Journal of Genetic and Environmental Resources Conservation, 2016, 4(2):162-170.
www.jgerc.com

Prognostic value of repeated measurements of CA125 and β-HCG as a predictor of the outcome of threatened miscarriage

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Abstract

The aim of this study was to compare CA-125 & βHCG level in threatened miscarriage pregnancy and normal pregnancy less than 20 weeks of gestation. Study designed a prospective case control study. This was a prospective case control study carried out on 70 healthy pregnant and 70 threatened miscarriage women. We compared the levels of CA-125 & βHCG in these groups and followed them to be informed of the outcome of pregnancy. Results revealed that in threatened miscarriage ended by abortion group the mean level of CA-125 was (73.48 ± 20.29 IU/ml) and the mean level of βHCG was (1188.20 ± 196.85 mIU/ml), while in threatened miscarriage with ongoing pregnancy group the mean level of CA-125 was (13.69 ± 4.01 IU/ml) and the mean level of (βHCG was (62566^67 ± 20674.31 mIU/ml). In the control group the mean level of CA-125 was (11.73 ± 4.74 IU/ml) and the mean level of (βHCG was (63682.86 ± 19367.34 mIU/ml). There was statistically significant difference between mean serum CA-125 levels of threatened miscarriage ended by abortion group and normal pregnant women and threatened miscarriage with ongoing pregnancy groups ($p < 0.05$), while there was no statistically significant difference between these levels in the patients of both groups who continued pregnancies ($p > 01$). In conclusion repeated measurements of serum CA-125 & βHCG may be an inexpensive, easily available, sensitive and specific predictor of the outcome in threatened abortion, that results loss of pregnancy.

Keywords: CA125, Pregnancy, Abortion, Threatened miscarriage.

Introduction

Threatened miscarriage is defined as vaginal bleeding before 20weeks, without dilatation of the cervix or expulsion of any products of conception (poc) (Monga, 2006). In pregnancy advancing after the diagnosis of threatened miscarriage, there is an increased risk of preterm birth and low birth weight infant (Wijesiriwardana *et al*., 2006). The risk of abruption placenta and placenta previa is also 2.5 fold greater than in general obstetric population (Paolo, 2003). Spontaneous Miscarriage occurs in around 10%-20% of confirmed pregnancies and is associated with psychological and physical morbidity (Edmonds, 2007; Medical Library, 2002). In 1997, Everett followed 550 pregnancies and found that, The risk of miscarriage increases with increasing maternal age and, in some cases, with paternal age. Eighty percent of all miscarriages occur before the twelfth week, whereas the remainder occurs between 12 and 20 weeks (Paolo, 2003) Chromosomal abnormalities are the most common cause of spontaneous abortion. About half (50%) of all clinically recognized first trimester losses are chromosomally abnormal, with 50% of these being autosomal trisomy, 20% polyploidy (typically result in empty sacs or blighted ova), and 10% with various other abnormalities (Kao, 2004). The remaining half of early miscarriage appears to have normal chromosomal components. Of these, 20% have other genetic abnormalities that may account for the loss (Decherney and Nathan, 2007).

Inadequate ovarianhormone production is one of common causes of a miscarriage (Decherney and Nathan, 2007), Immunologic disorders (Cunningham, 2005), autoimmune disease: antiphspholipid syndrome and systemic lupuserythematosus. alloimmune disease :blood group incompatibility due to ABO, RH , or other less common antigens. Maternal Infections :(eg, cytomegalovirus, rubella, toxoplasmosis, *Listeria Ureaplasma, Mycoplasma,* and syphilis).diabetes mellitus: Up to 30% of pregnancies in patients with poorly controlled diabetes mellitus result in

spontaneous miscarriage. Severe hypertension .Renal disease and Thyroid disease may account for pregnancy loss (Decherney and Nathan, 2007; Cunningham, 2005).

