Reducing Perinatal Mortality in India: Two-Years Results of the IRIA Fetal Radiology Samrakshan Program

Rijo M. Choorakuttil¹ Bavaharan Rajalingam² Shilpa R. Satarkar³ Lalit K. Sharma⁴ Anjali Gupta⁵ Akanksha Baghel⁶ Neelam Jain⁷ Devarajan Palanisamy⁸ Ramesh Shenoy⁹ Karthik Senthilvel¹⁰ Sandhya Dhankar¹¹ Kavita Aneja¹² Somya Dwivedi¹³ Shweta Nagar¹⁴ Sonali Kimmatkar Soni¹⁵ Gulab Chhajer¹⁶ Sunitha Pradeep¹⁷ Prashant M. Onkar¹⁸ Avni K.P. Skandhan¹⁹ Eesha Rajput²⁰ Renu Sharma²¹ Srinivas Shentar²² Suresh Saboo²³ Amel Antony²⁴ M.R. Balachandran Nair²⁵ Tejashree Y. Patekar²⁶ Bhupendra Ahuja²⁷ Hemant Patel²⁸ Mohanan Kunnumal²⁹ Rajendra K. Sodani³⁰ M.V. Kameswar Rao³¹ Pushparaj Bhatele³² Sandeep Kavthale³³ Deepak Patkar³⁴ Rajeev Singh³⁵ Amarnath Chelladurai³⁶ Praveen K. Nirmalan³⁷

- ¹ Department of Radiodiagnosis, AMMA Center for Diagnosis and Preventive Medicine Pvt Ltd, Kochi, Kerala, India
- ² Department of Radiodiagnosis, Fetocare Magnum Imaging and Diagnostics, Trichy, Tamil Nadu, India
- ³ Department of Radiodiagnosis, Antarang Sonography and Colour Doppler Center, Satarkar Hospital, Aurangabad, Maharashtra, India
- ⁴ Department of Radiodiagnosis, Raj Sonography & X-Ray Clinic, Baiju Choraha, Nayapura, Guna, Madhya Pradesh, India
- ⁵ Department of Radiodiagnosis, Anjali Ultrasound and Colour Doppler Centre, 2nd floor, Shanti Madhuban Plaza, Delhi Gate, Agra, Uttar Pradesh, India
- ⁶ Department of Radiodiagnosis, Baghel Sonography Center, Harda, Madhya Pradesh, India
- ⁷ Department of Radiodiagnosis, Jain Ultrasound Centre, Sonari, Jamshedpur, Jharkhand, India
- ⁸Department of Radiodiagnosis, Nethra Scans and Genetic Clinic, Tiruppur, Tamil Nadu, India
- ⁹Department of Radiodiagnosis, Consultant Radiologist, Lisie Hospital, Ernakulam, Kerala, India
- ¹⁰ Department of Radiodiagnosis, MS Hospital, Trichy, Tamil Nadu, India
- ¹¹ Department of Radiodiagnosis, Faith Diagnostic Center, Chandigarh, India
- ¹²Department of Radiodiagnosis, Images Ultrasound Center, Naveda Healthcare Centre, New Delhi, India
- ¹³Department of Radiodiagnosis, Qura Diagnostics & Research Center, Bhopal, Madhya Pradesh, India
- ¹⁴Department of Radiodiagnosis, Dr. Shweta Nagar's Ultrasound Clinic & Imaging Centre, Indore, Madhya Pradesh, India
- ¹⁵ Department of Radiodiagnosis, Navya Diagnostic Center, Near Nissan Motors, Walmiki statue, Gawal mandi, Putlighar, Amritsar, Punjab, India
- ¹⁶Department of Radiodiagnosis, Kushal Imaging & Diagnostic Center, Sumerpur, Pali, Rajasthan, India
- ¹⁷ Department of Radiodiagnosis, JIPMER, Puducherry, India
- ¹⁸ Department of Radiodiagnosis, NKPSIMS, Nagpur, Maharashtra, India
- ¹⁹Department of Radiology, Aster MIMS, Kottakkal, Kerala, India
- ²⁰ Department of Radiology, INHS Dhanvantari, Minnie Bay, Port Blair, Andaman & Nicobar Islands, India
 - Indian J Radiol Imaging 2022;32:30-37.

published online April 19, 2022 DOI https://doi.org/ 10.1055/s-0041-1741087. ISSN 0971-3026. Address for correspondence Rijo M. Choorakuttil, MD, AMMA Center for Diagnosis and Preventive Medicine Pvt Ltd, Kochi, Kerala 682036, India (e-mail: rijomc@gmail.com).

