

# Uterine artery Doppler at 11–14 weeks of gestation in chromosomally abnormal fetuses

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## ABSTRACT

**Objective** To determine whether the major chromosomal abnormalities are associated with impaired placentation in the first trimester of pregnancy.

**Methods** This was a prospective study of 692 singleton pregnancies undergoing fetal karyotyping at 11–14 weeks of gestation. Uterine artery Doppler was carried out and the mean pulsatility index was calculated just before chorionic villus sampling.

**Results** The fetal karyotype was normal in 613 pregnancies and abnormal in 79, including 39 cases of trisomy 21, 11 of trisomy 18, 11 of trisomy 13, eight of Turner syndrome and 10 with other defects. There were no significant differences in the median value of uterine artery mean PI between any of the individual groups. Although in the combined group of trisomy 18, trisomy 13 and Turner syndrome fetuses, the median pulsatility index (1.60) was significantly higher than in the chromosomally normal group (median pulsatility index, 1.51;  $P = 0.021$ ), in the majority of abnormal fetuses (24 of 30) mean pulsatility index was below the 95th centile of the normal group (mean pulsatility index, 2.34). There was no significant association between uterine artery mean pulsatility index and fetal nuchal translucency thickness or fetal growth deficit.

**Conclusions** The high intrauterine lethality and fetal growth restriction associated with the major chromosomal abnormalities are unlikely to be the consequence of impaired placentation in the first trimester of pregnancy.

## INTRODUCTION

Impaired trophoblastic invasion of the maternal spiral arteries is associated with increased impedance to flow in the waveforms obtained by Doppler ultrasound examination of the uterine arteries<sup>1</sup>. Several Doppler studies in the second trimester have reported that increased impedance identifies

a group at high risk for subsequent development of pregnancy complications, such as pre-eclampsia, fetal growth restriction and fetal death<sup>2</sup>. There is some evidence that Doppler assessment of the uterine arteries can be carried out at 11–14 weeks of gestation and that screening at this early gestation can also identify pregnancies at risk of developing complications associated with impaired placentation<sup>3</sup>.

Major chromosomal defects are associated with high intrauterine lethality. It has been estimated that the rate of fetal death between 12 and 40 weeks of gestation associated with trisomy 21 is 30%, whereas for trisomy 18, trisomy 13 and Turner syndrome the rate is approximately 80%<sup>4,5</sup>. Furthermore, chromosomal defects are associated with fetal growth restriction<sup>6,7</sup> and in the case of trisomies 18 and 13, but not in trisomy 21, the growth restriction is evident from the first trimester of pregnancy<sup>8–11</sup>.

The aim of this study was to examine whether the high lethality and fetal growth restriction associated with the major chromosomal abnormalities could be related to impaired placentation, demonstrated by increased impedance to flow in the uterine arteries at 11–14 weeks of gestation.

## PATIENTS AND METHODS

The study involved Doppler ultrasound examination of the uterine arteries in 692 singleton pregnancies undergoing chorionic villus sampling after nuchal translucency screening at 11–14 weeks of gestation<sup>12</sup>. The study was approved by the hospital ethics committee and written informed consent was obtained from all women before the examination. The Doppler studies were carried out immediately before chorionic villus sampling and the sonographers were not aware of the fetal karyotype results.

Doppler studies were carried out by one of five doctors who had obtained The Fetal Medicine Foundation Certificate of Competence in placental Doppler. Women were placed in the semirecumbent position and transabdominal ultrasound was used to obtain a sagittal section of the uterus and cervical canal. The internal cervical os was first identified. Subsequently,

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the transducer was tilted from side to side and color flow mapping was used to identify the uterine arteries as aliasing vessels coursing along the side of the cervix and uterus<sup>3</sup>. Pulsed wave Doppler was used to obtain flow velocity waveforms from the ascending branch of the uterine artery at the point closest to the internal os. When three similar consecutive waveforms were obtained, the pulsatility index (PI) was measured and the mean PI of the left and right arteries was calculated. Demographic characteristics and Doppler findings were recorded in a fetal database and the karyotype was entered after the results of chorionic villus sampling became available.

The Mann–Whitney *U*-test was used to determine the significance of differences in the median values of uterine artery mean PI between the chromosomally normal and abnormal groups. Regression analysis was used to determine the significance of the association between uterine artery mean PI and fetal nuchal translucency thickness. Similarly, we examined the association between uterine artery mean PI and the degree of fetal growth restriction in the chromosomally abnormal fetuses. For this analysis, we selected women with regular menstrual cycles of 26–30 days who were certain of the date of their last menstrual period and in these cases we calculated the difference in gestation between that estimated by measurement of fetal crown–rump length and menstrual dates.