Abnormalitie of the reproductive system (Cunningham 2005; Berek 2007) Cervical incompetence. Congenital (eg, septate uterus) or acquired defects (eg, uterine synechiae). Fibroids Trauma (Decherney and Nathan, 2007) Either *direct* trauma to the uterus, or indirect trauma such as surgical removal of an ovary containing the corpus luteum of pregnancy *Emotional disturbanc;*It is possible that elevated stress hormones (e.g. catecholamines and cortisol) may be able to reduce fetal vascularization and oxygen supply and thereby induce miscarriage (Edmonds, 2007).

Little is known about paternal factors in the genesis of spontaneous miscarriage. Certainly, chromosomal abnormalities in sperm have been associated with miscarriage (Cunningham, 2005). There are several risk factors associated with a higher rate of pregnancy loss:

1. Age: Advancing maternal age is the most important risk factor for spontaneous miscarriage. 2. Previous miscarriage: Past obstetrical history is an important predictor of subsequent pregnancy outcome. The risk of miscarriage in future pregnancy is approximately 20 percent after one miscarriage. By comparison, miscarriage occurred in only 5 percent of women in their first pregnancy or in whom the previous pregnancy was successful (Pfeifer, 2008; Bhattacharya *et al*., 2008). 3. Gravidity: Some studies have shown an increased risk of miscarriage with increasing gravidity (Pfeifer, 2008). 4. Fever: Fevers of 100 F (37.78 C) or more may increase the risk of miscarriage (Paolo, 2003). 5. Nonsteroidal anti-inflammatory drugs: The use of nonsteroidal anti-inflammatory drugs (NSAIDs), may be associated with an increased risk of miscarriage if used around the time of conception (Paolo, 2003). 6. Smoking: Heavy smoking (greater than 10 cigarettes per day) is associated with an increased risk of pregnancy loss (Kao, 2004). 7. Alcohol: Consumption of more than 30 ounces of alcohol per month doubled the risk of a miscarriage (Paolo, 2003; Cunningham, 2005). 8. Caffeine: More spontaneous abortions occurred in women who ingested at least 100 mg of caffeine per day than in women who ingested less than 100 mg per day (Wang X *et al*., 2003; Paolo, 2003). 9. Cocaine: Use of cocaine is associated with preterm birth, and may also be a risk factor for spontaneous abortion (Cunningham, 2005; Wang X *et al*., 2003).

Evaluation: There is usually a history of vaginal bleeding with or without abdominal cramping or low back pain, (Drife and Magowan, 2004) Bleeding associated with threatened miscarriage is typically scanty (Scott and Gibbs, 2003) History should include the date of last menstrual period, gestational age, the amount of and time of vaginal bleeding, the passage of tissue, abdominal cramping, last intercourse, drug use, general medical and surgical histories, and risk factors (Paolo, 2003)The abdomen is usually not tender , the uterus is soft and enlarged appropriate for gestational age . speculum and digital examination revealed blood coming from the cervical os without tissue in the cervical canal and the internal os is closed (Chan and Johnson, 2006), and usually there is no cervical motion or adenxial tenderness (Berek, 2007). Sonography can usually differentiate between an intrauterine pregnancy (viable or non-viable) from ectopic pregnancy or molar pregnancy (Bourgeois and Bray, 2008). The size of the *gestational sac* (GS) also correlates with the health of the developing fetus. If a (GS) is small for gestational age it carries a poor prognosisand a serial sonographic examination should be performed to assess the rate of growth. A (GS) with a growth rate of <1 mm/day usually has a poor prognosis (Reljic, 2001). A small (GS) may be due to oligohydramnios, which is a predictor of poor outcome, even in the presence of normal embryonic cardiac activity (Dighe *et al*., 2008). Demonstration of embryonic cardiac activity in a patient with vaginal bleeding does not ensure future fetal viability, but its presence significantly decreases the risk of future pregnancy loss (Wang X *et al*., 2003).

Maternal serum biochemistry has also been proposed as predictors of the outcome (Sotiriadis *et al.,* 2004).

