Early first-trimester growth restriction as a predicator of miscarriage

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LIST OF ABREVIATIONS

RCOG	Royal College Of Obstetricians And Gynecologists
MSD	Mean Sac Diameter
ERCP	Evacuation of retained products of conception
IVF	In vitro fertilization
HCGH	Human chorionic gonado tropin hormone
PCO	Poly cystic ovary
LH	Luteinizing hormone
APL	Anti Phospholipids
TVS	Transvaginal scanning
ECC	Exocelomic cavity
SYS	Secondary Yolk Sac
FVW	Flow Velocity Waveform
DNA	Deoxyribonucleic acid
AC	Amniotic cavity
PO2	Preasure oxygen
ROS	Reactive oxygen species

ART	Assisted reproductive technique
IUH	Intra-uterine hematoma
PPROM	Preterm premature rupture of membranes
GSD	Gestational Sac Diameter
FHR	Fetal Heart Rate
3D	Three dimensional
CRL	Crown-Rump Length
GA	Gestational Age
BMUS	British Medical Ultrasound Society
NICE	National Institute of Clininal Excellence
HC	Head Circumference
BBT	Basal Body Temperature
BPD	Bi-parietal Diameter
LMP	Last Menstrual Period
TAS	Trans-Abdominal Scanning
ET	Embryo Transfer
SD	Standard deviation
NT	Nuchal Translucency
EPAU	Early Pregnancy Assessment Unit

IGFBP-1	Insulin growth factor binding protein
HRQL	Health related quality of living
HER	Embryonic Heart Rate
YS	Yolk Sac
Yst	Yolk Sac Stalk
AFP	Alpha Fetoprotein
PCO	Polycystic Ovary
aPL	Anti-Phospho-Lipid

Introduction

The diagnosis of miscarriage is made in at least 10–20% of pregnancies in the first trimester (Makrydimas et al., 2003).

One in three women miscarries at some time during reproductive life and the incidence of early embryonic demise is high compared with other early pregnancy complications. The diagnosis of failed pregnancy has implications for further management, with associated emotional impact on the mother (jeve et al., 2011).

However, in pregnancies where fetal viability is demonstrated, the rate of subsequent miscarriage is lower (2–16%) but depends on the population studied, the indication of scan and gestational age (Mukri et al., 2008).

If an embryo has developed up to 5 mm in length, subsequent loss of viability occurs in 7.2% of cases. Loss rates drop to 3.3% for embryos of 6–10 mm and to 0.5% for embryos over 10 mm (Goldstein et al., 2008).

Fetal growth is an increasingly important area of study and has mainly focused on fetal size assessment from the end of the first trimester, only recently addressing early growth (Bukowski et al., 2007).

Studies which examine influences on fetal size at this early stage may contribute to further understanding of the patho-physiology of miscarriage and hence its treatment.

Ultrasound examination is the method of choice in the diagnosis of early embryonic demise, TVS (Trans-vaginal Ultrasound) with

its ability to provide accurate in-vivo images of the early gestational sac, has also provided pivotal clues to the epidemiology and patho-physiology of early pregnancy failure (Jauniaux et al., 2005).

Previous studies have evaluated various factors in the prediction of pregnancy outcome. Ultrasound findings that have been associated with subsequent miscarriage include a slow embryonic heart rate, a small gestational sac diameter and a larger-than-expected yolk sac diameter (Cho et al., 2006).

Early pregnancy dating by crown to rump length (CRL), rather than estimation of gestation from last menstrual period (LMP) dates, is commonly performed to date pregnancies up to 14 weeks, assuming no growth variation (NICE recommendation, 2008).

Studies among women with a regular menstrual cycle suggest that maternal age, ethnicity, and fetal sex affect fetal (CRL) (Bukowski et al., 2007; Bottomley et al., 2009).

Previous studies have shown that the observed CRL in pregnancies destined to miscarry is smaller than that expected for gestational age (Mantoni and Pedersen., 1982 ; Falco et al., 1996 ; Reljic et al., 2001 ; Choong et al., 2003).

In one study Relic et al. (2001) there was an increased likelihood of miscarriage with increasing discrepancy between observed and expected CRL; 13.7% of fetuses with a CRL more than 2SD below that expected for gestational age miscarried compared with an 8.3% miscarriage rate in those with less than 2SD difference (Quoted from Bottomley et al., 2009).

There is conflicting evidence for association between early growth restriction, as defined by a deficit between the CRL and that predicted by the last menstrual period, and karyotypic abnormalities (Jauniaux et al., 2005).

One possible link between a small CRL and subsequent miscarriage is that chromosomal defects not only have a high intrauterine lethality rate but can also be associated with fetal growth restriction in the first trimester of pregnancy (Mukri et al., 2008).

The classical study by Robinson and Fleming on crown–rump length (CRL) is still the main reference for the assessment of gestational age in early pregnancy (Jauniaux et al., 2005).

Because TVS provides superior resolution and more accurate identification of the embryonic structures than abdominal ultrasound, new charts have been developed for the period of gestation before 7 weeks (Jauniaux et al., 2005).

The first demonstration of an early intrauterine pregnancy by means of trans-vaginal ultrasound (TVS) was reported by Kratochwil in 1967 (Jauniaux et al., 2005).

The routine use of TVS in the investigation and diagnosis of early pregnancy problems has also led to improvements in the management of early pregnancy loss and the patient's perception of normal and abnormal fetal development in utero.

Up to 70% of women will choose expectant management of miscarriage if given the choice (Luise et al., 2002).

The ability to make an accurate risk estimate for the prediction of subsequent pregnancy failure is therefore important not only for counseling individual prospective parents, but also from the broader public health perspective.

Multiple ultrasound examinations are costly and an accurate estimate of the likelihood of spontaneous miscarriage would serve to rationalize the use of additional scans (Choong et al., 2003).

Aim Of Work

The objective of this study is:

- To Test the hypothesis that viable early pregnancy that subsequently ends in miscarriage is associated with first-trimester growth restriction i.e. CRL is 2 SD less than expected mean CRL for certain GA.