Intrauterine Growth Restriction
Diagnosis and Management

Practice Resource for Healthcare Providers

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ALBERTA
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PROGRAM

Intrauterine Growth Restriction: Diagnosis and Management

The Alberta Perinatal Health Program provides this practice resource to health practitioners with a goal towards improving perinatal outcomes for pregnancies at risk for intrauterine growth restriction. The information is based on a review of the current literature and in consultation with clinical experts in the field of perinatology and obstetrics.

Intrauterine growth restriction (IUGR) and small for gestational age (SGA) are associated with increased morbidity and mortality of the fetus and newborn. The study of the perinatal mortality in Alberta has shown that in a number of cases, SGA and/or IUGR was evident and that in some cases SGA and/or IUGR were not recognized during the pregnancy. The prevalence of SGA in Alberta in 2006 was 8.1% according to the Alberta reproductive health report[1]. This is above the Canadian national rate of 7.9%[2].

Prenatal recognition of the intrauterine growth restriction determines investigations for etiology, management of pregnancy, timing and place of delivery, and follow-up of the newborn.

In Canada, conditions of pregnancy that impact fetal growth and well being, such as decreased fetal growth in pregnancy, is the leading cause of childhood death[3].

The International Stillbirth Alliance identified recognition of poor fetal growth, evidence for fetal surveillance and management of pregnancies with diagnosis of intrauterine growth restriction as an international issue (ISA Conference Japan 2006).

Quick Reference Guide: IUGR Diagnosis and Management

Ensure Accurate Dating of Pregnancy

- If certain of date of LMP, and uterine size correlates, ultrasound to confirm at 18 to 20 weeks.
- If not certain of date of LMP, early ultrasound at 8 to 13 weeks.
- If no early ultrasound – estimate date of birth by ultrasound between 14 to 21 weeks, LMP, early uterine sizing, quickening and detection of fetal heart tones.

Assess for Risk Factors Associated with SGA/IUGR

- Past medical and obstetrical history:
  - diabetes
  - hypertension
  - vascular disease
  - thrombophilia
  - previous fetus/newborn diagnosed with SGA/IUGR
- Refer to Alberta Prenatal Record for risk profile and Table 1.
- Maternal hypoxemia, severe anemia, cyanotic heart disease.
- Medications, anticonvulsants, warfarin, antineoplastic agents.
- Recent infections/illness/viral and parasitic infections (TORCH, Malaria).
- Occupational or toxic exposures.
- History of smoking/alcohol/substance abuse.
- Assisted reproductive technology.
- Uterine malformations/fibroids.

Assess Physiologic Factors Affecting Fetal Growth

- Maternal height and weight (obesity/underweight).
- Age (extremes).
- Parity.
- Ethnic group.
- Sex of fetus (if known).
- Results of prenatal screening for fetal aneuploidy.

Measure Symphysis Fundal Height (SFH)

- Measure at each prenatal visit.
- Consistent technique – plotted on growth curve.
- Consistent maternal positioning, empty maternal bladder.
- Due to inaccuracy of SFH in the presence of multifetal gestation, increased maternal BMI or uterine fibroids, schedule serial ultrasounds to assess fetal growth.
- If ultrasound evaluation confirms fetal growth restriction, consider referral to specialist.

Evaluate Fetal Well Being

- Should include non-stress tests and serial ultrasounds when there is a discrepancy of ≥3 cm **or** lag in growth identified when compared to gestational age, no growth measured and women with risk factors.
- Assessment by ultrasound to include: fetal abdominal circumference, head circumference, biparietal diameter, biometric measurements, amniotic fluid volume, biophysical profile.
- Doppler velocimetry of fetal vessels is recommended when there is suspected or diagnosed IUGR. Umbilical artery Doppler is considered abnormal if diastolic flow is reduced, absent or reversed after 20 weeks gestation.
- Fetal movement count starting from 26 weeks.

Management of IUGR

Confirm Diagnosis of IUGR

- Confirm estimated date of birth.
- Assess for fetal anomalies through screening and ultrasound at 18 to 21 weeks.
- Evaluate environmental and physiological risk factors as per prenatal record.
- Measure fundal height with each visit and plot on growth chart.
- Counsel women on smoking cessation – refer to AADAC.
- Refer to obstetrician or perinatal specialist.

