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# Doppler ultrasound of the uterine arteries: the importance of bilateral notching in the prediction of pre-eclampsia, placental abruption or delivery of a small-for-gestational-age baby

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## ABSTRACT

*The use of Doppler studies of the uterine arteries in the prediction of pre-eclampsia and intrauterine growth retardation has had mixed success. The introduction of color Doppler imaging and the use of the 'notch' to define an abnormal waveform have helped to improve the predictive value of uterine artery Doppler screening.*

*The aim of this study was to evaluate the use of uterine artery Doppler in a group of women of mixed race and parity. This study was a prospective, cross-sectional analysis of 1326 unselected women who were screened with continuous wave uterine Doppler at 19–21 weeks, as part of a fetal anomaly/dating scan. A total of 214 women with abnormal uterine artery waveforms (notching) were referred for assessment at 24 weeks; 191 attended and had color Doppler imaging/pulsed Doppler studies of both uterine arteries. Data from 185 pregnancies were suitable for analysis.*

*There were abnormal uterine Doppler findings (uni- or bilateral notching) in 110 patients at 24 weeks; 48 had bilateral notching. The sensitivity of notching for the prediction of proteinuric pregnancy-induced hypertension (PPIH) was similar in primiparas (76.9%), multiparas (77.7%), African–Caribbean women (82.6%) and Caucasian women (71.4%). The sensitivity of bilateral notching for the prediction of PPIH requiring delivery before 34 weeks was 81.2%, and 57.6% for babies small for gestational age (SGA), with positive predictive values of 27% (PPIH), 31.2% (SGA) and 37.5% (any complication).*

*Patients with persistent bilateral notching are particularly at risk of developing PPIH or delivering an SGA baby before 34 weeks' gestation; they warrant increased surveillance, and may be a group that could benefit from prophylactic therapies.*

## INTRODUCTION

One of the main purposes for providing antenatal care is to identify women whose pregnancies are at risk of complications that arise as a consequence of impaired uteroplacental perfusion, such as pre-eclampsia or proteinuric pregnancy-induced hypertension (PPIH), intrauterine growth retardation (IUGR), or placental abruption. Early detection of disease should lead to an improved outcome, through increased surveillance and the use of prophylactic therapies such as low-dose aspirin[1,2]. Although clinical factors such as parity[3] and race[4] can help in selecting groups that have a relatively increased risk of developing complications, they are neither sufficiently sensitive nor sufficiently specific to be used alone. The advantage of a more accurate antenatal screening test is twofold: the selection of a high-risk group of women suitable for increased monitoring and prophylactic treatment, and by exclusion a low-risk group that would be suitable for less intensive 'community-based' antenatal care.

The placenta, through implantation and development, modifies the uterine circulation from one of low flow and high resistance to one of high flow and low resistance. The primary defect that predisposes pregnancies to uteroplacental complications appears to be a partial or complete failure of trophoblastic invasion[5], although the reason for

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this failure is still not clear. Doppler ultrasound examination of the uterine circulation provides indirect evidence of uterine blood flow changes in pregnancy (Figures 1 and 2). The original pulsed wave studies established the relationship between high-resistance waveforms and pre-eclampsia[6], and the potential usefulness of uterine artery Doppler scanning as an early predictor of subsequent PPIH and IUGR[7].

Subsequent continuous wave Doppler studies, seeking to expand on this finding, led to conflicting and often disappointing results[8–11]. The variation in study results has been attributed to a number of causes. One of these may be related to inherent problems with continuous wave Doppler as a 'blind' investigation, for it has been shown that the impedance indices obtained from the uteroplacental circulation vary, depending on the sampling site. Another source of error is that non-uterine pelvic vessels may be interrogated by mistake.

With the use of continuous wave Doppler, however, a clear relationship between high-resistance uterine waveforms and an increased risk of an adverse outcome to the pregnancy was established[12], but the poor sensitivity limited its value as a screening test. More recently, the introduction of color Doppler imaging to identify a reproducible point in the uterine circulation[13] (Figure 2), and the use of the early diastolic notch[8,14] as the definition of abnormality have improved the reliability and predictive value of uterine Doppler studies in pregnancy.

