Review of Literature
REVIEW OF LITERATURE

HISTORICAL ASPECTS:

Fetal growth retardation ranks third after prematurity and malformation as a cause of prenatal deaths. Antenatal fetal monitoring has emerged as the most important means of reduction in the number of still births and improvement in the quality of survival of infants who are born alive. Clinical finding combined with biochemical and ultrasonographic testing will identify as many as 70% of growth retarded fetuses. It should be the obstetrician’s aim to identify all growth retarded fetuses at risk of death from hypoxia.

With present day methods of antenatal diagnosis and treatment and timing of delivery the physical and intellectual prognosis of growth retarded infants is most satisfactory with ideal set ups follow up studies have shown that only about 2% of the infants are severely handicapped.

In 1947, Mac Burney first introduced the concept of IUGR. Clifford in 1954, actually claimed that clinically significant intrauterine malnourishment can occur in utero associated with intrauterine asphyxia and soft tissue wasting and the attributed these changes to the decreasing placental function with advancing maturity. Karn and Penrose (1951) showed that the weight at which the mortality curve reaches its minimum
is several hundred grams heavier than the mean birth weight; a findings
which was true for all human population later investigated (Wilcox and
Russill, 1983).

Subsequently many workers entered into this field and much
research has been done into the aetiology, pathology, diagnosis and
management of this condition, its immediate and long term effects on the
fetus and neonate.

Much confusion has occurred for describing IUGR, with a number
of synonyms------------------⁴ Small for Gestational age (SGA), small
for date, dysmature’ low birth weight, placental insufficiencies, all being
basically used to refer to the growth retardation.

The most widely accepted definition is that given by Lubchenko
A foetus whose birth weight is below the tenth percentile for that period
of gestation. The various birth weight tables used by different workers are
– Brenner et al.

The birth weight tables by different authors for different
populations vary.
EXAMPLES OF DIFFERENCES IN THE WEIGHT TABLES USED TO IDENTIFY IUGR INFANTS.

<table>
<thead>
<tr>
<th>Gestational age (wks.)</th>
<th>10th Percentile</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Thompson (gm)</td>
<td>Kloosterman (gm)</td>
<td>Lubchenko (gm)</td>
<td>Persson (gm)</td>
<td>Bronner (gm)</td>
</tr>
<tr>
<td>36</td>
<td>2330</td>
<td>2100</td>
<td>2050</td>
<td>2100</td>
<td>2190</td>
</tr>
<tr>
<td>38</td>
<td>2650</td>
<td>2650</td>
<td>2430</td>
<td>2500</td>
<td>2510</td>
</tr>
<tr>
<td>40</td>
<td>2884</td>
<td>2800</td>
<td>2630</td>
<td>2800</td>
<td>2750</td>
</tr>
<tr>
<td>42</td>
<td>3000</td>
<td>2720</td>
<td>3000</td>
<td>2830</td>
<td>3200</td>
</tr>
</tbody>
</table>

HISTORICAL ASPECT-ULTRASOUND DIAGNOSIS OF IUGR

Criteria used in the prenatal detection of IUGR in different investigations are:

Campbell (1974) BPD growth rate less than 5th percentile

Whetham (1976) BPD growth rate below- 2SD

Queenan (1976) BPD below- 2 SD any time

Crane (1977) BPD below- 2SD with normal growth rate

Arrias (1977) BPD growth rate below mean for gestational age.

Campbell (1977) HC\AC above 95th percentile within 7 days of delivery.

Sabaggha (1978) BPD growth rate between 26 weeks and 30 to 33 week below 25th percentile.

Perrson (1978) Single BPD below 5th percentile
Crane (1979)  
Single BPD below -2SD serial BPD’s below-2 SD during 3rd trimester. HC/AC above 95th percentile using.

(1979)  
Normal values published by Campbell and Thomson.

