1st Trimester Maternal Serum Retinol Binding Protein 4 as a Predictor of Subsequent Fetal Growth Restriction

Thesis

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Presented by

Ola Gamal Fathi El-Falal

M.B.B.CH., 2009- Ain Shams University

Supervised by

Prof. Hazem Amin El-zeniny

Professor of Obstetrics & Gynecology
Ain Shams University

Dr. Mostafa Ibrahim Ibrahim

Professor of Obstetrics & Gynecology
Ain Shams University

Dr.Mohamed Abd-Elhameed Abd- Elhafeez

Assistant Professor of Obstetrics & Gynecology
Ain Shams University

Faculty of Medicine
Ain Shams University
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Abstract

All women were subjected to full history taking, full general and abdominal examination; in addition, blood samples were collected by venipancture to measure RBP4 levels. All participants were followed up by sonography and Doppler study until delivery to calculate Estimated fetal weight and abdominal circumference.

At the current study, there was no statistically significant correlation between RBP4 versus gestational age and maternal age.

SRBP4 had good predictive value as evidenced by an area under the ROC curve (AUC).

After adjustment for the age of patient and the gestational age at sampling, SRBP4 was an independent predictor for IUGR.

Keywords: Intra uterine growth restriction - small for gestational age

INTRODUCTION

Intra uterine growth restriction (IUGR) remains a challenging problem for obstetricians and pediatrician and continues to be an important determinant of perinatal mortality and morbidity in modern obstetrics ***(Kady and Gardosi, 2004)***.

IUGR has a massive short term (increase fetal morbidity and mortality) and long term (increase incidence of cardiovascular disease in adulthood) health complications ***(Wareing et al., 2005).***

It is uncertain how many neonates who really are IUGR.

Vandenbosche and Kirchner (1998), suggest 4-7 % of neonates to be IUGR, whereas ***Brodsky and Cristou (2004),*** refer that the incidence of IUGR is 5-7% suggesting that up to 15% is identified when SGA and IUGR are defined as equivalent.

Before the development of ultrasonography, delayed fetal growth was indicated by low maternal weight gain, and fundal height measurement. IUGR is frequently detected in a pregnancy with a less than expected third-trimester weight gain (100 to 200 g [3.5 to 7 oz] per week) or as an incidental finding on ultrasound examination when fetal measurements are smaller than expected for gestational age ***(Calvet et al., 1982).***

Physical evidence of abnormal fetal growth becomes typically apparent in the second half of pregnancy ***(Gluckman***

and Liggins, 1992), although recent studies have suggested that indicators of aberrant fetal growth may be present as early as in the first trimester ***(Smith, 2004).***

Intrauterine growth restriction (IUGR) is a common diagnosis in obstetrics and carries an increased risk of perinatal mortality and morbidity. Identification of IUGR is crucial because proper evaluation and management can result in a favorable outcome. Certain pregnancies are at high risk for growth restriction, although a substantial percentage of cases occur in the general obstetric population. Accurate dating early in pregnancy is essential for a diagnosis of IUGR. Ultrasound biometry is the gold standard for assessment of fetal size and the amount of amniotic fluid. Growth restriction is classified as symmetric and asymmetric. A lag in fundal height of 4 cm or more suggests IUGR. Serial ultrasonograms are important for monitoring growth restriction, and management must be individualized. General management measures include treatment of maternal disease, good nutrition and institution of bed rest. Preterm delivery is indicated if the fetus shows evidence of abnormal function on biophysical profile testing. The fetus should be monitored continuously during labor to minimize fetal hypoxia.

Fetal growth is dependent on genetic, placental and maternal factors. The fetus is thought to have an inherent growth potential that, under normal circumstances, yields a healthy newborn of appropriate size. The maternal-placental-

fetal units act in harmony to provide the needs of the fetus while supporting the physiologic changes of the mother. Limitation of growth potential in the fetus is analogous to failure to thrive in the infant. The causes of both can be intrinsic or environmental.

Fetal growth restriction is the second leading cause of perinatal morbidity and mortality, followed only by prematurity. The incidence of intrauterine growth restriction (IUGR) is estimated to be approximately percent in the general obstetric population. However, the incidence varies depending on the population under examination (including its geographic location) and the standard growth curves used as reference. In assessing perinatal outcome by weight, infants who weigh less than 2,500 g (5 lb, 8 oz) at term have a perinatal mortality rate that is five to 30 times greater than that of infants whose birth weights are at the 50th percentile. The mortality rate is 70 to 100 times higher in infants who weigh less than 1,500 g.

Perinatal asphyxia involving multiple organ systems is one of the most significant problems in growth-restricted infants.

Timely diagnosis and management of IUGR is one of the major achievements in contemporary obstetrics. If the growth-restricted fetus is identified and appropriate management instituted, perinatal mortality can be reduced, underscoring the need for assessment of fetal growth at each prenatal visit.