- ²¹ Department of Radiodiagnosis, Dr Renu's Diagnostic Center, Sikar, Rajasthan, India
- ²² Department of Radiodiagnosis, Delta Diagnostic Services, Basavanagudi, Bengaluru, Karnataka, India
- ²³ Department of Radiology, JIJU, IIMS Medical College, Jalna, Maharashtra, India
- ²⁴ Department of Radiology, Lisie Hospital, Kochi, Ernakulam, Kerala, India
- ²⁵ Department of Radiology, Jubilee Mission Hospital, Thrissur, Kerala, India
- ²⁶Department of Radiology, Innovision Sonography and Imaging Center, Gangapur, Nashik, India
- ²⁷ Department of Radiodiagnosis, Dr. Ahuja Ultrasonography and Colour Doppler Center, Delhi Gate, Agra, (Dr. Sarkar Market), Uttar Pradesh, India
- ²⁸ Department of Radiodiagnosis, Gujarat Imaging Center, Navrangpura, Ahmedabad, Gujarat, India
- ²⁹ Vice Chancellor, Kerala University of Health Sciences, Thrissur, Kerala, India
- ³⁰Department of Radiodiagnosis, Sampurna Sodani Diagnostic Clinic, Indore, Madhya Pradesh, India
- ³¹ Department of Radiodiagnosis, MKCG Medical College, Berhampur, Odisha, India
- ³²Department of Radiodiagnosis, MRI Centre, NSCB Medical College, Jabalpur, Madhya Pradesh, India
- ³³Department of Radiodiagnosis, Indian Radiological and Imaging Association (IRIA), India & Vision Diagnostic Center, Maharashtra, India
- ³⁴Department of Radiodiagnosis, Nanavati Super Speciality Hospital, Mumbai, Maharashtra, India
- ³⁵ Department of Radiodiagnosis, Radiodiagnosis, Jaipur, Rajasthan, India
- ³⁶Department of Radiodiagnosis, Stanley Medical College, Chennai, Tamil Nadu, India
- ³⁷ Department of Research, AMMA Education and Research Foundation, AMMA Healthcare Research Gurukul, Kochi, Kerala, India

© 2022. Indian Radiological Association. All rights reserved. This is an open access article published by Thieme under the terms of the Creative Commons Attribution-NonDerivative-NonCommercial-License, permitting copying and reproduction so long as the original work is given appropriate credit. Contents may not be used for commercial purposes, or adapted, remixed, transformed or built upon. (https://creativecommons.org/ licenses/by-nc-nd/4.0/)

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India



Abstract Aim The aim of the study is to determine improvements in perinatal mortality at the end of the first 2 years from the initiation of the Samrakshan program of the Indian Radiological and Imaging Association. Methods Samrakshan is a screening program of pregnant women that uses trimester-specific risk assessment protocols including maternal demographics, mean arterial pressure, and fetal Doppler studies to classify women as high risk or low risk for preterm preeclampsia (PE) and fetal growth restriction (FGR). Low dose aspirin 150 mg daily once at bedtime was started for pregnant women identified as high risk in the 11–13^{6/7} weeks screening. The third-trimester screening focused on the staging of FGR and protocol-based management for childbirth and risk assessment for PE. Outcomes of childbirth including gestational age at delivery, development of PE, and perinatal mortality outcomes were collected. **Results** Radiologists from 38 districts of 16 states of India participated in the Samrakshan program that screened 2,816 first trimester, 3,267 second trimester, and 3,272 third trimester pregnant women, respectively. At 2 years, preterm PE was identified in 2.76%, preterm births in 19.28%, abnormal Doppler study in 25.76% of third trimester pregnancies, and 75.32% of stage 1 FGR delivered at term. The neonatal mortality rate was preeclampsia 9.86/1,000 live births, perinatal mortality rate was 18.97/1,000 child-► fetal growth births, and maternal mortality was 58/100,000 live births compared with 29.5, 36, and 113, respectively in 2016.

Conclusion Fetal Doppler integrated antenatal ultrasound studies in

Samrakshan led to a significant reduction in preterm PE rates, preterm

birth rates, and a significant improvement in mean birth weights. Perinatal,

neonatal, and maternal mortality rates are significantly better than the

targets for 2030 set by the Sustainable Development Goals-3.

Keywords

- restriction
- fetal Doppler
- perinatal mortality
- neonatal mortality

Introduction

Perinatal and maternal mortality rates are declining in India but remain high compared with the global rates.¹ The higher perinatal and maternal mortality rates in India indicate a high burden of maternal and fetal morbidity with short-andlong-term consequences on the health of the baby. Hales and Barker proposed undernourishment during critical periods of fetal development as a major cause for structural and functional changes in the developing systems of the fetus.² These changes are hypothesized as potential causes for the incidence of cardiovascular diseases (CVDs), diabetes, and non-communicable diseases later in life.³⁻¹⁰ Fetal undernourishment may be related to malnutrition of the pregnant woman that continues from preconception periods and placental insufficiency during pregnancy.¹¹ Pregnancy-induced hypertension can lead to placental insufficiency and consequent fetal growth restriction (FGR) and insulin resistance.^{12–14} The magnitude of CVDs is high in India with an age-adjusted CVD death rate of 272 per 100,000 population compared with the global average of 235 per 100,000 population.¹⁵ India is an epicenter of the global diabetes pandemic with a rapid increase in the prevalence of type 2 diabetes mellitus (DM).¹⁶ The fetal origin hypothesis may partly explain the high prevalence of these conditions in India as

pregnancy-induced hypertension and FGR are the major causes for perinatal morbidity and mortality in India.^{17,18}

Samrakshan is a national program of the Indian Radiological and Imaging Association (IRIA) that addresses high perinatal rates in India through an approach that integrates fetal Doppler imaging biomarkers with routine antenatal screening for pregnant women in India.¹⁹ The initial phase of Samrakshan focused on the use of a multiparametric Bayesian model for early identification and risk stratification of pregnant women at high risk for the development of preterm preeclampsia (PE) and FGR.¹⁹ Early identification of high-risk women, initiation of low dose aspirin and closer monitoring integrated with routine antenatal care as part of the Samrakshan program was expected to reduce perinatal mortality rates in India. We present the results of the first 2 years of the Samrakshan program in this manuscript.

Material and Methods

The methodology of the Samrakshan program is described in a previous publication.¹⁹ Briefly, Samrakshan aimed at the upgradation of technical skills with a focus on the diagnostic, interpretative, prognostic, and therapeutic efficacy integrating fetal Doppler with antenatal studies, online and offline learning platforms for continuous medical education (CME), improved synergy with other stakeholders involved with fetal and maternal care and building an evidence pool based on data analysis of the program. Samrakshan aimed to focus on two priority areas in the first couple of years-preterm PE and FGR.

