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Intrauterine growth retardation

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Abstract
Intrauterine Growth Retardation is defined as the rate of fetal growth that is less than normal for the growth potential of the infant and for the population. Insufficient endometrial surface for placental invasion and growth, along with abnormal placental perfusion, may combine to restrict nutrient delivery to the fetus, leading to IUGR. Poor placental growth and function limit placental supply of growth promoting hormones to the fetus such as hPL, steroid hormones and IGF-1 and limit effective maternal-fetal nutrient exchange.

Keywords: Fetus, intrauterine growth retardation, placental perfusion

Introduction
Intrauterine Growth Retardation is defined as the rate of fetal growth that is less than normal for the growth potential of the infant and for the population. Insufficient endometrial surface for placental invasion and growth, along with abnormal placental perfusion, may combine to restrict nutrient delivery to the fetus, leading to IUGR. Poor placental growth and function limit placental supply of growth promoting hormones to the fetus such as hPL, steroid hormones and IGF-1 and limit effective maternal-fetal nutrient exchange [1]. Preeclamptic mothers have poor endometrial vascular support for growth of the placenta, hence leading to placental growth failure, fetal nutrient deficit and IUGR [2]. Fetal hypoxemia, acidosis and hypoglycaemia are usually present in such cases of poor placental development and perfusion. These factors lead to increased production of prostaglandins and the activation of labour promoting cytokines, leading to preterm delivery [3].

Placental and fetal growth both depends on an adequate supply of maternal blood to the placenta. Inadequate development of the uteroplacental circulation is associated with IUGR. Radioisotope studies have demonstrated more than a twofold blood flow reduction in these pregnancies compared to normal pregnancies [4]. IUGR in the second half of gestation is primarily due to a failure of the normal villous vascular tree, mostly in the phase of nonbranching angiogenesis, because the terminal villi are critical for oxygen and nutrient transport to the fetus [5]. This angiogenesis is in turn dependant on the cytotrophoblast invasion of the uterus and its arterioles. Cytotrophoblast invasion is actually a differentiation process whereby the cells lose the ability to proliferate and modulate their expression of state-specific antigens. These antigens include members of the integrin family of cell-extracellular matrix receptors that are required for migration and invasion of the decidua and endometrium of the uterus [6].

Preeclamptic placentas have decreased growth of terminal villi, which limits glucose, aminoacid and oxygen transport to the fetus. Preeclampsia begins with shallow cytotrophoblast invasion [7]. Abnormal cytotrophoblast invasion also occurs, as evidenced by the cells inability to switch on their integrin repertoire [8]. Hence hypoxia of the invading cytotrophoblast cells increases cytotrophoblast proliferation over differentiation and invasion, thus causing a stage for deficient placental development that can result in deficient growth factor and nutrient supply to the fetus, producing fetal growth restriction.

Therefore IUGR produces infants who are Small For Gestational Age(SGA), but also infants who are Appropriate For Gestational Age (AGA) who experienced reduced fetal growth rates in utero. Small For Gestational Age (SGA) infants can be the result of normal but slower than average rates of fetal growth [9]. SGA infants are being classified as having symmetric or asymmetric IUGR.

Symmetric IUGR means that both body and brain growth are limited relatively equally. Asymmetric IUGR means that body growth is restricted to a much greater extent than the brain growth. Eventhough growth of the brain is spared relative to overall fetal growth, head circumference is mostly below the 10th percentile for gestational age and there is reduced brain volume [10]. The heart is also larger for body weight and spared in these babies, whereas the thymus and liver are smaller for body weight. Contributing factor includes an increased rate of cerebral blood flow relative to the systemic and umblical circulations.

Hence, the factors intrinsic to the fetus cause symmetric growth restriction, whereas extrinsic factors cause asymmetric growth restriction. Intrinsic factors that limit the growth of both the fetal body and brain include congenital infections (toxoplasmosis, rubella, cytomegalovirus), chromosomal anomalies, some inborn errors of metabolism and some drugs. Due to their intrinsic nature, a pattern of symmetric growth restriction develops during the early periods of gestation.

Asymmetric growth restriction typically develops during the late second and third trimesters. This has been due to the reduction in energy substrate supply to the fetus, thereby limiting fat and glycogen storage and the growth of skeletal muscle, but allowing for continued bone and brain growth. Extremely premature infants are often Small for Gestational Age (SGA) and have asymmetric growth, most probably due to common underlying pathology such as placental insufficiency, that produced the preterm delivery and growth restriction. More extreme limitations of nutrients for prolonged periods affect both energy storage and growth, hence causing reductions in head circumference and length as well as soft tissue mass and body weight. With decreased nutrient supply early in gestation, growth of all body organs is restricted, whereas decreased nutrient supply later in gestation primarily restricts the growth of skeletal muscle and adipose tissue [11-14].

Intrauterine growth retardation related to impaired placental function is usually associated with increased umbilical artery impedance, typically followed by brain sparing. In the course of worsening obliteration of placental vessels, venous shunting across the ductus venosus occurs and results in an increased blood flow to the heart at the sparing of liver. The increase in right ventricular afterload causes further shunting of blood to the left ventricle that improves the left ventricular output. Increased end diastolic pressure in the right ventricle, combined with decreased cardiac compliance, is reflected as a decrease, absence or reversal of blood flow in the ductus venosus during the atrial systolic component of the waveform. Further worsening of the placental function will lead to increased central venous pressure and umbilical venous pulsations which can be seen in the Doppler ultrasound. These may lead to abnormal biophysical profile or loss of fetal heart rate variability [15-16].

The concepts of 'fetal malnutrition' was first developed by Clifford and was defined by Scott and Usher as a clinical state of babies characterized by obvious intrauterine loss of failure to acquire normal amount of subcutaneous fat and muscle [17, 18]. The assessment of nutrition at birth has been made using several systems:

1. Anthropometry- Weight, Length, Head and Chest circumference
2. Proportionality indices- Ponderal Index (PI), head circumference to length ratio, chest circumference or midarm circumference to head circumference ratio (MAC/HC).
3. Clinical Assessment of Nutrition (CAN) of the fetus and the score- CAN score is a scoring system based on nine 'superficial' readily detectable signs of malnutrition in the neonate.

CAN score has nine superficial readily detectable signs, which are rated 1(worst-severe FM) to 4(best well nourished). The highest possible score is 36 and lowest possible score is 9. A CAN score of < or equal to 24 was taken as fetally malnourished [19].

Conclusion

Intrinsic factors that limit the growth of both the fetal body and brain include congenital infections (toxoplasmosis, rubella, cytomegalovirus), chromosomal anomalies, some inborn errors of metabolism and some drugs.

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