ORIGINAL ARTICLE

Serial Measurements of Fetal Head Circumference and Abdominal Circumference to Predict Fetal Growth Restriction in a Sri Lankan Study Population

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Abstract

Aim and objective: Prediction of fetal growth restriction (FGR) by serial ultrasound measurement of head circumference (HC) and abdominal circumference (AC) of the fetus applied routinely to all mothers irrespective of risk status for FGR and small for gestational age.

Materials and methods: A prospective study was done of 508 pregnant women who underwent two successive growth scans 4 weeks apart at Sri Jayewardenepura General Hospital, Sri Lanka. FGR was identified by graphically plotting serial fetal AC and HC. Postnatally, growth restriction was diagnosed based on ponderal index (PI). Sensitivity, specificity, positive predictive value, and likelihood ratio of predicting FGR by successive serial ultrasound measurements of fetal AC and HC were calculated.

Results: Based on fetal AC and HC, FGR was present in 223 of 508 fetuses (43.89%). Based on PI, 224 of 508 (44.1%) neonates were growth-restricted. Sensitivity, specificity, positive predictive value, positive likelihood ratio, and negative likelihood ratio of predicting FGR by serial fetal AC and HC were 82.59, 86.62, 82.59%, 6.2, and 0.2, respectively.

Conclusion: Serial ultrasound measurements of fetal AC and HC plotted on a fetal growth centile chart routinely carried out in all mothers irrespective of risk status for FGR increases the detection of FGR.

Keywords: Fetal growth restriction, Noncommunicable diseases, Ponderal index, Serial ultrasound scans, Thrifty phenotype.

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Synopsis

Detection of fetal growth restriction irrespective of risk status is paramount to prevent unexplained intrauterine fetal deaths (IUFD) and adult noncommunicable diseases.

Introduction

About 60–80% of the four million neonatal deaths that occur worldwide every year are associated with low birthweight (LBW) caused by fetal growth restriction (FGR) or preterm delivery or both.[1] Majority of FGR results from placental dysfunction which affects fetal nutrition and oxygen supply. Antenatal detection of FGR and optimized delivery would significantly reduce related perinatal morbidity and mortality.

FGR is defined as an inability to achieve the genetic growth potential by the fetus.[2,3] The causes of FGR can be categorized as maternal, fetal, and placental. In the majority of cases, reduced oxygen transfer to the fetus across the placenta is the underlying cause. Placental insufficiency is thought to be a result of improper invasion of maternal spiral arterioles by extra villous trophoblast cells. Leading maternal causes include medical disorders, infectious diseases, malnutrition, and smoking. Main fetal causes include fetal congenital anomaly and fetal infection.

Small for gestational age (SGA) is often synonymously and erroneously used with FGR because most of the immediate complications after birth are related to LBW irrespective of the underlying reason for LBW.[4,5] However, following the "thrifty phenotype" hypothesis, this approach has to be reconsidered in view of the long-term medical complications which have been found to be related to FGR irrespective of the birthweight.[6–9] SGA includes some fetuses that are genetically determined to be constitutionally small. The growth trajectory of these fetuses is normal. They are not growth-restricted, but just physically small (SGA without FGR). However, some fetuses in the SGA group could actually be ones who could not reach their genetically determined weight, thus becoming SGA. These fetuses are the ones actually growth-restricted (SGA with FGR). This should now point to another group of fetuses whose weight is actually above the 10th centile but who have not reached their growth potential. They are not SGA but are nevertheless growth-restricted (FGR without SGA). The last group of course would be fetuses who are neither growth-restricted nor below the 10th centile (no FGR and no SGA). Hence, it should be clear that birthweight or estimated fetal weight (EFW) alone could not be used to detect true FGR.

FGR could be symmetrical or asymmetrical. Symmetrical FGR which is less common and usually begins in early gestation.

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Asymmetrical FGR is more common and is detected at later gestational ages. Here, the fetal head continues to grow at normal or near-normal rates (head sparing effect) while fetal abdominal growth trajectory lags behind. However, persistent severe placental insufficiency may eventually lead to restriction of the growth of the head as well.