The aim of this study was to assess the potential benefit of uterine artery Doppler as a two-stage screening test for the selection of women at risk of subsequently developing PPIH, delivering a small-for-gestational-age (SGA) baby, or suffering a placental abruption, to establish its value in a group of mixed race and parity, and to evaluate the predictive value of bilateral notching in identifying women at risk of developing complications before term.

## PATIENTS AND METHODS

The study was undertaken in a university hospital ultrasound department. Approval for the study had been granted by the Hospital Ethics Committee. The hospital antenatal population consists of women who are of mixed race and parity[12]. At this hospital, continuous wave Doppler studies are performed as part of the fetal anomaly scan between 18 and 21 weeks[15]. The continuous wave artery Doppler measurements were obtained with a 4-MHz pencil probe (Doptek, Chichester, UK). The probe was placed in the iliac fossa on each side, just above the level of the inguinal ligament. It was then moved medially until a reproducible uterine artery waveform could be identified[12]. Patients with persistent notching of the uterine artery waveform or a resistance index (RI) above the 95th centile were referred for a second assessment at 24 weeks. Informed consent was obtained from each patient for the ultrasound investigation.

At 24 weeks the patients were allowed to rest for 10–15 min in a semi-recumbent position prior to the commencement of the ultrasound investigation. The investigations were performed with an Acuson 128 ultrasound machine (Mountain View, California) with 3.5- and 5-MHz linear transducers. To obtain recordings from the right or left uterine artery, the transducer was placed longitudinally in the right or left lower quadrant of the abdomen. Color Doppler imaging was employed to identify the uterine artery at the point where it crossed the external iliac artery, as previously described[13]. Pulsed Doppler was then used to obtain a flow velocity waveform. An angle of insonation of 50° or less was used to obtain waveforms acceptable for analysis. The RI and the presence or absence of a notch were noted. The procedure was then repeated on the opposite uterine artery.

A flow velocity waveform was defined as abnormal if there was persistent notching (Figure 3, trace A), or if the RI was > 95th centile, whether or not a notch was present (Figure 3, trace B). For the more detailed analysis of prediction of outcome, women with a high RI were included in the unilateral notch group if the RI was > 95th centile on one side only, and into the bilateral group if the RI was > 95th centile on both sides. Although determining the presence or absence of notching is qualitative, there is very close agreement between operators when a notch is identified[14]. Where there is ambiguity about the presence of a notch, it is usually in a low-resistance waveform and is not significant. For this reason, it was decided that, if the mean RI was < 0.55 (50th centile), the waveforms were considered to be normal.

Outcome variables included gestational age at delivery, mode and indication for delivery, the delivery of an SGA baby (< 10th centile)[16], admission to a neonatal intensive care unit where prematurity was not the primary indication for admission, and development of moderate-to-severe PPIH. The definition of moderate-to-severe PPIH was the finding of a rise in blood pressure (from the blood pressure reading before 20 weeks' gestation) of ≥ 30/25 mmHg on at least two occasions 4 h apart, with ≥ 500 mg proteinuria, or a diastolic pressure of ≥ 110 mmHg with ≥ 500 mg proteinuria[21]. Moderate-to-severe PPIH was used for two reasons: this group carries the greater morbidity, and previous studies[15] have suggested that notching of the uterine artery Doppler waveform is useful at identifying this particular group of women. Placental abruption was diagnosed if vaginal bleeding was associated with abdominal pain and tenderness, or if there was evidence of a retroplacental clot at delivery. An intrauterine death was defined as a stillbirth if it occurred after 24 weeks' gestation, and a neonatal death as one occurring within the first 4 weeks of life. A complication was considered to be one or more abnormal events occurring in the pregnancy.

Labor ward records, neonatal records and patient notes were used to confirm the outcome for all the patients in the study. Statistics were analyzed with the statistical package for the social sciences (SPSS). The odds ratio, 5th/95th confidence intervals and $\chi^2$ tests were used to compare the outcome of pregnancies with normal waveform vs. persistent notching of the uterine artery Doppler waveform at 24 weeks' gestation. Predictive tests, the sensitivity, specificity, positive and negative predictive values, including the

