The umbilical artery pulsatility index in the first trimester: is there an association with increased nuchal translucency or chromosomal abnormality?

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ABSTRACT

Objective The aim of this study was to examine the possible association between umbilical artery pulsatility index (PI) at 10–14 weeks of gestation and either increased fetal nuchal translucency (NT) or fetal chromosomal abnormality.

Design This was a prospective study of women undergoing chorionic villus sampling (CVS).

Subjects A total of 458 women undergoing CVS were studied; in 418 cases the karyotype was normal and in 19 cases fetal trisomy 21 was identified.

Methods Data from the women with a normal fetal karyotype and in whom the NT was also normal were used to calculate reference ranges for the umbilical artery PI. Associations were sought between umbilical artery PI and increased NT and between the PI and fetal trisomy 21.

Results We found no association between umbilical artery PI and NT, nor was there a difference in the PI between chromosomally normal pregnancies and those with fetal trisomy 21.

Conclusion The results suggest that fetoplacental vascular resistance per se does not contribute to increased NT and that measurement of the umbilical artery PI does not contribute to the first-trimester detection of fetal trisomy 21.

INTRODUCTION

Increased fetal nuchal translucency thickness (NT) at 10–14 weeks of gestation is associated with a wide range of chromosomal abnormalities and in particular is found in 80% of chromosomally abnormal fetuses. In the majority of cases, increased NT is a transient phenomenon; in trisomy 21, for example, by 20 weeks’ gestation increased NT will be found in only 30%, and this difference cannot be accounted for by the intrauterine lethality rate alone, which is approximately 20%.2-4

In both chromosomally normal and abnormal fetuses with increased NT there is a high prevalence of cardiac defects and also of narrowing of the aortic isthmus. This raises the possibility that these defects may be the cause of the increased NT through the mechanisms of cardiac failure, resulting in peripheral edema, or direct overperfusion of the head and neck.5-9 Fetoplacental vascular resistance, which is a determinant of the fetal cardiac afterload, falls with advancing gestation10-12 and it has been speculated that, in some fetuses, the higher afterload in earlier gestation may contribute to fetal cardiac failure and therefore to increased NT. There have also been reports suggesting an association between the umbilical artery pulsatility index (PI), an estimate of resistance in the fetoplacental circulation, and trisomy 21 in the first trimester, although existing data are contradictory.13-15

In light of these observations, this study was undertaken to examine the association between the umbilical artery PI and NT in both chromosomally normal and abnormal fetuses in the first trimester.

MATERIALS AND METHODS

The data presented here are taken from an ongoing prospective study in which, to date, 458 patients with live singleton pregnancies undergoing chorionic villus sampling (CVS) at 10–14 weeks’ gestation have been examined. In all cases, patients had attended for screening for fetal
chromosomal abnormalities because of a combination of maternal age and fetal NT\textsuperscript{8,16}. Of the women screened, only those who chose to undergo invasive testing (CVS), either as a consequence of the results of the screening test, in view of their age, anxiety or past history or because of a desire to be certain of the fetal karyotype irrespective of the results of the screening result were examined further.

The fetal crown–rump length (CRL) and NT were measured by transabdominal ultrasound as previously described\textsuperscript{16}. Gestational age was estimated from the measurement of the CRL. Prior to CVS, color flow Doppler imaging was used to identify a free-floating loop of the umbilical cord. Doppler examination was commenced with the color-gain at its lowest setting and increased until flow was detected. The pulsed Doppler sample gate was then positioned over the cord to obtain a blood flow waveform. Waveform analysis was performed by the calculation of the PI (peak systolic velocity − minimum diastolic velocity/mean velocity). At least two waveforms of satisfactory quality were selected and the PI was calculated using built-in computer software. All examinations were performed using a 3.5-MHz curvilinear sector array abdominal probe (Toshiba SSA380A, Toshiba Ultrasound, Japan) with the high-pass filter set at 50 Hz and the sampling width at 3 mm. In all imaging modes the system operated at power levels below 50 mW/cm\textsuperscript{2}.

The reference range for the umbilical artery PI was calculated using regression analysis and calculation of the 5th and 95th centiles. Both NT and umbilical artery PI are known to vary with CRL. To control for the variation of each variable with CRL the delta values (the differences between the values of individual measurements and the normal means at their given CRL) were calculated for NT, using the normal range that has previously been reported by our unit\textsuperscript{16} and umbilical artery PI, using the reference range described here. Comparison of the delta values for NT and PI allows the association between these variables to be assessed irrespective of the variation of each with gestation. The Mann–Whitney \textit{U} test and Kendall’s rank correlation coefficient were used to analyze the data.