Wladuimiroff (1979)  
(BPD)2/AA above 95th percentile

Sittman (1979)  
Single BPD, TA, CRL and CRL x TA below 10th percentile

Kuejak (1980)  
Single BPD, BPD growth rate or AC or HC/AC below 10th percentile

(parameters used or in combinations).

Dater (1980)  
One or more HC/AC above 95th percentile using the normal values published by Campbell and thomson.

**TYPE OF GROWTH RETARDATION**

The classical picture of the growth retarded infant increased body length in relation to weight, relatively large head with wide skull sutures muscle wasting prominent ribs, an alert look and a dry wrinkled skin is readily recognised. Reduction in length and in brain weight is much less then the fall in body weight whereas weight of liver and spleen are relatively more reduced than body weight. In the past with unreliable data on gestational age, such disproportion, mainly expressed in terms of birth
weight compared with length and/or head circumference, were important criteria to distinguish preterm infants from growth retarded infants (Gruehwald, 1963).

In general these clinical types of IUGR can be subdivided into a 'soft tissue type' in which there is reduced soft tissue mass, mainly adipose tissue and muscle wasting) a skeletal type (In which length and head circumference are more affected), and a combined type with shows features of both the skeletal and soft tissue type. Various term have been used by investigators to indicate differences between the first two type. One thus encounters subdivision of sub acute versus chronic, symmetric versus asymmetrical, disproportional versus proportional, waste versus symmetrically small, soft tissue wasting versus underweight for gestational age, low ponderal lindex versus short for dates, and so on.

**Symmetric & Asymmetric IUGR**

Symmetric growth restriction emplied a fetus whose entire body is proportionally small. Asymmetric growth restriction implied a fetus who is under nourished & is directing most of its energy to maintaining growth of vitals organs such as brain & heart at the expense of liver muscle & fat this is due to placental insufficiency.

Asymmetric IUGR fetus has a normal head dimension but a small abdominal circumference (d/t decrease size). Scrawny limbs (b/o
decrease in mass) & thinned skin (b/o decrease fat). Arrested head growth is of great concern to the developmental potential of fetus.

Distinction between disproportionally and proportionally grown or growth retarded infants is usually made on the basis of the ponderal index, a measure introduced some 60 years ago by Roghrer (1921) for comparing nutritional status of infants. This index the product of (birth weight in g) x 100/(length in cm)^3 – shows how heavy the infant is for his length and increases with accumulation of muscle mass and adipose tissue.

Ultrasonic assessment of fetal growth has revealed two principal types of growth retardation (Campbell, 1974). The first, called late flattening can be detected by serial measurements of Biparietal diameter, the BPD is within the normal range until after 30 weeks of gestation when its rate of growth slows or stops. Generally retardation of growth, of trunk if affected earlier and more severely. Comparisons of head and trunk growth have revealed a disproportionate decrease in the latter in 84.2% and 100% of such cases in studies of 19 and 7 fetuses respectively (Campbell, S. Thums A. 1977) Thus disproportion is a common feature and therefore also the term asymmetric growth retardation. Basically this type of IUGR is due to factors which compromise nutrition in an otherwise potentially healthy infant. There is a brain affect and there is preferential supply of fetal circulation to head and brain over the trunk.
Campbell has shown that approximately 70% of SGA infants show late flattening BPD growth pattern in utero. However, Sabbagha found that 67% of SGA babies have abnormally slow BPD growth. A second type of growth retardation is called low profile. This growth pattern is characterized by a BPD that grows consistently slower than normal at least after 2 weeks. The fetus exhibits growth retardation which begins in 2\textsuperscript{nd} trimester and affects all parts of the body more or less uniformly. Campbell considered it a manifestation of reduced growth potential and has also referred to it as hypoplastic IUGR, as the total number of cells are reduced, comparision of head and trunk growth have revealed a disproportionate decrease in trunk growth in 40% of the cases in a study (Campbell, 1977) Campbell has shown that about 30% of SGA infants show a low profile pattern. The low profile child has a relatively trouble free delivery, but later it found to be of subnormal IQ and stature (Fancourt et al, 1976). Affected fetuses are at much greater risk for congenital malformations than the general population (Ramzin et al (1973) according to Hansman. (1976) a significant number of these fetuses suffered intrauterine infections.