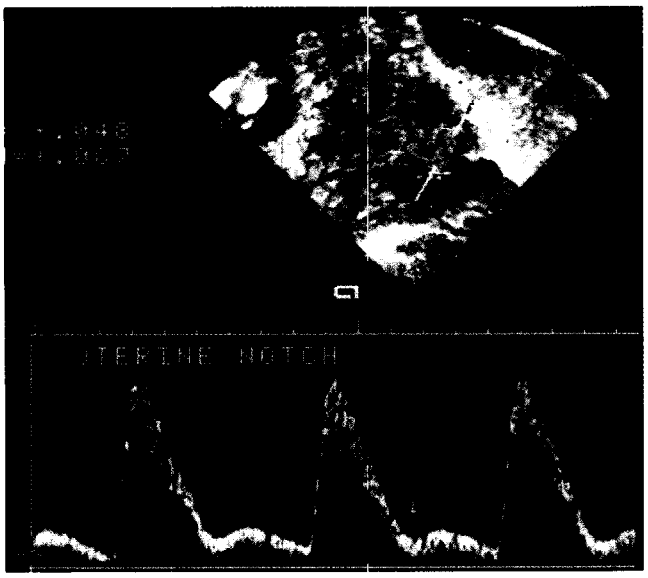

**Figure 1** A flow velocity waveform, obtained with a transvaginal probe, of the uterine artery in a non-pregnant woman. The high-resistance waveform with early diastolic notching is a normal feature of the non-pregnant uterine circulation

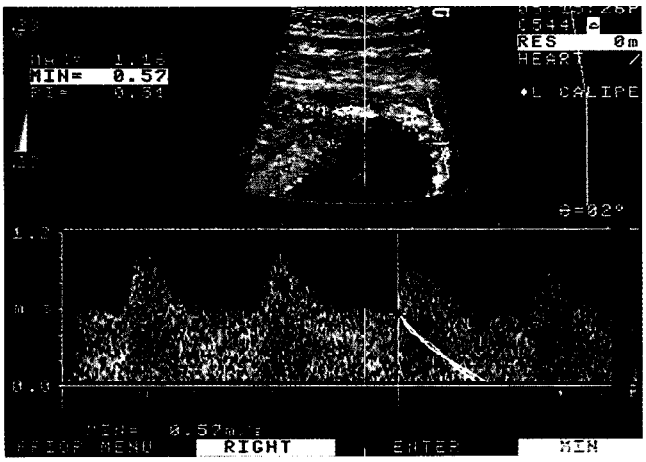


**Figure 2** Physiological changes in pregnancy result in a lowering of resistance and disappearance of the notch (see Figure 1). By using the external iliac artery as a point of reference, a consistent site for measuring uterine artery waveforms can be established

relative risk were calculated for PPIH, SGA, placental abruption and any complication (PPIH, SGA, placental abruption, stillbirth/neonatal death).

## RESULTS

### General data

A total of 1326 women underwent continuous wave Doppler studies between 19 and 21 weeks: 26 of these were excluded (15 with multiple pregnancy and 11 with a fetal abnormality or intrauterine death at the time of scan). A total of 214 (16.1%) were referred for repeat assessment at 24 weeks (median 24 weeks, range 24.0–25.6 weeks); 23 of those referred did not attend. Color Doppler studies were performed on 191 women; four were excluded from

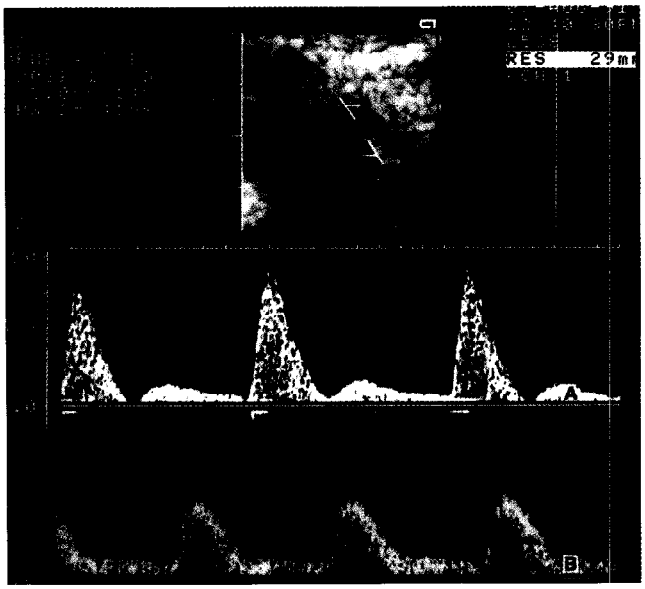


**Figure 3** Abnormal uterine artery Doppler waveforms at 24 weeks. Failure of physiological change in the uterine circulation results in a waveform (A) that is similar to that of a non-pregnant woman (compare with Figure 1). In a small number of cases there is no apparent notch, but resistance remains elevated (B). If the resistance index was > 95th centile, a waveform was defined as abnormal, irrespective of the presence or absence of a notch

