Nuchal translucency thickness measurements for fetal aneuploidy screening: Log NT-MoM or Delta-NT, performer-specific medians and ultrasound training

Wilfried J A Gyselaers, Annie J Vereecken, Erik J H Van Herck, Dany P L Straetmans, Willem U A M Ombelet, Jan G Nijhuis

INTRODUCTION

In fetal aneuploidy screening today, mathematical algorithms are used to calculate an individual’s risk for fetal chromosomal abnormalities using parameters derived from maternal serum and/or obtained by ultrasound. As the measured values for every parameter vary throughout gestation, the observed values are expressed as a function of the median at the same gestation, either as a multiple (multiples of the median [MoM]) or as a difference (Delta). For fetal nuchal translucency thickness (NT) measurements, the measured values are expressed in relation to the median values at the corresponding fetal crown-rump lengths (CRL). The CRL-related medians can be derived from a standard reference curve, such as the one published by the Fetal Medicine Foundation (FMF), or can be performer-specific or population-specific.

In the fetal aneuploidy screening programme organized by the Algemeen Medisch Laboratorium (AML) in Antwerp, Belgium, NT-related screening was introduced in 1999. In this programme, NT was implemented into first or second trimester screening algorithms, expressed as logarithmic NT-MoM values (Log NT-MoM) in relation to the FMF reference range. We reported the results of an audit on the methodology of NT measurement in this programme by comparing the observed Delta-NT values with those from the standard FMF curve. This audit showed a systematic underestimation of the NT measurements by the ultrasonographers, who were not enlisted as FMF trainees at the official FMF website, compared with the measurements of the ultrasonographers who were on this list.

In the present study, we compare the performer-specific CRL-related NT medians from the FMF-trainees with those from the other ultrasonographers. We also evaluate the effect of the NT distribution curves of introducing population- or performer-specific median NT values for calculation of NT-MoM or Delta-NT values.

MATERIALS AND METHODS

Between 1 January 2001 and 30 April 2004, maternal serum samples for first trimester fetal aneuploidy screening have been analysed by AML. These samples were recruited from 264 obstetricians active in 35 centres located in all geographic regions of Flanders. All serum samples were accompanied with data on first trimester NT and CRL in mm. The first trimester ultrasound scans were performed by the obstetricians referring the blood samples for analysis. The FMF-accredited ultrasonographers were identified at...
NT measurements for fetal aneuploidy screening

RESULTS

We evaluated NT measurements from a total of 16,096 unaffected pregnancies. These measurements were performed by a total of 264 ultrasonographers, of whom six were enlisted at the FMF website between 1 January 2003 and 1 May 2004. FMF trainees A–F performed 600, 352, 144, 140, 194 and 83 NT measurements, respectively. The five most active non-FMF trainee ultrasonographers in the AML screening programme (V–Z) performed 483, 658, 518, 262 and 361 NT measurements, respectively. The NT measurements of all other ultrasonographers were not evaluated individually.

Figure 1 shows the plot of CRL-related NT measurements of the group of FMF trainees and of the group of all other ultrasonographers, expressed as NT-MoM. The FMF trainees have systematically higher NT medians compared with the other ultrasonographers. Figure 1a shows the NT measurements expressed in relation to the FMF reference range. In Figure 1a, NT-MoM values are calculated in relation to the FMF reference or to AML- or performer-specific reference values. All distribution curves were plotted graphically.