The Samrakshan CMEs were organized by the state IRIA associations with larger states conducting several regional CMEs within the state to encourage wider participation. The offline CMEs included didactic lectures, workshops, and demonstrations, and case presentations and panel discussions on perinatal status in India, trimester-specific fetal Doppler studies, the use of risk assessment algorithms available online, and the collection and submission of data through online forms. The CMEs were supported by the creation of state-specific WhatsApp groups to facilitate long term follow-up and mentoring of participants. The dedicated WhatsApp groups provided a platform for participants to access instructors easily and clarify their doubts and encouraged peer to peer learning through sharing of interesting cases, dilemmas and learning and practice tips, audits of images and fetal radiology research. The offline CMEs were shifted to an online mode due to the lockdown and public health measures that resulted from the COVID-19 pandemic. The CMEs were subsequently conducted through dedicated fetal radiology webinars that catered to a larger pan India pool of Radiologists.

The skill upgradation focused on two important aspects. The measurement of mean arterial blood pressures²⁰ and fetal Doppler studies^{21,22} using standardized methodologies was a primary focus. The trimester-specific fetal Doppler studies of interest included the mean uterine artery pulsatility index (PI), umbilical artery PI, the middle cerebral artery (MCA) PI and the cerebroplacental ratio (CPR), and ductus venosus and absent/reversed end-diastolic velocity flow studies. The second priority was to encourage the use of a multiparametric risk algorithm based on a Bayesian model that helped to stratify pregnant women as high or low risk for preterm PE and FGR.²³

Clinical and demographic details were collected from all pregnant women screened using the Samrakshan protocol. Each woman was assigned a unique identification number that was used for all subsequent visits. The height and weight of the woman were recorded, maternal age and ethnicity, type of conception, history of smoking, any maternal history of PE or PE in a previous pregnancy, parity and interpregnancy intervals were collected. The number of fetuses was documented. Information regarding the last menstrual period (LMP) was obtained and accurate dating was performed based on the LMP and ultrasound parameters. The dating was not changed subsequently. In the first trimester $(11-13^{6/7})$ weeks), the blood pressure of the pregnant woman was measured simultaneously in both upper arms with the woman seated upright with feet flat on the floor in a quiet environment. The fetal crown-rump length (CRL) was measured with a range of 45 to 84 mm between 11 and 14 weeks of pregnancy considered acceptable. The mean uterine artery PI was estimated, and the information was input into the online calculator of the Fetal Medicine Foundation to estimate an individualized risk for the pregnant woman. We used a criterion of 1 in 150 to categorize pregnant women as high or low risk for the development of preterm PE and FGR. Any pregnant woman determined at high risk for preterm PE or FGR was recommended the use of low dose aspirin 150 mg once daily at bedtime till 36 weeks, development of preterm PE or childbirth, whichever was earlier.²⁴ The findings of the Doppler studies, risk assessment, and recommendations were shared with the managing physician. The detailed protocol of Samrakshan for the assessment of PE in India has been published earlier.²⁵ The screening protocol was repeated in the second trimester besides a targeted study for fetal abnormalities. In the third trimester, each pregnant woman had fetal Doppler studies focused on the mean uterine artery PI, the umbilical artery PI, and the MCA PI. The CPR was ascertained from the umbilical artery PI and the MCA PI. A mean uterine artery PI >95th percentile, umbilical artery PI >95th percentile, MCA <5th percentile, and CPR <5th percentile was considered abnormal. Estimated fetal weights were determined and fetal biometry parameters were charted for all women. Fetal growth was staged and managed using a composite model involving fetal weight and Doppler indices.²⁶ A fetus was considered as small for gestational age (SGA) if the EFW was third to 10th percentile with normal Doppler indices. The details of the third-trimester examination processes of Samrakshan have been published earlier.²⁷ The Samrakshan protocol was integrated with routine trimester-specific antenatal studies including studies for nuchal translucency, targeted imaging for fetal abnormalities, and fetal structural studies.

The processing of data and images in Samrakshan adhered to the tenets of the Declaration of Helsinki, anonymized data from each pregnant woman screened in Samrakshan was uploaded by individual radiologists onto trimester-specific online Google Forms and stored in a password protected centralized database. A childbirth outcomes form was used to collect information on childbirth with a focus on stillbirths, neonatal mortality, development of preterm PE in the mother, gestational age at delivery and birth weight. The childbirth outcomes were uploaded online to a specific Google Form and stored in a database. The data was exported from the database to statistical software (STATA version 14.0, College Station, Texas, United States) for further analysis. The data was cleaned to identify and remove any duplicate entries. An analysis of the Samrakshan data up to July 2020 was used to determine baseline indices to compare subsequent progress. The major indices of interest included the proportion of women in the first trimester identified as high risk, abnormal fetal Doppler studies in the third trimester, the stage-based proportion of FGR in the third trimester, the proportion of SGA babies in the third trimester, preterm births, preterm PE, birthweights, stillbirths, neonatal and maternal mortality. Categorical data were expressed as proportions and continuous data were expressed as mean \pm SD, 95% confidence intervals (CI) were estimated around relevant point estimates. Neonatal mortality is expressed as the number of neonatal deaths per 1,000 live births, perinatal mortality as number of stillbirths and early neonatal deaths

States/Union Territory covered through state specific CMEs	Chandigarh, Chhattisgarh, Gujarat, Haryana, Kerala, Madhya Pradesh, Maharashtra, Odisha, Puducherry, Punjab, Rajasthan, Tamil Nadu, Uttar Pradesh
Number of Fetal Radiology Webinars conducted	30 (700–900 participants in each webinar)
Outreach programs	Guna, Harda, Sagar—Madhya Pradesh Kollam, Calicut—Kerala Jalna—Maharashtra
Multilingual Health Education articles	24 (English, Hindi, Malayalam, Tamil, Kannada, Telugu, Marathi, Gujarati, Odia)
Educational Videos	11
Original Research Articles	11
Protocols, Editorials, and Interviews	6

 Table 1
 Educational programs as part of the Samrakshan Program

per 1,000 childbirths, and maternal mortality as the number of maternal deaths per 100,000 live births.

