A Comparison of Changes in the Mean Arterial Blood Pressure and Mean Uterine Artery Pulsatility Index from 11–14 to 19–24 + 6 Gestation Weeks in Low-Risk and High-Risk Asian Indian Pregnant Women


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Abstract

Aim The aim of this study was to determine the changes in the mean arterial blood pressure (MAP) and mean uterine artery (UtA) pulsatility index (PI) from 11-14 to 19-24 + 6 gestation weeks in Asian Indian pregnant women.

Methods Clinical and demographic details, MAP, and mean UtA PI measures were ascertained for pregnant women at 11 to 14 gestation weeks and 19–24 + 6 gestation weeks. Women were categorized as a high-or-low risk for preterm preeclampsia using the Fetal Medicine Foundation algorithm and 1 in 150 cutoff. High-risk pregnant women were recommended low-dose aspirin 150 mg daily at bedtime. Changes in MAP and mean UtA PI were compared for gestational age intervals and high-and-low risk women using nonparametric tests.

Keywords► mean arterial blood pressure
► mean uterine artery pulsatility index
► Doppler ultrasonography
► fetal ultrasonography
► pregnancy

The study analyzed the results of 1,163 pregnant women. Both MAP (mean difference: 5.14, p < 0.001) and mean UtA PI (mean difference: 0.14, p < 0.001) remained significantly higher at the second-trimester assessment in high-risk pregnant women compared to low-risk pregnant women. Seventy-seven (35.16%) of the 219 pregnant women with abnormal mean UtA PI in the first trimester had an abnormal mean UtA PI in the second-trimester assessment. One hundred (10.59%) of the 944 pregnant women with normal mean UtA PI in the first trimester had an abnormal mean UtA PI in the 19–24 + 6 weeks assessment. Seventy-seven pregnant women (6.62% of 1,163 women, 95% confidence interval: 5.33, 8.20) had an abnormal mean UtA PI at both gestation age intervals. High-risk pregnant women taking low-dose aspirin daily showed a larger reduction in mean UtA PI compared to high-risk pregnant women that did not report the use of low-dose aspirin (0.89 vs. 0.62, p < 0.001)

Conclusion
MAP and mean UtA PI decreased significantly from the first to the second trimester of pregnancy. Sequential assessment of the MAP and mean UtA PI in the first and second trimesters of pregnancy will be useful for fetal radiologists in India to identify a subgroup of women with abnormal mean UtA PI at both trimesters that may need more intense surveillance and follow-up till childbirth.

Introduction

The Samrakshan protocol utilizes maternal clinical and demographic details, mean arterial blood pressure (MAP), and mean uterine artery (UtA) pulsatility index (PI) measurements to assess the risk for preterm preeclampsia (PE) and fetal growth restriction (FGR) in pregnant women in India.1–3 MAP and mean UtA PI measurements are noninvasive, painless tests that are integrated with routine antenatal assessments. Several studies have confirmed the utility of mean UtA PI measurements during pregnancy to assess uteroplacental circulation and the risk for PE and FGR.4–10 Previous studies have reported that earlier reduction in UtA flow resistance results in better placentation and higher birthweights and that late normalization of UtA blood flow was associated with higher perinatal mortality.11–14 We aimed to determine the sequential changes in the MAP and mean UtA PI between two gestational week intervals, the 11 to 14 gestation week period and the 19–24 + 6 gestation week period, in a population of Asian Indian pregnant women.

Methods

The study protocol adhered to the tenets of the Declaration of Helsinki and all patient data were anonymized before analysis to protect patient confidentiality. The study sample was an opportunistic, purposive sample from fetal radiology centers that are participating in the Samrakshan program of the Indian Radiological and Imaging Association.1 Fetal radiologists certified by the Fetal Medicine Foundation performed all fetal Doppler assessments. The sample size for the study was estimated as a minimum of 957 first-trimester pregnant women using the likelihood ratio test for proportions. The assumptions underlying the sample size estimate included a 1:2 ratio for pregnant women at high risk and low risk for preterm PE in the 11 to 14 gestation weeks assessment, an alpha of 0.05, 80% power and an anticipated delta of 0.07. The least required sample size was revised upwards to 1,149 after factoring in a maximum anticipated 20% loss to follow-up between the 11 to 14 weeks and 19–24 + 6 weeks assessment. We estimated that study recruitment must include at least 1,264 pregnant women (based on an anticipated exclusion of 10% for maternal comorbidities and missing data) to achieve the minimum sample size of 1,149. The study data were prospectively collected between March and July 2022.

