

Maternal Factors Affecting Fetal Growth: Review Series 2

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Abstract

Successful pregnancy is unique achievement in women's life. Fetal weight is interplay of maternal, genetic, environmental, placental, hormonal and fetal factors. In this article, maternal factors affecting fetal growth will be explored. Both low birth weight and macrosomia have impact on neonatal mortality and morbidity. Advanced maternal age, adolescent pregnancy, maternal height, parity, maternal weight, social economic status and nutrition affect fetal weight. Environmental factors like drugs, alcohol, smoking are determinants of low birth weight. Maternal infections, chronic medical disorders are other causes of IUGR. Maternal diabetes, obesity, previous macrosomic infant, excessive weight gain during pregnancy, prolonged gestation are risk factors for macrosomia. Prevention, early detection and timely interventions are cornerstones of optimisation of fetal weight.

Keywords: Maternal Factors; Fetal Nutrition; Low Birth Weight; Macrosomia; Environment.

Introduction

"Giving birth and being born brings us into the essence of creation, where the human spirit is courageous and bold and the body, a miracle of wisdom".

-Harriette Hartigan

Care for safe and successful pregnancy begins before conception and it continues with appropriate antenatal care, ensuring optimum fetal growth. Pregnancy and healthy child have a huge impact on physical, mental, emotional and socioeconomic health of women and families. Fetal weight is interplay of maternal, fetal, placental, environmental, hormonal and genetic factors [1]. In the last article, Review series 1, we had discussed fetal factors. In this Review series 2, we will explore maternal factors affecting fetal growth. Large for gestational age is usually taken as more than 90th percentile and small for gestational age is below the 10th

percentile [2]. Fetal growth is not linear but occurs in a stepwise progression fetus undergoes periods of accelerated growth interspersed with period of slower growth [3]. As the human race walks with time and as the year roll by, so do we acquire changes in our Lifestyle. The modern era is witnessing a change in child bearing patterns. There is increasing number of pregnancies in advanced maternal age. Low birth weight is reported to be common in elderly mothers. The causes include:

- Increased spontaneous and induced Preterm deliveries
- IUGR
- Poor maternal nutrition
- Smoking
- Pregnancy complications
- Biological aging of maternal tissue and system

Poor fetal growth is caused by maternal factors

by following mechanism

- * Reducing utero placental perfusion
- * Inducing hypoxemia
- * Decrease nutritional substrates [4]

Altered maternal uterine environment, vascular system and endocrine system, lead to decrease of transfer of nutrients to the fetus [5].

Maternal Nutrition

Undernutrition in pregnant women may result from low intake of dietary nutrients owing to either a limited supply of food or severe nausea and vomiting known as hyperemesis gravidarum. Poor maternal nutrition is major risk factor of IUGR in both developed and developing countries. Maternal nutrition is modifiable factor for lbw. It is one of the major environmental cause of IUGR in developing world.

Maternal nutrition imbalance, metabolic disturbances during critical time window of development may have persistent effect on health of the offspring and may be transmitted to the next generation.

If supply of glucose, a critical fetal nutrient is reduced, IUGR may result.

- * Protein malnutrition before 26 week can cause IUGR
- * Intergenerational effect Women who were born as LBW are more likely to have LBW child (and even grandchild)
- * Pre pregnancy micronutrient intake or status is related to LBW. Increasing intakes shortly before and during pregnancy may increase birth weight [6].
- * Studies on the Siege of Leningrad during World War 2 and the Dutch famine during winter 1944 demonstrated that severe protein calorie malnutrition especially during second half of pregnancy causes decreased fetal weight.
- * Nutritional supplementation during pregnancy is best targeted at nutritionally disadvantaged populations during all three trimesters of pregnancy.
- * Another example of IUGR secondary to maternal malnutrition may occur in women who become pregnant after gastric bypass operation for treatment of morbid

obesity. In this condition the incidence of IUGR babies is 20 to 40%.

- * The concept of 'Eat for two' during pregnancy leads to massive increase in maternal weight gain which increases fetal weight [7].

Maternal Overnutrition: Why it Causes IUGR

Overnutrition can result from increased intake of energy and/or protein. Extensive studies have shown that maternal overnutrition retards placental and fetal growth. Many overweight and obese women unknowingly enter pregnancy and continue overeating during gestation. Maternal obesity or overnutrition before or during pregnancy may result in fetal growth restriction [8].