the analysis (three with a diagnosis of pre-eclampsia at 24 weeks, one with a diagnosis of IUGR). The outcome is unknown for 69 pregnancies (67 scanned at 19–21 weeks' gestation, and two pregnancies scanned at 24 weeks' gestation). Thus, a total of 1233 (19–21 weeks) and 185 pregnancies (24 weeks) were suitable for analysis (Figure 4). In the cases with no outcome data, the distribution of race and parity was similar to that of the study population[12].

### Outcome

Of the total population studied ($n$ = 1233), 44 women (3.57%) developed PPIH, 131 (10.62%) delivered an SGA baby (below the 10th centile) and 13 (1.05%) had a placental abruption. Abnormal waveforms were found in 185 women at 20 weeks: 36(19.4%) developed PPIH, 47 (25.4%) babies were SGA (below the 10th centile) at birth and six (3.2%) were diagnosed with placental abruption. In the group of women with abnormal uterine artery Doppler findings (notching or RI > 95th centile) at 24 weeks ($n$ = 110), 34 (30.9%) developed PPIH, 42 (38.1%) delivered an SGA baby (below the 10th centile), and four (3.6%) had a placental abruption. Table 1 presents the outcome for the total population compared with pregnancies with persistent notching of the uterine artery Doppler waveform at 24 weeks.

### Abnormal uterine artery Doppler studies

A total of 1094 women (1019 at 19–21 weeks, 75 at 24 weeks) had normal uterine artery waveforms; 113 women had a uterine artery waveform with a notch when they

were scanned at 24 weeks' gestation. Three were considered normal because the mean RI was < 0.55. The remaining 110 women were considered screen-positive. A total of 62 women had unilateral notching and 48 had bilateral notching. Women with notching had a significantly greater risk of developing PPIH ($\chi^2 = 247.0$, $p < 0.00001$), delivering an SGA baby ($\chi^2 = 90.0$, $p < 0.00001$), or suffering a placental abruption (Fisher's exact test, $p < 0.025$), compared with women with normal uterine artery waveforms. The predictive values for persistent notching (one or both uterine arteries) are presented in Table 2.

The sensitivity in primiparas (76.9%) and multiparas (77.7%) for the prediction of PPIH is similar. The lower positive predictive value in primiparas (29.4%), compared with multiparas, reflects the greater proportion of primiparas with persistent notching at 24 weeks, rather than a lower incidence of PPIH in primiparas. The predictive values are presented in Table 3.

The sensitivity and positive predictive value for the prediction of PPIH in African–Caribbean women (82.6% and 40.4%, respectively) are greater than the sensitivity and positive predictive value in Caucasian women (71.4% and 23.8%, respectively). The incidence of PPIH in African–Caribbean women (4.2%) is greater than in Caucasian women (3.06%), and a greater proportion of African–Caribbean women developed PPIH that required delivery before term. The predictive value of persistent notching in women of different races and parities is presented in Table 3.

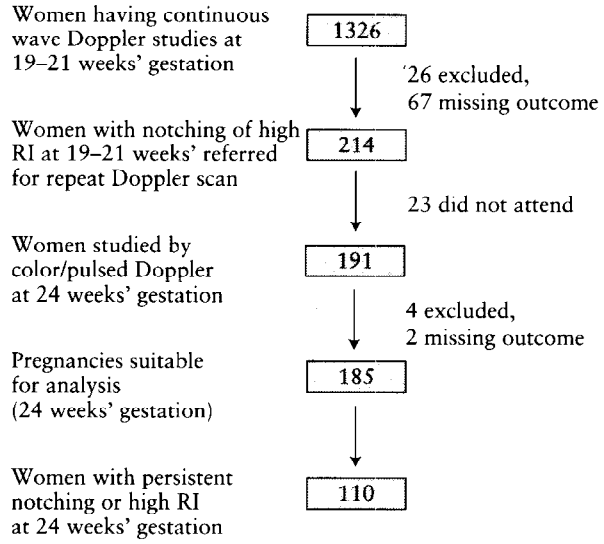


**Figure 4** Patients entered into the study at 19–21 weeks' gestation, those subsequently referred for repeat uterine artery Doppler assessment at 24 weeks' gestation and exclusions from the analysis, as indicated

