REVIEW ARTICLE

THE ULTRASOUND EVALUATION OF FETAL BIOMETRY IN INTRAUTERINE GROWTH RESTRICTION: A NARRATIVE REVIEW

Nazeeha Waseem[1], Rehan Afsar [2],Narjis Batool[3],Waqas Aleem[4]

Authors' Affiliation

[1]Medical Imaging Doctor, Department of Radiological Sciences and Medical Imaging, The University of Lahore Gujrat

[2,3,4]Lecturer, Department of Radiological Sciences and Medical Imaging, The University of Lahore Gujrat

Corresponding Author

Nazeeha Waseem
Medical Imaging Doctor
Department of Radiological Sciences and Medical Imaging
The University of Lahore, Gujrat
Email:drnazeehawaseem@gmail.com

ABSTRACT

Intrauterine growth restriction is a dilemma in the field of obstetrics and poses challenges in definition, terminology, cut-off values, and establishment of a standard. Since the advent of ultrasonography, after four decades, there is still debate on the best ultrasound biometric parameter that can give a definitive diagnosis of intrauterine growth restriction with the highest accuracy. Most commonly used parameters includes abdominal circumference, biparietal diameter, head circumference and femur length, which have a wide range of accuracy in predicting Intrauterine growth restriction, while each poses a certain limitation on their use. In this paper, we evaluate these individual parameters and dig the present literature for their accuracy, limitations, and standards in the estimation of intrauterine growth restriction.

Key Words: Biometry, Fetus, Growth, Intrauterine, Ultrasound.

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INTRODUCTION

Major advances in obstetrics would reliably detect and evaluate fetal development defects. It is correlated with infant morbidity and mortality and utilizes this knowledge for effective therapies.[1] The literature-wide concept of intrauterine growth restriction (IUGR) is contradictory and scientifically specified by weight percentile compared to gestational age. For gestational-age-reference-curve, the American College of Obstetricians and Gynecologists (ACOG) describes it as less than 10 percent ultrasonically measured fetal birth-weight. It can be triggered by maternal, infant, infant-maternal or external factors, and is correlated with perinatal morbidity and mortality, rendering detection in antenatal treatment imperative.[2]

Fetal ultrasound examination will provide considerable insight into foetal antenatal diagnosis with IUGR and boost perinatal complications. Some dimensions include Abdominal Circumference (AC), Biparietal Distance (BPD), Femur Length (FL), and Head Circumference (HC). In this article, in evaluating IUGR, we will address the precision of different foetal biometry parameters and their instructure.[3]

FETAL GROWTH RESTRICTION

IUGR definition lacks consensus and is critically defined as a decreased fetal growth rate that is lower than the infant's growth potential of a specific race and gender.[4] The estimation of newborns weight at a particular gestational age gives an important insight into the intrauterine development. Its anomalies in weight have been associated with neonatal and postnatal morbidity & mortality and put a question mark on long-term health.[5]

It affects approximately 10-15% of pregnancies 1. It may result in various intrauterine complications (like polyhydramnios), stillbirth

or delayed effects like cerebral palsy, stroke, hypertension, type 2 diabetes, impaired cognitive functions, endocrine disorders in adulthood.[6,7,8,9,10] According to Battaglia and Lubchenco [3], Neonates are classified according to the weight at a specific gestational age as Large for Gestational Age (LGA), Small For Gestational Age (SGA) and appropriate for Gestational Age (APA). The term IUGR, more accurately known in the literature as fetal growth retardation (FGR), and SGA are often used synonymously. Still, there exists an arcane difference between the two, or they should be strictly distinguished. SGA represents birth weight less than 10 % at a particular gestational age (GA) and may represent physiological variation, while IUGR determines pathologically decelerated fetal growth rate. A neonate may be born SGA but not IUGR and have better outcomes than an infant with birth weight greater than 10 percent and has suffered from IUGR during developmental phase.

