The value of serum CA-125 and yolk sac ultrasonographic morphology in predicting the outcome of threatened miscarriage

Thesis

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CONTENTS

Subject	Page No.
Contents	I
List of Tables	ii
List of Figures	iv
Introduction	1
Aim of the Work	6
Review of Literature	7
Diagnosis of Pregnancy	7
Miscarriage	17
Development of Yolk Sac	49
CA-125	73
Role of Ultrasound in Early Pregnancy	88
Conclusions& recommendations	185
Summary	186
References	189
الملخص العربى	-

LIST OF TABLES

Table No.	Title	Page No.
Table (1):	Diagnosis of different types of miscarriages according to clinical presentation and ultrasound picture	103
Table (2):	showing data descriptionamong all study group (no = 192) :	124
Table (3):	showing data description among all study group (no = 192) :	125
Table (4):	showing parity distribution of study group:	128
Table (5):	Comparison between two groups regarding pregnancy outcome:	129
Table (6):	comparison between two groups regarding maternal age:	131
Table (7):	comparison between two groups regarding parity:	132
Table (8):	comparison of MGSD between two groups:	133
Table (9):	comparison of CRL between two groups:	134
Table (10):	distribution of yolk sac abnormalities in two groups:	135
Table (11):	comparison between two groups in mean level of serum CA-125:	136
Table (12):	Relation between abnormal yolk sac and pregnancy loss:	137
Table (13):	prediction of pregnancy loss by abnormal yolk sac:	137
Table (14):	Relation between large yolk sac and pregnancy loss:	138
Table (15):	prediction of pregnancy loss by large yolk sac:	139
Table (16):	Relation between small yolk sac and pregnancy loss:	140
Table (17):	prediction of pregnancy loss by small yolk sac:	141
Table (18):	Relation between echogenic yolk sac and pregnancy loss:	142
Table (19):	prediction of pregnancy loss by echogenic yolk sac:	143
Table (20):	Relation between irregular yolk sac and pregnancy loss:	144
Table (21):	prediction of pregnancy loss by irregular yolk sac:	145
Table (22):	cutoff value of (MGSD, CRL, YSD, FHR) in study group(n=192) :	146
Table (23):	cutoff value of CA-125 in study group(n=192):	148
Table (24):	Prediction of pregnancy loss in study group by using combined risk of FHR<105 bpm and MGSD<16.25mm in study group(n=192):	148
Table (25):	The correlation between miscarriage and maternal age in study group (n=192):	149
Table (26):	Cutoff value of CRL in control (group a) :	151
Table (27):	cutoff value of MGSD in control (group a):	152
Table (28):	cutoff value of FHR in control (group a):	153
Table (29):	cutoff value of CA-125 in control (group a):	154
Table (30):	comparison of CA-125 in control (group a):	154
Table (31):	relation between early fetal FHR<100bpm in control (group a):	155
Table (32):	relation between early fetal FHR<100bpm in control group.	155
Table (33):	Relation between abnormal yolk sac and pregnancy outcome in control (group a) :	156
Table (34):	prediction of pregnancy outcome in control(group a) by abnormal yolk sac :	156

LIST OF TABLES (COM)

Table No.	Title	Page No.

Table (35): Relation between large yolk sac and pregnancy outcome in control(group a) : 157
Table (36): prediction of pregnancy outcome in control(group a) by large yolk sac : 157
Table (37): Relation between small yolk sac and pregnancy outcome in control (group a): 158
Table (38): prediction of pregnancy outcome in control (group a) by small yolk sac : 158
Table (39): cutoff value of CRL in cases (group b): 160
Table (40): cutoff value of MGSD in cases (group b): 161
Table (41): cutoff value of FHR in cases(group b): 162
Table (42): cutoff value of CA-125 in cases (group b): 163
Table (43): comparison of CA-125 in cases (group b): 163
Table (44): Relation between early fetal loss and FHR < 100 bpm in case (group b): 164
Table (45): Relation between yolk sac abnormalities and pregnancy outcome in cases (group b): 165
Table (46): prediction of pregnancy outcome in cases (group b) by yolk sac abnormalities: 165
Table (47): Relation between large yolk sac and pregnancy outcome in cases (group b): 166
Table (48): prediction of pregnancy outcome in cases (group b) by using large yolk sac: 166
Table (49): Relation between small yolk sac and pregnancy outcome in cases (group b) : 167
Table (50): prediction of pregnancy outcome in cases (group b) by small yolk sac: 167
Table 51: Some studies comparing pregnancy outcome in relation to yolk sac abnormalities 175
Table 52: Some studies comparing pregnancy outcome in relation to embryonic heart rate : 180