\textbf{Aetiology :}

Fetal growth can be defined as time – dependent increases in specific geometrical characteristics of the fetus and it depends on a complex interrelay of fetal, maternal and placental factors. Malfunction
of any of these factors lead to growth retardation. Thus, IUGR is multifactorial in origin and it is important to note that in over half the cases no obvious cause can be implicated potentially.

Potential causes of IUGR are dealt with below.

Although chromosomal abnormalities are estimated to occur in about 6% of conceptions (weight, 1976) and in 5% of recognized conspectuses (Hood 1981).

The presence of multiple Congenital malformations often leads to a clinical diagnosis of IUGR. Swab et al (1978) found that at 40 weeks of gestation the mean anencephalic birth weight was about 1000g. less than mean normal birth weight minus the weight of the brain. Of the congenital deformities those which affect the central nervous system and/or skeletal system have the most marked effect on fetal growth. IUGR is also common in fetuses with gastrointestinal abnormalities such as duodenal atresia (Girvans and Stephen S 1974). Omphalocele (Columbani and Cunnigham, 1977). Potter's syndrome and renal agenesis too are associated with IUGR.

IUGR may be caused by infections of viral and bacterial origin. Upto 60% of infants with congenital rubella may be below the10th percentile of weight for gestation (Cooper et al, 1965). The rubella virus show a prediction for infecting vascular endothelium and may cause
placental villous atrophy by introducing in the endothelium of villous capillaries (Driscoll, 1969).

C.M.V. is currently a common cause of congenital viral infection with an incidence ranging from 0.2 to 2.2% in different population (Stanzo et al, 1983). Growth retardation occurs in about 40% of infants who present with clinical manifestations at birth (Stanzo et al, 1983). Varicella Zoster infection especially early in pregnancy can cause IUGR (Waterson and Lynel, 1947). Growth retardation is common in malarious mothers. In an endemic Malarious area McGregor, Wilson, ad Billsicz (1983) found that 20% of placenta were infected and in these cases birth weight was reduced by about 170g.

According to Brent and Jensch (1967) high dosage ionizing radiation during pregnancy may result in severe growth retardation.

Several drugs have been reputed to cause impaired fetal growth (Jhons and Chernoff, 1978). Howard and Hill 1979, Redmond 1979). Certain drugs appear to affect some but not all parameters of growth e.g. Hulesmaa et al (1981) found smaller head circumference without much changes in others parameters with use of the antiepileptic carbamezepine or with a combination of phenobarbitone and phenytoin, Chronic administration of corticosteroid are possible causes of growth retardation (Scott, 1977). More then 50 publications based or over ½ a million births reported that woman who smoked during pregnancy had babies of lower
birth weight than woman who did not. The size of differences (above 175 to 200g. or a depression of approximate 5%) was remarkably consistent in all investigations (Peters et al, 1983).

Effect of alcohol abuse on fetal growth may be mediated in a number of ways, direct effect of alcohol or its metabolite acetaldehyde are probably the most important. These include malabsorption of nutrients across the intestinal musoca, alleged maternal hepatic function, effects on amino acid transport across the placenta and effects of fetal metabolism and endocrine function (Rosett et al, 1983) Reduced fetal growth is most marked in the fetal alcohol syndrome which is characterized by:

(a) Prenatal growth retardation.

(b) Congenital malformation.

(c) Facial dysmorphology

(d) Disturbances of mental development. In these cases fetal weight is reduced by as much as 1200g. at term compared with controls and 5cm. length (Brerich 1978).