Late diagnosis of FGR may be hazardous to the fetus since gradually reducing nutrients and oxygen supply may compromise development of organ systems of the body. It may eventually cause intrauterine fetal deaths (IUFDs). The thrifty phenotype hypothesis describes that reduced fetal growth is strongly associated with a number of chronic adult diseases due to fetal adaptations to survive in an environment which has limited availability of nutrients.[6–8] The said adaptations can be permanent and could lead to chronic medical disorders.[9] Therefore, it is paramount that a sensitive method is developed to correctly diagnose FGR to minimize perinatal morbidity, mortality, and adult disease.

Plateauing of growth trajectory plotted on fetal growth charts and umbilical artery Doppler waveform abnormalities are frequently used in the diagnosis of FGR worldwide.[2] Fetal growth charts utilizing ultrasonic fetal biometry parameters have been developed to monitor fetal growth.[10,11] Customized fetal growth charts, taking into consideration of maternal variables, have been introduced to increase the accuracy of FGR detection.[12,13] WHO global survey of fetal weight standards has been adopted to Sri Lanka with the aim of detecting the trend of fetal growth.[14] Ponderal index (PI) is a neonatal counterpart of body mass index, illustrates the degree of nourishment, and could be used to confirm the diagnosis of FGR after delivery.[12,15–23] PI is calculated by birthweight divided by the cube of the birth length (weight/length^3). Babies, who are confirmed postnatally to have had FGR in utero, have to be followed up with a tailored plan as they are vulnerable to adult disease irrespective of the birthweight.

Materials and Methods

A prospective cohort study was done including a cohort of 508 pregnant mothers attending the antenatal clinic of ward 9, Sri Jayewardenepura General Hospital, Sri Lanka. Ethical approval was obtained from the ethics review committee of the hospital prior to the study. Criteria for inclusion for the study were as follows: mothers with a singleton pregnancy, having an accurate dating scan prior to 20 weeks and mothers who gave their written consent for the study. Those who had booked later than 30 weeks and who had medical disorders complicating their pregnancy were excluded from the study. Recruitment started in August 2013 and was completed in March 2014. All were followed up until delivery without dropouts. All subjects had two serial ultrasound scans. First scan was carried out between 24 and 30 weeks, and a second scan after 2–4 weeks from the first scan. Measurements of biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), femur length (FL), amniotic fluid index, umbilical artery Doppler resistance index, and pulsatility index were recorded. AC and HC were plotted on the growth chart developed by Loughna et al.[10] as Sri Lanka is yet to develop its own population-based AC and HC standard nomograms. A visual assessment, as would be done in a clinic setting, was carried out after the second scan to determine whether the trajectory lines for both HC and AC followed the expected centile line on the chart.

The mothers whose trajectory line for AC alone or both AC and HC deviated to the right of the original centile line were assigned to the "antenatally growth-restricted" group, whose trajectory line for AC alone or both AC and HC followed the original centile line or deviated to its left were assigned to the "antenatally non-growth-restricted" group.

All were followed up and were delivered in the same unit of Sri Jayewardenepura General Hospital during November 2013–June 2014. Weight and length of neonates were recorded soon after the delivery, and PI was calculated using the following formula:

$$PI = \text{Birthweight (kg)}/\text{Length (m)}^3$$

The neonates with a PI below fifth centile in Landmann's PI centile chart,[24] were assigned to the "confirmed growth-restricted newborn" group. The neonates whose PI was on or above the fifth centile were assigned to the "confirmed non-growth-restricted newborn" group. Sensitivity and specificity of serial ultrasound measurements of fetal HC and AC to detect antenatal FGR were calculated.

Results

The range of age was 18–41 years with an average age of 29.9 years. Median age was 30 years. Standard deviation was 4.57 years. Figure 1 shows the distribution of age.

Out of 508 mothers, 243 (47.83%) were primigravidae. Distribution of parity is shown in Table 1.

Out of 508 deliveries, 256 (50.3%) were vaginal deliveries and 252 (49.6%) were caesarean sections for varied indications. Period of amenorrhea (POA) at delivery ranged from 33 + 1 to 41 weeks. Average POA was 37 + 5 days with a standard deviation of 8.1 days. Figure 2 shows the distribution of POA at delivery.

