

# Doppler studies of the placental and fetal circulation in pregnancies with preterm prelabor amniorrhexis

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## ABSTRACT

*This study has investigated the effect of intrauterine infection on placental perfusion, fetal circulation and fetal oxygenation in patients with preterm prelabor amniorrhexis. In 69 pregnancies with preterm prelabor amniorrhexis, Doppler ultrasound studies of the uterine and umbilical arteries and the fetal middle cerebral artery and thoracic aorta were performed. Within 1 h after the Doppler studies, cordocentesis and amniocentesis were carried out for microbiological investigations and measurement of blood pO<sub>2</sub> and pH. In the amniorrhexis group, there were no significant differences from the appropriate normal mean for gestation in any of the Doppler indices or blood gas results. Furthermore, there were no significant differences between the groups with positive fetal blood or amniotic fluid cultures and those with no evidence of infection. These data demonstrate that, in preterm prelabor amniorrhexis, microbial invasion of the amniotic cavity and fetal bacteremia are not associated with detectable changes in placental perfusion, fetal circulation or fetal oxygenation.*

## INTRODUCTION

Preterm prelabor amniorrhexis (rupture of membranes) is associated with intrauterine infection. Infection of the amniotic fluid and choriodecidua causes constriction of the umbilical cord and chorionic vessels and may consequently impair fetal perfusion and oxygenation<sup>1–7</sup>. However, Doppler studies of the umbilical arterial circulation in pregnancies with chorioamnionitis have provided conflicting results with some reporting an increase and others no change in impedance to flow<sup>8–11</sup>. Possible reasons for these conflicting results are the small number of patients that were examined and differences in the end-point for the diagnosis of infection which included histological and clinical chorioamnionitis.

The aim of this study was to evaluate the use of Doppler ultrasound of the uteroplacental and fetal circulation in the prediction of microbial invasion of the amniotic cavity and fetal bacteremia<sup>12</sup>. Furthermore, the study examined the possible influence of infection on fetal oxygenation by measuring umbilical venous blood pO<sub>2</sub> and pH in samples obtained by cordocentesis at the time of Doppler assessment.

## MATERIALS AND METHODS

During a 12-month period, 62 women were referred to our center for further assessment within 5 days of preterm prelabor amniorrhexis and 53 of these agreed to have amniocentesis and cordocentesis for the diagnosis of intrauterine infection. During the same period there were an additional 16 women who had amniocentesis and cordocentesis for preterm prelabor amniorrhexis, but in whom membrane rupture occurred 11–76 (mean 41) days before referral. The study was approved by the Hospital Ethics Committee.

Gestation was determined from the maternal menstrual history and by an ultrasound scan in early pregnancy. The diagnosis of preterm prelabor amniorrhexis was confirmed by the ultrasonographic demonstration of decreased or absent amniotic fluid and the visualization of Nitrazine<sup>®</sup>-positive fluid in the vagina.

Written informed consent was obtained for amniocentesis and cordocentesis, which were performed using a single uterine transabdominal entry of a 20G needle under ultrasound guidance. None of the patients had taken antibiotics or tocolytics shortly before or at the time of testing. In all cases umbilical venous blood was obtained and the Kleihauer–Betke test demonstrated that all blood samples contained only fetal blood. Fetal blood pO<sub>2</sub> and pH were measured by an automated blood gas

analyzer (Radiometer ABL 330, Copenhagen, Denmark). Fetal blood was inoculated into aerobic and anaerobic blood culture bottles (Bactec, Becton-Dickinson, Towson, USA). The amniotic fluid was cultured using standard microbiological techniques and was also inoculated into Mycofast<sup>®</sup> liquid cultures for *Ureaplasma urealyticum* and *Mycoplasma hominis* (International Mycoplasma, Toulon, France).

Within 1 h before amniocentesis and cordocentesis, Doppler studies were performed. Color flow imaging was used to identify the uterine and umbilical arteries and the fetal middle cerebral artery and descending thoracic aorta (Acuson 128, Acuson, California, USA: 5-MHz linear array and 3.5-MHz sector transducers). Pulsed wave Doppler was then used to obtain flow velocity waveforms from these vessels. In each case, three consecutive waveforms of satisfactory quality were obtained and the mean pulsatility index (PI) was recorded. During the studies, care was taken to apply minimal pressure to the maternal abdomen with the transducer, as fetal head compression is associated with alterations of intracranial arterial flow velocity waveforms<sup>13</sup>. All Doppler studies were performed in the absence of gross fetal body or breathing movements<sup>14</sup>.