The first-trimester assessments that included the collection of clinical and demographic details, measurement of MAP, and Doppler assessment of the uterine artery (UtA PI) were performed between 11 and 14 gestation weeks. Clinical and demographic details that were collected in the first trimester included maternal age, parity, prior obstetric history, prior and current comorbidity, type of conception, personal risk behaviors, and height and weight measurements to estimate the body mass index (BMI). Dating of the pregnancy was done at the first-trimester visit to assign an expected date of delivery and the crown-rump length (CRL) was measured. The study included singleton live pregnancies and fetuses with a CRL between 45 and 84 mm at 11 to 14 gestation weeks. The details were entered in the Fetal Medicine Foundation online calculator for risk assessment of PE (available at https://fetalmedicine.org/research/assess/preeclampsia/first-trimest-er) to determine a customized risk for the development of preterm PE and FGR for each woman. Pregnant women at high risk for the development of preterm PE (based on a 1 in 150 cutoff) were recommended low dose aspirin 150 mg once daily at bedtime to be continued up to 36 weeks of gestation, development of preterm PE or childbirth, whichever is earlier.

MAP was measured at each trimester of pregnancy after explaining the procedure to the woman. The blood pressure was measured in both upper arms simultaneously using
calibrated digital oscillometry machines with the pregnant woman seated in a comfortable upright position, legs uncrossed and placed flat on the floor, and forearms resting at the level of the heart on a table in front, and the digital monitor facing away from the woman.\(^2\) The blood pressure measurement was repeated after at least 1 minute.\(^2\) The blood pressure measurements were done in a silent environment avoiding any distraction for the pregnant woman during the measurement.\(^2\)

The mean UtA PI was measured using the transabdominal approach.\(^3\) A mid sagittal section of the uterus and cervix was obtained, and the transducer tilted gently sideways while using color flow mapping. The pulsed wave Doppler sampling gate was set at approximately 2 mm and positioned on the UtA (ascending or descending branch) at the point closest to the internal cervical os. The insonation angle was less than 30 degrees and as close to 0 as possible with a peak systolic velocity more than 60 cm/sec. The pulsatility of the right and left UtA was measured and the PI was measured when at least three identical waveforms were obtained. An abnormal UtA PI was defined as mean UtA PI more than 95\(^{th}\) percentile.

The second-trimester assessments were done between 19 and 24 + 6 weeks of pregnancy. These assessments included the collection of clinical and demographic details including self-reported use of low-dose aspirin, a targeted assessment for fetal anomalies (TIFFA scan), measurement of MAP and Doppler studies of the UtA, umbilical artery, and ductus venosus.

The data were entered into an MS Office Excel spreadsheet and subsequently exported to STATA version 12.0 (StataCorp, College Station, Texas, United States) for further analysis. Continuous data were expressed as mean (standard deviation) and categorical data as frequencies and proportions. The median and interquartile range (IQR) was estimated for continuous variables. The Shapiro–Wilk test was used to determine the normality of the data distribution and nonparametric tests were used for analysis as MAP and mean UtA PI were not normally distributed. The data of pregnant women who did not provide information on the use of low dose aspirin or reported irregular use of low dose aspirin and women with chronic hypertension or polycystic ovarian syndrome were excluded from further analysis. The nonparametric K sample equality of medians test was used to compare the medians of normally distributed data. The data of pregnant women who did not provide information on the use of low dose aspirin and 14 (2.89%) women who reported irregular use of low dose aspirin in the second-trimester follow-up visit were not considered for further analysis. The final cohort for analysis included 1,163 pregnant women including 390 women identified as high-risk for preeclampsia at the first-trimester ultrasound assessment and with sequential ultrasound scans in the first and second trimester of pregnancy.