(e) Narcotics alone can impair growth (Reneteria and Lotongknum, 1977). Amongst infants exposed to heroin in utero as many as 50% are growth retarded.
Placental Influences:

In the absence of gross pathology of the maternal-fetal unit, placental size shows a close correlation to fetal size. A large placenta is required to produce a large baby but the reverse is not necessarily true. Nevertheless, most growth retarded fetuses, have a fetal/placental weight ratio which is higher than that of normally grown fetuses. Thomson, Billewicz and Hitter (1968) showed that the fetal placental weight ratio increased from approximately 4.5 in the higher placental weight groups to about 7.3 in the lowest i.e. a growth retarded fetus shows some compensatory growth and tends to outgrow its small placental alterations (for e.g. calcification or so called infants that have been held responsible for otherwise unexplained fetal growth retardation, few have stood up to close scrutiny (Fox, 1981) placental abnormalities truly associated with low weight for gestation are haemangioma and extrachorial placenta (Fox, 1981).

Maternal Vascular Disease:

There appears to be general agreement that vascular pathology whether it is due to renal disease, essential hypertension, PIH, diabetes or collagen vascular disease, is the single most common denominator in the causation of IUGR frequency and severity of growth retardation is highest in pregnancy induced hypertension on superimposed in preexistent hypertensive disorders, lastly in PIH there is an undeniable
relationship with gestational age and the onset of disease. More and fedman (1983) formed that 82% of infants of mothers in whom they diagnosed pre-eclampsia before 34 weeks of gestation had birth weight below the 10th percentile of weight for gestation.

Anaemia and low haemoglobin levels, vary with poor socioeconomic status, poor general nutrition and other factors known to be associated with poor birth weight (Butler and Alberman, 1964) Harison and Ibeziako (1973) demonstrated clearly that severe chronic anaemia (defined as hematocrit of less than 30%, was associated with a reduction in birth weight about 100g. per 2% packed cell volume.

Perinatal mortality and morbidity and long term sequelae associated with IUGR:

20% of all fetal deaths can be attributed the impact of this problem is reflected in a marked increase in perinatal mortality and mordidity associated with IURG (Batteaglia, 1970 (Dobson et al 1981), William, et al 1982) it is associated with an eight fold increase in fetal mortality 9Butler at Behern, 1963), a seven fold increase in mortality at birth due to anoxia, asphyxia and decreased PH and a significant increase in the incidence of neonatal problems such as polycythaemia, hypothermia, hypocalcaemia.
**Diagnosis:**

The diagnosis of IUGR is difficult and must be done along the following lines. Step one is to pick the population at risk – these will account for 2/3\textsuperscript{rd} of the cases of IUGR step two is making a confirmatory diagnosis of IUGR then the following questions have to be answered.

1. What is aetiology of growth retardation?
2. Can progression be modified. If so, how?
3. What reliable parameters are available to monitor fetal well being.
4. Is delivery preferable, and if so when and how?

A maternal obstetrical history accompanied by a physical examination will identify many of the pregnancy at risk of growth retardation. A maternal history of a previous small for gestational age infant puts the current pregnancy at 20-30\% risk of again manifesting growth retardation. (Tejani, 1982). Maternal condition associated with IUGR are