Etiology of IUGR are broadly classified into maternal, fetal and placental, although the underlying pathophysiology may vary, but they often all result into suboptimal uterine–placental perfusion and fetal nutrition. Some causes may include pregnancy-related vascular disorders like Hypertensive disease, Substance use and abuse, maternal nutrition status, multiple gestation, diseases like CMV, placental and umbilical cord abnormalities.[3,5] IUGR still remains one of the significant problems in maternity and child care, and imposes a major problem for developing countries especially Pakistan, where many of the newborn population suffer from some degree of IUGR. Approximately 13.7 million children are born with low birth weight (LWB, birth weight <2500g); that's 11 % of all neonates in developed countries, and the incidence is six times higher in developing countries. IUGR accounts for 23.8%, or 30 million cases each year, of which 75% of all affected newborns are born in Asia, particularly South-east Asia, followed by Africa. The advancement in ultrasonography and establishing clear standards and extensive research has dramatically affected this value.4

TYPES

Normal fetal growth represents the association between fetal intrinsic growth potential and fetal, placental, and maternal health status. The Normal Fetal Growth follows 3 phases: Hyperplasia till 16 weeks, Hyperplasia and Cellular hypertrophy from 16 to 32 weeks, and Hypertrophy from 32 weeks onward and form the basis for the classification.

Symmetric (type 1)

Also known as primary type, accounts for approx. 20-25% of total IUGR cases. It includes diminished intrinsic fetal growth potential, and shows symmetrical decrease in size of head and abdomen. Various etiological factors that affect the absolute number of fetal cells (hyperplasia) at the early stage of growth include: genetic factors, infections etc.

Asymmetric (type 2)

Also called "Head sparing type "and accounts for 70-80% of total IUGR cases. It occurs in the late 3rd trimester (late onset) and causes late changes in growth in the Cellular hypertrophy phase, resulting in an asymmetric decrease in fetal growth. Ultrasound parameters, abdominal circumference (AC) is reduced (decreasing the fetal weight) while Biparietal Diameter (BPD), HC FL, is normal. The most common etiology includes placental insufficiency. [11, 12, 13] A less common type of IUGR involving both the factors of type 1 and type 2. Occur during the 2nd trimester; thus the embryonic growth shows semi-disharmony with hypo-trophic phase. Etiology is associated with fetal infection caused by cytomegalovirus, rubella, toxoplasma gondii, and toxic drugs. At present, most commonly used is chronological classification based on the time of onset. Papers by Gratacós [14] and Baschat [15] showed difference in pathophysiological behaviour of fetus with IUGR before and after 32 weeks.

Early onset

The foetus demonstrates strong immunity to low oxygen and hypoxemia at < 32 weeks owing to significant placental implantation and improved uterine resistance. Early Doppler umbilical artery follow-up is important in early FGR.

Late onset

Occurs at 32 weeks, there is little cardiovascular adaptation however, degree tolerance to hypoxia is low. The major challenge is Diagnosis as normal UA doppler findings may mask the disease. Late-onset FGR is determined by only one parameter: estimated fetal weight and/or AC < 10 percentile.[12]

DIAGNOSIS

Accurate and early diagnosis offers the best chance of decreasing the poor neonatal outcomes associated with IUGR.

Patient history

One of the earliest identifications can be made by thorough patient history and identifying the high-risk pregnancies. IUGR may be due to maternal, fetal or placental causes. Identifying the causes for high risk pregnancy greatly increases the positive predictive value of whatever diagnostic test chosen for IUGR.

Physical examination

Diagnosis through physical test is unreliable, sometimes incomplete or misdiagnosed.[16,17] Diagnostic rates of fundal height estimation for SGA range substantially from 41 percent to 86. Fundamental height measurement by non-elastic tape in centimeters from the tip of uterine fundus to the edge of pubic symphysis is equivalent to gestational age, and a measurement below the suspected GA of 4 indicates growth limit. However, it may be used as a diagnostic tool to diagnose deficiency of foetal development and early referral for further ultrasound examination. Only about 30% of IUGR foetuses, 33 were identified with abdominal palpation.[18-27] Fetal factors contribute between 7-10% in all cases, including chromosomal anomalies, hereditary disorders, and confined placental mosaics.

Ultrasound fetal biometry

Currently, foetal ultrasound assessment is the foundation for correct gestational age estimation, foetal growth assessment, and diagnosis of impaired or premature foetal growth.[17] Estimating foetal weight by ultrasound procedures utilizing foetal biometric scales is the most popular and agreed foetal growth tracking standard. Ultrasound assessment of foetal development, foetal conduct, and blood flow impedance measurement in foetal arterial and venous vessels is the foundation of foetal condition evaluation and decision-making. Fetal biometry includes non-invasive measurement of gestational age in early infancy, evaluation of SGA foetus, and later tracking of foetal development in pregnancy. Serial ultrasound measurements may offer a reasonable estimate of foetal gestational age and weight based on individual and composite foetal biometric measurements and provide the advantage of reasonably accurate foetal weight estimation, period development potential and growth pattern abnormality (asymmetric or symmetric).The most appropriate description for IUGR is a sono-graphically determined foetal weight (EFW) below 10th percentile for gestational age 16
Ultrasound is the tool of option, since it is extremely accurate and reproducible [29,30]

