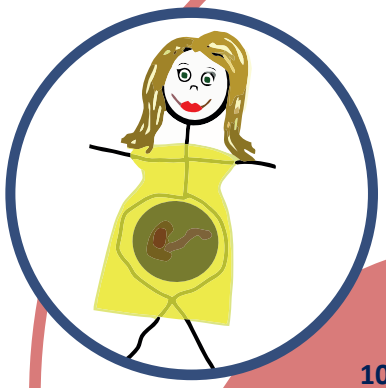


10° Corso A.O.G.O.I.
9° Turin IAN DONALD Course

TEST DI SCREENING E DI DIAGNOSI PRENATALE FRA PASSATO E FUTURO

PRENATAL SCREENING AND DIAGNOSTIC TESTS BETWEEN THE PAST AND THE FUTURE

Torino, 15-16 marzo 2024
Hotel NH S. Stefano

10°

DIRETTORE DEL CORSO
Elsa Viora - Torino

Nella pratica clinica:
esaminiamo insieme alcuni casi…

ILARIA DUSINI

S. BASTONERO, E. FORNACIARI, A. PERTUSIO
A. SCIARRONE

SSD di Ecografia Ostetrica e Ginecologica
e Diagnosi Prenatale

AZIENDA OSPEDALIERO - UNIVERSITARIA
Città della Salute e della Scienza di Torino

CASO CLINICO ♀ **37 anni**

Dettagli anamnestici di rilievo:

- partner non consanguineo
- anamnesi familiare non significativa
- buona salute
- fumo 3 sigarette/die, stop al test di gravidanza positivo
- **PARA 1051**
- 4 aborti spontanei nel I trimestre con necessità di RCU
- 1 gravidanza da FIVET nel 2021, con figlia vivente in buona salute
- 1 aborto spontaneo con RCU da gravidanza FIVET con PGT-A
- 1 successivo tentativo di FIVET fallito

GRAVIDANZA ATTUALE

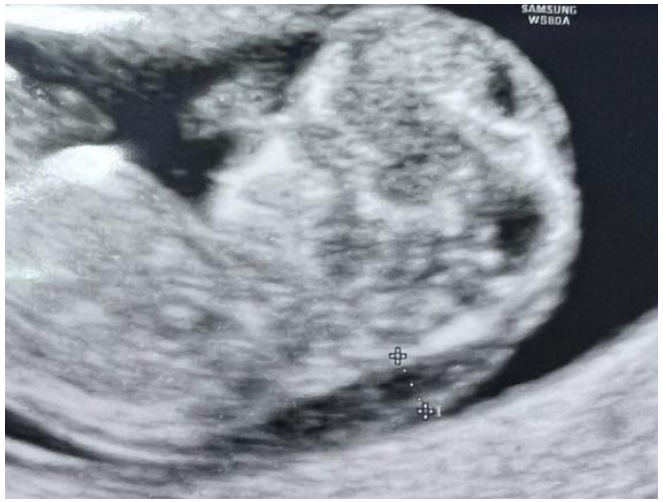
UM 26/10/2023, EPP 01/08/2024
FIVET con ET di blastocisti in V giornata
Test genetico preimpianto per aneuploidie (PGT-A): negativo

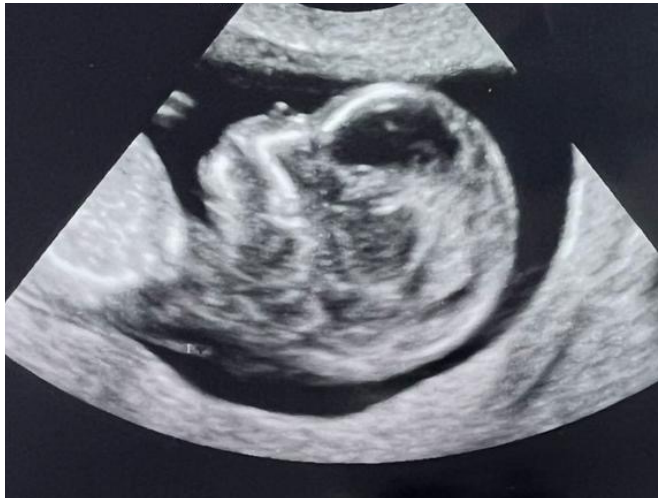
Cronologia degli accertamenti effettuati:

- **NIPT** (aneuploidie cromosomiche + pannello microdelezioni + ricerca trisomie cr. 9 e 16) a