1. β hCG*:* Women with threatened miscarriage in their first trimester who eventually miscarried have lower serum β hCG values compared with women continuing the pregnancy and asymptomatic pregnant women (Sotiriadis *et al*., 2004). A prospective study showed that a free β hCG cut-off value of 20 ng/ml could differentiate between normal (control and threatened continuing) and abnormal (non-continuing threatened miscarriage and tubal) pregnancies, with 88.3% sensitivity and 82.6% positive predictive value (Sebai *et al*., 1996).

2. Progesterone: Progesterone concentrations show a narrow variation in the first trimester. According to data from mixed obstetric populations, the lowest serum progesterone concentration associated with a viable first trimester pregnancy is 5.1 ng/ml, (Plant and

Blume, 2008).

3. Inhibin A, activin A: Women with threatened abortion and fetal heart activity at presentation, serum inhibin A and activin A concentrations were much lower in cases in which the women eventually miscarried (Bhattacharya *et al*, 2008).

4. Pregnancy associated placental protein A (PAPP-A) Low-level of (PAPP-A) have been implicated in spontaneous miscarriage in two studies (Yaron *et al*., 2002; Kabili and Striker, 2004) other study showed that, although pregnancy associated placental protein A (PAPP-A) concentrations were much lower in a series of 128 symptomatic women with fetal heart activity at presentation than in normal controls, its predictive value for miscarriage was only 18.7% (Sotiriadis *et al*., 2004).

*5.*Cancer antigen 125 (CA125) CA-125 (cancer antigen-125) is a cell-surface antigen with high molecular weight. It is a mucin like coelomic antigen, which is detected in 80% of non-mucus epithelial carcinomas of ovary. This antigen is secreted from normal tissues, such as; coelomic epithelium, amnion and their derivatives: respiratory system, mesenteric organs and epithelium of female genital system. Therefore, a basal serum CA-125 level is due to secretary Function of these organs (Ayaty *et al*., 2007).

Serum CA 125 levelspeak during the first trimester of pregnancy, and drop to non-pregnant values in the secondand third trimester. Elevated CA 125 levels in maternal serum originate from the decidual cells affected by chorionic invasion or placental separation (Condous *et al*., 2005). Mean value of CA125 in a 3rd stage of labor was significantly higher than in a 2nd day of puerperium, when it dropped to the levels similar to that of nonpregnant women (Fiegler, 2005).

What is a normal CA125 level?

Usually CA125 levels range between 1-35 u/ml, but can vary (Thomas, 1998). High values: (Thomas, 1998; Bonnar and Dunlop, 2005; Kafali *et al*., 2004). Conditions other than cancer that can cause high CA-125 are:

Pelvic inflammatory disease (PID). Endometriosis. Uterine fibroids.

The first trimester of pregnancy. During menstruation. Liver disease (such as hepatitis or cirrhosis).Renal failure. Peritonitis. Pancreatitis Systemic Lupus Erythmatosis Pericarditis. Serum levels of CA125 turned out to be a valuable parameter not only as a marker of ovarian carcinoma but also in other fields of obstetrics and gynecology (Fiegler *et al*., 2003). Types of cancer that can cause high CA-125 values include: (Thomas, 1998; Bonnar and Dunlop, 2005) Ovarian cancer or cancer of the fallopian tubes or endometrium. Most women with an ovarian cancer lump that can be felt in the pelvic area have CA-125 values higher than 65 U/mL Cancer of the pancreas, stomach, esophagus, liver, breast, colon, or lung. Cancers that have spread to the lining of the abdomen (peritoneum), including lymphoma. Maternal serum CA125 have prognostic power in patient with threatened miscarriage (Cenk and Petek, 2006). Women with threatened abortion who eventually miscarried had constant or increasing concentrations of Women ovarian carcinoma antigen CA125 over 5-7 days, whereas those who continued with pregnancy had a constantly low or steeply declining CA125 concentration (Scarpellini *et al*., 1995). The CA 125 levels in the threatened pregnancies were positively correlated with the tropho-decidual hematoma, (Foth and Romer, 2000) furthermore an elevated CA125 level in pregnant women with abdominal pain and vaginal bleeding is associated with a higher likelihood of spontaneous abortion (Urbancsek *et al*., 2005; Hauzman *et al*., 2006).