**Generic predisposition:**

- Previous IUGR infant
- Family history

**Cardiovascular**

- Chronic hypertension
- Pre-eclampsia
- Congenital heart disease

16
Infection
   Rubella
   CMV
   Malaria etc.

Social
   Cigarette smoking
   Drug abuse

Metabolic
   Malnutrition
   Chronic renal disease
   Phenylketonuria

Others
   Anaemia
   Placentapraevia

   Previous congenital malformations H/O still birth

Many scoring systems have been proposed over the last few years to identify, more accurately the pregnancy at risk of development of IUGR (Galbraith et al, 1979, Gaziano et al, 1981. of these the eight factor scoring system proposed by Wennnergren and Karlsson, 1982) currently appears to offer the best result and least complexity. The system result in 100% sensitivity and 95.5% specificity. The following table gives this scoring system.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Weighted Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>H/O proved IUGR, still birth or neonatal death</td>
<td>1</td>
</tr>
<tr>
<td>B.. 140/90 or more after 34 weeks</td>
<td>1</td>
</tr>
<tr>
<td>History of renal disease or urinary tract infection in this pregnancy.</td>
<td>1</td>
</tr>
<tr>
<td>Smoking</td>
<td>2</td>
</tr>
<tr>
<td>Bleeding or preterm labour</td>
<td>1</td>
</tr>
<tr>
<td>Inadequate weight gain</td>
<td>1</td>
</tr>
<tr>
<td>Decrease (or non increase) in fundal height (Score = 4 + at risk of IUGR)</td>
<td>3</td>
</tr>
</tbody>
</table>

**Methods of Diagnosis of IUGR**


2. Ultrasound Assessments: Single or battery of parameters single or serial measurement.

3. Cardiotocography

4. Tests of fetal conditions ± placental function.

5. Urinary or Plasma oestroil assay

6. Plasma placental lactogen

   Urinary pregnanediol or plasma progesterone, plasma pregnancy specific beta-1, glycoprotein. Serum cystyl aminopeptidatase maternal haemoconcentration in pre-eclampsia amnioscopy, Aminiocentesis, Vaginal cytology.
The Role of Ultrasound in the Evaluation of IUGR

Since the introduction of pulsed echo ultrasound into obstetric diagnosis in 1958 (Donald, Mac Vicar and brown, 1958). Ultrasonic diagnosis is concerned with the diagnosis of pregnancy, the viability and normality of the fetus, and in particular the accurate establishment of gestational age. In the latter half of pregnancy the major use of ultrasound is the fetal growth which is the outcome of complex interactions between the fetal genotype and numerous constraining and growth accelerating factors within the fetomaternal environment.

Dating the pregnancy – A necessary pre-requisite:

The correct interpretation of any ultrasonic parameter used for the diagnosis of IUGR requires knowledge of gestational period at the time of examination. Menstrual history unreliable in the quarter to one third pregnant woman (Campbell, 1974), Grennert person and Gennser, 1978) and clinical examination is of increasingly limited help as a means of assessing gestational length as pregnancy advances (Beazley and Underhill 1970, Campbell, 1976). Ultrasonic CRL measurements of the embryo have an accuracy of ± 6 days. Upto 11-12 weeks gestation which improves to ± 3.4 days when these measurements are average (Robinson and Fleming, 1975, Pederson, 1982). In malmo the following formula has been developed for between 12-24 weeks-BPD x 1.2 + FL x 1.0 + 29.0 =
Gestational age in days, addition of femur length considerably adds the accuracy.

Measurements and functional tests of use / potential use in the diagnosis of IUGR.

One and two dimensional growth:

Skeletal: BPD, head circumference, Long bone lengths.

Soft tissues: Trunk diameters, area, circumference Thigh thickness, Subcutaneous fat thickness

Combination: Head / Trunk ratios

Three dimensional growth:

Weight: Fetal weight estimation, fetal volume
Total intrauterine volume, intra-amniotic volume.

Functional (dynamic test):

Fetal breathing movements
Fetal umbilical vein/aortic blood flow
Fetal urinary bladder volume
Uterine blood flow

Placental Grading

1. Bi Parietal Diameter:

Since the observation by Willocks et al. (1904) that dysmature infants have on average a smaller BPD than normal infants. The BPD has remained the basic fetal measurement in IUGR in spite of
its limitation which were pointed out in 1965 by Thompson et al. The BPD is often measurable as early as 11 weeks after the last menstrual period and by the 13th week is visible and measurable with ease. From the 13th until the 30th week, the BPD represents a reasonably accurate method of detecting the fetal age. This accuracy is generally of ± 6 days. In the last trimester the accuracy decreases significantly the standard deviation maybe of ± weeks to ± 3 weeks.