## Unilateral vs. bilateral notching

For the purpose of more detailed analysis, women with abnormal waveforms were divided into three subgroups: any (right, left, or both sides), unilateral (one side only) or bilateral (both sides) notching. The sensitivity of unilateral notching only was poor (22.7% for PPIH, 13.7% for SGA[10]) (Table 4). Women with persistent bilateral notching of the uterine artery waveform had lower sensitivities for PPIH (54.5%), SGA (21.8%) and placental abruption (15.3%), when compared with any notching (Table 2), but a much higher specificity (Table 4). The positive predictive value of bilateral notching for PPIH was 50%, and 54.2% developed some complication.

Table 4 also shows the predictive value of bilateral notching in the prediction of complications that were associated with delivery of the patient before 34 completed weeks of pregnancy. The sensitivity for the prediction of early delivery (< 34 weeks) secondary to PPIH was 81.2%, SGA 57.6%, placental abruption 33.3%, and any complication 52.9%. The lower positive predictive value of bilateral notching for predicting 'any complication' before 34 weeks reflects the fact that most of the small babies identified before 34 weeks were also complicated by PPIH, whereas the ability of bilateral notching to predict 'any complication' at all gestations identified many SGA fetuses that did not have associated PPIH.

**Table 1** The prediction of the outcome for pregnancies found to have normal uterine artery Doppler studies, compared with those pregnancies found to have persistent notching of the uterine artery Doppler waveform at 24 weeks

| | *Normal (n = 1094)* | | *Abnormal (n = 110)* | | | | |
|---|---|---|---|---|---|---|---|
| | *n* | % | *n* | % | *Odds ratio* | *CI (95%)* | *p-Value* |
| PPIH | 10 | 0.91 | 34 | 30.9 | 48.5 | (23.4, 105.7) | < 0.0001 |
| SGA | 89 | 8.1 | 42 | 38.1 | 6.98 | (4.45, 10.81) | < 0.0001 |
| Abruption | 9 | 0.82 | 4 | 3.6 | 4.55 | (1.20, 14.8) | 0.049 |
| SB/NND | 11 | 1.01 | 1 | 0.91 | 0.90 | (0.041, 5.36) | 1.0 |
| Any | 98 | 7.7 | 59 | 53.6 | 11.75 | (7.67, 18.0) | < 0.0001 |
| NICU | 33 | 3.0 | 32 | 29.1 | 13.19 | (7.64, 22.6) | < 0.0001 |
| CSFC | 59 | 5.39 | 35 | 31.8 | 8.19 | (5.02, 13.2) | < 0.0001 |
| Delivery (≤ 34 weeks) | 27 | 2.47 | 22 | 20.0 | 9.88 | (5.33, 18.1) | < 0.0001 |

PPIH, proteinuric pregnancy-induced hypertension; SGA, small for gestational age, < 10th centile; abruption, placental abruption; SB/NND, stillbirth or neonatal death; Any, any complication (PPIH, SGA, placental abruption or SB/NND); NICU, admission to neonatal intensive care; CSFC, Cesarean section because of concern about fetal hypoxia/asphyxia or PPIH; CI (95%), exact 95% confidence intervals, mid-*p* corrected; *p*, exact significance

**Table 2** The prediction of different complications of pregnancy by single or bilateral abnormal uterine artery flow velocity waveforms (persistent notching or resistance index > 95th centile) at 24 weeks