About 223 neonates out of 508 (43.89%) were found to be in the "antenatal growth-restricted" group and 285 (56.11%) qualified to be in the "antenatal non-growth-restricted" group. Distribution

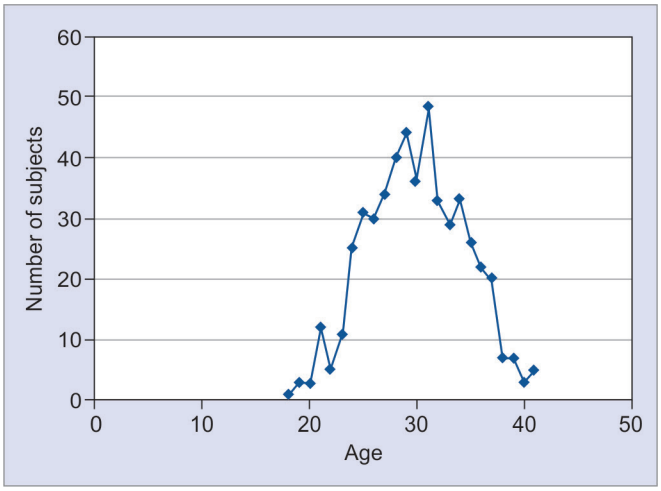

Fig. 1: Distribution of age

Table 1: Distribution of parity

Parity	*Number*	*Percentage*
0	243	47.83
1	198	38.97
2	51	10.03
3	16	3.15
Total	508	100

plots of lines connecting two scans for AC of growth-restricted cases are shown in Figure 3. Same plot of non-growth-restricted cases is shown in Figure 4.

Two hundred and twenty four (44.1%) neonates were assigned to the "confirmed growth-restricted newborn" group, and 284 (59.9%) neonates were assigned to the "confirmed non-growth-restricted newborn" group. We considered postnatal detection of growth restriction by PI as true growth restriction and calculated the sensitivity of predicting FGR by serial ultrasound measurements of fetal HC and fetal AC. Thus, 185 out of 223 in the "antenatal growth-restricted" group found to have growth restriction postnatally (PPV = 82.95%). About 246 out of 285 in the "antenatal non-growth-restricted" group found to have normal growth after delivery (NPV = 86.31%). Therefore, sensitivity and specificity of predicting FGR by serial ultrasound measurements of fetal HC and fetal AC were 82.59 and 86.62, respectively. Likelihood ratio of the test is thus 6.2. The pretest probability of a fetus having FGR is 44.1%. Therefore, the probability of having FGR is predicted beyond 80% by a positive test result. Analysis is given in Table 2.

Sensitivity = True positives/[True positives + False negatives] = 82.59

Specificity = True negatives/[True negatives + False positives] = 86.62

Likelihood ratio = Sensitivity/1 − Specificity = 6.2

Out of 508 newborns, 89 (17.5%) were LBW (birthweight below 2.5 kg) newborns. Out of 89 LBW newborns, only 50 (56.2%) were growth-restricted according to the PI. Remaining 39 (43.8%) newborns were not growth-restricted. About 419 out of 508 (82.5%) were of adequate birthweight newborns. Out of that 419 newborns, 175 (41.5%) were growth-restricted, and 245 (58.5%) were not growth-restricted (Table 3).