**RESULTS**

The fetal karyotype was normal in 418 cases, and abnormal in 40 cases. Of the latter, 19 were trisomy 21 and the remainder a variety of aneuploidies, the numbers of each being too small for further analysis at this stage. In pregnancies with a normal fetal karyotype, the median maternal age was 35 years (range 16–44), the median CRL was 63 mm (range 40–105) and the median fetal NT was 2.3 mm (range 0.9–10.3). In the trisomy 21 pregnancies, the median maternal age was 35 years (range 28–41), the median CRL was 65 mm (range 48–93) and the median NT was 3.8 mm (range 2.8–10.6).

In fetuses with a normal karyotype, the NT was above the 95th centile\textsuperscript{16} in 184 cases and within the normal range in 234 cases (Figure 1). The data in the latter group were used to calculate the reference range for the umbilical artery PI \((3.747 – 0.02 \times \text{CRL}; 95\% \text{ confidence interval } 3.461–4.032; \ t = 25.871, \ p < 0.0001; \text{ Figure 2})\). The umbilical artery PI measurements in the group with increased NT and a normal karyotype were not significantly higher than in the group with normal NT \((U = 22 \text{,}329, \ p = 0.5136; \text{ Figure 3})\). Furthermore, there was no significant association between δNT and δPI in the 418 cases with a normal fetal karyotype \((r = 0.031, \ p = 0.357; \text{ Figure 4})\).

In all 19 trisomy 21 pregnancies, the fetal NT was above the 95th centile of the normal range\textsuperscript{16} (Figure 5), but the umbilical artery PI was not significantly different from that in the chromosomally normal group and the PI was above the 95th centile in only two of the cases (Figure 6; \(U = 4749; \ p = 0.149\)).
DISCUSSION

The findings of this study demonstrate that at 10–14 weeks the umbilical artery PI decreases with gestation and is not significantly associated with fetal NT or trisomy 21.

The decrease in vascular resistance in the fetoplacental circulation with advancing gestation is compatible with the findings of previous studies11–13. This is believed to be a consequence of the increase in the number of vessels, and their relative volume, within the chorionic villi and an expansion of the intervillous circulation as evidenced by the coinciding fall in uterine arterial resistance17–19.

It has been suggested that the fall in fetoplacental vascular resistance with increasing gestation could lead to a reduction in the fetal cardiac workload. In fetuses with increased NT, in which this is wholly or partly due to cardiac failure, it is speculated that this could result in an improvement in cardiac function, which might in turn contribute to spontaneous resolution of the increased NT.

Although the data of this study do not disprove such a theory for fetuses with increased NT and cardiac defects, certainly in chromosomally normal fetuses we found no significant correlation between NT and umbilical artery PI in either those fetuses with a normal NT or those with an increased NT in the 10–14-week period. These findings suggest that peripheral vascular resistance per se is unlikely to be a contributory factor for increased NT.

There is contradictory evidence on the possible association of trisomy 21 at 10–14 weeks of gestation and increased umbilical artery PI. Martinez and co-workers13 reported that the umbilical artery PI was above the 95th centile in 55% of their nine cases of trisomy 21 and that this was not always associated with an increased NT. They
estimated that the measurement of both factors might in combination allow detection of up to 89% of cases of trisomy 21. In contrast, Jauniaux and colleagues examined 11 cases of trisomy 21 and reported that there was no significant difference in umbilical artery PI compared to normal fetuses and in none of these cases was the PI above the 95th centile. We also found no significant difference in umbilical artery PI between fetuses with trisomy 21 and chromosomally normal fetuses.

The differences between the findings of Martínez and colleagues and those of our own study and that of Jauniaux and colleagues may largely be accounted for by differences in the reference ranges used and also by the relatively small numbers of cases of trisomy 21 previously reported. The reference range described by Martínez and co-workers is lower than those published by Coppens and colleagues, Arduini and Rizzo and the range that we describe, this difference being most marked at earlier gestations.

We have not identified an association between umbilical artery PI and NT in chromosomally normal fetuses, nor have we identified an association between umbilical artery PI and fetal trisomy 21. Although measurement of the umbilical artery PI may prove to be of value in the assessment of pregnancies in the first trimester, our data demonstrate that this measurement does not contribute to the detection of fetal trisomy 21 at 10–14 weeks’ gestation.

REFERENCES