Macrosomia

Fetuses above 4000 grams are labelled as macrosomic. Macrosomia affects between 3-15% of all populations depending upon sample size population. Prepregnancy obesity should be considered as one of the predictors for macrosomia. Antenatal increase in BMI of 25% or greater is a most sensitive predictor for fetal macrosomia, other predictors being maternal diabetes, maternal impaired glucose tolerance, multiparity, previous history of macrosomic baby and post maturity [9].

Maternal Micronutrients

There are 3 general pathways through which micronutrient deficiency during gestation may affect fetal development:

1. hormonal changes in both the mother and the fetus,
2. epigenetic gene regulation.
3. restricted fetal growth and development.

Maternal Height

Height of a mother is an outcome of several factors including nutrition during her childhood and adolescence. The cut-off point for height below which a woman can be identified as nutritionally at risk varies across populations and ethnic origins. 145 cm in India, [12] 155 cm in United Kingdom, [13] 156 cm in Sudan, [14] and 165 cm in Israel [15].

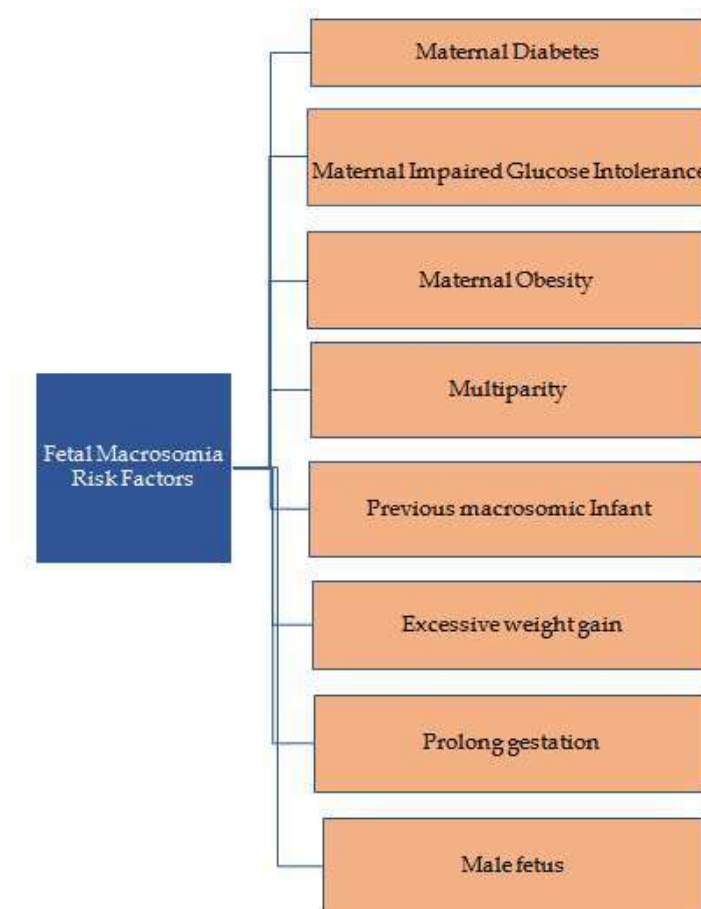


Table 1: Risk factors of fetal macrosomia [10,11]

Maternal Bmi

Low maternal BMI is a marker for marginal tissue nutrient reserves and a predictor of protein-energy malnutrition, which may affect fetal growth [16,17].

Impact of Parity on Fetal Growth

Primiparity seems to be associated with preterm births and LBW infants. It is well known that second and third children weigh more than the first [18]. Beginning with the fourth pregnancy, this increased birth weight is inverted, so that the risk of LBW again increases with the fourth and subsequent children [19].

Maternal Socio-Economic Status

Maternal socio-economic status, nutritional status and antenatal care are important determinants of LBW in India. These key mediating factors that need to be considered to improve birth weight of infants and targeted public health interventions are needed to improve these factors [20]. Low socioeconomic status is determinant of low birth weight. It is one

of the strongest predictors of LBW in low income countries [21,22].

Inter Pregnancy Interval

Short inter-pregnancy intervals may result in depletion of maternal nutrient stores and lead to reduced birth weight [23]. A short interval between deliveries results in poor outcome. Short interval often results from reproductive compensation to replace a lost child as soon as possible and the extra risk results from the tendency of adverse outcome to recur [24].

Maternal Weight Gain

Maternal weight gain is a sensitive index of acute nutritional stress during pregnancy. There is association between maternal weight and LBW/IUGR, especially in undernourished women.