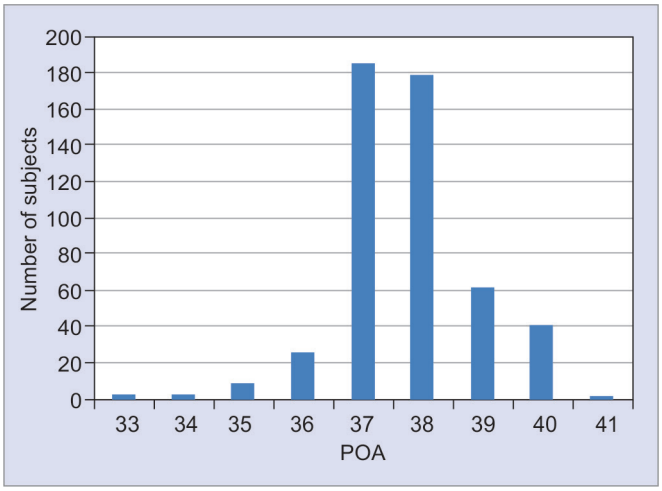

Fig. 2: Distribution of gestational age at delivery

Discussion

In most of the term IUFD, an underlying undetected FGR is noted.[1,5] This means many term IUFDs can be prevented if FGR is detected early. Sensitivity of clinical palpation alone to detect SGA, without measuring symphysio-fundal height (SFH) in low-risk populations, is about 20% and is highly unsatisfactory.[2]

Clinical detection of SGA is also done by relating a spot measurement of SFH to the 10th centile of a growth chart.

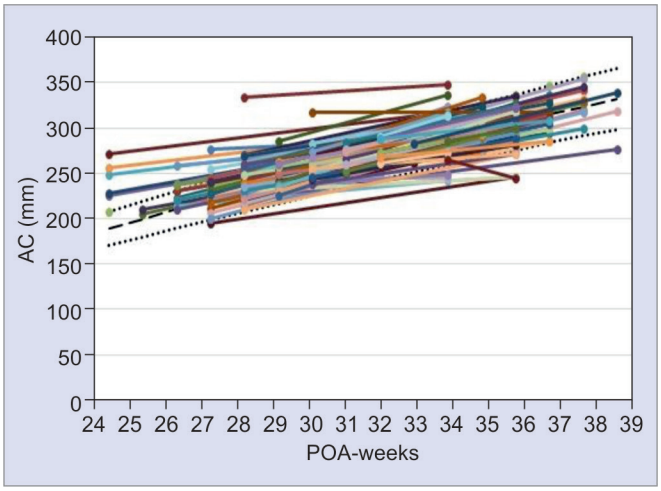

Fig. 3: Distribution of lines connecting two scans of AC in growth-restricted fetuses. Dotted lines represent centile of the nomogram

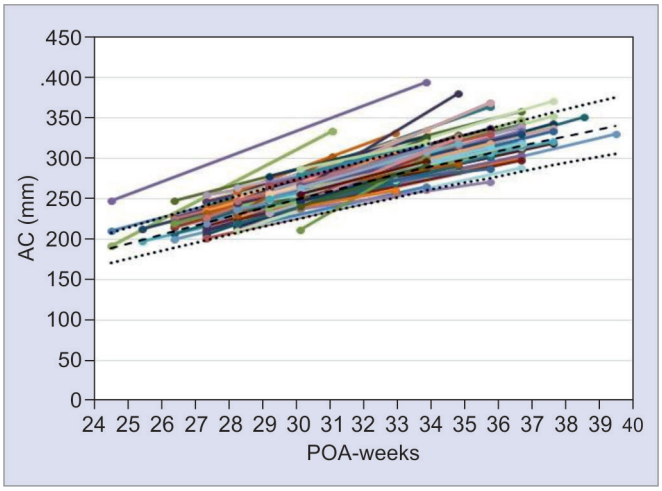

Fig. 4: Distribution of lines connecting two scans of AC in non-growth-restricted fetuses. Dotted lines represent centile of the nomogram

Table 2: Two by two table to calculate sensitivity, specificity, and likelihood ratio

	Confirmed growth-restricted newborns	*Confirmed non-growth-restricted newborns*	
Antenatal growth-restricted	185	38	223
Antenatal non-growth-restricted	39	246	285
	224	284	

Table 3: Relationship between LBW and FGR

	FGR	*Not FGR*	*Total*
LBW (<2.5 kg)	50	39	89
Adequate birthweight (2.5 kg)	174	245	419
Total	224	284	

Naturally, this is not satisfactory due to high inter- and intra-observer variability during measurement as well as the fact that the particular spot measurement, even if above the 10th centile, may well be a FGR. The sensitivity and specificity of detecting SGA by a single measurement of SFH is about 27 and 88%, respectively.[2] Introduction of a customized SFH chart which is adjusted for maternal characteristics, such as height, weight, parity, and ethnicity, has further improved the detection rate of SGA. Sensitivity of customized SFH chart for detection of SGA is superior to single SFH measurement (48 vs. 27%).[2,5,13]