Results

Samrakshan was launched in June 2019 and training programs initiated from August 2019. Radiologists from 38 districts of 16 states of India participated in the program. **- Table 1** presents the details of educational programs conducted by Samrakshan.

• Table 2 presents the clinical and demographic details of the 2,816 women with first-trimester pregnancy which were screened through Samrakshan till August 2021. The first trimester screening program identified 923 (32.78%, 95% CI: 31.07, 34.53) and 1,232 (43.75%, 95% CI: 41.93, 45.59) first trimester pregnant women at high risk for preterm PE and FGR, respectively. Six hundred and sixty-five (23.62%, 95% CI: 22.08, 25.22) first-trimester pregnant women were identified as high risk for both preterm PE and FGR. The proportion of pregnant women at high risk for preterm PE was 23.05% (95% CI: 21.53, 24.64) using a 1 in 100 criteria and

Table 2 Clinical and demographic details of the 2,816 first

 trimester pregnant women screened through Samrakshan

Characteristic	N (%)
Nulliparous	1,632 (57.95%)
Spontaneous conception	2,716 (96.45%)
Mean age \pm SD	27.45 ± 4.74
Maternal Age >35 y	231 (8.20%)
Body mass index <18.5 kg/m ²	204 (7.24%)
Body mass index 25–29.9 kg/m ²	788 (27.99%)
Body mass index $\geq 30 \text{ kg/m}^2$	328 (11.65%)
Chronic hypertension	30 (1.07%)
Diabetes mellitus	17 (0.60%)
Pregnant woman mother had preeclampsia	26 (0.92%)
Preeclampsia in previous childbirth	111 (9.38%)

11.29% (95% CI: 10.18, 12.51) using a 1 in 50 criteria. All pregnant women identified as high risk in the first-trimester screening were recommended low dose aspirin 150 mg once daily at bedtime as per the protocol. The mean \pm SD of the mean arterial blood pressure was 83.94 ± 9.68 mm of Hg (median: 83.33, interquartile range 60–123).

Three thousand two hundred and sixty-seven women were screened in the second trimester of pregnancy. Ninety-seven (2.97%) women had developed PE and 82 (2.51%) fetuses were identified as early FGR at the time of screening. An additional 182 (5.57%) of pregnant women were identified as high risk for preterm PE. Structural abnormalities were identified in 106 (4.65%) fetuses in the second-trimester screening. Three thousand two hundred and seventy-two pregnant women were screened in the third trimester of pregnancy (**Table 3**). Preterm PE developed in 20.51% of the high-risk women who had received low dose aspirin and only 1.20% of the pregnant women were classified as low risk. The mean estimated fetal weight was 2,214.83 $\pm\,580.09\,g\,(medi$ an 2,240, interquartile range 1,820 to 2,610 g). An abnormal Doppler study was found in 371 (20.98%, 95% CI: 19.15, 22.94) of 1,768 fetuses with an EFW 10th to 50th percentile and 172 (20.36%, 95% CI: 17.78, 23.20) of fetuses with an $\text{EFW} > 50^{\text{th}}$ percentile. The presence of preterm PE was significantly associated with mean uterine artery PI >95th percentile (p < 0.001), umbilical artery PI >95th percentile (p = 0.002), MCA PI < 5th percentile (p < 0.001) and CPR < 5th percentile (p < 0.001). Childbirth outcomes were available for 1,740 of the 3,272 women screened in the third trimester (**Table 4**) at the time of analysis. **Table 5** compares the baseline data derived from the Samrakshan database till July 2020 with the Samrakshan data till August 2021. Significant improvements were found in the preeclampsia rates, the proportion of stage 1 and stage 3 FGR, the proportion of stage 1 FGR delivered at term, preterm birth rates, mean birth weights, and perinatal and neonatal mortality rates.

Discussion

The NFHS-4¹ reported that the perinatal and neonatal mortality of India was 36 per 1,000 childbirths and 29.5 per 1,000 **Table 3** Clinical details of the 3,272 third trimester pregnant

 women screened in Samrakshan

Characteristic	N (%)
Pregnant woman developed preeclampsia	108 (3.30%, 95% Cl: 2.74, 3.97)
Preterm preeclampsia	97 (89.81%) of 108
Abnormal Doppler study	843 (25.76%, 95% Cl: 24.29, 27.29)
Mean uterine artery PI >95 th percentile	421 (12.87%, 95% Cl: 11.76, 14.06)
Umbilical artery PI >95 th percentile	198 (6.05%, 95% Cl: 5.28, 6.92)
Middle cerebral artery PI <5 th percentile	305 (9.32%, 95% Cl: 8.37, 10.37)
Cerebro-placental ratio <5 th percentile	443 (13.54%, 95% Cl: 12.41, 14.75)
No FGR	2,616 (71.95%, 95% Cl: 78.54, 81.29)
Stage 1 FGR	362 (11.06%, 95% Cl: 10.03, 12.18)
Stage 2 FGR	5 (0.15%, 95% Cl: 0.06, 0.36)
Stage 3 FGR	14 (0.43%, 95% Cl: 0.26, 0.72)
Stage 4 FGR	5 (0.15%, 95% Cl: 0.06, 0.36)
Small for gestational age	270 (8.25%, 95% Cl: 7.36, 9.24)
Estimated fetal weight (EFW)< 3 rd percentile	225 (6.88%, 95% Cl: 6.06, 7.80)
EFW 3 rd to 10 th percentile	434 (13.26%, 95% Cl: 12.14, 14.47)
EFW 10 th to 50 th percentile	1,768 (54.03%, 95% CI: 52.32, 55.75)
EFW >50 th percentile	845 (25.83%, 95% Cl: 24.35, 27.35)

