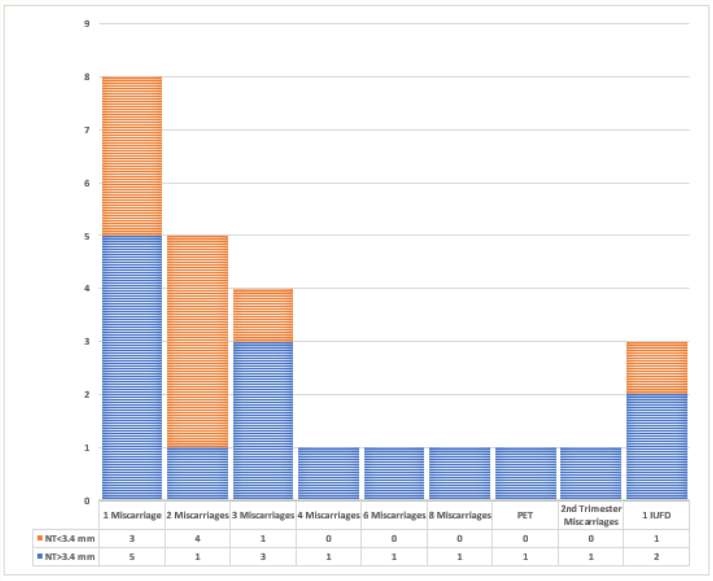
Graph 2: *No correlation between maternal age and NT (r -0,02 and p value 0,87).*

We took 3.4 mm (the median) to create two groups (below and above 3,4 mm).

Past history was an important finding, as 10.9% of the patients had a previous baby(ies) with single/multiple anomalies or genetic syndromes (details of which are found in table 2), essential to notice that all these cases had an NT of > 3 mm.

		NT < 3.4 mm (N = 24)	NT > 3.4 mm (N = 32)	P Value	Significance
Maternal Age (Mean ± SD) Years		32.5 ± 2.3	31.8 ± 2.6	0.87	NS
Gravida (Median)		3	3.5	0.26	NS
Parity (Median)		2	2	0.27	NS
Previous Abnormalities (table 2 for details)		4.2%	15.6%	0.5	NS
Previous Obstetrics Complications (See Graph 3 for details)		37.5%	50%	0.6	NS
Gestational Age at the Measurements (Mean ± SD) Weeks		13 ± 0.3	12.9 ± 0.3	0.69	NS
CRL at the Measurements (Mean ± SD) mm		68.9 ± 4.5	69.3 ± 4	0.9	NS
Associated Findings at the 1st trimester Scan		12.5%	25%	0.007	S
Karyotype Results	46 XX	45,8%	50%	0,76	NS
	46 XY	54,2%	50%	0,76	NS
Miscarriage		None	9.4%	0.18	NS
Associated Abnormalities on follow up		None	20.7%	0.017	S
IUGR		8.3%	13.8%	0.57	NS
Preterm Labour		4.2%	10.3%	0.75	NS
Gestational age at delivery (Mean ± SD) Weeks		38.7 ± 0.6	38.2 ± 0.8	0.39	NS
Birth Weight (Mean ± SD) Grams		3311.7 ± 249	3041.4 ± 253.4	0.13	NS
NICU Admission		4.2%	20.7%	0.19	NS
Neonatal Death		None	6.9%	0.2	NS

Table 1: *Patients' Biodata/Variables among the two groups.*



Graph 3: *Details Of Previous Obsteric Complications (N = 25).*

Case (N = 6)	Number of Babies affected	Descriptions
1	2	2 Babies with Congenital Heart Disease
2	2	1. Edward's Syndrome ended as Stillbirth, 2. Congenital Heart Disease died At 4 years of age.
3	1	Microcephaly and Delayed Milestones
4	3	1. Baby with Cystic Hygroma, Normal Anatomy At 20 Weeks but IUFD At 8 Months) 2. Cystic Hygroma Missed Miscarriage At 11 Weeks 3. One Baby with Skeletal Anomalies
5	1	Complex Congenital Heart Disease (Coarctation Of the Aorta +ASD and AV Septum Under development + MVP)
6	3	3 Babies with Complex Congenital Heart Disease (2 Neonatal Death)

Table 2: *Details of the Previous pregnancies with genetic/structural abnormalities (N = 6).*

19.6% of the case had other associated anomalies at the time of High NT measurement. Below a table 3 with these findings among the two groups.

	NT < 3.4 mm (N = 24)	NT > 3.4 mm (N = 32)	P Value	Significance
Absent/Hypoplastic Nasal Bone	2	2	0.3	NS
Absent/Hypoplastic Nasal Bone, Distended Bladder	None	1	0.76	NS
Cystic Hygroma	None	3	< 0.007	S
Distended Bladder, Single Umbilical Artery	None	2	0.9	NS
Echogenic Focus in the Heart	1	None	0.7	NS

Table 3: *Associated 1st trimester anomaly/marker.*

All these cases with high NT underwent invasive prenatal testing, 19.6% had CVS, and 80.4% had an amniocentesis. The results were all normal Karyotype as shown in the following diagram; the distribution was almost equal between both genders (48.2% and 51.8% were 46 XX and 46 XY respectively) with no significant difference among the two groups (See table 1).