### Statistical analysis

In normal pregnancy, blood  $pO_2$ , pH and PI in the different vessels that were examined change with gestation. To correct for the effect of gestation in the patients with amniorrhexis, individual values were expressed as the number of standard deviations (SD) by which they differed from the appropriate normal mean for gestation

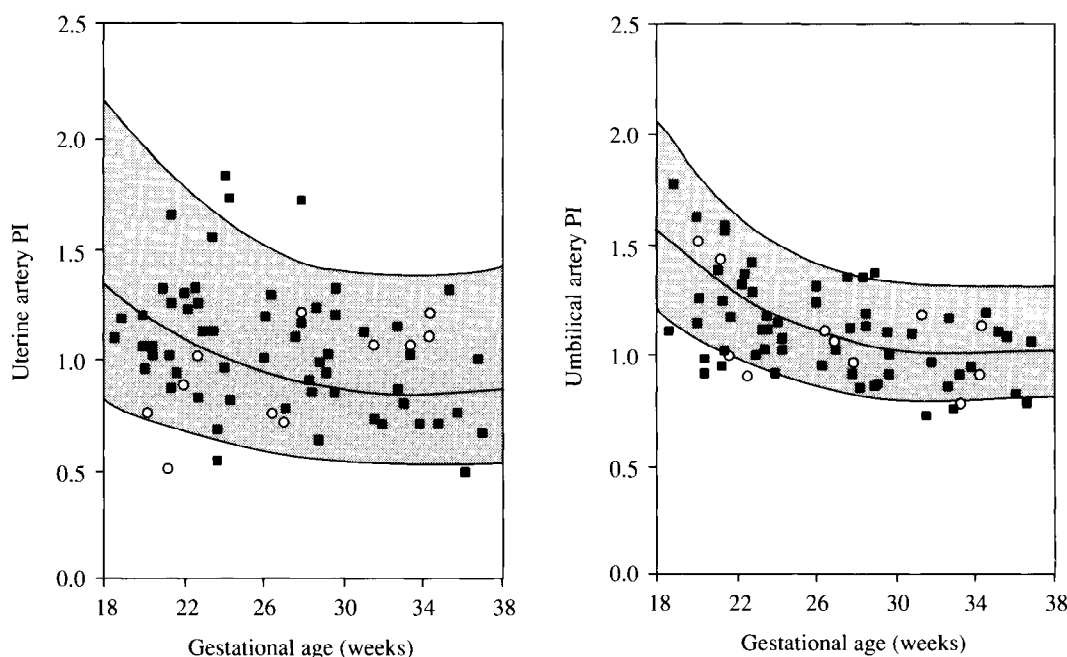
(delta values). Student's *t*-test was used to examine the significance of differences of the total amniorrhexis group from the normal mean and ANOVA was used to examine the significance of differences between those with and those without evidence of intrauterine infection.

### RESULTS

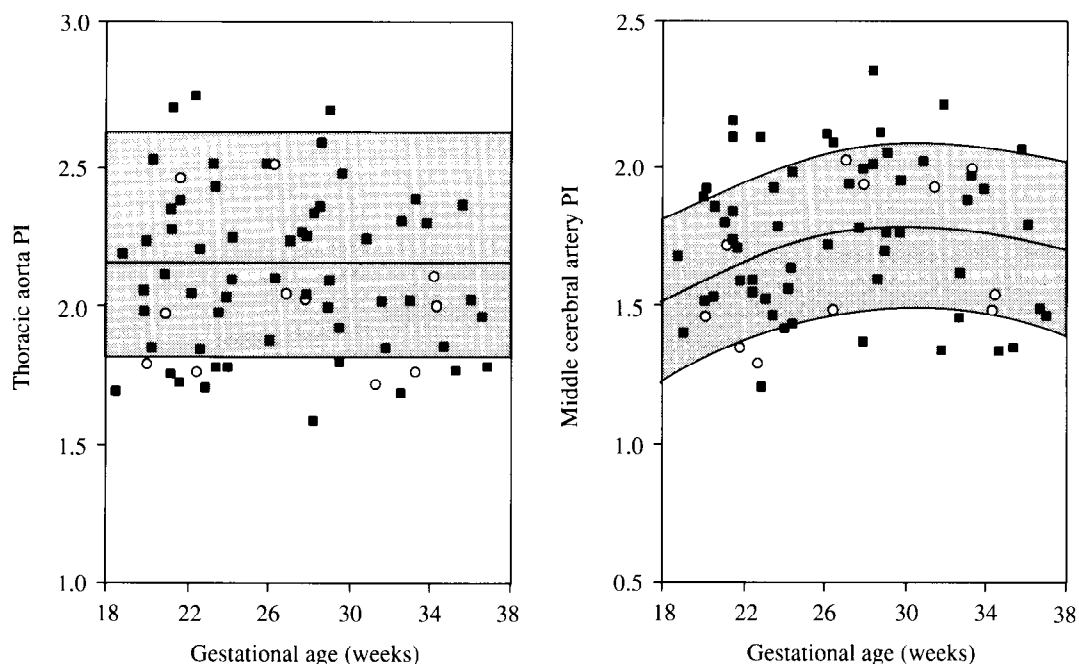
Fetal blood was successfully obtained from all cases but amniotic fluid was not taken from nine. The patients were divided into four groups, depending on the results of cultures. Groups 1, 2 and 3 included those patients with negative fetal blood cultures and where the amniotic fluid culture was negative (Group 1) or positive (Group 2) or no fluid was obtained (Group 3). In Group 4, the patients had positive fetal blood cultures.

