

Hormonal Assay
For Oestradiol and progesterone
In Saliva and plasma
In threatened abortion

A Thesis Presented
In partial Fulfilment
For the Master Degree in
Obstetrics & Gynaecology

by

Osama Saleh El Kadi
M.B.B.CH

Supervised by

Dr. Mahmoud El Shourbagy

Ass. Prof. of Obstetrics & Gynaecology
Faculty of Medicine . Ain Shama University

Dr Hussien Abd El Haliem

Lecturer in Obstetris & Gynaecology
Faculty of Medicine Ain Shams University

Faculty of MEDICINE
Ain Shams University

CAIRO - EGYPT

1986

بسم الله الرحمن الرحيم

" سبحانك لا علم لنا الا ما علمتنا انك أنت
العليم الحكيم "

صدق الله العظيم
(سورة البقرة)
آية ٣١



INDEX

Acknowledgement	
Introduction	1
Aim of work	3
Review of literature	
-Abortion	4
-Aetiology	6
-Types, clinical picture	13
-Assessment of threatened abortion	16
-Clinically	16
-Ultrasound	17
-Non Hormonal	22
-Hormonal	30
Material, Methods	46
Sample taking	52
Hormonal assays	54
Hormonal results	62
Discussion	68
Conclusion	71
Summary	72
References	74
Arabic Summary	85

Acknowledgement

I would like to express my appreciation and gratitude to professor Dr. Mahmoud El Shourbagy, Ass. professor of Gynaecology and Obstetrics Ain Shams University and to the soul of professor Dr. Hussein Abd El Haliem, Lecturer of Gynaecology and Obsterics Ain Shams University.

Also my thanks are extended to Dr. Abd-El Hameed E.Abd- El Aal for his help in the practical part. For their Masterly guidance and kind support during the preparation of the present thesis.

REVIEW

I N T R O D U C T I O N

Threatened abortion is a common gynaecological problem which confronts the clinician who is asked to judge the fate of threatening and to predict the out-come of pregnancy.

Studies of different parameters have been conducted to predict the outcome of pregnancy in cases of threatened abortion. Some studies depend upon the ultrasonic examination of the gestational Sac and reliable findings have been obtained in pregnancies from the tenth week and onwards. However, before this gestational age, hormonal parameters have been reported to be more informative in predicting pregnancy out-come in threatened abortion (Hertz 1984).

Such supplementary hormonal parameters as estradiol 17- β or h.P.L. (human placental lactogen)

As in Hertz's study in 1980 for combined E_2 and ultrasound study in cases of threatened abortion was with 100 % reliable.

In other studies a combination of hormonal parameters were used to give better predictive values reaching 100 % accuracy by combining pathological values for estradiol - 17- β + progesterone. This was proved by Kunz & Keller(1976) and Jouppita et al(1980.).

Other studies have used enzymatic activity as a predictive parameter for fate of threatened abortion, as Duff et al (1980), who used cystyl amino-peptidase activity for evaluation of early threatened abortion, and the predictive value was 71 %.

Non hormonal substances as alphafeto-proteins (A.F.P.) and pregnancy - specific glycoproteins were also measured in plasma of patients with early threatened abortion and gave good prognostic values. The predictive value for A.F.P. was 81 % and for pregnancy-specific B glycoproteins was 82 % (Hertz 1984).

Saliva was recently the field of study for estriol, and it was found that there was a parallelism between plasma level of unconjugated estriol and salivary estriol, (Gillian et al 1984). Many advantages for salivary assay such as being easy, quick, simple, cheap and non invasive have been reported.

AIM OF THE WORK

Threatened abortion is a common problem for both doctors and patients. Reliable parameters help the clinician to give the proper management and help the patients who need to know the out-come of their pregnancy. Hormonal assay in threatened abortion has a reliable predictive value especially in the first ten weeks during which ultrasound assessment is not equally informative, (Hertz 1984). Assay of both estradiol and progesterone have high predictive values, which if they are combined can give a prognostic value of up to 100 %, (Kunz and Keller 1980).

This study aims at evaluating the predictive value of combined estimation of estradiol and progesterone in the serum of patients with threatened abortion. However, the aim extends to compare the salivary and serum hormonal levels in such patients.

ABORTION

Definition

In 1977, the World Health Organization defined abortion as, "The expulsion or extraction from its mother of a fetus or an embryo weighing 500 grams or less (approximately equal to 20 - 22 completed weeks of gestation), or an otherwise product of gestation of any weight and specifically designated (e.g. hydatiform mole) irrespective of gestational age and whether or not there is evidence of life..." (Huisjes 1984).

The incidence of abortion is 10 - 15 % (pritchard and MacDonald, 1980), although it is much higher because of undiagnosed abortion in early pregnancy and unregistered cases. In a prospective study on the Island of Kauai, French and Bierman (1962); found that the incidence of abortion was 23.6 % and in another study by Shapiro et al (1963) who studied a well defined part of New York, they found that the incidence of abortion was 21.6 %.

Another study by Roth (1963) which has the advantage of being based on 3549 ^{the}gravidae personally treated by ~~a~~ mother between 1945 and 1962, reported an overall incidence of 15.6 %.