Abbreviations: CI, confidence interval; EFW, estimated fetal weight; FGR, fetal growth restriction.

live births, respectively, and stillbirths were 0.7%. Analysis of data from Samrakshan showed a significant reduction in perinatal (18.97 per 1,000 childbirths) and neonatal (9.86 per 1,000 live births) mortality rates compared with the national rates. The stillbirth rates from Samrakshan (0.92%) were similar to the national rates reported from NFHS-4.¹ The maternal mortality rate in Samrakshan was 58 per 100,000 live births compared with a national rate of 130 per 100,000 live births. The rates of maternal and neonatal mortality in Samrakshan are much lower than the goals set by the sustainable development goals-3 (SDG-3) that aimed for fewer than 70 maternal deaths per 100,000 childbirths and as low as 12 per 1,000 live births for neonatal mortality by 2030. However, participation, data collection, and submission are voluntary in Samrakshan and hence the sample is not representative of the general population of pregnant **Table 4** Childbirth outcomes of 1,740 pregnant women screened in the 3rd trimester of Samrakshan

Characteristic	N (%)
Gestational age at delivery <34 wk	43, 2.48% (95% Cl: 1.84, 3.31)
Gestational age at delivery 34 to <37 wk	292, 16.78% (95% Cl: 15.1, 18.61)
Overall preterm births (<37 wk)	335, 19.28% (95% Cl: 17.47, 21.17)
Mother developed preeclampsia	62, 3.56% (95% Cl: 2.79, 4.54)
Preeclampsia <37 wk	48 (77.41%) of 62
Birthweight <2,500 g	357, 20.51% (95% Cl: 18.69, 22.48)
Stillborn	16 (0.92%)
Neonatal deaths	17 (0.99%)
Neonatal mortality rate	9.86 per 1,000 live births
Perinatal mortality rate	18.97 per 1,000 childbirths
Maternal mortality rate	58.00 per 100,000 live births

women in India. We decided to additionally measure changes against baseline benchmarks estimated from the 1st year of Samrakshan as an internal validation to address the lack of representation. Samrakshan showed a marked reduction in perinatal and neonatal mortality compared with the baseline estimates.

The key elements of the first-trimester screening protocol are the identification of pregnant women at risk for preterm PE and FGR and the initiation of low-dose aspirin between 11–13^{6/7} weeks as a preventive measure. The Fetal Medicine Foundation (FMF) algorithm used for the prediction of preterm PE and FGR is better than the American College of Obstetricians and Gynecologists (ACOG) and the National Institute for Health and Care Excellence (NICHE) guidelines.²⁸ The FMF recommends a 1 in 100 criteria to classify risk for preterm PE and FGR and also recommends a risk of 1 in 150 for gestational ages <34 weeks and 1 in 100 for gestational ages <37 weeks to initiate low-dose aspirin.²⁹ The criteria for risk classification must consider the background risk in the local population and the purpose of the screening program. A study from the Netherlands reported that the optimal cut-off in their study population for preeclampsia <34, <37, and <42 gestational weeks were 1:250, 1:64, and 1:22, respectively.²⁹ A multicentric study from Asia has reported significant differences in the mean arterial blood pressure, mean uterine artery PI, and biochemical marker Multiple of Medians (MoMs) between the Asian populations and the FMF algorithm based on European populations.³⁰ A recent study from Brazil reported that the risk factors for the Brazilian population differed from those that that were incorporated in the FMF model and emphasized the need to derive a fitted model relevant to the Brazilian population.³¹

We chose a 1 in 150 criteria to classify risk based on (a) the higher background prevalence of PE and FGR in India, (b) the

Characteristics	Data up to July 31, 2020	Data up to August 1, 2021	p-Value
Stage 1 FGR	27.27%	11.06%	< 0.0001
Stage 2 FGR	0.38%	0.15%	0.41
Stage 3 FGR	5.30%	0.43%	<0.0001
Stage 4 FGR	0.76%	0.15%	0.05
Small for gestational age	4.92%	8.25%	0.06
Stage 1 FGR delivered at term	56.94%	75.32%	< 0.001
Preterm births	29.54%	19.28%	0.0001
Mean birthweight \pm SD (g)	2636.99 ± 568.95	2747.89 ± 515.39	0.001
Maternal preterm PE	9.85%	2.76%	< 0.0001
Neonatal mortality rate	15.32	9.86	0.007
Perinatal mortality rate	26.52	18.97	0.004

Table 5	Comparison of	the July 2020 Samrakshai	n data with the August 2021 data

Abbreviations: EFW, estimated fetal weight; FGR, fetal growth restriction.

lower uptake of antenatal services in India (51.6% had four or more antenatal care visits and only 21% utilized full antenatal care), (c) a large number of dropouts from the health care system or loss to follow-up³² and a balance between the minimal consequences of low dose aspirin dosage compared with the more severe consequences of PE and FGR in pregnancy. The 1 in 150 risk cut-off identifies more pregnant women at risk for the development of PE and FGR compared with a 1 in 100 risk cut-off but covers the large incidence of FGR in India. This cut-off allows the possibility to initiate low dose aspirin in the first-trimester for a larger proportion of pregnant women who enter the maternal health care system.