The limitation with the use of BPD for detection of IUGR are that fetal head size is spared until the 3rd trimester of pregnancy and does not fall out side the normal range until very near term. Thus its use alone would result in a low sensitivity and a high number of false negative results. Secondly the variation if fetal head shape due to moulding and particularly, dolichocephaly which is observed in cases of ruptured membranes, twins breech – will result in abnormally low values and a high number of false positive cases diagnosed as IUGR.

Campbell (1971) was the first investigator to link foetal BPD to gestational age and also standardized method for recording BPD since many worker have developed normograms for assessing fetal growth from BPD measurements.
In the series of Campbell and Kurjak (1972) 16% of fetuses with retarded ultrasonic growth pattern had a normal birth weight and 25% of the fetuses with normal cephalometric growth were small for gestational age.

Stocker et al (1974) showed that BPD measurement alone used to predict. Birth weight had too wide a range of predicted weights to be of clinical use, 1 SD ranging from 320 to 480 g.

Aanto and Korss (1974) also showed in their study that the growth curve flattened especially during the last month of pregnancy, in their series the weekly growth increment towards the end of pregnancy was 1 mm.

Queenan et al (1976) found BPD growth rate of 0.26 cm/week (18-38 weeks) in 468 normal pregnant females. He then studied 100 high risk patients and found two patterns of IUGR – those with BPD less than 2SD below mean and those with decreased growth rate of BPD or a combination of the two patterns.

Crame et al (1977) determined mean rate of growth of BPD at different gestational age.

The mean rates of growth given by them were:

3.1 mm/week between 19 to 30 weeks.
2.0 mm/week between 30 to 36 weeks
1.3 mm/week after 36 weeks.
Fernando Arias (1977) using the above, mentioned criteria to detect IUGR found that only 43 of the fetuses suspected of IUGR by ultrasonic cephalometry were found to be small for gestational age. He too found-two patterns of abnormal BPD growth. The most common, finding in 17 patients corresponded to ‘low growth profile’ type of IUGR and was characterized by continuous growth of the fetal head but at a rate below normal and with measurements falling consistently below the third percentile of normal growth. The second type observed in 11 patients, corresponded to the late flattening type of IUGR and minimal growth (<1mm/wk) of fetal biparietal diameter in the last trimester pregnancy.

Sabaggha (1978) used the GASA method (Growth adjusted sonographic age) to detect IUGR in 463 high risk pregnancies. He found 4 categories.

1. 75\textsuperscript{th} percentile – 3.5 had IUGR (asymmetrical)
2. 25\textsuperscript{th} – 75\textsuperscript{th} percentile – 3.5 had IUGR (asymmetrical)
3. 25\textsuperscript{th} percentile – 52.1\% had IUGR (symmetrical)
4. Decreasing BPD – 20\% IUGR (symmetrical)

Regarding the diagnosis of IUGR by serial BPD Campbell (1971), whethan (1976), reported an accuracy of 70-73\%.

M. Sood et al (1976), reported accuracy of 75.4\% while Sood et al (1985) reported an accuracy of 43-100\%.
Lee and Chard (1983) measured fetal BPD by ultrasound at 18-21 weeks gestation in 1023 women and tried to assess its predictive value for diagnosis of IUGR. The sensitivity was 24.2%, predictive value was 18.2% and the specificity was 92.5% fetal head measurement.

**Fetal Femur Length:**

The shaft of the femur is the easiest fetal long bone to visualize and measure. However, the accuracy of estimating dates from femur length is controversial.

Jenaty and associates (1984-1985) conducted a large study involving femur length and showed that the accuracy of this parameter is within +/- 2.8 weeks (2SD) regardless of pregnancy used.

Further ward and associates (1985) showed that a straight line measurement of the slightly bowed femur bone (usually noted after 18 weeks of gestation) does not alter femur length in at least 69% of period comparisons. They felt that a straight line measurement is appropriate particularly because the resolution of most machines in any case is approximately 2mm and (b) the inter - observer variability is large namely 4.4mm.

