Introduction

Small for gestational age (SGA) babies are those who are smaller in size than normal for the gestational age, most commonly defined as a weight below the 10th percentile for the gestational age ***(Andrea Lausman andJohn Kingdom, 2013).***

Not all feti that are SGA are pathologically growth restricted and, in fact, may be constitutionally small. If small for gestational age babies have been the subject of intrauterine growth restriction (IUGR), formerly known as intrauterine growth retardation the term SGA associated with IUGR is used ***(Dogra, 2007).***

Intrauterine growth restriction (IUGR) refers to a condition in which a fetus is unable to achieve its genetically determined potential size. This functional definitionseeksto identify a population of fetuses at risk for modifiable but otherwise poor outcomes. This definition intentionally excludes fetuses that are small for gestational age (SGA) but are not pathologically small ***(Ross, 2010).***

The average term infant at birth weights about 3000 to 3600 gm. During the second half of pregnancy, the fetal weightincreases in a linearmanner with time until about the

37th week of gestation and then the rate slows variably. A relatedterm is Low birth weight (LBW), defined as an infant with a birth weight less than 2500 g (5 lb 8 oz), regardless of gestational age at the time of birth. Related definitions include Very Low Birth Weight (VLBW) which is less than 1500 g, and Extremely Low Birth Weight (ELBW) which is less than 1000 g ***(Farah et al., 2009).***

Moderate and severe fetal growth restrictions (FGR) are defined as: birth weight in the 3^{rd} to 10^{th} percentile and less than 3^{rd} percentile, respectively. Normal term infants typically weigh more than 2500 g by 37 weeks gestation ***(Schwartz et al., 2012).***

The identification of fetuses and babies that are small for gestational age (SGA) is essential for antenatal as well as postnatal care. SGA often represents placental pathology, and may precede the clinical manifestation of preeclampsia, preterm labour, placental abruption, intrapartum complications or stillbirth ***(Gardosi, 2005).***

It has been estimated that only 50% of cases of fetal growth restriction (FGR) are correctly diagnosed in the antenatal period**.** While no proven intervention to prevent FGR has been identified, early prediction would allow for

improved patient counseling and for appropriate triage to a regimen of increased fetal surveillance ***(ACOG, 2008).***

However, it is highly unlikely that a single stand-alone diagnostic test could provide sufficient accuracy. Rather, a multivariable model combiningseveralindicators ofabnormal placental development is most probably necessary ***(Schwartz et al., 2012).***

Some investigators have focused on placental volume as a predictor of adverse pregnancy outcome***(Hafner et al., 2006).***Shown that three-dimensional (3D) placental measuresIn fact, such as volume and a placental morphology index, taken as early as 11–14 weeks' gestation, may be predictive of small-for-gestational-age (SGA) infants***(Schwartzet al., 2010).***

However, 3D scanning is more complex and time-consuming, and requires specialized equipment, limiting its clinical utility. Recently, two-dimensional (2D) placental measurementshave exhibited potential utility for predicting adverse outcomes in certain high-risk patients, possibly by serving as a marker of normal chorionicregression & placental growth ***(Proctor et al., 2009).***

While these simpler placental measurements may not perform sufficiently well to serve as a stand-alone test, they may act as a valuable component of a multivariableprediction model We recently demonstrated how subtle lags in fetal measurements from the first to second trimesters especially abdominal circumference (AC) lag, may serve as early indicators of SGA. While biometric lags(the difference between the actual gestational age and the biometry-derived gestational age) remain suboptimal for clinical use, their significant association with SGA and their availability as a standard element of the anatomic survey make them promising candidates for inclusion in multivariable models for the early prediction of SGA***(Scwaartz et al., 2011).***

Aim of the Work

The aim of this study was to investigate the potential utility of 2D placental measurements in the early prediction ofSGAand to determine whether these placental measurements could be combined with fetal biometriclags to improve the early prediction of SGA.

Chapter (1):

Normal Fetal Growth and Weight

The normal range of term birth weight is typically referenced to the mean birth weight for pregnancies delivered at 38-42 weeks' gestation (ie, mean term gestational age ±2 SDs). During this 4-week interval, the typical fetus gains approximately 12.7 ±1.4 g/day, with a difference of ±0.3 g/day depending on the sex of the fetus (male fetuses gain weight morerapidly thanfemalefetuses***(Nahum et al.,2013).***

Best method to determine the reference range for termbirth weight:

Perhaps the best method for defining the reference range of term birth weight is to examine fetal weights at the 2 extremes of the range (ie, below the 5^{th} -10^{th}percentile and above the 90^{th} -95^{th} percentile**.** By using this approach to establish a criterion, the reference range of term birth weight can be defined somewhat narrowly as about 3250-4250, or 3750 ± 500 g***(Nahum et al.,2013).***