  10 sett. + 0 gg di EG: negativo con FF 8%
- **ecografia ostetrica** a **10 sett. + 6 gg di EG**: BPD 16 mm, CRL 38 mm, **NT 3 mm**
- **ecografia ostetrica** a **11 sett. + 6 gg di EG**: BPD 20 mm, CRL 54 mm, **NT 2 mm**
- **ecografia ostetrica** a **12 sett. + 5 gg di EG**: BPD 23 mm, CRL 62 mm, **NT 1,7 mm**

invio al **centro di riferimento** per consulenza genetica





CONSULENZA GENETICA a **16 sett. + 4 gg di EG**:

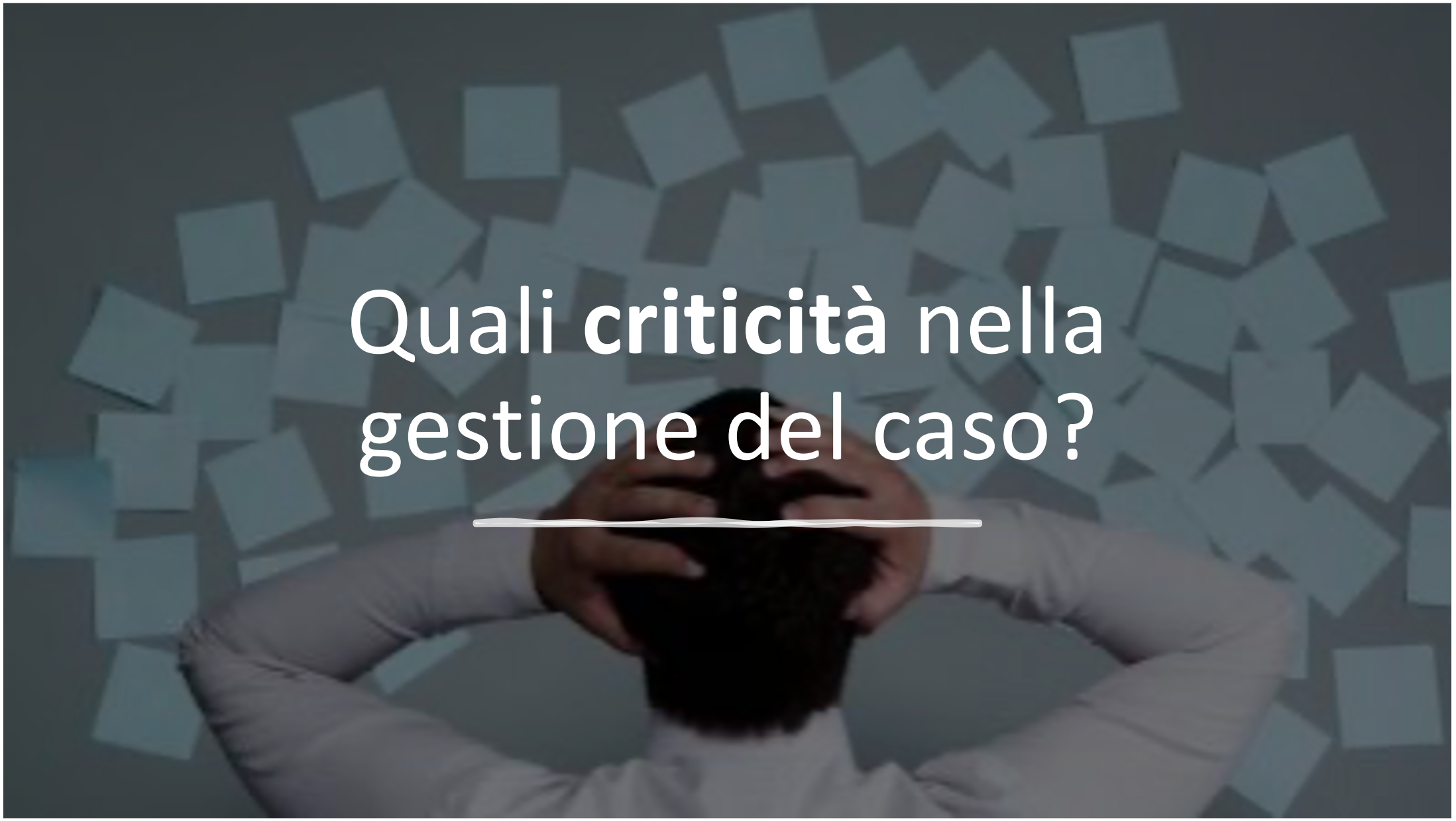
- proposta diagnosi prenatale invasiva (amniocentesi) per analisi del cariotipo ed arrayCGH
- consigliata valutazione ecografica di riferimento a 16-18 settimane di EG
- consigliata ecocardiografia fetale

"La consultanda appare più orientata a valutare la possibilità di una diagnosi invasiva dopo un controllo ecografico."

