Prioritizing Fetal Structural Abnormalities Over Risk for Pre-Eclampsia and Fetal Growth Restriction in the 20-24 Gestation Week Assessment in India: Missing the Woods for the Trees?

Rijo Mathew Choorakuttil\textsuperscript{1} Shilpa R. Satarkar\textsuperscript{2} Lalit K. Sharma\textsuperscript{3} Anjali Gupta\textsuperscript{4} Akanksha Baghel\textsuperscript{5} Praveen K. Nirmalan\textsuperscript{6}

\textsuperscript{1}Department of Clinical Radiology, AMMA Center for Diagnosis and Preventive Medicine, Kochi, Kerala, India
\textsuperscript{2}Department of Clinical Radiology, Antarang Sonography and Colour Doppler Center, Satarkar Hospital, Tilaknagar, Aurangabad, Maharashtra, India
\textsuperscript{3}Department of Clinical Radiology, Raj Sonography & X-Ray Clinic, Baiju Choraha, Nayapura, Guna, Madhya Pradesh, India
\textsuperscript{4}Department of Clinical Radiology, Anjali Ultrasound and Colour Doppler Centre, Shanti Madhuban Plaza, Delhi Gate, Agra, Uttar Pradesh, India
\textsuperscript{5}Department of Clinical Radiology, Baghel Sonography Center, Harda, Madhya Pradesh, India
\textsuperscript{6}Department of Research, Chief Research Mentor, AMMA Education and Research Foundation, AMMA Healthcare Research Gurukul, Kochi, Kerala, India

Address for correspondence Rijo Mathew Choorakuttil, MD, AMMA Center for Diagnosis and Preventive Medicine Pvt Ltd, Kochi 682036, Kerala, India (e-mail: rijomc@gmail.com).

Indian J Radiol Imaging

\textbf{Abstract}

\textbf{Aim} To compare the magnitude of fetuses with congenital anomalies, pregnant women identified at high risk for preterm pre-eclampsia (PE) or with preterm PE, and with early fetal growth restriction (FGR) or high risk for FGR at the second trimester assessment at 20 to 24 weeks of gestation.

\textbf{Methods} A standardized trimester-specific protocol that included clinical and demographic details, fetal biometry, estimated fetal weight (EFW), fetal abdominal circumference (FAC), mean arterial blood pressure and fetal Doppler studies was used to identify high risk for preterm PE and FGR. The Targeted Imaging for Fetal Anomalies (TIFFA) scan was used to identify congenital anomalies. In addition, 95\% confidence intervals of the point estimates were derived, and the \(p\)-value was estimated to assess the statistical significance of the difference in proportions.

\textbf{Results} Analysis of the data of 4,572 pregnant women screened between 20 and 24 gestation weeks showed a significantly lower prevalence (\(p < 0.001\)) of congenital abnormalities (3.81\%) compared to women diagnosed with early PE (2.71\%) or with a high risk for PE (4.00\%) and women (6.80\%) with early FGR or at higher risk for fetal growth restriction with both EFW and FAC < 10th percentile.

\textbf{Conclusions} The data on prevalence from Samrakshan show that the second-trimester assessment of pregnant women in India must expand its scope from the TIFFA scan to also focus on screening to identify women at high risk for preterm PE and FGR.
Introduction

Antenatal assessments of pregnant women in the second trimester in India focus almost exclusively on the identification of structural and congenital abnormalities through a targeted imaging for fetal anomalies (TIFFA) at 20 to 24 gestation weeks. A systematic review from India reported a pooled prevalence of congenital anomaly of 184.48 per 10,000 births (95% CI 164.74 - 204.21) and 472.177 (95% CI: 421.652 to 522.676) congenital anomaly affected births in India each year. Congenital heart defects (65.86 per 10,000 live births) and neural tube defects (27.44 per 10,000 live births) were the most common congenital abnormalities reported. The congenital anomaly termination of pregnancy rate was 4.39 per 1,000 births in India. Pre-eclampsia (PE) and fetal growth restriction (FGR) cause adverse consequences that can be minimized by early identification of pregnant women at high-risk. However, the assessment of PE and FGR is a lower priority than congenital abnormalities in the second trimester study at 20 to 24 gestation weeks. We estimated the comparative prevalence of congenital abnormalities, PE and FGR among pregnant women screened between 20 and 24 gestation weeks in the Samrakshan program of the Indian Radiological and Imaging Association (IRIA) to determine if the data support the larger focus on congenital abnormality.

Method

A standardized trimester specific protocol was used to screen pregnant women between 11 and 14 weeks, 20 and 24 weeks and 28 gestation weeks onward in Samrakshan. Briefly, the assessments included clinical and demographic details, fetal biometry, estimated fetal weight (EFW), fetal abdominal circumference (FAC), mean arterial blood pressure, and fetal Doppler studies. An individualized risk for PE was determined using the online Fetal Medicine Foundation calculator and a cutoff of 1 in 150 was used to stratify risk. The diagnosis of PE was based on documented evidence in the medical records for a clinical diagnosis and management of PE after 20 gestation weeks. EFW and/or FAC <10th percentile were considered as high risk for FGR or suggestive of the presence of early FGR or small for gestational age (SGA) fetus. Congenital abnormalities were determined based on a TIFFA scan and fetuses that required further study and fetal interventions were referred to tertiary care units for further assessment.