There were 34 cases in Group 1, 15 in Group 2, nine in Group 3 and 11 in Group 4. The organisms recovered from the amniotic fluid in Group 2 were *M. hominis* and/or *U. urealyticum* in 11 cases, *Streptococcus agalactiae* in two, *Streptococcus milleri* in one and *Cryseomonas* in another. The organisms recovered from fetal blood in Group 4 were, in two cases, *Streptococcus agalactiae* and, in one case each, *Lactobacillus*, *Fusobacterium*, *Enterobacter*, *Citrobacter*, *Candida albicans*, *Haemophilus influenzae*, *Streptococcus milleri*, *Streptococcus viridans* and *Streptococcus sanguis*.

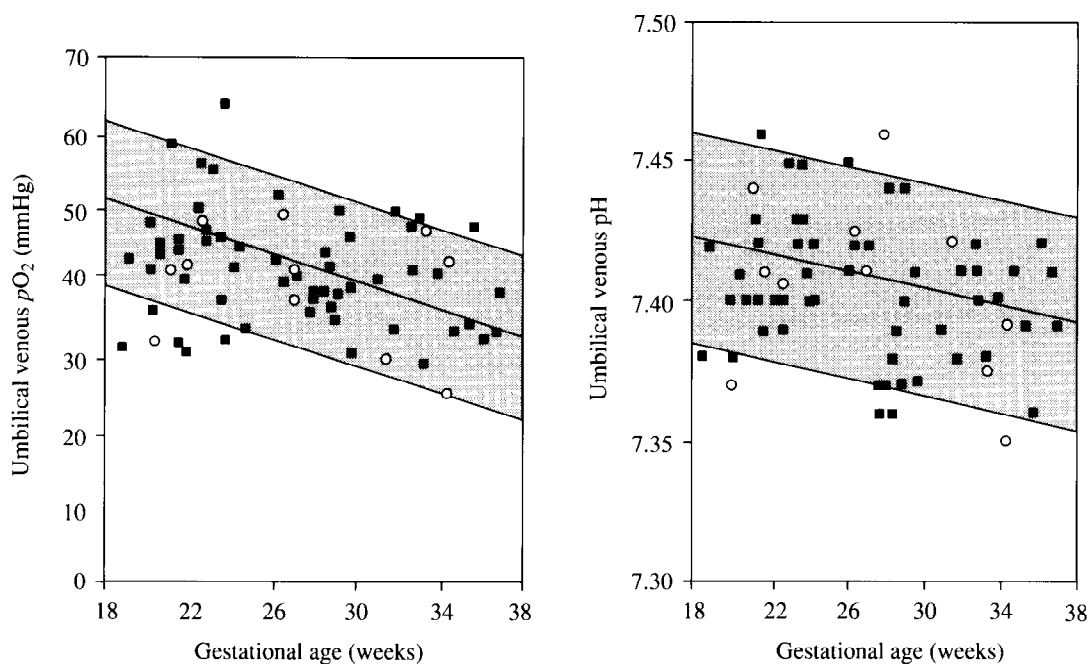
The median gestations at assessment of Groups 1,2,3 and 4 were 26, 28, 28 and 27 weeks, respectively. In the 53 cases where the interval between membrane rupture and cordocentesis was less than 6 days, there were 21 cases in Group 1, 14 in Group 2, seven in Group 3 and 11 in Group 4. Of the 16 cases where the interval was at



**Figure 1** Pulsatility index (PI) of the uterine and umbilical arteries in pregnancies with preterm prelabor amniorrhexis plotted on the appropriate reference range against gestation (mean, 5th and 95th centiles). Squares, Groups 1-3; circles, Group 4



**Figure 2** Pulsatility index (PI) of the fetal descending thoracic aorta and middle cerebral artery in pregnancies with preterm prelabor amniorrhexis plotted on the appropriate reference range against gestation (mean, 5th and 95th centiles). Squares, Groups 1-3; circles Group 4



**Figure 3** Umbilical venous blood  $pO_2$  and pH in pregnancies with preterm prelabor amniorrhexis plotted on the appropriate reference range against gestation (mean, 5th and 95th centiles). Squares, Groups 1-3; circles, Group 4

least 6 days, there were 13 in Group 1, one in Group 2 and two in Group 3.