The incidence of spontaneous abortion is commonly influenced by prior reproductive history as the incidence increases with the number of previous spontaneous abortions. This can be illustrated from the following table :

PARITY	INCIDENCE
PO+0	12.7%
0+1	22.8%
0+2	28.6%
0+3	33.3%
P1+0	14.0%
1+1	24.9%
1+2	26.9%
1+3	48.7%

(Dicky and
Richard 1984)

Different variables were found to influence abortion rate such as gravidity, Roman et al in 1980 published interesting data from 2917 female doctors responding to an enquiry in a general population, the curve of fetal loss was J. Shape indicating that, the best reproductive result obtained was in the second pregnancy and a steady rising rate of abortion with increasing pregnancy order.

Leridon in 1976 and Golding et al in 1983 suggested, that the increasing rate of abortion was with aging more than with gravidity. Other variables that influence the abortion rate are : Social Class, where the lower social class groups have a higher rate of abortion (Hemminki et al 1980) and a lady with twin pregnancy has a higher rate of abortion than with singleton (Livingston 1980).

The Aetiology of Abortion According to Huisjes (1984)

(A)- chromosomal abnormalities :

The Incidence of chromosome abnormalities in first trimester abortions is approximately 60% , modern studies utilizing Giemsa banding technique found abnormal karyotypes in 54.7% of 139, 61% of 288 and 61% of 1,498 first trimester abortions (Dicky and Richard 1984) . The frequency of Karyotypic abnormality was higher when, mothers had used oral contraceptives, when pregnancy followed ovulation stimulation, when either the mothers or the father's work resulted in exposure to excessive radiation and with increasing maternal age (Dicky and Richard 1984).

- Aging of ovum and ~~for~~ sperm was studied and it was found that there was increasing incidence of karyotype abnormalities with increasing age of ovum before fertilization or increasing age of sperms in the genital tract before fertilization (Dicky and Richard 1984) .

(B) Uterine Causes :

i. Congenital Anomalies

Congenital anomalies of uterus represent, the most important group of maternal causes of abortion, about 30 % (Hay, 1958; Stool 1978, Heinonen 1982). The group of congenital uterine anomalies has a prevalence of 8 % - 30 % in patients with recurrent abortion (Von Goecke, Pavenstadt 1961). The incidence of the congenital uterine anomalies in general ranges between 0.1 - 10 % (Huisjes 1984). Such anomalies include subseptate uterus, arcuate uterus and bicornuate uterus, either unicollis or bicollis.

Another group of congenital anomalies are those encountered in women who are exposed to D.E.S. (di-ethyl. stilbesterol) in utero resulting, together with vaginal adenosis and clear cell adeno carcinoma to intrauterine polypoid and cervical incompetence (Goldstein 1978, Singer and Hochman 1978).

ii. Intrauterine Synechiae

For example after evacuation of incomplete and missed abortion.

iii. Retro Verted Flexed Uterus (R.V.F.).

In a study by (Tupper et al 1957), they found that RVF occurred twice as often in patients with threatened abortion who mis-carried than those who carried their pregnancy to term.

iv. Leiomyomas

Submucons myomas are presumably more likely to cause abortion than subserous ones and in a study by Robin(1966,)he found that the incidence of fibroid was 14 % in recurrent abortion.

v. Cervical Incompetence

It is defined as " inability of the cervix to retain the contents of a pregnant uterus (No - vak 1976),among the causes of incompetent cervix are :

- a. Traumatic Group : After forceful dilatation especially beyond number 12 Hegar as in treatment of dysmenorrhea, after extraction in delivery before full cervical dilatation and after amputation of the cervix.
- b. Non-Traumatic Group : as in cases of congenital weakness of musculo-collagenous tissue of the cervix (Buckingham et al 1985), as well as the group of women exposed to diethyl. stilbesterol (D.E.S.) in utero (Cousins 1980).

(C) Endocrinal Group of Causes :

One of the most important cause of repeated abortion is corpus luteum defieiciency (C.L.D.), in which a low level of plama pregesterone is found in early pregnancy before the trophoblastic tissue takes the role of progesterone

Production from the 8th week onwards. Low progesterone level leads to increased intra uterine pressure, bleeding and cervical dilatation and thus causing abortion (Csapo et al 1972).

Dicky and Richard 1984 have identified 3 phases during early pregnancy which are associated with low progesterone, the first is the luteal phase insufficiency, where progesterone level is low at the time between ovulation and time at which H.C.G., human chorionic gonadotropin, is high enough to stimulate corpus luteum, corpus luteum insufficiency may be due to low L H level, incomplete maturation of graffian follicle and/or high prolactin level. The second phase is inadequate progesterone production by corpus luteum of pregnancy from the second till the seventh or the eighth week. The third phase is low progesterone level due to failure of the placenta and this may be due to poor placental plate development, partial placental separation and/or decrease uterine blood supply.

(D) Immunological Causes :

- i. Disturbed materno-fetal ; immune tolerance;
Of the major causes of disturbed materno-fetal immune tolerance is absence of blocking antibodies in mother plasma to prevent rejection of the feto-placental allograft (Stimson et al 1979).