MAP was significantly higher (K sample Equality of Medians test Fisher's exact p-value <0.001) in high-risk (median: 86, IQR: 81.42–90.8) compared to low-risk pregnant women (median: 79, IQR: 75.5–84) in the 11 to 14 weeks screening. Two (0.26%) of the 773 low-risk women and 10 (2.56%) of the 390 high-risk women had a MAP more than or equal to 100. The 11 to 14 weeks MAP was significantly associated with increasing gestational age (β coefficient: 0.27, 1.49, p = 0.18). MAP decreased (β coefficient: -0.008, 95% CI: -0.01, -0.001, p = 0.02) with increasing gestational age in the 11 to 14 weeks assessment.

Mean UtA PI was significantly higher (K sample Equality of Medians test Fisher’s exact p-value <0.001) in high-risk (median: 2.02, IQR: 1.72–2.4) compared to low-risk pregnant women (median: 1.50, IQR: 1.25–1.92) in the 11 to 14 weeks screening. Two hundred and nineteen (18.83%) women were identified with abnormal mean UtA PI in the 11 to 14 weeks assessment. One hundred and twenty-eight (58.45%) of the 219 women with abnormal mean UtA PI and 262 (27.75%) of the 944 women with normal mean UtA PI in the 11 to 14 weeks assessment were categorized as high-risk for

### Table 1 Clinidemographic details of the 1,163 pregnant women in the 11 to 14 gestation weeks’ assessment

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, median, IQR</td>
<td>28, 24 to 30.7 years</td>
</tr>
<tr>
<td>Body mass index, median, IQR</td>
<td>23.53, 20.57 to 26.84</td>
</tr>
<tr>
<td>Spontaneous conception, n, %</td>
<td>1137, 97.76%</td>
</tr>
<tr>
<td>Nulliparous, n, %</td>
<td>685, 58.90%</td>
</tr>
<tr>
<td>Multiparous, n, %</td>
<td>478, 41.10%</td>
</tr>
<tr>
<td>Mean arterial blood pressure, median, IQR</td>
<td>81.67, 76.83 to 86</td>
</tr>
<tr>
<td>Mean uterine artery PI, median, IQR</td>
<td>1.7, 1.35 to 2.13</td>
</tr>
</tbody>
</table>

Abbreviations: IQR, interquartile range; PI, pulsatility index.

### Results

The initial study dataset included 1,274 pregnant women with ultrasound scans over 2 gestational week intervals, 11 to 14 gestation weeks, and 19-24 + 6 gestation weeks. The 11 to 14 weeks assessment identified 484 pregnant women at high risk for preterm PE who were recommended low-dose aspirin. We excluded the data of 42 (3.30%) women with chronic hypertension and 12 (0.94%) women with polycystic ovarian disease from the analysis. The data of 48 (9.92%) of the 484 high-risk women who did not provide information on the use of low dose aspirin and 14 (2.89%) women who reported irregular use of low dose aspirin in the second-trimester follow-up visit were not considered for further analysis. The final cohort for analysis included 1,163 pregnant women including 390 women identified as high-risk for preterm PE in the first-trimester ultrasound assessment and with sequential ultrasound scans in the first and second trimester of pregnancy.
preterm PE. Abnormal mean UtA PI decreased with increasing maternal age (β coefficient: −2.20, 95% CI: −2.88, −1.52, p < 0.001), increasing gestational weeks (β coefficient: −0.31, 95% CI: −0.43, −0.19, p < 0.001) and increasing BMI (β coefficient: −1.16, 95% CI: −1.83, −0.50, p = 0.001) but was not associated with parity (β coefficient: 0.03, 95% CI: −0.03, 0.09, p = 0.31) in the first trimester.

Table 2 presents the changes in MAP from the baseline first-trimester to the second-trimester assessment. The MAP showed a significant reduction from baseline to the second trimester in all subgroup analyses except for obese pregnant women. The mean UtA PI showed a significant reduction from baseline to the second trimester in the subgroup analyses except for obese pregnant women. The mean UtA PI at both gestation age intervals. One hundred and ten (10.59%) of the 944 pregnant women with normal mean UtA PI in the 11 to 14 weeks assessment had abnormal mean UtA PI in the 19–24 + 6 weeks assessment. On further analysis, we observed that the mean UtA PI shifted from abnormal at 11 to 14 weeks to normal at 19–24 + 6 weeks in 59.38% of high-risk women. Among high-risk women, 40.63% had an abnormal UtA PI at both first- and second-trimester assessments. The proportion of women that shifted from a normal first-trimester UtA PI to an abnormal second-trimester UtA PI was significantly higher in the high-risk group compared to the low-risk group (13.74% vs. 9.38%, p = 0.048).