**RESULTS**

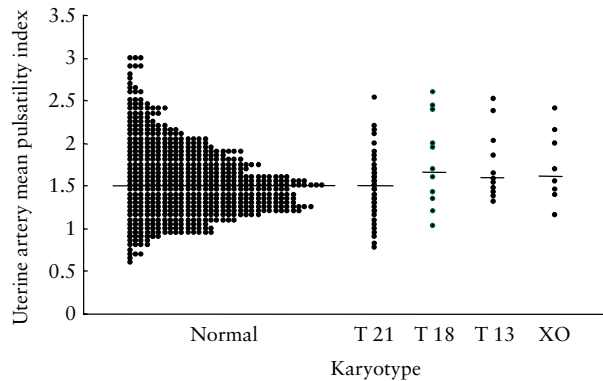
Satisfactory flow velocity waveforms from both uterine arteries were successfully obtained from all 692 women recruited to the study. The median gestation was 12 weeks (range, 10–14 weeks) and the mean CRL was 65 mm (range, 45–85 mm). The fetal karyotype was normal in 613 pregnancies and abnormal in 79 (Table 1). There were no significant differences in the median value of uterine artery mean PI between any of the individual groups (Figure 1). Although in the combined group of trisomy 18, trisomy 13 and Turner syndrome fetuses, the median PI (1.60) was significantly higher than in the chromosomally normal group (median PI 1.51;  $P = 0.021$ ), in the majority of abnormal fetuses (24 of 30), mean PI was below the 95th centile of the normal group (mean PI 2.34). In the chromosomally abnormal fetuses, there was no significant association between uterine artery

**Table 1** Median and range of uterine artery mean pulsatility index in the chromosomally normal and abnormal pregnancies

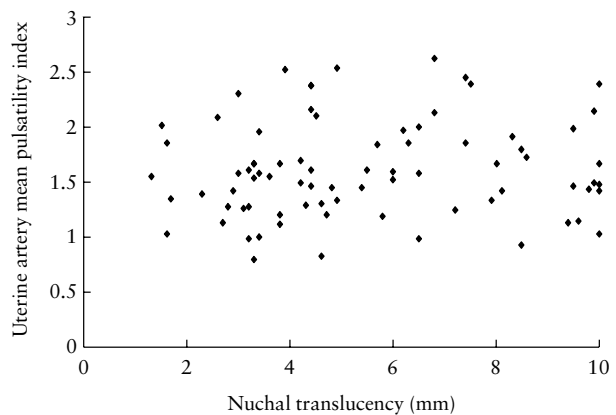
| Karyotype        | n   | Median PI (range) |
|------------------|-----|-------------------|
| Normal karyotype | 613 | 1.51 (0.6–3.0)    |
| Trisomy 21       | 39  | 1.52 (0.8–2.5)    |
| Trisomy 18       | 11  | 1.67 (1.0–2.6)    |
| Trisomy 13       | 11  | 1.59 (1.3–2.5)    |
| Turner           | 8   | 1.62 (1.2–2.4)    |
| Other*           | 10  | 1.56 (1.0–2.4)    |

There were no significant differences in median pulsatility index between any of the groups. \*Three cases of triple X syndrome, one of triploidy, one of Wolf–Hirschhorn syndrome, two cases of monosomy 21, one of tetrasomy 18p, one of trisomy 20q and one of monosomy 2. PI, pulsatility index.

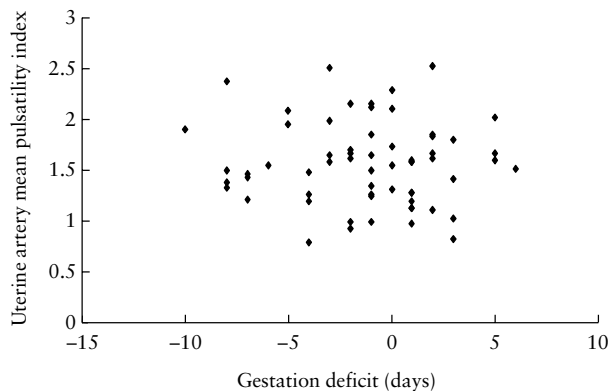
mean PI and fetal nuchal translucency thickness ( $r = 0.094$ ,  $n = 79$ ,  $P = 0.394$ ) (Figure 2) and in those with certain and regular menstrual cycles, there was no significant association between uterine artery mean PI and fetal growth deficit ( $r = 0.053$ ,  $n = 62$ ,  $P = 0.685$ ) (Figure 3).



**Figure 1** Distribution of uterine artery mean pulsatility index in the chromosomally normal and abnormal pregnancies. The horizontal lines in each group indicate the median values.



**Figure 2** Relationship between uterine artery mean pulsatility index and nuchal translucency thickness in 79 chromosomally abnormal fetuses.



**Figure 3** Relationship between uterine artery mean pulsatility index and gestation deficit (difference in gestation between that estimated by measurement of fetal crown–rump length and menstrual dates) in 62 chromosomally abnormal fetuses.

## DISCUSSION

The findings of this study demonstrate that the major chromosomal abnormalities are not associated with increased impedance to flow in the uterine arteries as assessed by Doppler ultrasound at 11–14 weeks of gestation. Consequently, the high intrauterine lethality and fetal growth restriction in these abnormalities cannot be attributed to impaired trophoblastic invasion of the maternal spiral arteries, which is thought to be the cause of increased uterine artery mean PI<sup>1–3</sup>.

Histological studies of the placenta in cases of autosomal trisomy have shown non-specific changes, including under-vascularization of the villi and increased basophilic stippling of the basement membrane, which was particularly prominent in trisomies 18 and 13<sup>14,15</sup>. These placental abnormalities may be responsible for the increased impedance to flow in the umbilical arteries reported in trisomy 18, but not in trisomy 21<sup>16,17</sup>.

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