→ **ecografia ostetrica** a **16 sett. + 6 gg di EG:** anatomia e biometria nella norma

→ **ecografia di screening del II trimestre**: anatomia e biometria nella norma per EG

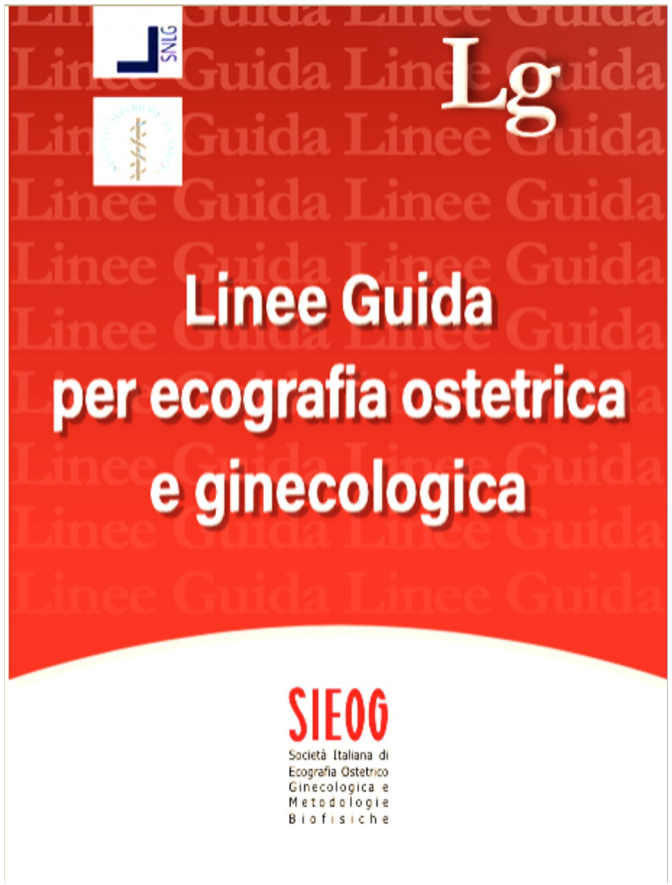
→ **ecocardiografia fetale** a **20 sett. + 1 gg di EG**: nella norma


Quali **criticità** nella
gestione del caso?

NIPT senza
NT a 10 sett.

misurazione
NT con CRL
< 45 mm

La translucenza nucale va misurata con CRL tra 45 e 84 mm!



Ultrasound Obstet Gynecol 2014; **43**: 520–524
Published online 1 April 2014 in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.13203

Is nuchal translucency a useful aneuploidy marker in fetuses with crown–rump length of 28–44 mm?

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KEYWORDS: chromosomal abnormalities; CRL; nuchal translucency

ABSTRACT

Objective *To investigate whether increased nuchal translucency (NT) in fetuses with a crown–rump length (CRL) below 45 mm needs to be re-evaluated at a later stage, or whether the early NT measurement can be used effectively as an aneuploidy marker.*

Methods *This was a prospective cohort study including all singleton fetuses with a CRL between 28 and 44 mm, scanned in our center during 2002–2012. The CRL, NT, fetal karyotype (when available) and pregnancy outcome were recorded. NT reference ranges were constructed using the Lambda-Mu-Sigma (LMS) method in non-referred pregnancies after exclusion of chromosomal anomalies. The 95th percentile was used to calculate detection rates for chromosomally abnormal fetuses.*

Results *NT was successfully measured in 643 of 672 fetuses with a CRL of 28–44 mm. Subsequent cytogenetic analysis revealed 11 cases of trisomy 21, 14 cases of trisomy 13 or 18, three cases of monosomy X, three sex trisomies, three triploidies and 12 balanced anomalies. NT was above the 95th percentile in 64% of the fetuses with trisomy 21, in 71% with trisomy 13 or 18 and in all three cases of monosomy X.*

Conclusion *NT appears to be useful as a marker for the early detection of fetal trisomies at 9–10 weeks' gestation (28–44 mm CRL). Copyright © 2013 ISUOG. Published by John Wiley & Sons Ltd.*

INTRODUCTION

First-trimester combined screening is a well-established method to screen for Down syndrome. Maternal age-derived risk is modified by deviations in the maternal serum β-human chorionic gonadotropin and pregnancy-associated plasma protein-A levels, together with those found in fetal nuchal translucency (NT) measurements[1]. In addition to being the best aneuploidy marker, NT also signals cardiac defects, other fetal malformations and genetic syndromes[2–5].