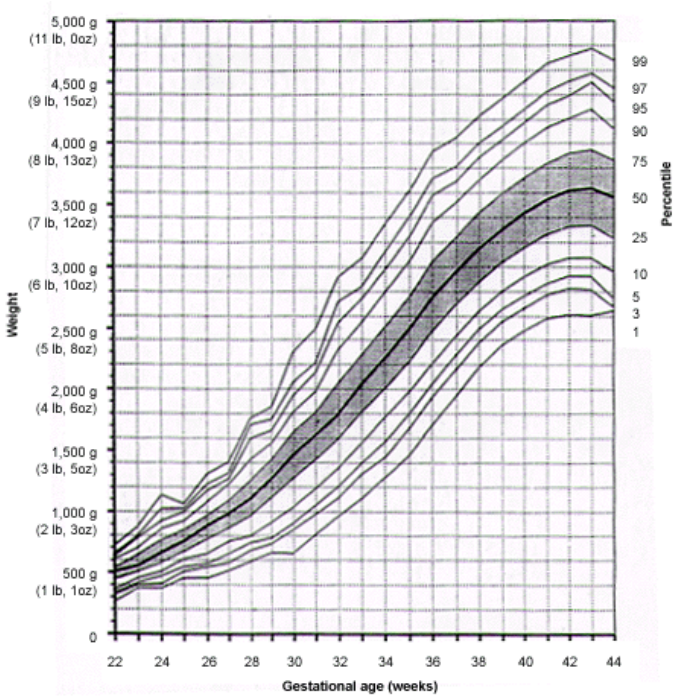

Figure (1): Fetal weight percentiles throughout gestation***(Gruenwald et al.,1967).***

Factors Influencing Intrauterine Growth:

Normal fetal growth depends on maternal, fetal, placental, and external factors combined with genetically predetermined growth potential ***(Miller et al., 2008).***

A-Maternal nutrition:

The nutritional status of a woman before and during pregnancy is important for a healthy pregnancy outcome. Maternal malnutrition is a key contributor to poorfetal growth, low birthweight (LBW) and short- and long-term infant morbidity andmortality, balancedprotein-energy

supplementation is an effective intervention to reduce theprevalence of LBW and small-for-gestational-age births, especially inundernourished women***(Imdad and Bhutta,2012).***

During the first two trimesters of pregnancy, maternal metabolism, mediated by placental and pituitaryhormones, is directed towardenergy storage and uteroplacental development. In addition toincreased maternal food intake, first-stage insulin secretiontypically increases by approximately 60%, whereas sensitivityto insulinand fasting glucose concentrations remains relativelynormal ***(Freemark, 2006).***

B-Placental size and function:

There is a direct relationship between placenta and fetal weight that becomes evident during the first trimester and less evident on ward; due to the rapid rate of growth of the fetus that exceeds the placental growth rate. The placental weight is not an indication of its function. The association of large placenta with large fetuses may be only a reflection of the somatic growth promoting influences the same for the small placenta associated with small fetus.It influences fetal growth via its functional size, capacity to transport oxygen and nutrient and its own metabolism. It's supported by the

fact that, via gestation placental growth closely parallels fetal growth***(Peter,2009).***

C-Maternal age and parity:

Maternal age has a little influence on birth weight. The second and subsequent babies grow faster than first babies,possibly due to enhanced efficiency of uterine circulation***(Claas et al., 2011).***

Parity is directly and independently associated with fetal size. The greater the maternal parity, the larger the fetus is likely to be. Maternal parity is closely linked to maternal age, but once maternal parity is specified, maternal age is not an independent predictor of fetal weight. At term, a fetus typically gains 0.2-0.5 g/day for each increase of 1 in maternal parity***(Nahum et al., 2013).***

D-Maternal Smoking:

Children whose mothers smoked during pregnancy had a birthweight 142 g lower than those of non-smoking mothe*r*. There was a direct dose-response association between the number of cigarettes smoked and the risk of growth retardation. Women whose partner smoked were also at higher risk of having a child with growth retardation***(Hortaet al., 2008).***

E-Physical activity during pregnancy:

The beneficial effect of maternal physical activity on fetal growth may be caused the impact of aerobic exercise on glucose tolerance. Fitness trainers and kinesiologists, as well as health care providers, should be educated on the benefits of regular exercise during pregnancy and safe physical exercise for pregnant women ***(Voltkatomic et al., 2013).***

F-Ambient altitude:

Ambient altitude predictably influences fetal weight such that, an increase in altitude of 1000 m accounts for a reduction in term birth weight of 102-145 g**.**In addition, adult hemoglobin concentrations increase by 1.52 g/dL for every 1000-m increase in ambient altitude***(Nahum et al., 2013).***

G- Genetic factors:

Population-based intergenerational studies of birth weight have found that genetic factors contribute 30 to 50 percent of the variation in birth weight.Maternal genes influence birthweight more than paternal genes, but both have an effect. Specific allelic variants associated with birth weight include mutations in GCK and HNF1beta, which have been associated with low birthweight, and mutations in HNF4 alpha, which have been associated with high birth weight Variants in ADCY5 and loci near CCNL1 also appear to lower birth weight***(Freathy et al., 2010***).