Low pregnancy weight=>LBW

Low weight gain during pregnancy=>LBW

Many researchers have found that prepregnancy weight of less than 40 kg is a cut off to predict women who will deliver lbw babies [6].

Antenatal Care

Good antenatal care improves pregnancy outcome. It enables the obstetricians:

- To counsel regarding diet
- To identify risk factors
- Early detection of complications
- Interventions
- To ensure iron, calcium intake.

Gender Factors

The study conducted by Manzur Kader et al found that male gender has a protective effect against LBW, the weight of a male infant is 150 g greater than that of a female infant and this difference in weight starts to appear after 28 weeks of gestation. It is hypothesized that the activity of androgen causes difference in maternal fetal antigen, or genetic material on the Y chromosome carrying genetic material for fetal growth [25].

Environmental Factors

Prenatal development is the process that occurs during the 40 weeks prior to the birth of a child. During each prenatal stage, environmental factors affect the development of the fetus. The developing fetus is completely dependent on the mother for life. The placenta provides nourishment and oxygen to the fetus. Illicit drugs such as asheroine, cocaine and amphetamine can cause problems for fetus, including preterm birth and LBW. Stressed mother's behaviour could negatively affect the fetus, such as smoking, drug use, and alcohol use [26].

Maternal Stress and Depression

When a mother is under stress, physiological changes occur in the body that could harm the developing fetus. Other factors that can put a person at risk for prenatal depression include

- Unplanned pregnancy,
- Difficulty in becoming pregnant,
- History of abuse,
- Economic or family problems [27].

Adolescent Pregnancy

Adolescent is a period when structural, functional and psychological development occurs in a girl. pregnancy in adolescent girl is a social hazard, she has to attain her full growth. In adolescent pregnancy there is double burden of reproduction and growth.

Inadequate nutrition, poor health before pregnancy, unmarried status and poor education are problems related to pregnancy in adolescent girls. Incidence of preterm birth and low birth weight is higher among adolescent mothers. Most teen parents do not have the maturity needed to provide for another life. Malnourished adolescent girls will give birth to LBW, IUGR babies [28].

Maternal Medical Disorders

Many medical conditions have been shown to be associated to increased risk for SGA. Among them diabetes with vascular disease, renal impairment (especially when associated with hypertension), antiphospholipid syndrome (APS) and chronic hypertension (CH) have been demonstrated to be the most important ones. For other conditions such as systemic lupus erythematosus (SLE) and congenital heart defect, SGA has been observed [29].

Maternal medical conditions associated with vascular disease cause reduce uteroplacental perfusion;

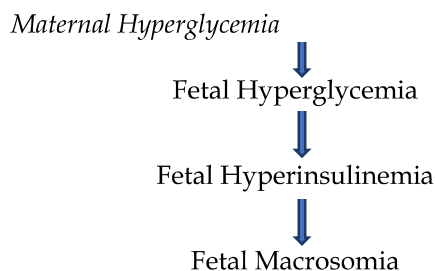
Factors decreasing placental perfusion are -

- * Placental microthrombi
- * Occlusion of vessels
- * Infaracts

Placental underperfusion is the commonest cause of intrauterine growth restriction in foetus without congenital anomalies [4]. Fetal growth restriction due to placental insufficiency is common in preeclampsia. Increase in perinatal mortality and morbidity in severe preeclampsia is due to fetal growth restriction and prematurity [30].

Maternal hyperglycemia is the most important cause of fetal complications. Fetal growth restriction occurs in women with Pre-gestational and gestational diabetes mellitus.

Macrosomia is the most common complication of diabetic patient and occurs in 50% of women with gestational diabetes mellitus and diabetes mellitus. Tight control of glycemia throughout the pregnancy reduces risk of macrosomia.



Contributing factors are:

- IGF's
- Leptin
- Maternal obesity

Hypothyroidism is associated with low birth weight and prematurity. Transplacental transfer of TSH antibodies may lead to fetal hypothyroidism and goiter leading to fetal growth restriction. Association between low calcium levels and adverse health outcome is documented. Low levels of vitamin D cause LBW babies. Obesity is a complex multifactorial disorder involving genetic, environmental and endocrine factors. Maternal obesity has impact on the fetus, resulting in increased risk of macrosomia [32].