The prognostic predictive value of maternal serum CA125 in recurrent pregnancy loss conflicting. In one study, the mean serum CA125 of patient with an unfavorable outcome was significantly higher than of the patient with favorable outcome (Cunningham, 2005). There is conflicting evidence regarding the use of CA 125 to differentiate between intrauterine pregnancies (IUP) and extra uterine pregnancies. Serum CA 125 levels have been reported to be significantly lower in ectopic pregnancies (EP) compared with IUP ; however, in a larger study single serum measurements of CA 125 failed to discriminate between spontaneous miscarriage, EP or normal pregnancies, Interestingly, serum CA 125 levels have been used to differentiate tubal abortion and viable EP (Condous *et al*., 2005; Berek, 2007).

Although there is no convincing evidence that any treatment favorably influences the course of threatened miscarriage, a sympathetic attitude by the physician along with continuing support and follow-up are important to patients. a later (Scott and Gibbs, 2003).

Bed rest and abstinence from intercourse: although often prescribed, does not alter the course of threatened miscarriage (Decherney and Nathan, 2007; Cunningham, 2005).

Progesteroneis prescribed in 13-40% of women with threatened miscarriage, according to published series (Sotiriadis *et al*., 2004).

Progestogens are a group of hormones, which bind to the progesterone receptors; they include both the natural female sex hormone progesterone and the synthetic forms.

Progesterone is secreted during early pregnancy from the ovary by corpus luteum ,It is an essential hormone for the establishment and maintenance of pregnancy by inducing secretary changes in the lining of the uterus, which are important for implantation of the fertilized ovum Progesterone modulates the immune response of the mother to prevent rejection of the embryo and it enhances uterine quiescence and suppresses uterine contractions ,local application of a progestogen was found to subjectively decrease uterine cramping more rapidly than bed rest alone in one small study (Sotiriadis *et al*., 2004).

Other regimen:

Human chorionic gonadotrophins (HCG) a small randomized controlled trial have shown some benefit in pregnancy outcome when hCG treatment was administrated to women with early threatened miscarriage (Qureshi *et al*., 2005).

The aim of this study was to evaluate the reliability of repeated measurements of CA125 & β-HCG as apredictor of the outcome of threatened miscarriage.

Materials and Methods

This prospective case-control study was carried out in Department of Obstetrics and Gynecology of Al-Imamain Al-Kadhemain Medical City, Baghdad, Iraq. The study was conducted over a period of twelve months: starting from the first of February2012 to the end of January 2013.

A total of 140 pregnant women were evaluated, seventy (70) normal pregnant women less than twelfth weeks of gestation and seventy (70) pregnant with threatened miscarriage matched by maternal age and gestational age. The patients were collected from antenatal clinic and outpatient clinics, all of the patients had single viable pregnancy documented by U\S. the control group were selected as normal pregnant women with gestational age and maternal age that were matched with the case group. Patients who had a history of maternal disease which would cause increase in CA125 level were excluded.

- *Selection criteria:* Gestational age 7-12 wk. Patients with vaginal bleeding ±abdominal pain. A closed cervical os . Single viable pregnancy by U\S.

Exclusion criteria:

- Gestational age less than 7wk and more than 12wk.
- Nonviable fetus by U\S. - opened cervical os.
- Maternal disease that increase CA125 include: PID, endometriosis, uterine fibroids, lupus erythematosis, lung, liver, renal and pancreatic disease; carcinoma of the ovary, endometrum, pancreas, colon and lung.