Assess Fetal Well Being

- Daily fetal movement count.
- Non-stress test.
- Biophysical profile if non-stress test is abnormal.
- Serial ultrasounds (growth documented on growth chart), increasing frequency with diminishing fetal growth or other abnormal parameters.
- Arrange for Doppler studies.
- Continue surveillance and deliver at term if results of antenatal testing are reassuring and fetal growth is noted.

Consider Delivery

- When risk of fetal death exceeds major neonatal morbidity and/or neonatal death[5, 20].
- When extrauterine survival is likely despite significantly abnormal antenatal testing.
- When complete cessation of fetal growth is assessed ultrasonically over a 2 to 4 week interval[5, 20].
- When fetus is at 32 to 34 weeks and antenatal test results are abnormal.
- When fetus is 32 to 34 weeks and the end diastolic flow (EDF) is absent or reversed and BPP is <6.
- When fetus is >37 weeks.

Outcomes for IUGR are improved when:

- Antenatal steroids are administered to promote fetal lung maturity if infant is below 34 weeks of gestation.
- Early referral for specialist care and delivering centre is able to manage the possible needs and complexities of preterm and term IUGR.
- Hypoxic episodes are minimized during labour and delivery.

Defining Small for Gestational Age (SGA) and Intrauterine Growth Restriction (IUGR)

The terms SGA and IUGR are often used interchangeably in discussions about poor fetal growth, however, IUGR must be differentiated from SGA.

SGA is when the estimated fetal weight (EFW) falls **below the 10th percentile** for gestational age.

Of the SGA fetuses that are diagnosed[4]:

- 40% are constitutionally small but healthy; these fetuses reflect the race, weight and stature of their parents.
- 20% are intrinsically small secondary to a chromosomal or environmental etiology and are unlikely to benefit from prenatal intervention.
- 40% are at high-risk for poor perinatal outcome including death and may have intrauterine growth restriction; a pathological process may have already been identified.

IUGR is the **inability of a fetus to maintain its expected growth along a standardized curve** regardless of whether this growth falls below the 10th percentile. Thus, the IUGR fetus may be growth-restricted but not SGA. Fetal growth at less than the 5th percentile should be considered absolute IUGR and investigations and management must be initiated immediately.

Intrauterine growth restriction (IUGR) is a multi-system disorder that results in a fetus unable to meet its full growth potential. Pregnancies with IUGR of the fetus are most often as a result of fetal abnormalities or abnormal placental vascular development. The growth restriction of the fetus may be identified as symmetrical or asymmetrical.

- **Symmetrical Growth Restriction** – Fetal growth is impaired proportionately during the first and/or second trimesters. This type is typically related to fetal causes of IUGR (i.e., chromosomal anomalies) and accounts for 20 to 30% of IUGR infants[5, 6].
- **Asymmetrical Growth Restriction** – This type of IUGR typically occurs as a result of decreased fetal growth velocity in the third trimester. This is the most common type of IUGR (70 to 80%) and is attributed to the ability of the fetus to adapt by redistributing its cardiac output to vital organs resulting in the head-sparing phenomenon[5]. Measurement of the asymmetric IUGR fetus will show a change in abdominal circumference below the expected percentile for gestational age[7].

Etiology

The etiology of IUGR may be maternal or fetal. Regardless of origin, uteroplacental insufficiency is a defining feature of IUGR and results in deficient nutrient delivery, placental uptake and distribution within the fetus as well as deficient delivery of waste to the placenta[8]. Many causes of IUGR are not amenable to antenatal therapies[6, 9]. Refer to table 1.

Perinatal Outcomes

Fetal and infant morbidity and mortality is increased in the presence of IUGR and is sharply increased when the birth weight is less than the 5th percentile[10, 11]. IUGR at birth may be associated with health risks which may persist into adulthood. Refer to table 2.