LIST OF FIGURES

Figure No.	Title	Page No.
Figure (1):	Almost completely implanted blastocyst at approximately 23 days menstrual age. (Moore et al, 1988).	53
Figure (2):	Formation of the secondary yolk sac.Day 26 menstrual age.Formation of cavities within the extraembryonic mesoderm that coalesce to form the extraembryonic coelom (Moore et al, 1988).	53
Figure (3):	As the extra-embryonic coelom enlarges, the secondary yolk sac forms, and the primary yolk sac is pinched off and extruded. (Moore , 1988)	54
Figure (4):	showing control (ANC) and cases(threatened miscarriage) group.	126
Figure (5):	showing pregnancy outcome in the study group.	126
Figure (6):	showing fetal heart rate of the study group.	127
Figure (7):	showing yolk sac morphology among study group.	127
Figure (8):	showing maternal age of the study group.	128
Figure (9):	comparison between two groups regarding pregnancy outcome	130
Figure (10):	comparison between two groups regarding MGSD.	133
Figure (11):	comparison between two groups regarding CRL.	134
Figure (12):	distribution of yolk sac abnormalities in two groups	135
Figure (13):	comparison between two groups in mean level of serum CA-125.	136
Figure (14):	The relation between miscarriage and yolk sac abnormalities.	137
Figure (15):	showinglarge yolk sac sonography(a) YSD 6.2mm,(b) YSD 6.8mm.	138
Figure (16):	Relation between large yolk sac and pregnancy loss.	139
Figure (17):	showing small yolk sac sonography (a) YSD 2.7mm. (b) YSD 2.1mm.	140
Figure (18):	Relation between small yolk sac and pregnancy loss.	141
Figure (19):	showing (a),(b),(c) echogenic yolk sac sonography.	142
Figure (20):	Relation betweenechogenic yolk sac and pregnancy loss.	143
Figure (21):	showing irregular yolk sac sonography.	144
Figure (22):	Relation between irregular yolk sac and pregnancy loss.	145
Figure (23):	ROC curve of (MGSD, CRL, YSD, FHR) in study group	146
Figure (24):	ROC curve of CA-125in all patients.	147
Figure (25):	The correlation between miscarriage and maternal age	149
Figure (26):	ROC curve of CRL in control group.	150
Figure (27):	ROC curve of MGSD in control group.	151
Figure (28):	ROC curve of FHR in control group.	152
Figure (29):	ROC curve of CA-125 in control group.	153
Figure (30):	comparison of CA-125 in control group.	154
Figure (31):	Relation between abnormal yolk sac and pregnancy outcome in control group.	156

LIST OF FIGURES (COM)

Figure No.	Title	Page No.
Figure (32):	Relation between large yolk sac and pregnancy outcome in control group.	157
Figure (33):	Relation between small yolk sac and pregnancy outcome in control group.	158
Figure (34):	ROC curve of CRL in cases group:	159
Figure (35):	ROC curve of MGSD in cases group:	160
Figure (36):	ROC curve of FHR in cases group.	161
Figure (37):	ROC of CA-125 in cases group.	162
Figure (38):	Comparison of CA-125 in cases group.	163
Figure (39):	relation between early fetal loss and FHR < 100 bpm in cases group.	164
Figure (40):	Relation between yolk sac abnormalities and pregnancy outcome in cases group.	165
Figure (41):	Relation between large yolk sac and pregnancy outcome in cases group.	166
Figure (42):	Relation between small yolk sac and pregnancy outcome in cases group	167