Women included in this study were subdivided into three groups:

1st group: 25 pregnant women with threatened miscarriage whom pregnancy ended with pregnancy loss. 2nd group: 45 pregnant women with threatened miscarriage with ongoing pregnancy (continued beyond 24 wk). 3rd group: 70 apparently healthy pregnant women without any complaint, of comparable age and gestational age with the previous two groups. From all included patients detailed history and thorough clinical examination were performed. The gestational age was determined depending on accurate dating of LMP and confirmed by U\S, the latter also confirm viability and exclude others pathology. Patients underwent general examination and pelvic examination to assess the condition of the cervical os. Blood sample for CA125& βHCG was taken in the first visit & then after by the following method:

Sample collection: Blood samples were collected for each patient by venipuncture and separate the serum. The serum sample were be stored at 2-8ċ for 24hr, for longer periods the sample stored at -70ċ or below. Serum CA125 was measured with radio-immuno assay (RIA) method using IEMA WELL KIT. Then all patients followed up till 24wk and then see who continued pregnancy and who aborted before 24 wk.

Statistical analysis: Data were analyzed using the computer facility with use of SPSS -15 (statistical package for social sciences version 15) software packages. The data were expressed as means and stander deviation of the means. ANOVA and t- test was used as the test of significance taking P value≤ 0.05 as significant value. Using the cut-off value of CA125 as one and two standard deviation from the mean. The sensitivity, specificity, positive predictive value and negative predictive value were calculated.

Results and Discussion

A total of 140 pregnant women included in this study, the mean level of maternal age, gestational age, CA125 & βHCG in the first and second visit(after 5-7days)

for the threatened miscarriage with ongoing pregnancy group (TMOP) and threatened miscarriage ended with abortion group (TMEA) compared to their matched normal pregnancy(control) group.

Table (1) shows that:

1: The mean maternal age for threatened miscarriage ended with ongoing pregnancy group was 23.91±4.29, while in threatened miscarriage

ended by abortion group was 23.96±5.05 and in normal pregnancy group was 24.10±4.56. which is statistically not significant (P value 0.975)

2: The mean gestational age for threatened miscarriage with ongoing pregnancy was 9.67±2.02, in threatened miscarriage ended by abortion was 9.36±1.96 and n normal pregnancy was 9.64±1.93. which is statistically not significant (P value 0.795).

3: The mean CA125 level in the 1st visit in threatened miscarriage ended by abortion group 58.76±20.61, was higher than the threatened miscarriage with ongoing pregnancy group which was 28.51±7.86 and in normal pregnancy which was 22.64±8.75 which is statistically significant. (P value < 0.001)

4: The mean βHCG level in the 1st visit for threatened miscarriage ended by abortion group was 23578.00±13837.37 while in threatened miscarriage with ongoing pregnancy was 41788.89±21875.73 and in normal pregnancy was 41741.43±22026.06. which is statistically significant. (P value 0.001)

5: The mean CA125 level in the 2nd visit for miscarriage ended by abortion group was 73.48±20.29 while in threatened miscarriage with ongoing pregnancy was 13.69±4.01 and in normal pregnancy was 11.73±4.74. which is statistically significant. (P value < 0.001)

6: The mean βHCG level in the 2nd visit for threatened miscarriage ended by abortion group was 1188.20±196.85 while in threatened miscarriage with ongoing pregnancy was 62566.67±20674.31 and in normal pregnancy was 63682.86±19367.34. which is statistically significant. (P value < 0.001).

Table (1): The mean level of maternal age (years), gestational age (weeks), CA125(IU/ml) & βHCG (mIU/ml) in the first and second visit for the three different studied groups.

Parameter	Control (n= 70)		TMOP (n= 45)		TMEA (n= 25)		P1	P2	P3	P4
	Mean	SD	Mean	SD	Mean	SD				
Age	24.10	4.56	23.91	4.29	23.96	5.05	0.829	0.896	0.966	0.975
GA	9.64	1.93	9.67	2.02	9.36	1.96	0.949	0.537	0.532	0.795
CA125(1)	22.64	8.75	28.51	7.86	58.76	20.61	0.009	<0.001	<0.001	<0.001
CA125(2)	11.73	4.74	13.69	4.01	73.48	20.29	0.278	<0.001	<0.001	<0.001
BHCG(1)	41741.43	22026.06	41788.89	21875.73	23578.00	13837.37	0.990	<0.001	0.001	0.001
BHCG(2)	63682.86	19367.34	62566.67	20674.31	1188.20	196.85	0.747	<0.001	<0.001	<0.001

TMOP: threatened miscarriage with ongoing pregnancy; TMEA: threatened miscarriage ended with abortion. P1: between control and TMOP; P2: Between Control and TMEA; P3: Between TMOP and TMEA; P4: Among all groups.