**Abdominal Circumference:**

Nelson et al (1965) realized that measurements (1980) performed a 2 stage ultrasound examination schedule as a screening procedure for small for date fetuses on 474 single term pregnancies. In the first stage
examination CRL and BPD were measured for an accurate assessment of gestational age. In the second stage at 34-36 weeks the abdominal area and abdominal circumference were measured and an accuracy of 61% and 83.7% respectively was reported.

Steven L, wars of et al (1986) designated a prospective screening programme of a large obstetric population. 3616 pregnancies were analysed. All pregnancies were dated before the 24th week by ultrasonic measurements. The study compared the effectiveness of three ultrasonic parameters. Biparietal diameter (BPD), head circumference and abdominal circumference. They concluded that abdominal circumference measurements were more predictive of IUGR than either head circumference or BPD measurements or the combination of these parameters. In view of the sensitivity of the test and the prevalence of the disorder, it is concluded that 34 ± 1 week of gestation is the optimal time to screen patients ultrasonically for IUGR.
Additional Criteria for diagnosis IUGR

Additional Sonographic Criteria for diagnosing IUGR have included elevated HC/AC ratio, elevated FL/AC ratio, presence of oligohydranmios without ruptured membrane, presence of advanced placental grade and other. Each of these sonographic parameters of features has been found to have a statistically significantly different mean value, or frequency of occurrence, in growth-restricted compared with normal fetuses. For a criterion to be clinically useful in a particular population of particular, to be useful for diagnosing IUGR, a criterion must have a high sensitivity and a high positive predictive value. That is, it must detect a substantial fraction of growth-restricted fetuses, and the likelihood of IUGR after a positive test result must be high (relatively few false-positive results). In analogous fashion, a criterion must have high specificity and negative predictive value to be useful for excluding IUGR.

The performance characteristics-sensitivity, specificity, predictive values-of sonographic (non-Doppler) criteria for IUGR are presented in Table 8-7 in order of increasing positive predictive value. Sensitivities and specificities were obtained by pooling data from the published literature, and predictive values were computed with Bayes’ theorem assuming a prevalence rate of 10%. The presence of a grade 3 placenta and an elevated FL/AC ratio have the lowest positive predictive values; the likelihood of IUGR is no more than 20% when either of these criteria
is positive. Seven of the nine criteria, including a low estimated fetal weight, have positive predictive values below 50%, so that a fetus meeting on these criteria is more likely to be normal than growth restricted. An elevated HC/AC ratio had the highest positive predictive value, 62% but even on the basis of this criterion IUGR cannot be diagnosed with confidence because 38% (100%-62%) of fetuses with an elevated HC/AC ratio will not be growth restricted.

In contrast to the poor positive predictive values, all parameters had negative predictive values of at least 92% (see Table 8-7). This is a reflection of the low prevalence of IUGR, not of the excellence of the criteria for excluding IUGR. Ninety percent of fetuses are not growth restricted, so any reasonable test will have a negative predictive value of at least 90%. Overall, no single non-Doppler sonographic parameter permits the confident diagnosis of IUGR.

**DIAGNOSIS OF IUGR USING MULTIPLE PARAMETERS**

Because no single criterion is reliable for diagnosing IUGR, more accurate diagnosis might be achieved by using multiple parameters (Table 8-9). In view of interrelationships between the various proposed criteria—a small AC and otherwise normal measurements, for example, will lead to an elevated FL/AC ratio, elevated HC/AC ratio, and low estimated fetal weight—a rule for diagnosing or excluding IUGR should be based on a subset, as opposed to the entire group of criteria. The optimal
subset and the rule for diagnosing IUGR using this subset can best be found by using logistic regression analysis.