Ultrasound Screening

Ideally ultrasound screening for any abnormality or suggestive signs should be done in every pregnant woman 2-3 times during pregnancy. Screening is organized differently all over the world. The German Society for Ultrasound in Medicine (DEGUM) organizes a 3 level system with increasing expertise of the person screening for abnormality and recommends 3 ultrasounds at 8-12 weeks, 18-12 weeks, and 28-32 weeks.23 In the UK, National Institute for Health and Clinical Excellence (NICE) specifies 2 scans, one in the first trimester, and second between 18-22 week,24 Same is recommended by Mayo clinic, US. [25,26]

Fetal Biometry

Fetal biometry includes sonographic measurements of various anatomical segments of the foetus. Measurement of foetal proportions has four major applications: assign GA to unknown hours, diagnose intrauterine growth retardation (IUGR), measure foetal weight in utero, and classify congenital defects. Different auxological criteria used in the diagnosis of antenatal foetal status are: Biparietal width (BPD), Head circumference (HC), Femur length (FL), Humerus length (HL), Abdominal circumference (AC), Crown rump length (CRL), Occipital-frontal width (OFW) and Amniotic

fluid index (AFI). Structures such as binocular scale, intraorbital scale, foetal foot length, transverse cerebellar diameter can be measured to refine the data gathered or correct details. It may become difficult to pick one parameter to detect gestational age, foetal development and quantify foetal weight. Main biometric parameters-CRL, BPD, HC, AC, and FL-can be quickly explored.[31-42]

BIOMETRIC PARAMETERS

Crown Rump Length (CRL)

CRL is used for the accurate determination of gestational age during the first trimester. The most favourable gestational age for determining CRL is 8-12 weeks, when the fetal size is above 10mm. Because the embryonic growth curve slope is less before this age and very early fetus is difficult to identify.[43,44] Means of 3 measurements of CRL should be taken with each measurement being in midsagittal plane with longitudinal view of genital tubercle and fetal spine, and the maximum length from cranium to caudal rump taken as a straight line.[45, 46] Various studies stress the accuracy of CRL in determination of GA and show a curvilinear relationship between CRL and GA during the first trimester, after which the CRL either overestimate or underestimate the true gestational age [47, 47, 49]

Head Measurements

BPD was the first ultrasonic test of foetal development and gestational age. Serial ultrasonic cephalometry by A&B scan ultrasonography was used in the diagnosis of SGA foetuses as demonstrated by Cambell et al in 1971 [50] BPD defies the strongest axial estimation of the skull from the outer edge of the proximal parietal bone to the outer edge of the distal parietal bone with thalami and cavum septi pellucidi as point 51. BPD accuracy in evaluating GA declines with 3rd trimester and establishes the optimum period for measurements at 53 54 55 maternity weeks 12-24.[51-53]

Head diameter is calculated as the skull's outermost perimeter and may be assessed at the same stage as BPD by ellipse process or by geometric formulae. Schmidt et al recently recommended the use of ellipse in HC clinical practice.[54-56]

BPD typically offers the same GA measurements as HC 56, but it depends on the standard head shape ovoid. Abnormal head shape, round ((brachycephalic), flattened or compressed head (dolichocephalic) can offer aberrant GA. [57-59] Ultrasound BPD estimation can also be impaired by placing the foetal head in the uterine cavity (breech head reduces BPD), inaccurate ultrasound plane and procedure, as well as congenital abnormality, so HC is favored as a more useful indicator in the evaluation of gestational age and foetal growth.[57-63] The occipitofrontal diameter is estimated at the same amount as the biparietal diameter from mid frontal echo to mid occipital echo.

Femur length

FL parameter include the ultrasonic measurement of ossified portion of the diaphysis and metaphysis, with proximal and distal epiphyseal cartilage being in sight for accurate measurement. FL can be accurately measured at the beginning of 14 week along with BPD. FL used in determination of Gestational age gives measurements in range +_ 2.8 weeks, with accuracy decreasing with increasing gestational age.[64-67] Measurement of FL can also be used as a cross-check of BPD in fetal age assessment.

