ENDOCRINOLOGICAL INDICES AND DOPPLER ULTRASONOGRAPHY USES FOR PREDICTION OF FIRST TRIMESTER ABORTION

THESIS

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بسم الله الرحمن الرحيم

(و في أنفسكم أفلا تبصرون)

صدق الله العظيم

الاية (٢١) من سورة (الذاريات)

Abstract

Threatened miscarriage occurs often and is a serious emotional burden for women. The aim of this work, was to study if there is a correlation between the different measured endocrinological (serum free β-HCG & Progesterone) and ultrasound and Doppler indices (corpus luteum volume & vascularity, decidual thickness & uteroplacental blood flow) and the occurrence of abortion, and the possibility of such markers to be used as predictors for first trimester abortion. In conclusion, our findings seem to suggest the possibility of using decidual thickness, corpus luteum volume and serum free β-HCG for the prediction of the prognosis of threatened first trimester abortion.

Key Words

Prediction - Abortion - Doppler - First trimesten - Hormonal inclices

TO MY FAMILY

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LIST OF ABBREVIATIONS

ACA	: Anti-cardiolipin antibody
AFP	: Alpha fetoprotein
Apla	: Antiphospholipid antibodies
B-hCG	: Beta subunit of human chorionic gonadotrophin
CRL	: Crown –rump length
CL	: Corpus luteum
DES	: Diethyl stilbestrol
DOC	: Deoxycorticosterone
FVW	: Flow velocity waveform
FET	: Frozen-thawed embryo transfer
hCG	: Human Chorionic Gonadotropin
HLA	: Human Leucocyte antigen
IRP	: International Reference Preparation
IS	: International Standard
IUP	:Intra Uterine Pregnancy
LDL	: Low density lipoprotein
LH	: Luteinizing hormone
LMP	: Last menstrual period
LPI	: Luteal phase insufficiency
LR	: Likelihood ratio
MHC	: Major histocompatibility complex
MHz	: Mega Hertz
MSD	: Mean sac diameter
PI	: Pulsatility index
PRF	: Pulse repetition frequency
PSV	: Peak systolic velocity
PV +	: Predictive Value of Positive Test
PV -	: Predictive Value of Negative Test
RI	: Resistive (resistance) index
ROC	: Reciever operator characteristic curve
RSA	: Recurrent spontaneous abortion
S/D	: Systolic diastolic ratio
T_{max}	: Time averaged maximum velocity
TVUS	: Transvaginal ultrasonography

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INTRODUCTION

Spontaneous abortion is one of the commonest complications of pregnancy. The rate of fetal loss after ultrasound-proved embryo viability in normally developing early pregnancy was shown to be low, approximately 3.2% (***Simpson et al., 1987***).

However, in patients with first –trimester threatened abortion and a living embryo, the rate of fetal loss is much higher, approximetly 15% (***Falco et al., 1996***). Threatened abortion complicates about 15% of pregnancies (***Arias, 1994***). Because of the high prevalence of spontaneous abortion in this group of patients, a technique that could predict pregnancy outcome would be extremely useful (***Alcazar and Ruitz-Perez, 2000***).

Therefore an important clinical problem is how to predict whether the pregnancy will continue to viability or not. This is more complex in cases of recurrent abortion which adds to the psychologic burden on both doctor and patient(***Alcazar and Ruitz-Perez, 2000***).

As the survival of pregnancy is dependent upon steroids from the corpus luteum of pregnancy until the 10^{th} week (***Speroff et al., 1999***), 1\3 of cases of first trimester abortion in recurrent miscarriage, could be attributed to luteal phase defect (***Peters et al., 1992***). Endovaginal ultrasonographic evaluation of corpus luteal volume in the first trimester in combination with serum progesterone may then be used as useful diagnostic tools for

predicting prognostic outcome in cases of first trimestric threatened abortion.

Free beta human chorionic Gondotropin is produced by the trophoplast; therefore, abnormal values could suggest abnormal placentation (***Goetzl et al., 2004***). So its estimation together with the measurement of decidual thickness might help in prediction of the fate of pregnancy in first trimester threatened abortion cases.