In the 69 cases with preterm prelabor amniorrhexis, the mean delta PI values in all vessels that were examined and the mean delta umbilical venous blood  $pO_2$  and pH were not significantly different from the appropriate normal mean for gestation and there were no significant differences between the four groups (Figures 1-3; Table 1).

**DISCUSSION**

The data of this study demonstrate that in pregnancies with preterm prelabor amniorrhexis, in both the presence and the absence of intrauterine infection, uteroplacental and fetoplacental perfusion, as assessed by Doppler, and fetal oxygenation are not impaired. The finding that intrauterine infection is not associated with a significant decrease in umbilical venous blood  $pO_2$  and pH is consistent with that of previous studies that examined

**Table 1** Mean delta values of pulsatility index (PI) of the uterine artery, umbilical artery, fetal aorta and middle cerebral artery and umbilical venous blood  $pO_2$  and pH in pregnancies with preterm prelabor amniorrhexis and in the individual groups with and without evidence of intrauterine infection. Values are expressed as number of standard deviations by which they differed from the appropriate normal mean for gestation

|                           | Total (n = 69) | Group 1 (n = 34) | Group 2 (n = 15) | Group 3 (n = 9) | Group 4 (n = 11) |
|---------------------------|----------------|------------------|------------------|-----------------|------------------|
| Uterine artery PI         | 0.17           | 0.17             | 0.27             | 0.34            | -0.13            |
| Umbilical artery PI       | 0.13           | 0.17             | 0.03             | 0.25            | 0.06             |
| Aorta PI                  | -0.24          | -0.19            | 0.02             | -0.44           | -0.58            |
| Middle cerebral artery PI | 0.14           | 0.19             | 0.41             | 0.14            | -0.40            |
| Umbilical venous $pO_2$   | -0.22          | -0.03            | -0.22            | -0.69           | -0.41            |
| Umbilical venous pH       | -0.18          | -0.11            | -0.34            | -0.33           | -0.09            |

umbilical cord blood obtained after delivery in patients with clinical chorioamnionitis or positive neonatal blood cultures<sup>15, 17</sup>.

Previous Doppler studies in pregnancies with preterm prelabor amniorrhexis examined only the uterine and/or umbilical arteries. In two cross-sectional studies, involving a total of 35 patients with clinical chorioamnionitis, impedance to flow in the umbilical arteries (measured as S/D ratio) was always normal<sup>9, 11</sup>. In a longitudinal study of 22 patients with preterm prelabor amniorrhexis and umbilical vasculitis, the mean umbilical arterial S/D of the last examination 24 h before delivery was significantly higher than previous ones; however, the measurements were not above the normal range<sup>8</sup>. In another longitudinal study of uterine and umbilical arteries in 60 patients with amniorrhexis, including 12 who developed clinical chorioamnionitis, there was no significant increase in S/D even in measurements taken within 24 h before delivery<sup>10</sup>.

The findings that uterine and umbilical arterial PI and umbilical venous blood  $pO_2$  and pH were within the normal ranges do not exclude the possibility that in intrauterine infection there is vasoconstriction in uterine, chorionic or umbilical vessels. In animal studies, uteroplacental and fetoplacental blood flow can be reduced by microsphere embolization of the uterine arteries and occlusion of umbilical vessels. These studies have demonstrated that, to produce fetal hypoxia, it is necessary to achieve a minimum of 50% reduction in placental perfusion<sup>18, 20</sup>. In the human, evidence for high reserve in the fetoplacental circulation is provided by the findings that, in labor, impedance to flow in the umbilical arteries is not increased during contractions<sup>21, 22</sup>.

These findings suggest that chorioamnionitis is not associated with a major degree of vasoconstriction in the uteroplacental or fetoplacental circulation. Consequently, Doppler does not provide a clinically useful distinction between infected and non-infected cases. However, Doppler studies in pregnancies with suspected amniorrhexis may be useful in the differential diagnosis from oligohydramnios due to uteroplacental insufficiency and intrauterine growth retardation. In the latter, there is an increase in impedance to flow in the uterine and/or umbilical arteries with decreased PI in the fetal cerebral vessels and increased PI in the descending thoracic aorta<sup>23</sup>.

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