With this technique, we found that IUGR can be diagnosed most accurately using a combination of three parameters: estimated weight percentile, amniotic fluid volume, and maternal blood pressure status (normotensives, hypertensive, using the commonly accepted definition of hypertension during pregnancy as a diastolic pressure of at least 90 mm Hg or a systolic pressure of at least 140mm Hg or a rise in the former of at least 15mm Hg or in the latter of at least 30mm Hg). Diagnostic accuracy is not improved by considering additional parameters such as the FL/AC and HC/AC ratios.

These parameters can be used for diagnosing IUGR in two ways: one quantitative and the other semi-quantitative. The quantitative method uses an IUGR score derived from the logistic regression analysis. Alternatively, a table based on that IUGR score can be used. To diagnose or to exclude IUGR in a particular fetus, the table provides "rule-in" and "rule-out" estimated fetal weights corresponding to gestational age, amniotic fluid volume, and maternal blood pressure status. If the estimated fetal weight is below the lower rule-in value, IUGR can be diagnosed with confidence; if it is above the rule-out value, IUGR can be excluded. An estimated weight be excluded. An estimated weight between these values is indeterminate for IUGR. When the gestational
age is known precisely, based on a prior sonogram before 20 weeks, the situation is better in that the indeterminate range can be eliminated; an estimated weight below the rule-in value is diagnostic of IUGR, and an estimated weight above this value excludes IUGR, both with greater than 85% confidence.

**Pregnancies at Elevated Risk for IUGR**

In some pregnant women, the clinical history or physical examination may indicate an elevated risk for IUGR. When this occurs, an active approach to the diagnosis of IUGR should be undertaken, including one or more sonograms at appropriate time in the pregnancy.

The factors associated with increased risk may predate the pregnancy. Woman with chronic hypertension, collagen vascular disease, or a history of IUGR fall into this category. In these patients, the scanning protocol should include a first trimester sonogram for precise gestational age assignment, followed by at least one additional sonogram in the early to middle third trimester to assess fetal growth. Additional sonograms may be indicated, depending on the nature and severity of risk factors. For example, a woman at high clinical risk for IUGR should have sonogram at regular intervals (e.g. every 2 to 4 weeks) in the third trimester.

In other woman, the indicators of increased risk arise during the pregnancy. Examples include lag in fundal height or development of
hypertension during the pregnancy. In these women, a sonogram should be performed as soon as the indicator of high risk is recognized. This sonogram will provide information about gestational age and the size of the fetus and will serve as a baseline to assess growth on future sonograms if the woman remains at elevated risk for IUGR.

Summary

IUGR has been defined differently by various authors. We advocate defining IUGR as a fetal weight below the 10th percentile for gestational age. Causes of growth restriction include primary placental insufficiency, placental insufficiency resulting from maternal disorders, fetal chromosomal abnormalities, and fetal infections.

Growth-restricted fetuses have a four to eightfold increased risk of perinatal mortality, and of those who survive, 50% have significant short- or long-term morbidity.

Sonography is useful for diagnosing IUGR has been diagnosed. Many sonographic and Doppler criteria have been proposed for diagnosing IUGR, but none on its own permits a confident diagnosis of IUGR. A multiparameter approach using a combination of estimated fetal weight percentile, amniotic fluid volume, and presence or absence of maternal hypertension is the most accurate method for diagnosing or excluding growth restriction.
Once IUGR has been diagnosed, an attempt should be made to
determine its cause, including an evaluation of the mother for a maternal
cause and a careful sonographic evaluation of the fetus, searching for
evidence of a chromosomal or infectious origin. When a chromosomal or
infectious cause is suspected, sonographically guided amniocentesis or
sampling of umbilical blood can be used for further evaluation.

Unless the growth restriction is due to a lethal cause such as
trisomy 18, the fetus should be monitored closely by sonography for the
remainder of the pregnancy. In particular, the estimated weight percentile,
amniotic fluid volume, biophysical profile score, and Doppler waveform
indexes should be followed up serially. A worsening trend in one or more
of these items should prompt consideration of early delivery.