Introduction

At first glance, achieving agreement on a generally accepted definition of fetal macrosomia seems a meaningful goal ***(Langer, 2000).***

Fetal macrosomia defined as infant birth weight ≥4000g, is associated with many adverse outcomes, which can be the cause of high rate perinatal maternal and fetal morbidity and mortality***(Chaabaneet al., 2013).***

However, in the last 3 decades, the overall proportion of women delivering macrosomic infants has increased in many countries ***(Lu et al., 2011).***

Fetal macrosomia is defined as a birth weight of at least 4000 gm or greater than the ninetieth percentile for gestational age after correcting for neonatal sex and ethnicity ***(Al-Inany, 2010).***

Fetal macrosomia is defined as fetus that is of large size for gestational age equal to or greater than the 90^{th} percentile. Large for gestational age fetuses can be a result of genetic variance, excessive growth secondary to overweight mothers, excessive maternal weight gain during pregnancy and gestational diabetes or insulin dependent diabetes mellitus ***(Haram et al., 2002).***

Based on these definitions, macrosomia affects 1-10% of all pregnancies***(Ratchanikon et al., 2006).***

Fetal macrosomia observed in gestational diabetes mellitus (GDM), by a mechanism involving maternal hyperglycemia--fetal hyperglycemia--fetal hyperinsulinemia, it is known that pregnant women with pre-gestational overweight not suffering from GDM still have a higher frequency of fetal macrosomia ***(Wahabi et al., 2014).***

Maternal obesity, excessive gestational weight gain and diabetes are independent valuable predictors of macrosomia, when adjusted for other recognized risk factors (parity, mother's height, gestational age at birth, neonate sex)***(Yu et al., 2013).***

Despite not being rare, having an incidence of 10% or even more, no method has been sufficiently accurate in predicting birth weight, many efforts have been dedicated to evaluate the accuracy with which clinical or ultrasonographic methods can predict birth weight ***(Pollack et al.,1997)***.

Accurate methods for prenatal prediction of macrosomia would therefore be very useful for planning labor and delivery strategies and consequently prevent from its complications ***(Kais Chaabaneet al., 2013).***

Excessive gestational weight gain has been extensively proven to be an important risk factor for the development of macrosomia, independently of pre-gestational BMI***(Ludwig et al., 2010).***

Women's perspectives on weight gain during pregnancy have been explored in a wide range of subpopulations, including low-income, overweight and ethnic minority groups, but not among women with a history of macrosomia ***(Paul et al., 2013).***

Shoulder dystocia, one of the worst obstetric emergencies, occurs in 0.15-1.7% of vaginal deliveries. About half of shoulder dystocia happen to macrosomic infants (birth weight of ≥4000 g) ***(Cunningham et al., 2005).***

Macrosomia is associated with many adverse outcomes, for example, prolonged labor, premature labor, increase risk of traumatic damage, increase risk of shoulder dystocia, increase risk of cesarean section, fetal distress, birth asphyxia, brachial plexus injury, stillbirth and cephalhaematoma. These adverse outcomes are associated with high rate of perinatal morbidity and mortality ***(Ferber, 2000).***

There is a strong association between fetal birth weight and gestational age in normal pregnancies. An infant who is above the 90^{th} percentile and/or more than 4000 g at birth,

however, may a chronologically and functionally normal fetus, whereas in pregnancies complicated by diabetes, a neonate of the same size may be abnormally large and have accompanying implications. These large infants have been associated with high maternal and perinatal morbidity and mortality rates. The morbidity of an abnormally large infant can result in trauma to both mother and fetus, and fetal metabolic and respiratory complications. Perinatal mortality associated with a large fetus is greater than that for normal size fetuses ***(Langer, 2000).***

There is some evidence of increased perinatal mortality and morbidity rates in cases of macrosomia. A number of problems during delivery, such as prolonged duration of delivery, an increased risk of cesarean section and postpartum hemorrhage have been widely reported ***(Boulet et al., 2006).***

Accurate perinatal diagnosis of fetal macrosomia would permit fetuses to be delivered by caesarian section, thus obviating these complications. On the other hand, liberal caesarian section may expose the mother to unnecessary operative and anesthetic risks. However, perinatal diagnosis of macrosomic fetuses is often difficult because more than 60% of such infants are born to mothers with no identifiable risk factors to macrosomia ***(Reece and Hagay, 1999)***.