AIM OF THE WORK

To assess the accuracy of first trimester maternal serum Retinol binding protein4 level in prediction of subsequent development of fetal growth restriction later in pregnancy.

Chapter One

INTRAUTERINE GROWTH RESTRICTION

- ***Defenition:***

Intrauterine growth restriction (IUGR) is failure of the fetus to achieve his or her intrinsic growth potential, due to anatomical/functional diseases or disorders in the feto-placental-maternal unit ***(Malamitisi et al., 2006).***

Intrauterine growth restriction (IUGR) is a condition whose name and definition have changed but consistently has contributed significantly to prenatal morbidity and mortality. The term Intrauterine growth restriction has evolved from being expanded as intrauterine growth retardation to current term, Intrauterine growth restriction this change probably better reflects the pathophysiology of this disorder and avoids the emotionally change and frequently misunderstood term retardation ***(Scott, 2002; Baschat, 2004).***

The common definition of IUGR is a birth weight less than the 10^{th} percentile for gestational age ***(Resnik, 2002)***

- ***Epidemiology:***

Regardless the definition of IUGR, the problem is widespread among developed as well as underdeveloped countries and population. Risk factors for IUGR include small

maternal size(height and pregnancy weight) and low maternal weight gain, but more importantly, this characteristics interacts and other risk factors to impact on fetal growth, especially in thin women ***(William et al.,1997).***

The epidemiology of fetal growth restriction varies internationally. In developed countries, the most frequently identified cause of growth restriction is smoking, while in developing countries, maternal nutritional factors (pregnancy weight, maternal height) and infections (malaria) are the leading identified causes ***(Kramer et al., 2000).***

Additionally, in developing countries, there is a direct correlation between the incidence of low birth weight (less than 2500 grams) and IUGR, the high incidence of low-birth-weight (LBW) infants is almost exclusively due to the incidence of IUGR. Data from developed countries show the opposite, rates of low birth weight being explained almost exclusively by prematurity rates ***(Martinez and Simmons, 2005).***

Outcome studies of the effect of IUGR have been confounded by heterogeneity of population studies. This includes various causes and definitions of intra uterine growth failure, the effects of the associated perinatal and neonatal complications on outcomes, the age of the children are studied, and postnatal influences on the children, especially those related to sociodemographic factors ***(William et al., 1997 and Menendez et al., 2000).***

▪ *Incidence of IUGR:*

Intrauterine growth restriction (IUGR) is considered a severe complication of pregnancy ***(Kiely et al., 2005)***. IUGR is associated with short and long term negative outcome in fetuses, infants and children. It may be associated with development of disease in adult life. IUGR also has adverse consequences for future generations. It forms part of an intergenerational vicious cycle of deprivation ***(Steketee, 2003).***

Intrauterine growth restriction (IUGR) is of public health importance as it is prevalent in developing countries. The highest rates are in South Asia and parts of sub-Saharan Africa affecting about 40% as compared to less than 10% in most developed countries ***(Bernstein and Gabbe, 1996).***

In accurately dated pregnancies, approximately 80-85% of fetuses identified as being small for gestational age (SGA) are constitutionally small but healthy, 10-15% is true IUGR cases, and the remaining 5-10% of fetuses is affected by chromosomal/structural anomalies or chronic intrauterine infection ***(Manning et al., 2004).***

The incidence of IUGR varies according to the reference population (with higher rates of IUGR in developing countries) and the percentile determined as indicted clinically significant growth restriction ***(Resnik, 2002).***

- ***Predection and diagnosis:***

Most cases of IUGR occur in pregnancies in which no prior risk factors are present; however the clinician must be alert to the possibility of a growth disturbance in all pregnancies. Furthermore, no single measurement or assessment helps secure the diagnosis; a complex strategy for diagnosis and assessment is necessary ***(Bricker and Neilson, 2003).***

Early recognition before fetal viability affords opportunities to direct women to regional perinatal care centers for enhanced maternal fetal surveillance. Screening programs are cost effective because existing patterns of care are utilized. This leads to the emergence of measurements in early pregnancy of a variety of biological, biochemical, and biophysical markers to predict faulty placentation before actual development of IUGR ***(Whittle et al., 2006).***

Early and accurate diagnosis of IUGR is all important but it is missed in 50-75% of cases. The aim is to identify those fetuses antenatally who are at risk for increased morbidity and mortality ***(Kay, 2005).***

The current therapeutic goals are to deliver the baby at the maximum gestational age possible and just before acidemia or hypoxia occurs ***(Bricker and Neilson, 2003).***

Clinical prenatal diagnosis remains difficult in spite of the fact that some clinical signs of (IUGR) have been recognized ***(Lin, 1985).***