In the last decade, the capabilities of ultrasound flow imaging have increased enormously. Color flow imaging is now commonplace and facilities such as ‘power’ or ‘energy’ Doppler provide new ways of imaging flow. With such versatility, it is tempting to employ such noninvasive technique for ever more demanding applications and to try to measure increasingly subtle changes in the uteroplacental (***Giacobbe et al., 2002***), and luteal circulations (***Gupta et al., 2004*****).**

So the main purpose of introducing tests to predict the outcome of threatened abortion is to identify failing gestations in order to accelerate definitive treatment. In this respect serial measurements waste time and expenses and add to the patient anxiety.Therefore, a single assessment, when adequetly reliable, will offer the ideal solution. The perfect test or the combination of tests, accurately predicting abortion as well as successful outcome from a single assessment in 100% of cases remains to be developed ***(Ledger et al., 1994).***

AIM OF THE WORK

The aim of this work, is to study if there is a correlation between the different measured endocrinological (serum free β-hCG & Progesterone) and ultrasound and Doppler indices (corpus luteum volume & vascularity, decidual thickness & uteroplacental blood flow) with the occurrence of abortion, and to study the possibility of such markers to be used as predictors for first trimester abortion.

SPONTANEOUS ABORTION

Terminology and incidence:

Spontaneous abortion refers to pregnancy loss at less than 20 weeks gestation in the absence of elective medical or surgical measures to terminate the pregnancy. The term "miscarriage" is synonymous and often is used with patients because the word "abortion" is associated with elective termination. "Spontaneous pregnancy loss" has been recommended to avoid the term "abortion" and acknowledge the emotional aspects of losing a pregnancy ***(Scroggins et al., 2000)***. Another emotionally neutral term is "early pregnancy failure" ***(Creinin et al., 2001)***

The recommended medical term for pregnancy loss under 24 weeks by the ***Royal College of Obstetricians and Gynaecologists,(2006)*** is 'miscarriage'. The word miscarriage' should be used as recommended in clinical practice and its' use should be strongly encouraged in textbooks and scientific journals.

Abortion is probably the most frequent outcome of human conception. The true incidence of spontaneous abortion is uncertain because of the difficulty in recognizing early conceptions and losses. Estimates have indicated that 76% of conceptions fail to result in a live birth, and the pioneering histological studies suggested an embryonic mortality rate of 40% by the time of the expected menstrual period ***(Grimes, 2003).***

The incidence depends on the country, the period, the design of investigation and on the social structure of the population studied. Even now, however, rates of spontaneous abortion should be adjusted for the rate of induced abortion in the population studied, but this is hardly ever done ***(Susser, 1988)*.**

At least one out of six pregnancies results in miscarriage, which makes it the most common pregnancy complication.And pproximately 80% of spontaneous abortions occur in the first trimester***(Engelhard, 2004).***

Juliano et al. (2008) reported that fetal loss before 20 weeks occurs in 9.2% of patients with live intrauterine pregnancy diagnosed by ultrasonography and that vaginal bleeding carries a higher fetal loss rate of 13.8%.

Following at least one successful pregnancy, the risk of abortion is 12.3% for those who had never had spontaneous abortion. And it is 23.75, 26.2% and 32.2% respectively, if one, two or three previous abortions had already occurred in addition to successful pregnancy.***(Cunningham et al. , 2001)***

Risk Factors for Spontaneous Abortion:

1-Advanced maternal age

2-Alcohol use

3-Anesthetic gas use (e.g., nitrous oxide)

4-Caffeine use (heavy)

5-Chronic maternal diseases: poorly controlled diabetes, celiac disease, autoimmune diseases (particularly antiphospholipid antibody syndrome)

6-Cigarette smoking

7-Cocaine use

8-Conception within three to six months after delivery

9-Intrauterine device use

10-Maternal infections: bacterial vaginosis; mycoplasmosis, herpes simplex virus, toxoplasmosis, listeriosis, chlamydia, human immunodeficiency virus, syphilis, parvovirus B19, malaria, gonorrhea, rubella, cytomegalovirus

11-Medications: misoprostol (Cytotec), retinoids, methotrexate, nonsteroidal anti-inflammatory drugs

12-Multiple previous elective abortions

13-Previous spontaneous abortion

14-Toxins: arsenic, lead, ethylene glycol, carbon disulfide, polyurethane, heavy metals, organic solvents

15-Uterine abnormalities: congenital anomalies, adhesions, leiomyoma

(Scroggins et al., 2000) and ***(Cunningham et al., 2001).***