DISCUSSION

In the fetal aneuploidy screening programme organized by AML, NT measurements were introduced as a screening parameter in 1999, first in combination with second trimester triple serum parameters and later also with first trimester serum screening. In these algorithms, NT measurements are expressed as Log NT-MoM, relative to a standard reference range established by FMF. Our audit on NT measurements, as used in our programme, showed a systematic underestimation of NT measurements from a group of ultrasonographers not enlisted as FMF trainees at the FMF website, compared with the measurements of FMF trainees. As a consequence,
our first trimester combined screening algorithm was less efficient at detecting T21-affected pregnancies compared with single-centre studies using FMF scanning criteria. Our results, however, were very close to those of multicentre studies using FMF scanning criteria or using group- or performer-specific reference values for NT. We have been investigating several pathways to improve the overall screening results of our programme. One of these measures was an attempt to increase the number of FMF trainees in the programme. Despite many efforts, the number of FMF trainees in Flanders enlisted at the FMF website has not yet increased, and many obstetricians do not intend to participate in the FMF programme for first trimester ultrasound screening and audit. In this study, we evaluated whether an improvement of screening performance could be expected from the introduction of performer-specific Delta-NT instead of Log NT-MoM values. For all ultrasonographers, the curves of CRL-related NT medians are different, both in the FMF trainee group and in the group of other ultrasonographers. The inter-individual variation between these curves is less for the FMF trainee and the five other ultrasonographers (see Figure 2), expressed as performer-specific Delta-NT values (3a) or performer-specific Log NT-MoM values (3b).

Figure 2 Medians of NT thickness measurements (in mm) in relation to fetal CRL for five ultrasonographers not enlisted as trainees at the FMF website (2a) and for six FMF trainees (2b)

Figure 3 Probability plots of NT-measurements from the six FMF-trainees and the five other ultrasonographers [see Figure 2], expressed as performer-specific Delta-NT values (3a) or performer-specific Log NT-MoM values (3b)
trainees, which indicate that some ultrasonographers may achieve acceptable NT measurements even without official accreditation by the FMF. Our results may perhaps be biased by our choice of the non-FMF trainee ultrasonographers with the most numerous NT measurements in the AML screening programme. These ultrasonographers perform ultrasound screening on a regular basis and are likely to have developed a specific method for ultrasonic measurement of NT. This may not be true for ultrasonographers who perform a lower number of ultrasound scans. The curve of non-FMF trainee ultrasonographer Y illustrates that some ultrasonographers may have NT measurements which deviate from the FMF criteria and from those of other ultrasonographers. This is likely to be the result of a lack of methodology, and training into ultrasound screening is recommendable for this person. One of the most important effects of ultrasound training is a reduction of inter- and intra-observer variability or standard deviation of NT measurement.11

Appropriate estimates of risk of Down’s syndrome can be calculated if it is reasonable to assume the NT measurements are sampled from a Gaussian distribution. In Figure 3, we examine the Gaussian assumption for the Log NT-MoM transformation and for the Delta-NT transformation. It is shown that the Log NT-MoM transformation fits a Gaussian distribution better above the 10th percentile, which is of relevance in screening given that high NT values contribute to an increased risk of Down’s syndrome. Thus, we think that Log NT-MoMs should be used in our screening algorithm.

We conclude from this study that (i) the use of screening would benefit from performer-specific NT medians based on Log NT-MoM values; (ii) the use of Log NT-MoM values is similar to or marginally better than the use of Delta-NT; and (iii) NT measurements are valid at about 10 weeks (CRL 40-45 mm) as well as at 11-14 weeks.

ACKNOWLEDGEMENTS

We thank the obstetricians in Flanders for their appreciated efforts to register pregnancy outcome in the AML-database of fetal aneuploidy screening.

REFERENCES


Authors’ affiliations
Wilfried JA Gyselaers, Consultant Obstetrician, Ziekenhuis Oost Limburg, Genk, Belgium
Annemie J Vereecken, Director, Algemeen Medisch Laboratorium (AML), Desguinlei 88/1, Antwerp, Belgium
Erik JH Van Herck, Scientific Assistant, AML, Antwerp, Belgium
Dany PL Strattemans, Senior Laboratory Assistant, AML, Antwerp, Belgium
Professor Willem UAM Ombelet, Head of Department, Obstetrics and Gynaecology, Ziekenhuis Oost Limburg, Genk, Belgium
Professor Jan G Nijhuis, Head of Division, Fetalmaternal Medicine, Academic Hospital Maastricht, The Netherlands