Current guidelines recommend the gestational period of 11 to 13 + 6 weeks, in which the fetal crown–rump length (CRL) is between 45 and 84 mm, as the time at which NT measurement should be performed[6,7]. The lower and upper limits were selected to allow the diagnosis of major structural abnormalities whilst also providing the option for an earlier termination in affected pregnancies[8]. However, these limits, as defined by Nicolaides' group, have changed in the last two decades, with NT being measured at 10–14 weeks[2,9,10], 10–13 weeks[11], 11–14 weeks[12] and finally 11 to 13 + 6 weeks[13].

Currently, the finding of increased NT at a CRL below 45 mm requires confirmation at a higher CRL. The aim of this study was to determine whether increased NT in fetuses with a CRL below 45 mm needs to be re-evaluated at a later stage, or whether the early measurement can be used clinically.

METHODS

During an 11-year period (2002–2012), 672 singleton pregnancies in which the CRL ranged from 28 to 44 mm, corresponding to 9 + 4 to 11 + 1 weeks according to the Robinson and Fleming (1975) charts[7], were scanned in our center. In 96 cases, the scan was routine and revealed a CRL that was lower than expected. In the other 576 cases, chorionic villus sampling (CVS) was performed because of advanced maternal age (≥ 38 years) (n = 326), previous aneuploidy (n = 119), molecular testing (n = 96),

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ORIGINAL ARTICLE

PRENATAL DIAGNOSIS WILEY

Increased nuchal translucency before 11 weeks of gestation: Reason for referral?

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Abstract

Objectives: In this era of non-invasive-prenatal testing (NIPT), when dating scans are usually performed around 10 weeks of gestation, an increased NT before the official established timeframe (CRL between 45 and 84 mm) may be encountered. Information on management of these pregnancies is limited. Therefore, we evaluated the relationship between an early increased NT and adverse pregnancy outcome. Secondary, we evaluated the rate of chromosomal anomalies that might have been missed in first trimester should solely NIPT be performed as first-tier test, and the rate of adverse pregnancy outcome if NT normalizes before 14 weeks.

Methods: We performed a retrospective cohort study that included all pregnancies between January 1, 2007 and June 1, 2020 in Amsterdam UMC locations AMC and VUmc. We included fetuses with a crown-rump length (CRL) < 45 mm (~11 weeks) and a nuchal translucency (NT) measurement ≥2.5 mm. Fetuses referred with an early increased NT and a major fetal anomaly at the dating scan were excluded, as were cases of parents with a family history of monogenetic disease(s) or recognized carriers of a balanced translocation.

Results: We included 120 fetuses of which 66.7% (80/120) had an adverse pregnancy outcome. Congenital anomalies were present in 56.7% (68/120), 45.8% (55/120) had a chromosomal anomaly. The prevalence of congenital anomalies was 30.3% in fetuses with NT 2.5–3.4 mm compared to 66.7% with NT ≥ 3.5 mm (p < 0.001). 16.7% (20/120) had a chromosomal anomaly that might have been missed by conventional NIPT in first trimester. We found an adverse pregnancy outcome of 24% in the group with a normalized NT compared to 78.1% in the group with a persistently increased NT (p < 0.001).

Conclusion: An early increased NT should make the sonographer alert. In this selected cohort, an early increased NT was associated with a high probability of having an adverse pregnancy outcome. Regardless of CRL, we deem that an early

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KATHMANDU UNIVERSITY MEDICAL JOURNAL

Nuchal Translucency in Normal Fetus and Its Variation With Increasing Crown Rump Length (Crl) and Gestational Age

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Citation

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ABSTRACT

Background

Nuchal translucency (NT) is the fluid collection behind the fetal neck which can be measured by ultrasound at 11-14 weeks of gestation. Increase in the nuchal translucency thickness is associated with various congenital anomalies.

Objective

To study the relationship between nuchal translucency thickness, crown rump length and gestational age in normal fetus.

