

**PREDICTION OF SPONTANEOUS ABORTION RISK BY THE USE
OF FIRST TRIMESTER ULTRASOUND MEASUREMENTS AND
MATERNAL SERUM PROGESTERONE LEVEL AT
THE 7TH WEEK OF PREGNANCY**

Thesis

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List of Abbreviations

APS.....	Antiphospholipid syndrome
CA125.....	Cancer Antigen 125
CRL.....	Crown rump length
ECC	Extra coelomic cavity
ELISAs.....	Enzyme-linked immune-sorbent assays
EP	Ectopic Pregnancy
FHR	Fetal heart rate
GS	Gestational sac
GSD	Gestational sac diameter
GTD	Gestational trophoblastic diseases
hCG.....	human Chorionic Gonadotropin
HER.....	Embryonic Heart rate
Hgb A1c.....	Glycosylated Hemoglobin
HIV	Human Immunodeficiency Virus
HSG	Hystrosalpingogram
IR	Insulin Resistance
IUHs.....	Intrauterine Hematomas
IUPs.....	Intrauterine pregnancies
IVF.....	In vitro Fertilization
LDL.....	Low density lipoproteins
LPD.....	Luteal Phase Defect
MSD.....	Mean sac diameter
OPU	Oocyte Pick up
PCOS.....	Polycystic ovarian syndrome
PR-A	progesterone receptors type A
PR-B	progesterone receptors type B
RPL.....	Recurrent pregnancy loss
SIS	Saline Infusion Hystrography
SYS	Secondary yolk sac
TVS.....	Transvaginal ultrasound
VEGF.....	Vascular Endothelial Growth Factor
YSD.....	Yolk Sac Diameter
β-hCG	Beta- Human chorionic gonadotropin

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INTRODUCTION

Spontaneous miscarriage is defined as the involuntary termination of pregnancy before the 20th week of gestation (dated from the last menstrual period) or spontaneous expulsion of fetus below a fetal weight of 500 gm (*Speroff and Fritz, 2005*).

Spontaneous miscarriage affects 15-20% of pregnant women, primarily in the first trimester whilst most are sporadic and non-recurrent (*Clark et al., 2003*).

Many researchers have tried to find some useful ultrasonographic markers in early pregnancy in order to predict the prognosis of the ongoing pregnancy; this includes gestational sac diameter, crown- rump length, fetal heart rate, and the growth rate of the gestational sac (*Metin et al., 2009*).

Mean gestational sac diameter is considered as one of the most predictive parameters in the outcome of pregnancy. Once a gestational sac has been documented on ultrasound, subsequent loss of viability in the embryonic period remains around 11% (*Goldstein, 1994*). In very early pregnancy, it appears that there is no difference in gestational sac diameter (GSD) when compared with pregnancy outcome (*Oh et al., 2002*). The

difference appears from the 5th week onwards. Unfortunately, the predictive value of smaller than expected GSD in isolation is variable and highly depends upon other presenting factors (*Jauniaux et al., 2005*).

Crown- rump length (CRL) still one of the main references for the assessment of gestational age in the early pregnancy (*Robinson et al., 1975*).

Mean GSD: CRL ratio have also been used to predict pregnancy outcome with varying degree of accuracy (*Choong et al., 2003*). Unfortunately, this technique is also of limited usefulness in isolation (*Jauniaux et al., 2005*).

Fetal heart rate in many studies is also used as a predictor of pregnancy outcome. With the widespread use of the transvaginal ultrasound (TVS) during the first trimester, we are able to study accurately the developing process of pregnancy. We can easily demonstrate the embryonic heart activity during the 6th postmenstrual week, and consequently calculate the embryonic heart rate. It shows that from the 5th to 9th weeks of gestation there is a rapid increase in the mean fetal heart rate from 110 to 175 beat per minute, it then gradually decrease to around 160 to 170 beat per minute (*Stefos et al., 1998*).

Some biochemical markers such as beta human chorionic gonadotropin (β -hCG), progesterone (P), and estradiol (E2), are reported to be very helpful in predicting the prognosis of pregnancy either used alone or in combination (*Hahlin et al., 1991*).

Progesterone secreted from the corpus luteum is solely responsible for the continuity of pregnancy until 6th to 7th week of pregnancy. Between the 7th to 11th weeks of gestation, both the corpus luteum and the developing placenta secrete progesterone. After the 10th week of pregnancy the placenta entirely takes over the production of progesterone. The half-life of the progesterone in serum is less than 1hr; therefore anything that affects the viability of the trophoblasts will reduce the progesterone level quickly (*Malatyaliogu, 2001*).