The abdominal circumference (AC) is the most important measurement in estimating fetal weight and only examination with high quality of the AC measurements must be accepted to calculate the EFW***(Ratchanikon et al.,2006).***

There is a high probability that the baby is macrosomic even when the estimated fetal weight indicates a smaller size if the AC measurement is 2 or more standard deviations above the mean ***(Ratchanikon et al.,2006).***

Unless there are additional indications, there is currently no solid evidence to support induced labour or elective cesarean section in non diabetic patient with suspected fetal macrosomia. Instead, it is recommended that spontaneous delivery should be awaited, or the labour should be induced only when indicated ***(Impey et al., 2000).***

Unfortunately, despite advances in ultrasound technology, our long-standing experience in obtaining fetal biometric measurement and research efforts to date, the diagnosis of macrosomia still remains problematic ***(Chauhan et al., 2005).***

The application of Doppler technique was used for the detection of complications of pregnancy, detection and characterization of certain fetal abnormalities, as well as assessment of the value of Doppler in the detection and management of the maternal diseases ***(Lee et al.,2003).***

Doppler ultrasound allows the investigation of feto-placental circulation, thus provides a non invasive monitoring tool for assessing fetal well being. Umbilical artery Doppler reflects downstream placental vascular resistance, which is strongly correlated with intrauterine growth restriction and placental insufficiency. When umbilical arteries become abnormal, Doppler information from systemic vessels is required. Middle cerebral artery changes begin when the redistribution of the cardiac output reflects rising placental resistance, demonstrating 'brain sparing' when cerebro-vascular dilation occurs. The Doppler information is combined with biophysical profile (BPP) scoring to determine the need for and timing of intervention ***(Harman and Baschat, 2003*)**.

Evaluation of the cerebral blood flow in the fetus has become an integrated part of the assessment of high-risk pregnancies. The middle cerebral artery (MCA) has been studied extensively, and its Doppler recordings are incorporated regularly into the management of fetuses at risk of developing placental compromise and fetal anemia ***(Ebbing et al., 2007).***

Combining the Doppler waveform analysis of the middle cerebral artery (MCA) with that of the umbilical artery (UA) by a common cerebroplacental ratio, i.e. the ratio of their pulsatility indices has been suggested as a useful clinical simplification ***(Ebbing et al.,2007).***

A cerebroplacental ratio reflects redistribution of the cardiac output to the cerebral circulation and has been shown to improve accuracy in predicting adverse outcome compared with MCA or UA Doppler alone ***(Vergani et al.,2005).***

Aim of the Work

The aim of this study is to assess the predictive value of the changes in middle cerebral artery versus sonographic fetal biometry of estimation of fetal weight in detection of fetal macrosomia.

The Research Question:

- Are the predictive values of the changes in middle cerebral artery better than sonographic fetal biometry of estimation of fetal weight in detection of fetal macrosomia?

Study hypothesis:

The present study hypothesizes that Doppler examination of the fetal middle cerebral artery has better predictive value for anticipation of fetal macrosomia compared with conventional ultrasound anthropometric measures.

Null hypothesis:

There is no difference between Doppler examination of the fetal middle cerebral artery and conventional ultrasound anthropometric measures for prediction of fetal macrosomia.

Alternative hypothesis:

There is a difference between Doppler examination of the fetal middle cerebral artery and conventional ultrasound anthropometric measures for prediction of fetal macrosomia.

Fetal Growth

Fetal growth is the result of the genetic potential of the fetus that is then in turn modified by environmental factors. Growth and development of the fetus are regulated by and dependent on numerous factors that include the maternal, uterine environment, the functioning of the placenta, and the availability of nutrients to mother and fetus ***(Carrera and Devesa, 1998a).***

Fetal under-nutrition, during the period of hypertrophy, results in a decrease in cell size that is reversible with improved nutrition.

In addition, disturbance of over growth are possible two patterns of excessive fetal growth are seen. First, some fetuses have a symmetric pattern, with head measures (bi-parietal diameter, abdominal circumference) measuring greater than 90^{th} percentile. This is the type of growth pattern in postdate pregnancies and infants of obese women. The second type is a more asymmetric pattern, with normal-for gestational-age head and limb measures but large abdominal circumference. This is the type of growth pattern in infants born to the diabetic patient.

Because the abdominal circumference is affected in each pattern of accelerated fetal growth, this measure tends to be the most reliable single parameter to detect fetal size ***(Campbell, 1998).***

Determinants of Fetal Growth

(1)Genetic factors:

Genetic factors such as parental height and weight may play a role in determining new born birth weight. Genes would be considered as non modifiable.

The relative contribution of genes to birth weight has been estimated at 25 – 80%***(Johnston et al., 2002).***

(2)Growth Factors:

Adequate fetal growth is dependent on a delicately balanced interplay of positive and negative regulators originating from maternal, fetal, and placental units.

Fetal growth curve

The intrauterine pattern of fetal growth and the progression of fetal weight are influenced by various factors. The most important of these are the genetic, ethnic, climatic, and socioeconomic ***(Carrera et al., 1998b).***

Differences in the makeup of the various statistical groups [different population, non homogenous distribution, and inclusion of dead or malformed newborns, uncertain dates] resulted in a large range of variation in the birth weights that were defined as normal. Figure (1) shows a percentile curve for fetal weight based on data published by ***Gallivan et al., (1993)*** there authors performed serial

ultrasound examinations in 67 Caucasian women and used the Hadlock formula***(Hadlock et al., 1991)*** and mathematical model to calculate normal date for fetal weight. It should be noted that the biparietal diameter used in this ultrasound weight calculation was outer-to-inner measurement.