Table 1

Maternal, Fetal and Placental Conditions Associated with IUGR[5, 6, 8, 12]		
Maternal	**Fetal**	**Placental**
• Hypertension and vascular disease (essential hypertension, gestational hypertension, autoimmune disease). • Diabetes. • Viral and parasitic infections (TORCH, malaria); less likely bacterial infections (sexually transmitted infections). • Maternal hypoxemia (pulmonary disease, cyanotic heart disease, severe anemia, residing at high altitude). • Toxins – medications (warfarin), anticonvulsants, antineoplastic agents. • Uterine malformations or fibroids. • Thrombophilias (antiphospholipid syndrome). • Maternal weight – underweight at start of pregnancy, protein-calorie malnutrition or maternal obesity (increased BMI). • Sociodemographic variables – childbearing at extremes of age, race. • Smoking and/or alcohol use, and/or substance use. • Assisted reproductive technologies (including those that result in singleton pregnancies). • Woman was growth restricted, had a previous IUGR pregnancy or sister had an IUGR pregnancy.	• Twin to twin transfusion syndrome. • Multiple gestations. • Chromosomal anomalies. • Congenital anomalies (including those as a result of maternal infection).	• Placental infarctions. • Thrombosis of fetal vessels. • Premature separation/chronic abruption. • Edema of the placental villi. • Placenta previa. • Abnormal cord insertion/ cord anomalies (single vessel, velamentous insertion).

Table 2

Morbidity and Mortality Associated with IUGR[5, 6, 11, 12, 13]		
Fetal Morbidity and Mortality	**Neonatal Morbidity and Mortality**	**Relationship to Adult Disorders**
• Risks associated with labour induction and preterm birth. • Fetal compromise in labour related to compromised placental function (atypical and/or abnormal fetal heart patterns). • Iatrogenic prematurity. • Stillbirth.	• Increased risk of: - meconium aspiration - respiratory distress - hypoglycemia - necrotizing enterocolitis - thrombocytopenia - temperature instability - renal failure • Risks associated with prematurity. • Risks associated with congenital malformations/ chromosomal anomalies. • Neonatal death	• May be at increased risk of: - ischemic heart disease - other related disorders (hypertension, diabetes, stroke and hypercholesterolemia)

Diagnosis

Diagnosis is made through the recognition of risk factors and fetal growth. A thorough maternal assessment should include an investigation for risk factors associated with IUGR and ongoing fetal growth monitoring to ensure it is within expected sizing for the gestational age. It is recommended that any deviations from expected growth, whether SGA or a lag in growth over time, be followed up with serial ultrasounds[14, 15]. Referral to a specialist should be considered.

Accurate Dating

Accurate dating is required to optimally assess fetal growth and to prevent iatrogenic prematurity[12, 16]. If the pregnant woman is confident in recalling the date of her last menstrual period (LMP) and the uterine size correlates with the estimated date of birth, routine 18 to 20 week ultrasound is acceptable. If the woman is uncertain of her LMP or the uterine size does not correlate with the estimated date of birth, dating by early ultrasound at 8 to 13 weeks provides the best estimate for date of birth. If early ultrasound is not done or available, ultrasound at 14 to 21 weeks is recommended in combination with the LMP, early uterine sizing, quickening and detection of fetal heart tones can be used to estimate the date of birth.

Physiologic Factors

Multiple regression analysis of term deliveries showed that physiologic variation impacts birth weight. Physiologic factors, at the first prenatal visit, that collectively may impact the growth, development and birth weight of the fetus include[5, 16, 17]:

- Maternal height and weight in early pregnancy.
- Parity (i.e., the term birth weight of the second child born to a mother is typically higher than the term birth weigh of the first).
- Ethnic group (i.e., Caucasian versus Asian).
- Sex of the fetus if known (i.e., female fetuses typically weigh less than male fetuses).

Use of customized fetal weight curves may help in discerning the constitutionally small yet healthy fetus from one who is SGA or IUGR[14]. Further research is currently being conducted regarding the use of customized fetal weight curves.

Risk Factors

Identification of risk factors that may lead to the development of IUGR should influence the degree of monitoring and assessment during the pregnancy. See Etiology for a complete listing of risk factors. Pregnancies in which risk for development of IUGR is identified should receive ultrasound evaluation of the fetus for growth[7]. Counseling for modifiable risk factors such as smoking in pregnancy, should be provided. Previous pregnancies and deliveries should be reviewed for the presence of IUGR.

Prenatal Screening

Resent research has shown early screening in pregnancy may identify those pregnancies at risk for chromosomal anomalies. Chromosomal anomalies are associated with SGA, IUGR and stillbirth.

The SOGC Clinical Practice Guideline for *Prenatal Screening for Fetal Aneuploidy*[18] recommends "All pregnant women, regardless of age, should be offered a prenatal non-invasive screening test for risk modification of Down Syndrome and trisomy 18".