The preventive strategy is based on the administration of low-dose aspirin between 11-13^{6/7} weeks and at a dose of 150 mg once daily at bedtime. The 150 mg dose is superior to lower doses for the prevention of preterm PE globally and in India.^{33–35} The ASPRE trial reported a significant reduction in the incidence of preterm PE with low-dose aspirin.^{33,36} We found that the early identification of risk and administration of low-dose aspirin resulted in the development of preterm PE in only 20.51% of the women classified as high risk. The screening model did not miss a significant proportion of women at high risk for PE because only 1.20% of the pregnant women classified as low risk and did not receive low-dose aspirin developed preterm PE. The significant reduction in the incidence of preterm preeclampsia, the reduction in the proportion of babies classified as FGR and improvement in mean birthweight from baseline also indicate the effectiveness of the first-trimester screening model.

The Samrakshan screening model focuses primarily on protocol-based management of FGR in the third trimester, besides the focus on PE. The integration of fetal Doppler studies was expected to lead to a reclassification of stage 1 FGR and SGA babies. This reclassification is expected to result in a lower incidence of stage 1 FGR and a higher incidence of SGA babies. Additionally, the integration of fetal Doppler studies was expected to provide more objective measures that could help decision making around the timing of childbirth and lead to a possible reduction in preterm birth rates. An increase in the mean birth weights was an anticipated outcome of the shift of childbirths from preterm to term. We found a significant change in the categorization of stage 1 FGR, and SGA compared with the baseline data. The integration of fetal Doppler studies reduced the proportion of fetuses classified as stage 1 FGR and led to an increase in the proportion of fetuses classified as SGA. We also found a significant increase in the proportion of stage 1 FGR babies that were delivered at term and an increase in the mean birth weight, which can impact the low-birthweight rates positively. The integration of fetal Dopplers is expected to positively impact the perinatal mortality rates due to improved risk stratification and monitoring. The perinatal, neonatal, and maternal mortality rates of Samrakshan showed significant improvement compared with the baseline and were consistent with the direction of results that were expected before the program implementation.

Fetal Doppler studies in the third trimester are important in populations with high rates of perinatal mortality, perinatal asphyxia, and low birth weights like India. An abnormal Doppler study was found in 25.76% of pregnant women screened in the third trimester. Umbilical artery Doppler studies primarily identify the severe placental disease and may not identify the mild placental disease which constitutes a proportion of early-onset cases and virtually all instances of late-onset FGR.³⁷ Increased impedance in the umbilical arteries is seen only when at least 60% of the placental vascular bed is obliterated.³⁸ This may explain the relatively low incidence of abnormal umbilical artery Doppler PI in this study as 93.78% of the identified FGR were classified as Stage 1 FGR. The middle cerebral artery provides information about brain vasodilation and is considered as a surrogate for fetal hypoxia. Abnormal MCA Doppler studies are useful to identify and predict adverse outcomes among late-onset FGR independent of the umbilical artery Doppler status.^{39,40} The CPR is a diagnostic index and is the best test to pick up the effects of fetal adaptation.²⁶ All cases with abnormal CPR may not progress to baseline hypoxia but rapid fetal deterioration may occur once baseline hypoxia is established as placental reserves are minimal.²⁶ This leads to an increased risk of intrauterine fetal death after 37 weeks due to a combination of higher susceptibility to hypoxia of the term-mature fetus and the presence of uterine contractions at term.²⁶ An abnormal CPR is considered a better indicator than an abnormal UA or MCA and independent of fetal size for emergency caesarean section.⁴¹ An abnormal CPR (13.54%) was the most common fetal Doppler abnormality in this series. Previous studies have reported that CPR is a useful diagnostic index even in AGA and LGA babies and that changes in umbilical Doppler based on fetal size suggest the need to adjust the Doppler reference ranges according to the fetal weight percentile.^{42,43} Prior et al, have previously reported that 11% of AGA fetuses had abnormal CPR.⁴¹ Nearly one-fifth of fetuses at the higher percentiles of EFW (>50th percentile) in this series had an abnormal Doppler study suggesting the need for routine assessment of fetal Doppler irrespective of fetal size.

There is scope for improvement in Samrakshan. The representativeness of Samrakshan data can be improved by involving fetal radiologists from more diverse areas. Samrakshan is initiating the use of software that will automatically collate anonymized data from the machine and store the data in the cloud. This will help reduce the need to enter and upload multiple forms as the data entered during the assessments will be collated into a cloud-based database. The automation and a larger pool of data will allow for the development of population-based biometry and fetal Doppler indices that are relevant to the Indian population. The lockdown imposed due to the COVID pandemic affected patient flow and examination for a large period. The COVID pandemic also affected the possibility of in-person CMEs which was a good platform for hands-on demonstrations of concepts. The shift to a webinar mode allowed for access and reach to a larger pool of radiologists but reduced the possibility of personal interactions to clarify concepts. We recognize the need for greater interactions with the neonatologists and obstetricians so that childbirth recommendations are team-based decisions with the fetal radiologist as an integral part of the team. Samrakshan encouraged greater synergy with stakeholders at the local level and several outreach programs were organized where neonatologists, obstetricians, geneticists, and other stakeholders discussed how to work synergistically to reduce perinatal mortality in India. Much of the focus in fetal radiology in India has been on the detection of structural abnormalities. Samrakshan provides evidence of the larger magnitude of PE and FGR compared with structural abnormalities and the significant impact preventive strategies have on perinatal mortality. We did not choose to include biochemical markers in the screening model due to issues of availability, accessibility, and affordability of these tests on a large scale. Fetal Doppler studies are widely available and affordable, provide rapid test results, and can be integrated with routine antenatal scans. There is a large readily available pool of trained radiologists that can perform fetal Doppler studies.