Abdominal circumference

Abdominal diameter can be determined at the level of the foetal intestine, a small section of the umbilical vein, the ductus venosus and the ellipse gallbladder used to calculate HC.AC is less reliable than BPD, HC, FL in assessing gestational age, but it is one of the main measurements of IUGE and macrosomi. [68- 73]. The AC offers a reliable assessment of foetal development, so much so that the IUGR definition is described by AC as below the 2.5th percentile. [37]

Evaluation of IUGR

Following are essential criteria needed to form the diagnosis of IUGR using ultrasonography:

Accurate gestational age

Accurate measurement of GA is important whether a foetal size is suitable for gestational age AGA or SGA. Clinically, LMP is used for GA and may be unclear or inaccurate. In the ultrasound examination during the 1st trimester, the CRL is the most accurate parameter for determining gestational age earlier in pregnancy.[37] However BPD maintains the closest correlation with the gestational age in the 2nd trimester with the highest accuracy of 2SD range of +_ 7 days.[38,39] And FL can be used to determine GA in case of head abnormally shaped or inability to image BPD accurately, but it's accuracy decreases with increasing GA. [40] HC can still give the best estimation of gestational age with the with random error (SD) of 3.77 days. [41] Using multiple factors significantly improved the sonographic estimation of gestational age as shown by Hadlock et al. [42]

Estimation of fetal weight

The exact estimation of gestational age is vital in the use of any of the biometric parameters. In unreliable dating, BPD or Serial scans with 2-3 weeks intervals are used with error potential increasing with increasing gestational age. [37,38] There exists a limit to the efficacy of each of these parameters and which factor accurately determine the fetal weight, length and ultimately IUGR. The parameter with highest diagnostic accuracy of IUGR is AC, as AC is classically affected in case of growth deceleration, with sensitivity as high as 95% if the values fall below 2.5 percentile. [71,72] Smith et al. in 1997 [32] analyzed 3512 nondiabetic women with a customarily formed singleton fetus. They concluded that AC was the most accurate single factor for predicting birth weight in IUGR; hence, the fetal size was completed by Campbell and Wilkin in 1975.[33] They first described the prediction of birth weight by using ultrasonography. Barry et al.[75] in 1982 evaluated the relationship of BPD in determining IUGR and found a positive predictive value of 42%. He reviewed the sensitivities of various parameters mentioned in literature present at that time and showed that none of the studies accurately predicted correct estimations and showed these parameters are limited in their accuracy in the determination of IUGR.

A combination of 3 or 4-factor model should be used to increase the accuracy and efficacy of ultrasonic determination of fetal weight. [28]

William J. Ott [35] compared the accuracy of various ultrasound parameters and showed that both AC and Estimated fetal weight had a high predictive value of around 65%, although Doppler studies showed the highest sensitivity. But when AC or Fetal weight was combined with Doppler studies, the positive predictive value increased to 95.9%.

Dashe et al. [34] reviewed the importance of HC/AC ratio in determining IUGR, and it's differentiating its different types (asymmetrical and symmetrical). Guidetti et al. [74] compared the efficacy of estimating fetal weight in IUGR fetus using BD, AC, and FL, either alone or in combination. He showed that in the fetus with IUGR, fetal weight estimates that included FL correlated best with the actual birth weight.

Although each of these parameters is being used in the diagnosis of IUGR, estimation of fetal weight is one of the most common methods used, and the ultrasound Doppler studies of umbilical vessels are the most effective in predicting morbidity and mortality. [30, 31] Requirements for birth weight and duration in many countries and regions can vary greatly due to ethnographic factors, dietary conditions and different healthcare systems.

Table 1: Ultrasound Parameters and the Diagnosis of Intrauterine Growth Restriction

	Fetal weight	AC	HC/AC	AC/FL	Doppler
Sensitivity	65.8	62.2	49.1	28.9	66.7
Specificity	88.9	90.7	83.7	47.8	68.5
Positive predictive value	63.6	67.3	47.1	47.8	38.4
Negative predictive Value	89.8	89.8	84.8	81.3	87.5
False positive feedback	8.6	7.2	12.6	7.2	24.4
False negative	7.8	8.0	11.6	16.2	17.7

CONCLUSION

There is a significant gap in the literature comparing different ultrasound biometric parameters in their accuracy and reliability for detecting IUGR. However, AC has the highest accuracy of all in IUGR estimation, as AC is linearly associated with fetal growth. Combining different factors significantly increases the positive predictive values of these parameters, whichever the equation is used. BPD was the first parameter used to detect GA and estimate IUGR. But latest studies showed various limitations in the accuracy of BPD in IUGR diagnosis

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