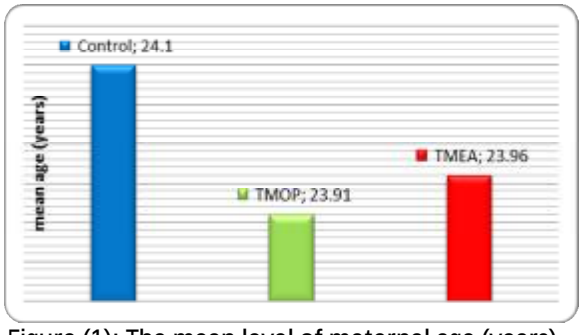

Figure (1): The mean level of maternal age (years) for the three different studied groups TMOP: threatened miscarriage with ongoing pregnancy, TMEA: threatened miscarriage ended with abortion.

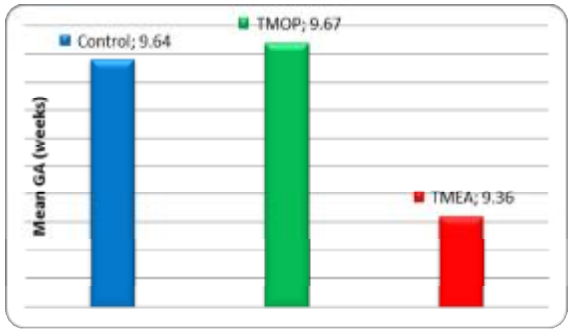

Figure (2): The mean level of gestational age (weeks) for the three different studied groups. TMOP: threatened miscarriage with ongoing pregnancy; TMEA: threatened miscarriage ended with abortion.

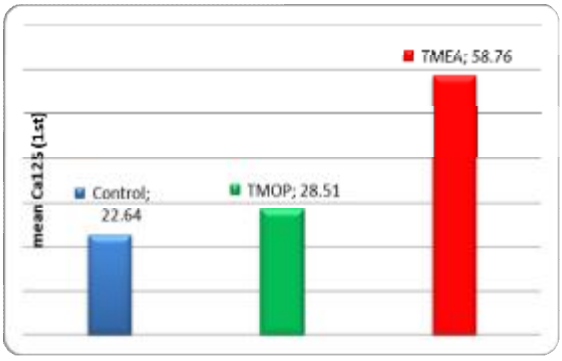

Figure (3) The mean level of CA125 (1st) visit for the three different studied groups. TMOP: threatened miscarriage with ongoing pregnancy; TMEA: threatened miscarriage ended with abortion.

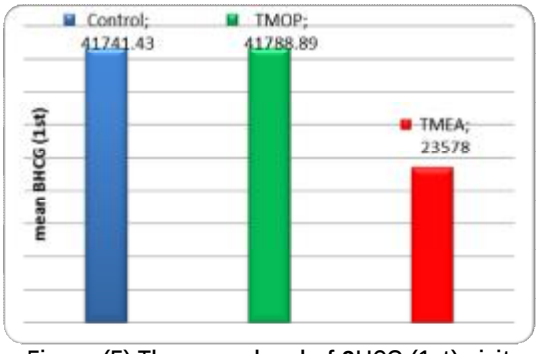

Figure (5) The mean level of βHCG (1st) visit (mIU/ml) for the three different studied groups. TMOP: threatened miscarriage with ongoing pregnancy; TMEA: threatened miscarriage ended with abortion.