| *Outcome* | *n* | *True positive* | *False negative* | *False positive* | *True negative* | *Sensitivity (%)* | *Specificity (%)* | *PPV (%)* | *NPV (%)* | *RR* |
|---|---|---|---|---|---|---|---|---|---|---|
| PPIH | 44 | 34 | 10 | 76 | 1084 | 77.3 | 93.9 | 30.9 | 99.1 | 34.7 |
| SGA | 131 | 42 | 89 | 68 | 1005 | 32.0 | 93.6 | 38.2 | 91.8 | 6.7 |
| Abruption | 13 | 4 | 9 | 106 | 1085 | 30.7 | 91.1 | 3.6 | 99.2 | 4.5 |
| SB/NND | 12 | 1 | 11 | 109 | 1083 | 8.3 | 90.8 | 0.9 | 99.1 | 0.9 |
| Any | 157 | 59 | 98 | 51 | 996 | 40.9 | 95.1 | 53.6 | 91.0 | 6.0 |
| NICU | 65 | 32 | 35 | 78 | 1059 | 30.7 | 93.1 | 29.1 | 96.8 | 9.6 |
| CSFC | 94 | 35 | 59 | 75 | 1035 | 37.2 | 94.1 | 31.8 | 94.6 | 6.1 |
| Del34 | 49 | 22 | 27 | 88 | 1067 | 44.8 | 92.4 | 20.0 | 97.5 | 8.4 |

PPV, positive predictive value; NPV, negative predictive value; RR, relative risk; PPIH, proteinuric pregnancy-induced hypertension; SGA, small for gestational age, < 10th centile; Abruption, placental abruption; SB/NND, stillbirth or neonatal death; Any, any complication; NICU, admission to neonatal intensive care; CSFC, Cesarean section because of concern about fetal hypoxia/asphyxia or PPIH; Del34, pregnancies that delivered before 34 completed weeks

**Table 3** Comparison of the predictive values of persistent notching of the uterine artery Doppler waveform at 24 weeks in primiparous and multiparous high-risk patients, and in Caucasian and African–Caribbean high-risk patients. The percentage of different races referred reflects the ethnic mix of the local antenatal population

| *Outcome* | *n* | *True positive* | *False negative* | *False positive* | *True negative* | *Sensitivity (%)* | *Specificity (%)* | *PPV (%)* | *NPV (%)* | *RR* |
|---|---|---|---|---|---|---|---|---|---|---|
| *Primiparous* (*n* = 558) | | | | | | | | | | |
| PPIH | 26 | 20 | 6 | 48 | 484 | 76.9 | 90.1 | 29.4 | 98.8 | 24.5 |
| SGA | 68 | 23 | 45 | 45 | 445 | 33.8 | 90.8 | 33.8 | 90.8 | 3.8 |
| *Multiparous* (*n* = 646) | | | | | | | | | | |
| PPIH | 18 | 14 | 4 | 28 | 600 | 77.7 | 95.5 | 33.3 | 99.3 | 51.8 |
| SGA | 63 | 19 | 44 | 23 | 560 | 30.1 | 96.1 | 45.2 | 93.3 | 6.4 |
| *African–Caribbean* (*n* = 536) | | | | | | | | | | |
| PPIH | 23 | 19 | 4 | 28 | 485 | 82.6 | 94.5 | 40.4 | 99.1 | 50.5 |
| SGA | 58 | 19 | 44 | 23 | 445 | 32.7 | 95.1 | 45.2 | 91.7 | 6.4 |
| *Caucasian* (*n* = 668) | | | | | | | | | | |
| PPIH | 21 | 15 | 6 | 48 | 599 | 71.4 | 92.6 | 23.8 | 99.0 | 24.7 |
| SGA | 73 | 26 | 44 | 37 | 558 | 35.6 | 93.8 | 41.2 | 92.7 | 5.5 |

PPV, positive predictive value; NPV, negative predictive value; RR, relative risk; PPIH, proteinuric pregnancy-induced hypertension; SGA, small for gestational age, < 10th centile

**Table 4** The predictive value of persistent unilateral and bilateral notching of the uterine artery Doppler waveform at 24 weeks. The predictive values of bilateral notching for pregnancies requiring delivery before 34 weeks for a particular complication are also presented