Multiparity (β coefficient: −0.19, 95% CI: −0.34, −0.04, p = 0.01) reduced risk and higher second-trimester MAP (β coefficient: 0.01, 95% CI: 0.004, 0.02, p = 0.007) increased risk for abnormal mean UtA PI in both trimesters in a multivariate regression model that adjusted for maternal age, parity, BMI, and second-trimester MAP. Maternal age (p = 0.30), BMI (p = 0.91), parity (p = 0.17), or second-trimester MAP (p = 0.72) was not significantly associated in the multivariate regression model with a shift from normal mean UtA PI in the first-trimester assessment to an abnormal mean UtA PI in the second trimester.

**Discussion**

We found that MAP and mean UtA PI measures decreased significantly from the first to the second trimester of pregnancy.

### Table 2 Changes in MAP from 11 to 14 to 19–24 + 6 gestation weeks by subgroups

<table>
<thead>
<tr>
<th></th>
<th>11–14 weeks MAP Mean (SD)</th>
<th>19–24 + 6 weeks MAP, Mean (SD)</th>
<th>Wilcoxon test p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nulliparous (n = 685)</td>
<td>81.39 (7.19)</td>
<td>79.76 (7.55)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Multiparous (n = 478)</td>
<td>82.00 (7.99)</td>
<td>78.92 (8.00)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Normal BMI (n = 612)</td>
<td>80.73 (7.28)</td>
<td>78.19 (7.53)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lean BMI (n = 99)</td>
<td>77.09 (9.53)</td>
<td>74.86 (8.14)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Overweight BMI (n = 320)</td>
<td>83.47 (6.62)</td>
<td>81.33 (7.18)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Obese BMI (n = 132)</td>
<td>84.87 (6.60)</td>
<td>83.86 (6.37)</td>
<td>0.08</td>
</tr>
<tr>
<td>No aspirin use (n = 773)</td>
<td>79.28 (6.97)</td>
<td>77.68 (7.56)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Daily aspirin use (n = 390)</td>
<td>86.32 (6.34)</td>
<td>82.82 (6.94)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Abbreviations:** BMI, body mass index; MAP, mean arterial blood pressure; SD, standard deviation.

### Table 3 Changes in mean UtA PI from 11 to 14 to 19–24 + 6 gestation weeks by subgroups

<table>
<thead>
<tr>
<th></th>
<th>11–14 weeks mean UtA PI Mean (SD)</th>
<th>19–24 + 6 weeks mean UtA PI Mean (SD)</th>
<th>Wilcoxon test p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nulliparous (n = 685)</td>
<td>1.73 (0.55)</td>
<td>1.00 (0.33)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Multiparous (n = 478)</td>
<td>1.77 (0.52)</td>
<td>1.05 (0.35)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Normal BMI (n = 612)</td>
<td>1.77 (0.52)</td>
<td>1.03 (0.32)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lean BMI (n = 99)</td>
<td>1.95 (0.52)</td>
<td>0.99 (0.43)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Overweight BMI (n = 320)</td>
<td>1.67 (0.55)</td>
<td>0.99 (0.33)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Obese BMI (n = 132)</td>
<td>1.66 (0.52)</td>
<td>1.07 (0.39)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No aspirin use (n = 773)</td>
<td>1.60 (0.49)</td>
<td>0.97 (0.33)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Daily aspirin use (n = 390)</td>
<td>2.05 (0.49)</td>
<td>1.11 (0.34)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Abbreviations:** BMI, body mass index; SD, standard deviation; UtA PI, uterine artery pulsatility index.
pregnancy in this study. Both MAP and mean UtA PI were significantly higher in high-risk pregnant women compared to low-risk pregnant women in the first trimester. We found that MAP measures were higher with increasing maternal age and BMI in the first trimester and reduced with an increase in gestational age. MAP reduced significantly between trimesters in both high- and low-risk subgroups and probably reflected the natural decrease of blood pressure in the early trimesters of pregnancy. Consistent with prior knowledge, we found that mean UtA PI decreased with older maternal age and higher BMI in the first trimester. The reduction in mean UtA PI with increasing gestational age is consistent with existing knowledge of a significant reduction within-and-between trimesters of pregnancy. The high-risk subgroup that received daily low-dose aspirin had MAP and mean UtA PI measures that were significantly higher than the low-risk subgroup in the second-trimester assessment. The reduction in mean UtA PI was significantly more among those taking low-dose aspirin daily compared to those not taking low-dose aspirin in the high-risk subgroup.