List of Abbreviations

YSD ------ **:** yolk sac diameter.
MGSD ---- **:** mean gestational sac diameter.
CRL------- **:** crown rump length.
FHR------- **:** fetal heart rate.
ELISA ---- **:** enzyme linked immunosorbant assay.
RCOG ---- **:** royal college of obstetricians abd gynaecologists.
TVUS ----- **:** transvaginal ultrasound.
TAUS ----- **:** transabdominal ultrasound.
PUL ------- **:** pregnancy of unknown location.
ERPC ----- **:** evacuation of retained products of conception.
B-HCG --- **:** beta human chorionic gonadotropin.
EPF ------- **:** early pregnancy factor.
HIV ------- **:** human immunodeficiency virus.
PCOS ----- **:** poly-cystic ovary syndrome.
SLE ------- **:** systemic lupus erythromatosis.
DM -------- **:** diabetes milletus.
APS ------- **:** anti phospholipid syndrome.
EPL ------- **:** early pregnancy loss.
CA-125 --- **:** cancer antigen 125.
SYS ------- **:** seconadry yolk sac.
GS --------- : gestational sac.
PAPP-A -- : pregnancy associated plasma protein A.
DIC ------- **:** disseminated intravascular coagulation.
YS --------- **:** yolk sac
BPD ------- **:** biparietal diameter.
FL --------- **:** femur length.
IUP-------- **:** intrauterine pregnancy**.**
2D --------- **:** two dimensional**.**
PROM---- **:** premature rupture of membrane.
PID-------- **:** pelvic inflammatory disease.
EEC------- **:** extra embryonic coelom.
IGF-------- **:** insulin-like growth factor.
CA19-9 --- **:** cancer antigen 19-9.
CA15-3 --- **:** cancer antigen 15-3.
CEA------- **:** carcinoembryonic antigen.
IUGR ----- **:** intrauterine growth restriction.

ABSTRACT

Background: Miscarriage is the termination of pregnancy by any means before the fetus is sufficiently developed to survive. It is the most common complication of early pregnancy. The miscarriage rate among females who know that they are pregnant is roughly 10-20%. Unfortunately, spontaneous expulsion of non viable pregnancy is frequently delayed for weeks following onset of clinical symptoms leading to problems of prolonged vaginal bleeding, infection and complications of mother anxiety. **Aim of the Work:** to evaluate the role of serum CA-125 and yolk sac ultrasonographic morphology in the prediction of pregnancy outcome in cases of threatened miscarriage. **Patients and Methods:** This was aprospective case control study. We recruited women from Ainshams Maternity Hospital Obstetrics Outpatient Clinics from October 2016 to July 2017. The study included 192 women (96 coming for routine antenatal care and 96 coming because of suspicion of threatened miscarriage such as vaginal bleeding or vaginal bloody discharge with or without pelvic pain), each participant was checked for inclusion and exclusion criteria. **Results:** Elevation of CA125 more than 50.68±11.37IU/Ml in threatened miscarriage is associated with increase risk of pregnancy loss especially if it was associated with abnormalities in yolk sac and fetal braycardia. **Conclusion:** First trimesteric ultrasound assessment is the corner stone in evaluating the potential of the ongoing pregnancy. It is crucial to assess the viability, the location of the pregnancy, the gestational age and wether it is singleton or multiple pregnancy. Measurement of gestational sac diameter, CRL and fetal heart rate in combination provides better prediction of the prognosis of the first trimester than when either parameter is used alone. **Recommendations:** Measuring serum level of CA-125 and performing transvaginal sonography for each woman complaining of threatened miscarriage especially between 6-10 weeks of gestation.

Key words: serum Ca-125, yolk sac ultrasonographic morphology, threatened miscarraige

Introduction

Miscarriage is associated with considerable physical and psychological morbidity, women with threatened miscarriage were found to have increased rate of antepartum hemorrhage, prelabor rupture of membrane, preterm delivery and intrauterine growth restriction when compared with women who did not have threatened miscarriage **(Saraswatet al, 2010).**

The emotional response of miscarriage can be profound. It includes depression, sleep disturbance, anger and marital disturbances **(Marcinko et al, 2011).**

Miscarriage is pregnancy loss before 20 weeks of gestation or if gestational age is unknown it is loss of a fetus of less than 400gm **(Zegers-Hochschild et al, 2009).**