| *Outcome* | *n* | *True positive* | *False negative* | *False positive* | *True negative* | *Sensitivity (%)* | *Specificity (%)* | *PPV (%)* | *NPV (%)* | *RR* |
|---|---|---|---|---|---|---|---|---|---|---|
| *Unilateral notching* (*n* = 62) | | | | | | | | | | |
| PPIH | 44 | 10 | 34 | 52 | 1108 | 22.7 | 95.5 | 16.1 | 97.0 | 5.6 |
| SGA | 131 | 18 | 113 | 44 | 1029 | 13.7 | 95.9 | 29.0 | 90.1 | 3.0 |
| Abruption | 13 | 2 | 11 | 60 | 1131 | 15.3 | 95.0 | 3.2 | 99.0 | 3.4 |
| Any | 157 | 23 | 134 | 39 | 1008 | 15.9 | 96.2 | 37.0 | 88.3 | 3.2 |
| *Bilateral notching* (*n* = 48) | | | | | | | | | | |
| PPIH | 44 | 24 | 20 | 24 | 1136 | 54.5 | 97.9 | 50.0 | 98.3 | 40.8 |
| SGA | 131 | 24 | 107 | 24 | 1049 | 21.8 | 97.8 | 50.0 | 90.8 | 5.5 |
| Abruption | 13 | 2 | 11 | 46 | 1145 | 15.3 | 96.1 | 4.1 | 99.0 | 4.5 |
| Any | 157 | 26 | 131 | 22 | 1025 | 18.0 | 97.8 | 54.2 | 88.8 | 4.8 |
| *Bilateral notching: complications associated with delivery ≤ 34 weeks' gestation* (*n* = 48) | | | | | | | | | | |
| PPIH | 16 | 13 | 3 | 35 | 1153 | 81.2 | 97.1 | 27.0 | 99.7 | 107.0 |
| SGA | 26 | 15 | 11 | 33 | 1145 | 57.6 | 97.2 | 31.2 | 99.0 | 33.7 |
| Abruption | 6 | 2 | 4 | 46 | 1152 | 33.3 | 96.2 | 4.0 | 99.7 | 12.3 |
| Any | 32 | 18 | 16 | 30 | 1140 | 52.9 | 97.4 | 37.5 | 98.6 | 27.7 |

PPV, positive predictive value; NPV, negative predictive value; RR, relative risk; PPIH, proteinuric pregnancy-induced hypertension; SGA, small for gestational age, < 10th centile; Abruption, placental abruption; Any, any complication

## DISCUSSION

This study supports the proposal that it is possible to identify, with uterine artery Doppler studies, a group of women at high risk of developing pre-eclampsia or delivering a growth-retarded baby. The use of notching, a qualitative assessment of the flow velocity waveform, provides a more sensitive screening test when compared to the RI alone. In women with bilateral notches, we present a cohort who had a 1 : 2 chance of developing a complication, and a 1 : 3 chance of developing complications that required delivery before 34 weeks. Abnormal uterine artery Doppler studies probably reflect the failure of placentation adequately to modify the uterine circulation, rather than necessarily the development of pathological complications. This may be the reason that uterine artery Doppler appears to be capable of identifying high-risk pregnancies well before the onset of complications. The failure thus far of biochemical markers to be sufficiently sensitive as early predictors of subsequent pre-eclampsia and intrauterine growth retardation may be because many simply reflect the pre-clinical onset of disease[17].

Although the incidence of notching and the predictive values in this study vary slightly from previous, similar work[14], there is general agreement about the potential for this test. The high sensitivity of notching for the prediction of PPIH in both studies suggests that the combination of color Doppler imaging to identify the uterine artery accurately, and notching as the definition of an abnormal waveform, has helped to provide a useful and reproducible test for the detection of high-risk pregnancies. Color Doppler imaging overcomes the limitations of blind investigation of the uterine arteries, a problem encountered with continuous wave Doppler studies, thereby providing a more reproducible test. It should be noted in this study that continuous wave Doppler was used for the purpose of initial screening at 20 weeks; it remains to be seen how the results would alter if color Doppler imaging were used at both stages.

Persistent notching of the uterine artery waveform is a qualitative assessment. Attempts to define the notch have thus far failed[18]. The use of a quantitative RI cut-off point can therefore be helpful in two ways: excluding women where trophoblastic invasion appears normal but the placenta is positioned laterally, and where there is any doubt in interpreting a low-resistance flow velocity waveform. Ultimately more reliable methods of defining an abnormal waveform will be required. However, there is very good agreement between experienced operators when waveforms are classified as normal or abnormal.

One of the aims of antenatal care is to identify the fetus that is both small and growth-retarded. Smallness may occur for a variety of reasons[19], not all pathological. Although the overall number of small babies identified with persistent notching of the uterine artery Doppler waveform represents approximately one-third of the SGA population (32.0%), the proportion of these babies that require delivery by Cesarean section for concern about the fetus (31.8%) or admission to a neonatal intensive care unit (29.1%) reflects the fact that many of these small babies are truly growth-retarded, and often associated with the need for early delivery (20.0%).