We found that the high-risk subgroup had a higher proportion of pregnant women that shifted from an abnormal first trimester mean UtA PI to a normal second trimester mean UtA PI (or normalized late) and a higher proportion of women with a UtA mean PI shifting from normal to abnormal between the two intervals studied. These results are consistent with a previous study that reported a similar pattern for complicated and normal pregnancies between the first and second trimesters. Previous studies have reported that delayed normalization of the UtA PI is associated with an intermediate risk for adverse perinatal outcomes. The subgroup of 77 pregnant women (6.62% of the overall study cohort, 95% CI: 5.33, 8.20) that had an abnormal mean UtA PI at both gestation age intervals is an important group for surveillance when we consider the effects of delayed normalization of the mean UtA PI. The estimate of 6.62% (95% CI: 5.33, 8.20) is consistent with the estimated magnitude of PE in India that ranges from 5 to 10%. We found that nulliparity and higher MAP increased the risk for abnormal mean UtA PI in the second trimester in the high-risk subgroup that is consistent with the known risk factors for PE. We did not find any specific associations for the transition from a normal first-trimester mean UtA PI to an abnormal second-trimester mean UtA PI in the low-risk subgroup and hence cannot comment on follow-up surveillance strategies for specific low-risk subgroups. However, we feel it is important to repeat the UtA PI measurements in the second trimester even for low-risk pregnant women as 1 in 10 low-risk pregnant women transitioned to an abnormal UtA PI in the second trimester.

The quantum of reduction in MAP between the gestation intervals was statistically significant. Previous studies have reported that maternal predisposing factors can cause vasoactive and atherosclerotic changes that affect the transformation of spiral arteries and influence the risk for PE. Any decrease in MAP must therefore be useful to minimize the risk for PE. Underlying maternal predisposing factors may contribute to the higher MAP and mean UtA PI measures in the second trimester in high-risk pregnant women even though there is a significant decrease from the first-trimester measures.

The inability to perform sequential assessments within trimesters may be considered a limitation of our study but is a pragmatic reality of clinical practice in India where it is not feasible to perform weekly ultrasound measurements routinely in a clinical setting. We did not collect information on childbirth outcomes as part of this study and hence cannot comment on the possible association of late normalization of mean UtA PI with adverse perinatal outcomes in this study. The large number of paired assessments at both gestational age intervals by radiologists certified for ultrasound assessments is a strength of the study. Since this was a real-life practice-based study, we had not masked the radiologist to the baseline measures. However, we do not anticipate the lack of masking to significantly impact the study results as both Doppler and MAP measures are objective measures.

Our results cannot be generalized to the larger population of pregnant women in India due to the diversity and variations in population characteristics within and between states and settings in India. However, our results suggest that a sequential assessment of the MAP and mean UtA PI in the first and second trimesters of pregnancy will be useful to identify a subgroup of women with abnormal mean UtA PI at both trimesters that may need more intense surveillance and follow-up till childbirth. We do not provide any specific recommendations on possible targets or management of MAP based on our results as further studies on the normative distribution of MAP in pregnant Asian Indian women, the potential associations of MAP in pregnancy in India, and the effectiveness of possible management strategies including optimal thresholds are required.

Note
This work has been attributed to: Indian Radiological & Imaging Association, New Delhi, India.

Conflict of Interest
None declared.

References