Samrakshan has shown that a significant reduction in perinatal mortality, neonatal mortality, preterm birth rates and rates of preeclampsia and FGR is possible with a systematic integration of fetal Doppler studies with routine antenatal ultrasound studies. The reduction was significantly lower than the targets of the SDG-3 for India for the year 2030 and lower than the projected rates of early neonatal mortality rate of 18 per 1,000 live births for 2020. Improved fetal and maternal wellbeing have short-term benefits and can impact the larger epidemic of non-communicable diseases prevalent in India in the long term.

Work Attributed to

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

Financial Disclosures

None of the authors have any financial interests to disclose with respect to this study and manuscript.

Conflict of Interest

None declared.

References

- International Institute for Population Sciences (IIPS) and ICF. 2017National Family Health Survey (NFHS-4), 2015–2016. Mumbai: IIPS
- 2 Barker DJP. In utero programming of chronic disease. Clin Sci (Lond) 1998;95(02):115-128
- 3 Barker DJ. Fetal origins of coronary heart disease. BMJ 1995;311 (6998):171–174
- 4 Stein CE, Fall CH, Kumaran K, Osmond C, Cox V, Barker DJP. Fetal growth and coronary heart disease in South India. Lancet 1996; 348(9037):1269–1273
- 5 Barker DJP, Gluckman PD, Godfrey KM, Harding JE, Owens JA, Robinson JS. Fetal nutrition and cardiovascular disease in adult life. Lancet 1993;341(8850):938–941
- 6 Eriksson JG, Forsén T, Tuomilehto J, Winter PD, Osmond C, Barker DJP. Catch-up growth in childhood and death from coronary heart disease: longitudinal study. BMJ 1999;318(7181):427–431
- 7 Rich-Edwards JW, Kleinman K, Michels KB, et al. Longitudinal study of birth weight and adult body mass index in predicting risk of coronary heart disease and stroke in women. BMJ 2005;330 (7500):1115–1118
- 8 Eriksson JG, Forsén T, Tuomilehto J, Osmond C, Barker DJP. Early growth and coronary heart disease in later life: longitudinal study. BMJ 2001;322(7292):949–953
- 9 Bhargava SK, Sachdev HS, Fall CHD, et al. Relation of serial changes in childhood body-mass index to impaired glucose tolerance in young adulthood. N Engl J Med 2004;350(09):865–875
- 10 Eriksson JG, Forsén TJ, Osmond C, Barker DJP. Pathways of infant and childhood growth that lead to type 2 diabetes. Diabetes Care 2003;26(11):3006–3010
- 11 Henriksen T, Clausen T. The fetal origins hypothesis: placental insufficiency and inheritance versus maternal malnutrition in well-nourished populations. Acta Obstet Gynecol Scand 2002;81 (02):112–114
- 12 Dekker GA, de Vries JIP, Doelitzsch PM, et al. Underlying disorders associated with severe early-onset preeclampsia. Am J Obstet Gynecol 1995;173(04):1042–1048
- 13 Lorentzen B, Henriksen T. Plasma lipids and vascular dysfunction in preeclampsia. Semin Reprod Endocrinol 1998;16(01):33–39
- 14 Kaaja R. Insulin resistance syndrome in preeclampsia. Semin Reprod Endocrinol 1998;16(01):41–46
- 15 Prabhakaran D, Jeemon P, Roy A. Cardiovascular diseases in India: current epidemiology and future directions. Circulation 2016;133 (16):1605–1620