The definition of placental abruption was made on clinical grounds: routine histology of the placenta was not available at the time of the study. Placental abruption probably occurs for a number of reasons, so it is improbable that any one test will successfully identify all patients at risk of developing this complication. The sensitivity of any notching for the prediction of abruption is low but encouraging, as almost a third (30.7%) of patients diagnosed with an abruption were identified with uterine artery Doppler studies.

The greater incidence of PPIH in African–Caribbean as compared with Caucasian women (4.2% vs. 3.0%) resulted in a high positive predictive value (40.4%) for the prediction of PPIH in this racial group. In addition, the majority of women who required delivery before 34 weeks' gestation for PPIH were of African–Caribbean origin (62.5%). There was a relatively high incidence (2.7%) of PPIH in the multiparous group (Table 3), which reflects the high-risk population used in this study. It probably also reflects a pattern of referring multiparas with a poor obstetric history for 24-week uterine artery Doppler assessment, irrespective of any previous investigation. The percentage of women with uterine artery Doppler waveform notching was greater in primiparas (11.9%) than in multiparas (6.3%). The combination of a relatively high incidence of complications and low percentage with notching resulted in a higher positive predictive value of notching in multiparas for PPIH (33.3%) and SGA (45.2%), compared to the primiparous group. The higher percentage of primiparas with notching at 24 weeks may be a chance finding. Alternatively, it may reflect chronological differences in the rate or extent of physiological changes that occur in first and subsequent pregnancies.

One of the problems with pre-eclampsia/PPIH is that the majority of patients are primiparous and therefore without a history to help determine surveillance and management. Persistent notching selects a group of women whose uterine circulation has failed to modify appropriately during pregnancy. It therefore holds the potential to identify pregnancies at risk of uteroplacental problems, regardless of race or parity.

By further subdividing the groups into those with persistent notching in only one (unilateral) or both (bilateral) uterine artery waveforms, it is possible to see the part each subset plays in the prediction of complications (Table 4). Although the sensitivity of unilateral notching was poor (22.7% for PPIH, 13.7% for SGA), removing this group of women diminishes the overall predictive value of the test. With a positive predictive value of 50.0% for PPIH, and 54.2% for any complication, it is clear that women with persistent bilateral notching at 24 weeks constitute a very high-risk group.

The overall sensitivities of bilateral notching for the prediction of pre-eclampsia (55%) and SGA (21.8%) were lower than the sensitivity for any notching, but the high sensitivity of bilateral notching for predicting early delivery

(before 34 weeks) due to PPIH (81.2%) or SGA (57.6%) highlights the potential of this test for diagnosing the most severe forms of these conditions. Thus, failure to modify either uterine artery (bilateral notching) by 24 weeks implies that there are significant problems with placental growth and development, and the findings in this study suggest that these patients constitute a very high-risk group. It is not known whether bilateral notching would be as useful in populations with a lower incidence of pre-eclampsia or growth retardation, especially where the requirement for preterm delivery for these complications is low.

Two of the largest placebo-controlled trials of low-dose aspirin to date[20,21] could not demonstrate a significant overall benefit by using low-dose aspirin, although the trend in the CLASP[20] study suggested that the earlier the delivery required for a complication, the more likely that aspirin might exert a beneficial effect. This supports the results from previous placebo-controlled randomized trials with aspirin[1,22]. Low-dose aspirin or other therapies are likely to be of benefit in only very high-risk pregnancies that end in preterm delivery, in particular pregnancies that require delivery before 34 weeks.

Women with bilateral notching appear to fulfil the criteria for pregnancies that may benefit from prophylactic therapy, especially primiparas who would otherwise not be identified at this early stage in the pregnancy. Furthermore, the negative predictive value of uterine Doppler should not be overlooked. Women with normal uterine Doppler waveforms constitute a very low-risk group, with less than 1% developing PPIH (Table 1). With the current trend in the UK for devolution of antenatal care to the community, uterine artery Doppler could be used to help define patients who are suitable for this type of care. To ascertain whether the selection of patients at this gestation can improve outcome, it will be necessary to perform randomized trials using uterine artery Doppler as the criterion for entry into the study; such studies are in progress.

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