Non-invasive screening for trisomy 13, 18 and 21 may be done through first trimester or second trimester screening[18].

Monitoring Fetal Growth

Monitoring of intrauterine fetal growth must be done in conjunction with continuing assessment of maternal and fetal-welling to determine risk of poor outcomes, continuing surveillance, referral for specialist consultation/care and timing of delivery.

Symphysis Fundal Height Measurement[14]

Fetal growth, during pregnancy, should be monitored by symphysis fundal height (SFH) measurements and confirmed by serial ultrasounds if indicated[12]. SFH measurements, to be clinically relevant, must be done in a consistent manner at each prenatal visit and plotted on a growth curve. The sensitivity of SFH is limited. Accuracy is improved with consistent provider technique and consistent maternal position. SFH cannot be relied on with a high maternal BMI or in multifetal pregnancies. SFH measurements may also be affected by a full maternal bladder or the presence of uterine fibroids. **Physical examination alone is not sufficient to make or exclude the diagnosis of IUGR**.

The SFH with a discrepancy of greater than or equal to three centimeters or detection of a lag in growth, when compared to gestational age, warrants ultrasound measurement of fetal growth.

Ultrasonography

Ultrasound examination of the fetus for serial growth and development should encompass the following measurements:

Estimated Fetal Weight (EFW)

An estimation of the fetal weight based on standardized percentiles, when combined with assessment of maternal and fetal risk factors and fetal biometric measurements, can provide confirmation of the diagnosis of IUGR.

Abdominal Circumference (AC)

In both symmetric and asymmetric growth-restricted fetuses, the AC is the first biometric measure to change due to depleted abdominal adipose tissue and decreased hepatic size[14]. Assessment of the HC:AC ratio (head circumference: abdominal circumference) assists in the identification of asymmetrically growth-restricted fetuses.

Fetal Growth

Comparison of biometric measurements, as well as the EFW and AC, provide an indication of the fetal growth over time. Serial ultrasounds, with examination of fetal growth and use of standardized growth curves, demonstrate growth velocity. Subsequently, loss of or decreased growth velocity can also be identified and is an important indicator of possible IUGR.

Amniotic Fluid Index (AFI)

Assessment for decreased AFI is not an appropriate screening tool for IUGR as it may or may not be present. However, given that oligohydramnios is one of the sequelae of IUGR, the AFI should still be assessed as low AFI will identify the fetus at risk for poor perinatal outcome[19].

Doppler Velicometry

"Use of Doppler ultrasonography to measure umbilical artery waveforms in the management of IUGR is associated with a reduction in perinatal death and may be considered a part of fetal evaluation once IUGR is suspected or diagnosed[20]."

Umbilical artery Doppler is considered abnormal if diastolic flow is reduced, absent, or reversed after 20 weeks gestation. Abnormal Doppler indices have shown to be strong predictors of poor perinatal outcomes including low Apgar score, late decelerations, severe variable decelerations, absent variability, low fetal scalp pH, presence of thick meconium, and admission to the neonatal intensive care unit[21]. **Abnormal umbilical artery Doppler is an indication for enhanced fetal surveillance or delivery**[22]. Management by enhanced surveillance or delivery depends on clinical factors, fetal well being, and gestational age[22].

Doppler assessment of the umbilical artery is a key component of assessment in the presence of risk factors or a SGA fetus to identify IUGR fetuses with placental insufficiency at risk for hypoxia and acidosis[10]. Doppler assessment of the umbilical artery in IUGR is not currently recommended as a screening tool in low-risk populations[10, 19].

Doppler assessment should be available for assessment of fetal placental circulation for suspected fetal growth restriction or placenta pathology[22]. In specialized tertiary care centers, Doppler assessment of fetal cerebral circulation and umbilical venous Doppler evaluation of the severe IUGR fetus may be performed. Although umbilical venous Doppler has been shown to predict fetal acid-base status, recent information suggests that fetal ductus venosus waveforms are better at predicating neonatal outcomes[7, 26].