- 16 Unnikrishnan R, Anjana RM, Mohan V. Diabetes mellitus and its complications in India. Nat Rev Endocrinol 2016;12(06): 357–370
- 17 Duley L. The global impact of pre-eclampsia and eclampsia. Semin Perinatol 2009;33(03):130–137
- 18 Bassani DG, Kumar R, Awasthi S, et al; Million Death Study Collaborators. Causes of neonatal and child mortality in India: a nationally representative mortality survey. Lancet 2010;376 (9755):1853–1860
- 19 Choorakuttil RM, Patel H, Bavaharan R, et al. Samrakshan: an Indian Radiological and Imaging Association program to reduce perinatal mortality in India. Indian J Radiol Imaging 2019;29(04): 412–417
- 20 Poon LC, Zymeri NA, Zamprakou A, Syngelaki A, Nicolaides KH. Protocol for measurement of mean arterial pressure at 11-13 weeks' gestation. Fetal Diagn Ther 2012;31(01):42–48
- 21 Bhide A, Acharya G, Bilardo CM, et al. ISUOG practice guidelines: use of Doppler ultrasonography in obstetrics. Ultrasound Obstet Gynecol 2013;41(02):233–239
- 22 Sotiriadis A, Hernandez-Andrade E, da Silva Costa F, et al; ISUOG CSC Pre-eclampsia Task Force. ISUOG Practice Guidelines: role of ultrasound in screening for and follow-up of pre-eclampsia. Ultrasound Obstet Gynecol 2019;53(01):7–22
- 23 O'Gorman N, Wright D, Syngelaki A, et al. Competing risks model in screening for preeclampsia by maternal factors and biomarkers at 11-13 weeks gestation. Am J Obstet Gynecol 2016;214(01):103. e1–103.e12
- 24 Rolnik DL, Wright D, Poon LC, et al. Aspirin versus placebo in pregnancies at high risk for preterm preeclampsia. N Engl J Med 2017;377(07):613–622
- 25 Choorakuttil RM for Team Samrakshan. The Samrakshan Screening Protocol for Pre-eclampsia in India. Journal of Fetal Radiology. 2020. Accessed September 8, 2021 http://fetalradiology.in/ 2020/04/03/the-samrakshan-screening-protocol-for-preeclampsia-in-india/
- 26 Figueras F, Gratacós E. Update on the diagnosis and classification of fetal growth restriction and proposal of a stage-based management protocol. Fetal Diagn Ther 2014;36(02):86–98
- 27 Bavaharan R, Choorakuttil RM, Ahuja B, et al. Routine 3rd Trimester Colour Doppler Ultrasound in Fetuses with Estimated Fetal Weight 10–50th centiles in India- Preliminary Results from the Samrakshan Program. Journal of Fetal Radiology. Accessed September 8, 2021: http://fetalradiology.in/2020/01/16/routine-3rd-trimester-colour-doppler-ultrasound-in-fetuses-with-estimated-fetal-weight-10-50th-centiles-in-india-preliminaryresults-from-the-samrakshan-program/
- 28 Chaemsaithong P, Pooh RK, Zheng M, et al. Prospective evaluation of screening performance of first-trimester prediction models for preterm preeclampsia in an Asian population. Am J Obstet Gynecol 2019;221(06):650.e1–650.e16
- 29 Zwertbroek EF, Groen H, Fontanella F, Maggio L, Marchi L, Bilardo CM. Performance of the FMF first-trimester preeclampsia-screening algorithm in a high-risk population in the Netherlands. Fetal Diagn Ther 2021;48(02):103–111

- 30 Chaemsaithong P, Sahota D, Pooh RK, et al. First-trimester preeclampsia biomarker profiles in Asian population: multicenter cohort study. Ultrasound Obstet Gynecol 2020;56(02):206–214
- 31 Rezende KBC, Cunha AJLAD, Pritsivelis C, Faleiro EC, Amim Junior J, Bornia RG. How do maternal factors impact preeclampsia prediction in Brazilian population? J Matern Fetal Neonatal Med 2019;32(07):1051–1056
- 32 Kumar G, Choudhary TS, Srivastava A, et al. Utilisation, equity and determinants of full antenatal care in India: analysis from the National Family Health Survey 4. BMC Pregnancy Childbirth 2019;19(01):327
- 33 Poon LC, Wright D, Rolnik DL, et al. Aspirin for Evidence-Based Preeclampsia Prevention trial: effect of aspirin in prevention of preterm preeclampsia in subgroups of women according to their characteristics and medical and obstetrical history. Am J Obstet Gynecol 2017;217(05):585.e1–585.e5
- 34 Sharma AK, Bhatla N. Aspirin for pregnancies at high risk for preterm pre-eclampsia. Natl Med J India 2018;31(01):26–27
- 35 Kumar N, Das V, Agarwal A, Pandey A, Agrawal S, Singh A. Pilot Interventional Study comparing fetomaternal outcomes of 150 mg versus 75 mg aspirin starting between 11 and 14 weeks of pregnancy in patients with high risk of preeclampsia: a randomized control trial. J Obstet Gynaecol India 2020;70(01): 23–29
- 36 Wright D, Nicolaides KH. Aspirin delays the development of preeclampsia. Am J Obstet Gynecol 2019;220(06):580.e1–580.e6
- 37 Oros D, Figueras F, Cruz-Martinez R, Meler E, Munmany M, Gratacos E. Longitudinal changes in uterine, umbilical and fetal cerebral Doppler indices in late-onset small-for-gestational age fetuses. Ultrasound Obstet Gynecol 2011;37(02):191–195
- 38 Giles WB, Trudinger BJ, Baird PJ. Fetal umbilical artery flow velocity waveforms and placental resistance: pathological correlation. Br J Obstet Gynaecol 1985;92(01):31–38
- 39 Eixarch E, Meler E, Iraola A, et al. Neurodevelopmental outcome in 2-year-old infants who were small-for-gestational age term fetuses with cerebral blood flow redistribution. Ultrasound Obstet Gynecol 2008;32(07):894–899
- 40 Hershkovitz R, Kingdom JC, Geary M, Rodeck CH. Fetal cerebral blood flow redistribution in late gestation: identification of compromise in small fetuses with normal umbilical artery Doppler. Ultrasound Obstet Gynecol 2000;15(03):209–212
- 41 Prior T, Mullins E, Bennett P, Kumar S. Prediction of intrapartum fetal compromise using the cerebroumbilical ratio: a prospective observational study. Am J Obstet Gynecol 2013;208(02):124. e1–124.e6
- 42 Sirico A, Diemert A, Glosemeyer P, Hecher K. Prediction of adverse perinatal outcome by cerebroplacental ratio adjusted for estimated fetal weight. Ultrasound Obstet Gynecol 2018;51(03):381–386
- 43 Sirico A, Rizzo G, Maruotti GM, et al. Does fetal macrosomia affect umbilical artery Doppler velocity waveforms in pregnancies complicated by gestational diabetes? J Matern Fetal Neonatal Med 2016;29(20):3266–3270
- 44 Sankar MJ, Neogi SB, Sharma J, et al. State of newborn health in India. J Perinatol 2016;36(s3)S3–S8