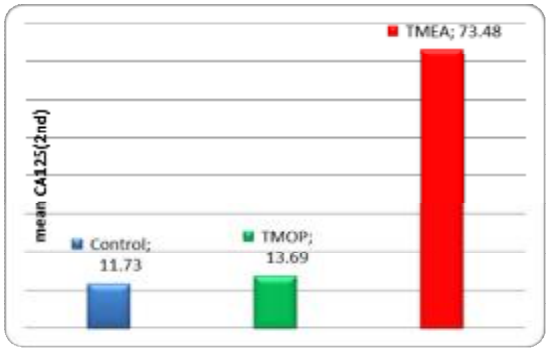

Figure (4) The mean level of CA125 (2nd) visit (IU/ml) For the three different studied groups. TMOP: threatened Miscarriage with ongoing pregnancy; TMEA: threatened miscarriage ended with abortion.

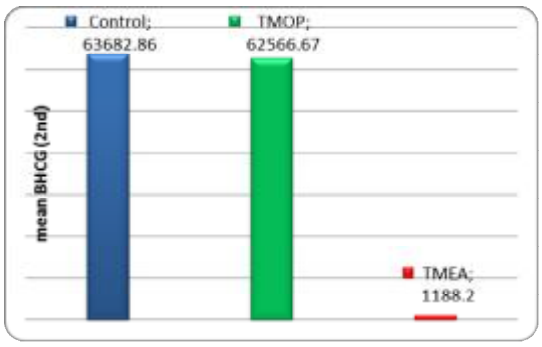

Figure (6) The mean level of βHCG (2nd) visit (mIU/ml) for the three different studied groups. TMOP: threatened miscarriage with ongoing pregnancy; TMEA: threatened miscarriage ended with abortion.

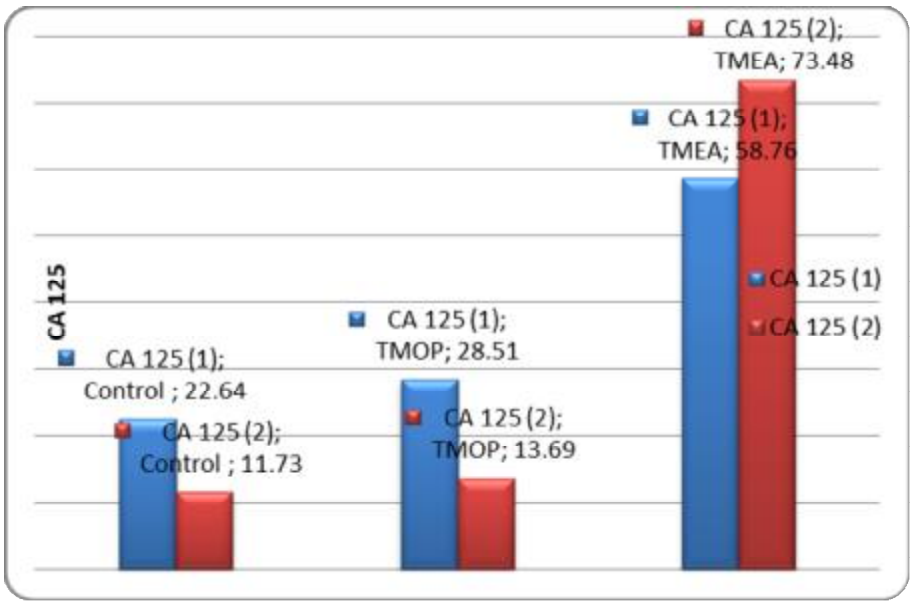

Figure (7): The mean level of CA125 in the (1st)& (2nd) visit (IU/ml) for the three different studied groups. TMOP: threatened miscarriage with ongoing pregnancy; TMEA: threatened miscarriage ended with abortion.