Ultrasound Reporting and Documentation

Ultrasound interpretation and timely reporting of ultrasound findings is an important step in management of the IUGR fetus. Ultrasonography is an operator-dependent technology and in obstetrics, accuracy and interpretation can be influenced by level of experience with normal and abnormal examinations. It is recommended that[23, 24]:

- A written report be included in the patient's medical record and sent to the referring clinician in a timely fashion.
- Clinically significant findings should be called to the referring physician to ensure and facilitate appropriate follow-up.
- Emergent findings should be called to the referring clinician while the patient is still in the ultrasound facility or en route to the physician's office or hospital.
- Estimated fetal weight should be reported as a percentile based on the gestational age of the fetus (as determined by early ultrasound crown-rump length); the gestational age should not be adjusted based on the estimated fetal weight.
- Variations from normal size should be accompanied by measurements.

Evaluation of Fetal Well Being

Fetal Movement

Given the association between IUGR and stillbirth, women should be taught the importance of awareness of fetal movement and to consult their physician if they notice a decrease or change in fetal movements. One method of increasing awareness is fetal movement counting. All women with pregnancies with risk factors for adverse perinatal outcome should perform daily fetal movement counts starting from 26 weeks until delivery[22].

Non-Stress Test

The non-stress test (NST) may be considered when risk factors for adverse perinatal outcome are present[22]. Frequency of regular NSTs to assess fetal well being should be based on severity of the IUGR as well as contributing factors and perceived risk to the fetus. Atypical and/or abnormal findings on NST require further evaluation of the fetus within the context of the complete clinical picture[22].

Biophysical Profile

Biophysical profile (BPP) of the fetus is a non-invasive method used to evaluate five parameters (gross movement, tone, breathing movements, amniotic fluid volume and NST) that may provide useful information in relation to fetal well-being. In the presence of hypoxemia and acidosis, one or more of these five variables may be affected.

"In pregnancies, at increased risk for adverse perinatal outcome and where facilities and expertise exist, a biophysical profile (BPP) is recommended for the evaluation of fetal well being[15]". The SOGC (2007) also recommends that in the presence of decreased fetal movement, abnormal NST, as well as suspicion or diagnosis, of IUGR, a BPP or amniotic fluid assessment is warranted.

It should be noted that BPP itself, should not be used as a single assessment tool in the evaluation of the IUGR fetus as it provides insufficient information related to cardiovascular compromise. BPP should be used in conjunction with umbilical arterial Doppler for more comprehensive fetal assessment[4].

Management of IUGR

When IUGR is suspected or diagnosed, ongoing teaching and support for the pregnant woman, referral to specialist, follow-up, and evaluation must be organized. Once non-treatable underlying fetal conditions and chromosomal anomalies have been ruled out, further antenatal surveillance should be instituted based on the severity of the maternal and/or fetal condition[8].

The challenges for healthcare providers are to:

1. Identify IUGR fetuses whose health is at risk and intervene appropriately.
2. Identify small, yet healthy, fetuses and support these pregnancies appropriately.

Surveillance

The timing of interventions for the management of IUGR is dependent on the cause and severity of the IUGR. Interventions may be therapeutic or preventative. Despite numerous approaches to managing IUGR, effective therapies that improve the growth pattern of the fetus have not been identified. Modalities that have been tested with little effect include bedrest, maternal nutritional supplementation, plasma volume expansion, maternal medications (low-dose aspirin), oxygen supplementation and antihypertensives[4, 13].

Frequency of re-evaluation of the IUGR fetus is dependant on many factors. Interval of repeat ultrasound for the assessment of fetal growth can be as frequent as every two weeks depending on the severity of IUGR, gestational age and evidence of fetal compromise. Assessment of fetal well being through biophysical profile (BPP), with or without Doppler flow assessment, and NST may be done more frequently based on the same factors.

Timing of Delivery

In the absence of successful intrauterine therapy, the timing of delivery is the most critical aspect of antenatal management.

Timing of delivery is individualized based on the gestational age of the fetus, maternal health, the severity of the IUGR and fetal well being.

In the preterm fetus, the effects of prematurity must be weighed against the risks of fetal compromise. Close monitoring of growth, BPP, Doppler assessment and assessment of amniotic fluid may identify evidence of fetal compromise that requires planning for delivery of a preterm fetus[3]. Outcome of preterm delivery of IUGR is improved when[4, 8, 25]:

- Antenatal steroids have been administered, and
- Delivery occurs at a care center with a neonatal unit that is able to manage the complexities of the IUGR affected preterm newborn.

Delivery should be considered for the term fetus (≥37 weeks) with evidence of IUGR. Consideration must be given to the ability of the delivering centre to manage the possible needs and complexities of the term IUGR affected newborn[4].

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