Anemia is multifaceted problem with many adverse perinatal effects. It is the commonest medical disorder in pregnancy resulting in preterm deliveries with IUGR [33]. Peripartum cardiomyopathy is associated with increased incidence of prematurity and LBW [34]. Fetal growth may be affected in Thalassemia and Sickle Cell disease due to chronic anaemia and placental insufficiency due to vascular occlusion. There is increased frequency of abnormal placenta with areas of infarcts and Fibrosis. Chronic vascular occlusion probably is the cause of impaired fetal blood flow rather than occlusion during painful crisis or acute chest syndrome [35].

Discussion

Genetic potential of an individual determines intrauterine growth and development of fetus, modulated by environmental factors. Normal intrauterine growth and development depend on the genetic potential of an individual, modulated by environmental factors including maternal health and nutrition, and the endocrine environment. The interaction between the genetic growth potential, the capability of the maternal-placental system to transfer nutrients to the fetus and the endocrine environment determine whether the fetus will follow its growth curve during intrauterine life [36].

Maternal conditions associated with IUGR interfere with fetal growth by one of the three mechanisms.

- * Aggravating placental vascular insufficiency.
- * Limiting the availability of substrates required for fetal growth
- * Transferring to the foetus substances that affect fetal growth [7]

Fetal origin of adult disease:

Individuals who display poor growth in utero are at increased risk for type 2 Diabetes mellitus, obesity, hypertension, dyslipidemia, cardiovascular disease in adulthood [37]. The risk of recurrent fetal growth restriction is increased in pregnant women who previously had IUGR. This is particularly true in women with antiphospholipid antibody and other continuing medical complications.

Birth weight of each infant born previously is important. If history of delivering a large size baby in the past is elicited, maternal diabetes must be ruled out. The condition may recur in current pregnancy [38].

Nutrition: Intrauterine Environmental Factors

Signalling molecules important for mediating actions of maternal growth factors in the placenta:

It should be possible to improve placental function by enhancing the response to maternal hormones. For some, but not all, of the growth factors, supplementing maternal levels could be of therapeutic benefit. Mechanisms to promote growth factor actions within the placenta should be explored; we suggest that methods to specifically target receptors and/or molecules within the placenta are more likely to prove beneficial [39].

Early detection, watchful expectancy and active intervention in complications are key factors for safe delivery and macrosomic fetus. Several potentially useful strategies may be useful to reduce incidence of macrosomia:

- During preconceptional period, women should be advised regarding changing life style and attain optimum weight before pregnancy.
- Monitor weight gain during pregnancy
- Diabetes in pregnancy: strict glucose control with insulin therapy.
- Interventions: management strategies for suspected fetal macrosomia include: early induction of labour and elective caesarean section.

An effective method for predicting outcome should be sensitive, specific, and applicable early enough in pregnancy to permit an intervention suitable to prevent or modify a predicted adverse outcome. Adverse outcome of pregnancy is quite repetitive. The risk factors present in an earlier pregnancy. Several kinds of factors relate to the course of pregnancy. There are obstetric events

such as threatened abortion and the onset of preeclamptic toxemia [40] Metcoff has stated in his paper that maternal genetic factors account for about 25% of the variance in birth weight, while paternal genetic factors account for 1 to 2%.

Key Points

- Maternal age affects pregnancy from conception to delivery. Advanced maternal age poses a challenge because of maternal risk factors and fetal risk factors such as chromosomal abnormalities and IUGR.
- Teenage mothers are in growth phase, they compete with their own foetuses for nutrients, causing IUGR.
- Maternal nutrition, both undernutrition and overnutrition will have an impact on fetal weight.
- Maternal height is a reflection of nutrition during her childhood and adolescence also.
- Maximum fetal weight is during the second and third pregnancy.
- Previous miscarriages have repercussions on current pregnancy also, leading to low birth weight babies.
- Good antenatal care will detect complications early and promote timely interventions to have a positive effect on fetal birth weight.
- Low socioeconomic status, short interpregnancy interval, malnourished status are causative factors for low birth weight.
- Maternal environmental factors like drugs, alcohol, smoking are strong determinants of low birth weight.
- During maternal stress, physiological changes will lead to low birth weight.
- Maternal infections, chronic medical disorders are other causes of IUGR.
- Maternal diabetes, obesity, previous macrosomic infant, excessive weight gain during pregnancy, prolonged gestation are risk factors for macrosomia.
- Prevention, early detection and timely interventions are the cornerstone of optimization of fetal weight.

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