Phases of weight gain:

Four different phases of fetal weight gain have been identified***(Carrera et al., 1998b).***

1) Slow phase
2) Acceleration phase
3) Maximum phase
4) Declining growth phase

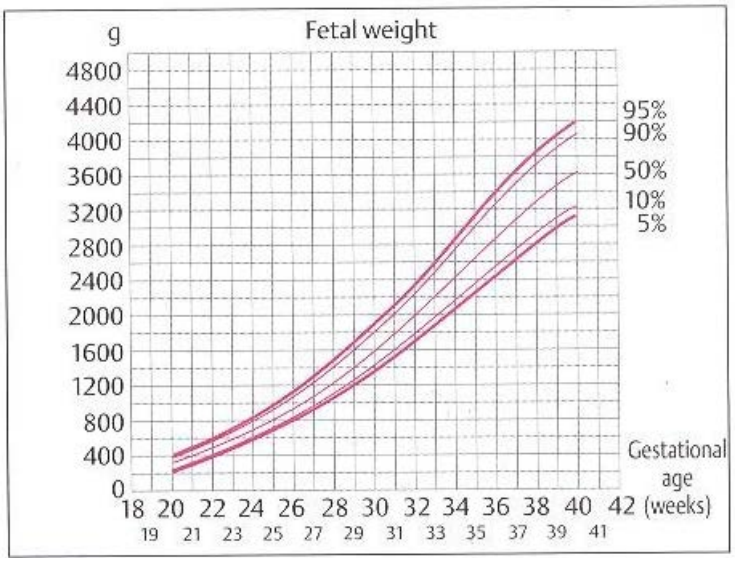

Figure (1): Percentile curves for fetal weight (5th, 10th, 50th, 90th, and 95th percentiles), calculated from a mathematical model based on measured ultrasound parameters [data from ***(Gallivan et al., 1993)].***

A fetus whose body weight is between the 10^{th} and 90^{th} percentile curve is defined as eutrophic. A percentile curve is the boundary line indicating the percentage of the population which falls above or below that line.Fetuses below the10^{th} percentile for body weight are generally classified as small for gestational age, while fetuses above the 90^{th} percentile are classified as hypertrophic.

Fetal Macrosomia

Definition:

Fetal macrosomia is defined as a birth weight of at least 4000 gm or greater than the ninetieth percentile for gestational age after correcting for neonatal sex and ethnicity ***(Al-Inany, 2010).***

Boulet et al.(2003)described a grading system of macrosomia as system has been used in the research setting to determine maternal and neonatal outcome associated with fetal macrosomia, it classified into 3 grades:

- Grade 1: 4000-4499 gm
- Grade 2: 4500-4999 gm
- Grade 3: ≥ 5000 gm

Incidence:

Macrosomia affects 1-10% of all pregnancies***(Ratchanikon et al., 2006).***

Pathogenesis of Fetal Macrosomia:

Determination of the mechanism that leads to in utero overgrowth has proved elusive because our knowledge has significantly expanded as a result of the generation of experimental mouse models engineered to disrupt the expression of one or more genes, and by detailed molecular and genetic analysis of infants and children with overgrowth

syndromes. Studies, which were done on mice, have largely defined the essential role of insulin like growth factors (IGF 1 and IGF II), insulin and their receptors in embryonic and fetal growth ***(Sotos, 1997)***.

The normal growth of a fetus is a delicate balance of several factors. The genetic drive for growth is environmental factors in utero and the supply of growth substrates to the fetus.Deviations in this balance my result in growth restriction or accelerated growth. Two growth pathways have been described-fetal hormone dependent growth and substrate-limited growth.It should be noted that the supply of substrate to the fetus is regulated by materno-placental factors. Insulin and Insulin-like growth factors are important regulators of fetal growth.

Insulin has been shown to be present in the fetus from 8-10 weeks of pregnancy but remains inactive until 20 weeks, when a response to glucose levels becomes evident.

Glucose in the fetal circulation is transferred from the maternal compartment via the placenta.The fetal glucose concentration is approximately 80% of the maternal level.Clearly, as maternal blood glucose increases, so will fetal blood glucose***(Langer, 1991).***Such changes in glucose concentration are monitored by fetal β cells.

Normal pregnant women have reduced insulin sensitivity, tending toward a state of hyperglycemia to provide substrate for the fetus ***(Catalano et al., 1998; Catalano et., al 1999).***

It is well documented that obesity reduces insulin sensitivity and increases insulin resistance***(Jolly et al., 2003; Surkan et al., 2004).***Likewise, increasing age associated with an increasing insulin resistance. The factors may compound the already suppressed insulin sensitivity of pregnancy leading to a state of increased carbohydrate intolerance, increasing the amount of glucose available for maternofetal transport, thus driving fetal hyperinsulinaemia and accelerated intra-uterine growth.

Additionally, Insulin resistance perturbs metabolism and increases the substrate availability to the fetus. Increased flux of nutrients across the placenta causes fetal hyperinsulineamia and accelerated fetal growth. Insulin resistance is associated with higher fasting triglyceride concentration.

Triglycerides are energy-rich and placental lipases can cleave them and transfer free fatty acids into the fetal circulation. This increases energy and substrate delivery to the fetus and may further increase insulin levels***(Jolly et al., 2003).***

The above factors may well combine in obsese, older and diabetic women to promote the development of