3/56 (5.4%) had a miscarriage at a mean gestational age of 15. 3 +/- 5.8 weeks with an interval of 2.9 +/- 7.8 weeks since high NT Diagnosis. (in two case; there were no fetal, and one miscarried due to cervical insufficiency at 18 weeks). No cases of IUFD after 24 weeks.

For those who continue the pregnancy (53 patients), 11.3% had associated antenatal anomalies during follow up morphology scans (all in the NT > 3.4 mm group), below are details of these anomalies.

6/53 (11.3%) had an IUGR that was diagnosed at mean Gestational Age of 33.4 +/- 6.7 weeks. The mean birth weight for the IUGR fetuses was 2066.7 +/- 349.1 grams.

1.	Outlet Ventricular Septa Defect.
2.	Hyper Echogenic Bowel, Echogenic Kidney and Mild Renal Dilatation.
3.	Microcephaly.
4.	Severe Lower Urinary Tract Obstruction.
5.	Skeletal Dysplasia.
6.	Polycystic Kidney Disease and Lung Hypoplasia.

Table 4: *Associated 1st trimester Anomaly/Marker.*

7.5% went into preterm labour with mean GA of 34.8 +/- 0.8 weeks. The remaining had a mean gestational age at delivery of 38.4 +/- 0.5 weeks.

For those babies, who delivered alive, in 7 cases (13.2%); the neonates were admitted to NICU, mean length of stay in NICU was 13.7 +/- 15.9 days. Moreover, 3.8% ended in neonatal death (2 babies) Below are the details:

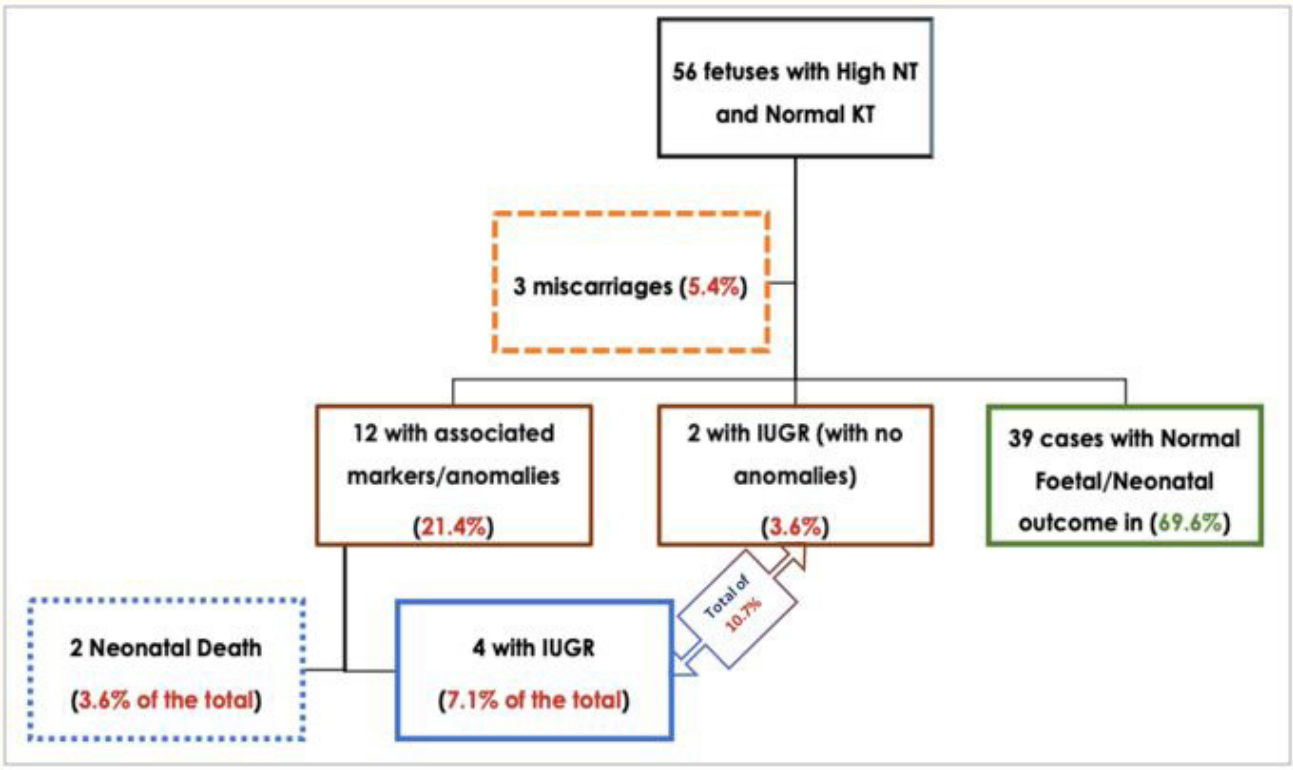


Figure 1: *The outcomes of our cohort.*

	NT Category	Course	Neonatal Death
IUGR	< 3.4 mm	Good	No
Mild RDS	> 3.4 mm	Good	No
Severe Lung Hypoplasia	> 3.4 mm	Deteriorated	Yes
Retracting and Cyanosis (Absent Left Kidney, Ectopic Right Kidney, and Lung Hypoplasia)	> 3.4 mm	Deteriorated	Yes
VACTREL Association for Further Management	> 3.4 mm	Good	No
Severe Dilated Cardiomyopathy.	> 3.4 mm	Stable	No
IUGR, Mild RDS	> 3.4 mm	Good	No

Table 5: *Reasons for the NICU admission.*

Discussion

NT should be measured between 11 and 14 weeks of pregnancy (or for a crown-rump length of 45 to 84mm), as recommended by Nicolaides., *et al.* [8] in 2002. During the study period all the patient included diagnosed with High NT underwent prenatal testing, and all had Normal Karyotype. Full counseling always provided in these cases emphasizing the importance of morphology ultrasound and fetal echo, as increased NT has been associated with other pathologic conditions, including structural fetal abnormalities, cardiac malformations, a high risk of miscarriage, and intrauterine death [10].

Form these results, almost 30% ended up with some complication (Figure1), however with the exclusion of morphological anomalies, most of the patient end up having the favourable outcome (more than two thirds) which is in line with most of the case-series published before.

As its previously mentioned in the literature [7,9], the rate of complications increases as the NT increases even with normal karyotype, which is supported by this study (even those with no statistical significance; we could see the significant clinical deference among those with < and > 3.4 mm respectively (see table 1 for details).

It is of great importance to providing detailed and comprehensive counselling at the diagnosis of High NT, indicating the importance of ruling out aneuploidy, structural abnormality, and growth abnormality (which was significantly high “10%”).

Limitations of our study are:

- Retrospective nature.
- Small number of the cohort.
- This research did not follow the neurodevelopment of those supposedly healthy, although in literature the incidence of neurodevelopmental pathologies in children with increased NT, a normal karyotype, and normal anatomy did not appear to be higher than that reported for the general population [11].

Conclusion

This study showed that; in the patient with High NT and Euploid karyotype, almost third of the patient would have a significant foetal/neonatal morbidity or mortality; hence detailed and comprehensive counselling, thorough morphology scan and echo are essential. Large cohort Prospective study will be needed to address many defects in the retrospective researches.

Bibliography

1. Pandya PP., *et al*. "Screening for fetal trisomies by maternal age and fetal nuchal translucency thickness at 10 to 14 weeks of gestation". *British Journal of Obstetrics and Gynaecology* 102.12 (1995): 957-962.

2. Taipale P., *et al*. "Increased nuchal translucency as a marker for fetal chromosomal defects". *New England Journal of Medicine* 337.23 (1997): 1654-1658.

3. Snijders RJM., *et al*. "UK multicentre project on assessment of risk of trisomy 21 by maternal age and fetal nuchal translucency thickness at 10-14 weeks of gestation". *Lancet* 352.9125 (1998): 343-346.

4. Souka AP., *et al*. "Defects and syndromes in chromosomally normal fetuses with increased nuchal translucency thickness at 10-14 weeks of gestation". *Ultrasound in Obstetrics and Gynecology* 11.6 (1998): 391-400.

5. Reynders CS., *et al*. "First trimester isolated fetal nuchal lucency: significance and outcome". *Journal of Ultrasound in Medicine* 16.2 (1997): 101-105.

6. Zoppi MA., *et al*. "Changes in nuchal translucency thickness in normal and abnormal karyotype fetuses". *BJOG: an International Journal of Obstetrics and Gynaecology* 110.6 (2003): 584-588.

7. Roberta De Domenico., *et al*. "Increased nuchal traslucency in normal karyotype fetuses". *Journal of Prenatal Medicine* 5.2 (2011): 23-26.

8. Nicolaides Kh., *et al*. "Increased fetal nuchal translucency at 11-14 weeks". *Prenatal Diagnosis* 22.4 (2002): 308-315.

9. Souka AP., *et al*. "Outcome of pregnancy in chromosomally normal fetuses with increased nuchal translucency in the first trimester". *Ultrasound in Obstetrics and Gynecology* 18 (2001): 9-17.

10. Socolov D., *et al*. "Increased nuchal translucency in fetuses with a normal karyotype-diagnosis and management". *Medicine* 96.29 (2017): e7521.

11. Sotiriadis A., *et al*. "Neurodevelopmental outcome of fetuses with increased nuchal translucency and apparently normal prenatal and/or postnatal assessment: a systematic review". *Ultrasound in Obstetrics and Gynecology* 39.1 (2012): 10-19.

Volume 8 Issue 8 August 2019