Diagnosis of SGA is based on EFW being below the 10th centile. However, an EFW, despite being above the 10th centile, could well be FGR. Clinical detection of FGR has to be done by detection of the increments in growth with time irrespective of whether the measurements are above or below the 10th centile. Plotting serial SFH on a chart, preferably a customized one, improves the accuracy of this clinical method.[2]Ultrasound scan is more accurate in detecting FGR. Fetal growth charts have been developed illustrating centile values of fetal BPD, HC, AC, FL, and EFW according to gestational age. Ultrasonically, FGR can be diagnosed when sequential fetal growth measurements show a trajectory deviating to the right of a centile line or cross the centile lines toward the right. Even though fetal growth velocity between two points would be able to detect FGR, there is no clear method of detecting FGR using growth velocity.[2] Growth velocity differs with the gestational age. In the early part of a gestation, growth velocity is high, whereas in the latter period, it is low, due to physiological senescence of the placenta.

Uterine artery Doppler flow analysis is used in the second trimester to predict FGR while umbilical artery Doppler can diagnose FGR in late pregnancy. RCOG Green-top Guideline recommends offering uterine artery Doppler to pregnant mothers between 20 and 24 weeks, having minor risk factors for FGR. They also recommend serial ultrasound measurement of fetal parameters and umbilical artery Doppler in those who had an abnormal uterine artery Doppler between 20 and 24 weeks.[2] With advancing FGR, umbilical artery diastolic flow gradually falls, and in late stages, it may be absent or even reversed. Doppler flow analysis can be done in the fetal middle cerebral artery and in the ductus venosus to predict the severity of the FGR.[25]

Antenatally detected SGA, but not FGR, can be verified postnatally by birthweight as all FGR neonates are not SGA. PI has been shown as a tool to identify FGR babies after birth.[12,15–23] It has been shown that the PI is superior to skin fold thickness, and midarm-circumference-to-occipitofrontal-circumference ratio in detecting growth restricted neonates.[12,16] It is also known to be better than birthweight centile in detecting growth restriction in neonates.[18] We used the PI for identification of true growth restriction among neonates.

Thrifty phenotype hypothesis suggests an increased lifetime risk of coronary artery disease, diabetes mellitus, and metabolic syndrome in growth-restricted neonates.[6,7] The current epidemic of noncommunicable diseases (NCDs) and the inability to improve the outcome of NCDs by late interventions, such as lifestyle modifications and medications, probably lie in the fact that most if not all of these patients with NCDs were programmed in utero during the period of restricted growth. These babies are born with physiological systems with inherently low thresholds for subsequent environmental insults, such as excessive food intake and lack of exercise during postnatal and adolescent life. The inability of the systems to cope with this additional load results in NCDs. Further studies are required to evaluate the outcome of obstetric interventions in mild forms of FGR in preventing NCDs.

Using serial ultrasound measurements of fetal AC and HC and plotting those values on a centile chart is the most accurate way of detecting a growth trajectory. As our results show, sensitivity and specificity of 82.59 and 86.62%, respectively, in the detection of FGR shows that this method enables detection of even mild cases of FGR which cannot be detected by routine methods.

In conclusion, our study has shown that serial ultrasound measurements of fetal AC and HC plotted on fetal growth centile charts, with sensitivity, specificity, and a likelihood ratio of 82.9, 86.63, and 6.2, respectively, provide a more precise method that can detect even milder forms of FGR that are not detected by conventional clinical methods. If ultrasound growth parameter charts and PI centile charts derived from the Sri Lankan population were available, accuracy of antenatal and neonatal confirmation of FGR could have been made even more accurate. Screening low-risk pregnancies for FGR by serial ultrasound scans is the way forward if we are to detect all growth-restricted fetuses and prevent related adult adverse health issues.

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Author Contributions

HP designed and planned the study, and supervised data collection and analysis; RD performed ultrasound scans, collected data, and analyzed and drafted the article. Both authors reviewed the article.

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