Results

We analyzed the data of 4,572 pregnant women screened between 20–24 gestational weeks. The prevalence of congenital abnormalities (3.81%) was significantly lower (p < 0.001) than women diagnosed with early PE (2.71%) or with a high risk for PE (4.00%) and women (6.80%) with early FGR or at higher risk for fetal growth restriction with both EFW and FAC <10th percentile (Table 1). Of the 4,572 women screened at 20 to 24 weeks, 721 (15.77%) had been started on low-dose aspirin based on the risk assessment at 11 to 14 gestation weeks. Third trimester assessments until 37 gestation weeks were available for 4,372 pregnant women. At the third trimester assessment, preterm PE had developed in 1.94% (95% confidence interval [CI]: 1.55%, 2.43%) of the women considered low risk in the first trimester assessment, and in 25.40% (95% CI: 21.98%, 29.15%) of women started on low-dose aspirin based on the first-trimester assessment. Preterm PE did not develop until 37 gestation weeks in 74.60% (95% CI: 70.85%, 78.02%) of pregnant women started on low-dose aspirin in the first trimester, which is consistent with the results of a recent systematic review and meta-analysis that reported a 62% reduction in the in risk of preterm preeclampsia with low-dose aspirin. The ASPRE trial had also reported a reduction in the risk (OR 0.38, 95% CI: 0.20, 0.74) for preterm PE in women receiving low-dose aspirin compared to placebo. Overall, 4.96% (95% CI: 4.46%, 5.65%) of pregnant women developed preterm PE before 37 gestation weeks. The comparative prevalence at 20 to 24 gestation weeks reaffirms that the identification of pregnant women with-or-at-risk for PE and FGR in the second trimester is a priority in this population.

Discussion

The identification of a congenital abnormality involves either continuation or termination of pregnancy, or fetal interventions based on the severity and lethality of the abnormality. Pregnant women identified as high-risk for PE and FGR are advised low-dose aspirin starting from 11 to 14 weeks as a preventative measure. Treatment-naive cases identified in the second trimester can be started on low-dose aspirin within 20 gestation weeks but with lower effectiveness.

Table 1: Prevalence of congenital abnormalities, pre-eclampsia, high risk for fetal growth restriction in the screened population at 20–24 gestation weeks

<table>
<thead>
<tr>
<th>Congenital abnormality</th>
<th>Prevalence</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital abnormality</td>
<td>174, 3.81%</td>
<td>3.28, 4.39</td>
</tr>
<tr>
<td>Diagnosed preeclampsia</td>
<td>124, 2.71%</td>
<td>2.28, 3.22</td>
</tr>
<tr>
<td>High risk for preeclampsia</td>
<td>178, 4.00%</td>
<td>3.46, 4.62</td>
</tr>
<tr>
<td>Fetal abdominal circumference (FAC) &lt;10th centile</td>
<td>378, 8.27%</td>
<td>7.50, 9.10</td>
</tr>
<tr>
<td>Estimated fetal weight (EFW) &lt;10th centile</td>
<td>395, 8.64%</td>
<td>7.86, 9.49</td>
</tr>
<tr>
<td>Both EFW and FAC &lt;10th centile</td>
<td>311, 6.80%</td>
<td>6.11, 7.57</td>
</tr>
</tbody>
</table>

*aExcludes already diagnosed preeclampsia.*
Longitudinal assessments of fetal growth velocity and interval assessments of FAC and EFW are useful to monitor growth. However, it is a pragmatic reality that patients do not necessarily follow up with the same doctor for care and do not have access to or carry their medical records with them for follow-up assessments. The use of fetal Doppler studies can help identify women at-risk for PE and FGR. The assessment of Doppler studies is not time consuming and can be integrated with routine antenatal ultrasound and TIFFA studies.

Clinical algorithms that can identify pregnant women at high risk for PE and FGR between 20 and 24 gestation weeks are available and can be used by fetal radiologists. Fetal radiologists in India must focus on the development of region-specific and representative normative biometry and Doppler parameters as a priority and integrate these with the sonography machines for more accurate risk estimates. The distinction between early FGR and SGA needs accurate normative data that allow optimal identification and monitoring of progress. The data on prevalence from Samrakshan show that a larger focus only on congenital abnormalities in the second trimester is a misplaced priority based on the magnitude of PE and FGR in the pregnant women population of India.

Work Attributed to
Indian Radiological & Imaging Association, IRIA House, C-5, Qutab Institutional Area, New Delhi-110016, India.

Conflicts of Interest
None declared.

References