Early pregnancy losses may be related to abnormal embryonic structural development whether or not they are associated with chromosomal abnormalities **(Bromley et al, 2010).**

Threatened miscarriage presenting with vaginal bleeding before 20 weeks is the commonest complication in pregnancy **(Makrydimaset al, 2003).**

The clinical diagnosis of threatened miscarriage is presumed when bloody vaginal discharge or bleeding appears through closed cervical os with or without pelvic pain in patients with an ongoing pregnancy **(Johns and Jauniaux, 2006).**

The introduction of ultrasound scans in the management of bleeding in early pregnancy improved the diagnosis by rapid confirmation of viability and improved the management by introducing prognostic factors such as fetal bradycardia and discrepancy between gestational age and crown rump length **(Makrydimaset al, 2003; Dede et al, 2010).**

There is significant relation between yolk sac abnormalities and embryonic morphology in missed miscarriage **(Ashoush et al, 2016).**

Yolk sac can be detected easily by transvaginalsonography between 5 to 12 weeks of gestation as a round and anechoic area **(Kaur and Kaur, 2011).**

Ultrasonographic findings of Yolk sac were classified into variations in the diameter, shape, and/or ultrasonographic appearance **(Lindsay et al, 1992; Kurjak et al, 2008).**

The Yolk sac diameter was classified into normal Yolk sac size (3 to 6 mm), absent Yolk sac, too large Yolk sac (>6 mm) and too small Yolk sac (<3 mm) **(Lindsay et al, 1992; Kurjak et al, 2008)**. Absence of yolk sac on transvaginalsonography is abnormal and indicates subsequent embryonic death (**Varelas et al, 2008**).

Large yolk sac with diameter >6mm is associated with increased risk of spontaneous miscarriage (**Berdahl et al, 2010).**

Abnormalities in yolk sac diameter were much more common than the abnormalities in yolk sac shape and yolk sac ultrasonographic appearance **(Ashoush et al, 2016)**

The shape of Yolk sac was divided into normal round shape and abnormal irregular shape **(Lindsay et al, 1992; Kurjak et al, 2008) .** Irregular yolk sac is defined as a sac with wrinkled margins or indented wall or both **(Tans et al, 2011)**. which may be used to indicate adverse gestation outcome **(Cho et al, 2006).**

Ultrasonographic appearance of Yolk sac was divided into normal and hyperechoic or echogenic (degenerative changes, abundant calcifications, and decreased translucency).Calcified yolk sac has not been reported to be

associated with aliving embryo before 12 weeks of gestation **(Lyson and Levis, 2005).**

The number of yolk sacs should be equal to the number of the embryos **(Lindsay et al, 1992; Kurjak et al, 2008).**

When the 10-11th weeks of gestation is completed the yolksac begins to shrink rapidly and eventually disappears **(Berdahl et al, 2010)**

Another parameter which could be used as a predictive marker for spontaneous miscarriage or subsequent outcome of pregnancy is the tumor marker Cancer Antigen 125 (CA-125). The latter is a cell surface high molecular weight glycoprotein, it is a mucin-like celomic antigen which is detected in 80% of cases of non-mucinous epithelial carcinoma of ovary , this antigen is secreted from normal tissue such as celomic epithelium amnion and their derivatives including respiratory system, mesenteric organs and epithelium of females genital origin **(Berek, 2002).**

An increase of CA-125 is usually due to genital origin. Non-genital origins include hepatitis, renal failure, tuberculosis, breast, colonic and lung carcinoma, genital causes as pelvic inflammatory disease (PID), endometriosis, leiomyoma, adenomyosis, ectopic pregnancy, endometrial

and ovarian carcinoma, serum CA-125 increases in early pregnancy and immediately after birth **(Cunnigham, 2005).**

Elevation of CA-125 in cases of threatened miscarriage may be related to the disintegration of the maternal decidua **(Ayaty et al, 2007).**

AIM OF THE WORK

The aim of this work is:

To evaluate the role of serum CA-125 and yolk sac ultrasonographic morphology in the prediction of pregnancy outcome in cases of threatened miscarriage.