Methods

Prospective analytical study conducted on 211 pregnant women from March 2011 to August 2012. Measurement of Nuchal translucency thickness and crown rump length was performed by ultrasound at 11-14 weeks of gestation. The relationship between nuchal translucency thickness, crown rump length and gestational age was studied by using linear regression analysis.

Results

The mean CRL was 63.67±13.48mm (range 41.2-88mm) and mean NT thickness was 1.55±0.35mm (range 0.8-2.7mm), respectively. The median gestational age was 12.9 weeks. The regression equation which shows relation between median NT thickness and CRL was described as follows: expected NT thickness = 0.013CRL+0.725, (R2 = 0.258, p <0.001). There was increase in the incidence of NT thickness more than or equal to 2.5mm; 1.7% in fetus between 12-12.9 weeks of gestation to 15.1% in fetus between 14.0-14.9 weeks.

Conclusion

Our study offers normative data of NT thickness in normal fetus, which can be used as reference to screen various chromosomal and congenital abnormalities between 11-14 weeks of gestation. NT thickness increased with increasing CRL and a false positive rate increases with increasing gestational age.

KEY WORDS

Crown Rump length, gestational age, nuchal translucency

INTRODUCTION

Collection of fluid behind the neck of fetus occurs partly because of fetus's tendency to lie on its back and laxity of the skin of the neck. It can be detected as nuchal translucency (NT) by ultrasound scanning. More the fluid that has accumulated, the greater the risk of an abnormality being present.[1] It can represent the end point of several pathological processes, including heart failure like ankle edema in adult population.

Although the pathophysiologic mechanism leading to a thickened NT in fetuses during first trimester remains undetermined, the association of a thickened NT and fetal aneuploidy has been demonstrated.[2]

NT measurement of ≥2.5 mm between 10th and 13th week of gestation is associated with a higher rate of fetal chromosomal defects. It is particularly important in early detection of Down's syndrome.[3]

NT IN EPOCA GESTAZIONALE PRECOCE

Studio prospettico su **210 embrioni** con **CRL 10-27 mm** con duplice obiettivo di valutare la fattibilità della **misura della NT in EG precoci** e di costruire **tabelle di riferimento** con percentili di valori di NT
→ misura NT possibile nel **91,4%** dei casi
(fallimento soprattutto in caso di EG < 8 w)

LIMITI:
- bassa numerosità campionaria
- nessuna trisomia individuata
- nessun dato sulla variazione del valore di NT
...ma soprattutto **impossibilità a studiare adeguatamente l'anatomia fetale!**

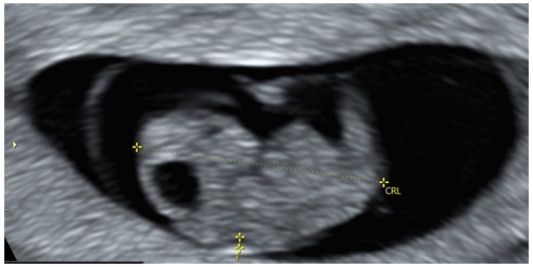
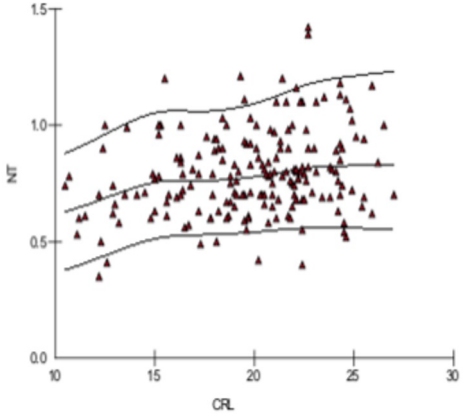


Table 3: Nuchal translucency (NT) reference ranges according to crown-rump length (CRL) in mm between 7 to 9 weeks of pregnancy

CRL (mm)	5th percentile	50th percentile	95th percentile
10	0.38	0.63	0.88
11	0.39	0.64	0.90
12	0.42	0.67	0.93
13	0.45	0.70	0.98
14	0.48	0.73	1.01
15	0.50	0.75	1.04
16	0.52	0.76	1.05
17	0.52	0.76	1.05
18	0.53	0.77	1.06
19	0.53	0.77	1.07
20	0.54	0.78	1.08
21	0.54	0.79	1.12
22	0.55	0.80	1.15
23	0.55	0.81	1.19
24	0.56	0.82	1.21
25	0.56	0.83	1.22
26	0.57	0.85	1.23
27	0.59	0.88	1.24

CRL: crown-rump length.