The susceptibility to FGR is also heritable; in epidemiologic studies, women who were SGA themselves at birth have a two-fold increase in risk of FGR in their offspring .Women who give birth to a growth restricted fetus are at high risk of recurrence, and the risk increases with increasing numbers of FGR deliveries.**(Sellinget al.,2006**).

Karyotypic abnormalities account for up to 20 percent of all FGR. The presence of a chromosomal abnormality often results in restriction of fetal growth early in pregnancy; as many as one-quarter of fetuses with early onset FGR have chromosomal abnormalities. Most cases are symmetric, but asymmetric early FGR also occurs one mechanism may be a reduced number of small muscular arteries in the tertiary stem villi of affected fetuses***(Freathyet al., 2010).***

H-Gestational age at delivery:

Gestational age at delivery is the most significant determinant of newbornweight*;* Preterm delivery is the leading cause of low birth weight newborns in the United States***(Nahumet al., 2013).***

I-Maternal race:

A systematic difference is observed in the mean birth weight of babies born to mothers of different races and ethnicities. Depending on the mother's race, mean birth

weights differ by as much as 141-395 g at term***(Nahum et al., 2003).***

True racial difference in birth weight occurs; showed that the mean birth weight can differ by as much as 700 gm between different races ***(Jacquemyn et al., 2002).***

J-Maternal height:

Maternal height is an easily measurable physical characteristic that is positively correlated with term fetal weight***(Miletic et al., 2005).***

There is increase of about 16 gm in birth weight for every centimeter of maternal height above the base line value(160)cm***(Thame et al., 2004).***

K-Maternal obesity:

The level of maternal obesity independently influences fetal weight such that the more a mother weighs, the larger her fetus is likely to be. This occurs because maternal weight and fetal weight are directly related, and women with high BMIs are at increased risk for developing diabetes during pregnancy***(Miletic et al., 2005).***

L-Fetal sex:

There are known sex specific differences in fetal and neonatal morbidity andmortality. There are also known differences in birthweight centile with malesgenerally being

larger than females at birth. These differences are generallyignored when studying obstetric complications of pregnancy and the mechanismsthat confer these differences between the sexes are unknownfetal growthand survival with males adapting placental function to allow for continued growthin an adverse maternal environment while females reduce growth in an attempt tosurvive further maternal insults ***(Clifton, 2010).***

M-Maternal hemoglobin concentration:

Maternal hemoglobin concentration at constant altitude independently explains 2.6% of the variance in birth weight. The relationship between birth weight and circulating maternal hemoglobin concentration is inverse; such that for each 1.0-g/dL increase in maternal hemoglobin concentration, term birth weight is reduced by 89g.This effect may be as the result of changes in blood viscosity. This effect may partly explain why increasing altitude (which increases circulating hematocrit and hemoglobin concentrations) results in progressively lower mean birth weights***(Nahumet al., 2004).***

N-Paternal height

There is increase of about 9 gm in birth weight for every centimeter of father's height above the base line value ***(Bernstein et al.,2010).***

Chapter (2):

Abnormal Fetal Growth

1-Small for gestational age:

Definition:

The definition of small-for-gestational age for a fetus in uterois an estimated fetal weight that measures < 10th percentileon ultrasound. This diagnosis does not necessarily implypathologic growth abnormalities, and may simply describe afetus at the lower end of the normal range***(Andrea Lausman andJohn Kingdom, 2013).***

2-IUGR:

Intrauterine growth restriction refers to a fetus with anestimated fetal weight < 10th percentile on ultrasoundthat, because of a pathologic process, has not attainedits biologically determined growth potential. A clinicalestimation of fetal weight or symphysis-fundal height has poorsensitivity and specificity and should not be relied upon todiagnose intrauterine growth restriction. Intrauterine growthrestriction should be considered in the differential diagnosiswhen the fetus is found to be small for gestational age***(Andrea Lausman and John Kingdom, 2013).***

Fetal growth restriction constitutes only a fraction of small for gestational age (SGA) newborn.Up to-70% of SGA infants are small simply due to constitutional factors determined by maternal ethnicity, parity, weight, or height. But, some infants with physical characteristics of IUGR may demonstrate weights beyond the ranges for IUGR Therefore, Ponderal index defined as the birth weightin grams divided by the cube of the height in centimeters, has been proposed as a better indicator of newborn infant with fetal growth retardation ***(Cunningham et al., 2005).***

Classification of SGA:

Limitations in the categorization of SGA can be attributed to the routine practice of grouping all growth-restricted fetuses based on fetal weight. One proposed alternative grouping is as follows:

1) Small for gestational age (SGA) refers to those small fetuses with no discernible pathology and with normal umbilical artery and middle cerebral artery Doppler results.
2) Growth-restriction refers to small fetuses with recognizable pathology and abnormal Doppler studies.
3) Idiopathic growth restriction applies to small fetuses with no discernable pathology and abnormal Doppler studies.

(Mari and Hanif, 2008)