The knowledge of the ultrasound appearance of normal early pregnancy development and a good understanding of its pitfalls are essential for the diagnosis and management of early pregnancy failure. No single ultrasound measurement of the different anatomical features in the first trimester has been shown to have high predictive value for determining early pregnancy outcome. Ultrasound parameters combined with maternal serum hormone levels, maternal age, obstetric history

and occurrence of vaginal bleeding have all been combined in multivariate analyses, with mixed results (*Jauniaux et al., 2005*).

AIM OF THE WORK

The aim of this study is to assess the accuracy of using first trimester ultrasound markers as mean gestational sac diameter (MGSD), crown- rump length (CRL), MGSD: CRL ratio, fetal heart rate (FHR), and progesterone (P) level at the 7th week of pregnancy to predict spontaneous abortion risk.

MISCARRIAGE

Definitions:

Abortion is the pregnancy termination before a live birth is possible. It can occur spontaneously or by induction (*Vern Katz et al., 2012*).

Spontaneous miscarriage is the involuntary termination of pregnancy before 20 weeks of gestation or spontaneous expulsion of fetus below a fetal weight of 500 g (*Speroff and Fritz, 2011*). The definition varies in duration of gestational age according to the countries and available facilities (*Chayachinda et al., 2012*).

Incidence:

Early pregnancy loss is the most common pregnancy complication. About 15% of gestation results in pregnancy loss and 1% of women experience recurrent miscarriage (*McNamee et al., 2012*).

The true incidence of abortion, including unrecognized early pregnancy losses, is 2-4 folds higher (30-60%). Miscarriage risk increases with the number of previous pregnancy loss, but rarely exceeds 40-50% (*Speroff and Fritz, 2011*).

Pathophysiology:

The exact pathophysiology resulting in the expulsion of the early pregnancy remains unknown. Abnormal placentation can either leads to reduced or shallow uterine invasion. In this situation, the usual reduction in maternal vascular tone cannot occur. It is presumed that blood flow enters the intervillous space and dislodges the conceptus, thereby leading to embryonic demise if this has not already occurred. Once the conceptus is dislodged, there is further intrauterine bleeding. Local prostaglandins release will lead to pain and ultimately expulsion of the conceptus and any associated blood (*Backett and Regan, 2003*).

The mechanisms responsible for abortion are not always apparent, but in the first trimester of pregnancy, death of the embryo or fetus nearly always precedes spontaneous expulsion of the ovum. For this reason, finding the cause of early abortion involves ascertaining the cause of fetal death. In subsequent months, the fetus frequently does not die before expulsion; therefore, other explanations for its expulsion should be sought (*Cunningham et al., 2010*).

Etiology:

More than 80% of abortion occurs in the first 12 weeks of pregnancy; at least half result from chromosomal

anomalies. After the first trimester, both the abortion rate and the incidence of chromosomal anomalies decrease. The causes of spontaneous abortion include fetal, maternal and paternal factors. A definite reason cannot always be established because analysis of all causative factors is impossible (*Cunningham, Leveno et al., 2010*).

1-Fetal factors:

In 50- 60% of spontaneously aborted embryos and early fetuses, abnormalities in chromosomal numbers (aneuploidy) account for most wastage. Chromosomal errors (Euploidy) become less common with advancing pregnancy and are found in approximately a third of 2nd trimester losses(*Cunningham et al., 2010*).

A)Aneuploid abortion:

Chromosomal abnormalities are common among embryos and early fetuses that are aborted spontaneously, and it accounts for 50 to 60 percent of early pregnancy wastage (*Cunningham et al., 2010*).

Over than90% of the chromosomal abnormalities observed among abortuses are numerical. Trisomy accounts for 50- 60% of chromosomally abnormal abortuses, monosomy (45 XO) accounts for 25% and

polyploidy accounts for 15- 20%. The reminder is split between structural abnormalities (translocation, inversion) and mosaicism (*Phillip et al., 2003; Cunningham et al., 2010*).

•Autosomal trisomy:

Autosomal trisomy is the most frequently identified chromosomal anomaly associated with first trimester abortion. Although most trisomy result from isolated non-disjunction, balanced structural chromosomal rearrangements are present in one partner in 2 to 4 % of couples with a history of recurrent abortions. Trisomy for all autosomes except chromosome number 1 have been identified in abortuses, but autosomes 13, 16, 18, 21 and 22 have been found most commonly. These defects usually have a lethal effect on conceptus, thereby causing very early abortion (*American college of Obstetricians and Gynecologist, 2001; Phillip et al., 2003; Cunningham et al., 2010*).

•Monosomy X (45, X):

Monosomy is the second most frequent chromosomal abnormality, usually result in abortion and much less frequently in live born infant (turner syndrome) females (*Cunningham et al., 2010*).