Michos G et al, *"Is nuchal translucency measurement feasible in early pregnancy?"*, Hippokratia 2021

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Disappearance of enlarged nuchal translucency before 14 weeks' gestation: relationship with chromosomal abnormalities and pregnancy outcome

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KEYWORDS: Down syndrome; first trimester; NT; nuchal translucency measurement; prenatal; serial; transient; ultrasound

ABSTRACT

Objective *The aim of this study was to investigate the natural course of enlarged nuchal translucency (NT) and to determine if its disappearance before 14 weeks' gestation is a favorable prognostic sign in relation to fetal karyotype and pregnancy outcome.*

Methods *A total of 147 women with increased NT (> 95th centile) at first measurement were included in this study. A second measurement was performed in all cases, at an interval of at least 2 days. Both measurements were taken between 10 + 3 and 14 + 0 weeks. All women underwent chorionic villus sampling or amniocentesis for subsequent karyotyping. In those women with a normal karyotype, a fetal anomaly scan was performed at 20 weeks' gestation. Pregnancy outcome was recorded in all cases. The finding of persistent or disappearing NT enlargement was analyzed in relation to fetal karyotype and pregnancy outcome.*

Results *Of the 147 paired measurements, NT remained enlarged at the second measurement in 121 (82%) cases. An abnormal karyotype was found in 35% of these cases. In 26 (18%) fetuses the NT measurement was found to be below the 95th percentile at the second measurement and in only two of them an abnormal karyotype was found (8%). In the 103 chromosomally normal fetuses an adverse outcome (i.e. fetal loss or structural defects) was recorded in 22 fetuses with persistent enlargement (28%) and in four fetuses with disappearing enlargement (17%).*

Conclusions *Disappearance of an enlarged NT before 14 weeks' gestation is not a rare phenomenon and seems to be a favorable prognostic sign with respect to fetal karyotype. Overall, no significant difference in pregnancy outcome was found between chromosomally normal fetuses with persisting or disappearing NT enlargement.*

INTRODUCTION

Since the introduction of nuchal translucency (NT) measurement in 1992[1], screening using this sonographic marker has proven to be effective in the detection of Down syndrome and other chromosomal abnormalities[2]. Adequate training of sonographers and the development of technical guidelines have led to improvement and uniformity of results in centers performing NT screening.

Studies have shown that in normal fetuses the fluid collection known as NT increases with gestational age until about 13 weeks' gestation[3] and usually disappears after 14 weeks[3,4]. In the case of an enlarged NT the fluid collection also tends to disappear after this period[5], although sometimes it persists or even progresses into generalized hydrops or enlarged nuchal fold[6–8]. Because of its transient nature NT measurement must be performed between 11 and 14 weeks' gestation.

Since the widespread introduction of NT screening an increasing number of pregnancies with enlarged NT are referred to specialized centers for fetal karyotyping. In our center we witnessed several cases of enlarged NT normalizing at subsequent scanning, within the period of 11–14 weeks' gestation. This may lead to conflicting risk assessments and complicate parental counseling, especially in young women in whom the initial NT enlargement was the only risk factor.

The phenomenon of 'disappearing enlargement' before 14 weeks has been reported by Maymon *et al.*[9] and more

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Accepted: 3 May 2004

Studio prospettico su **147 feti** con riscontro di NT >95° centile, sottoposti a una **ulteriore misurazione** a distanza di 2 settimane dalla prima e a CVS per lo studio del cariotipo fetale.

La **scomparsa di una NT aumentata** prima della 14ma settimana di gestazione non è un fenomeno raro (6% del totale) e sembra essere un **segno prognostico favorevole** rispetto al cariotipo fetale.

L'accumulo di liquido nucale è stato osservato in una varietà di difetti fetali, suggerendo **diversi meccanismi patogenetici**.
Supponendo che nei difetti genetici, cromosomici o strutturali un eccessivo accumulo di liquido nucale sia il risultato di uno sviluppo fetale anomalo, ci si aspetterebbe una persistenza durante tutto il periodo tra 11 e 14 settimane in cui tutti i feti hanno un po' di liquido nucale, ma **la normalizzazione dell'eccessivo accumulo di liquidi** prima della 14ma settimana di gestazione suggerisce un **diverso meccanismo di fondo** per cui non sorprende che i feti in cui la normalizzazione è documentata alla seconda misurazione abbiano una **minore incidenza di anomalie cromosomiche**.

qualche spunto di riflessione...


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GRAZIE PER L'ATTENZIONE