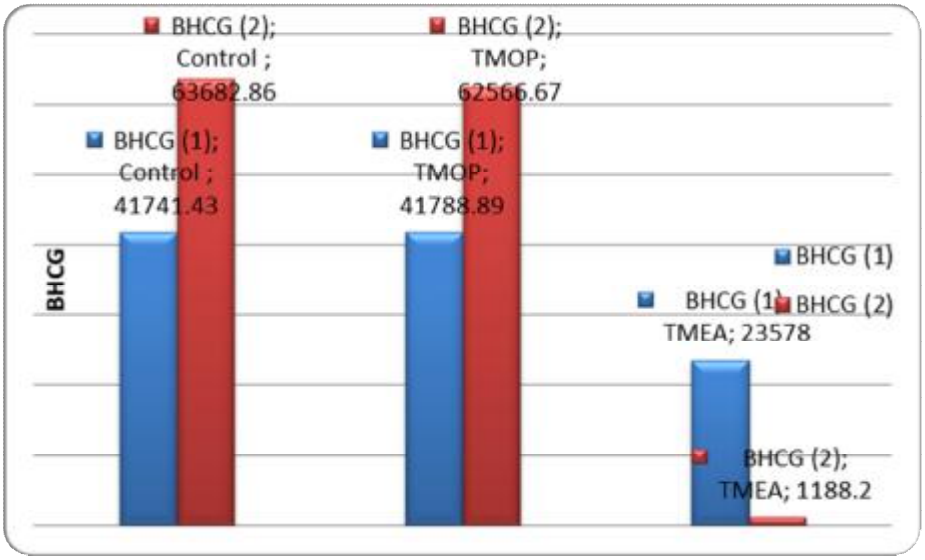

Figure (8): The mean level of βHCG in the (1st) & (2nd) visit (mIU/ml) for the three different studied groups. TMOP: threatened miscarriage with ongoing pregnancy; TMEA: threatened miscarriage ended with abortion

sensitivity and specificity: Table (2) shows the sensitivity and specificity of CA125 & βHCG in the 1st & 2nd visit when cut-off value for CA125 1st = 37.5(IU/ml), CA125 2nd = 36 (IU/ml), βHCG 1st = 31000(mIU/ml) & βHCG 2nd = 6725(mIU/ml). The sensitivity for the CA125 in the 1st visit was 92% & in the 2nd visit was 94%. The specificity for CA125 in the 1st visit was 91.1% & in the 2nd visit was 92%. The sensitivity for the βHCG in the 1st visit was 90% & in the 2nd visit was 91%. The specificity for the βHCG in the 1st visit was 92% & in the 2nd visit was 95%.

Table (2): The sensitivity and specificity of CA125 & βHCG, cut-off value in the 1st & 2nd visit.

Cut off value	CA 125 (1)=37.5*	CA 125 (2)= 36*	BHCG (1)= 31000†	BHCG (2)= 6725†
AUC	0.980	1.000	0.780	1.000
P	<0.001	<0.001	<0.001	<0.001
Sensitivity	92 %	94 %	90 %	91 %
Specificity	91.1 %	92 %	92 %	95 %

AUC: area under the curve. P: p value *Equal or above; † equal or bellow

Our study showed that mean level of CA125 was higher in threatened miscarriage ended by abortion group (73.48±20.29) than threatened miscarriage with ongoing pregnancy group (13.69±4.01) and both were higher than normal control group (11.73±4.74) the difference was statically significant (p value <0.001), while the mean level of βHCG was lower in threatened miscarriage ended by abortion group (1188.20±196.85) than threatened miscarriage with ongoing pregnancy group (62566.67 ±20674.31) and both were lower than normal control group (63682.86±19367.34) the difference was statically significant (p value <0.001). In our study the measurement of CA125 with a cut-off value =36 showed sensitivity 94% and specificity of 94% while βHCG measurement with cut-off value =6725 showed sensitivity 91% & specificity 95%.

Serum CA-125 levels are increased in early pregnancy and immediately after birth, implicating the disintegration of the maternal decidua (*i.e.,* blastocyst implantation and placental separation) as a possible source of the tumor marker elevation (Fiegler *et al*., 2003).This is consistent with the study of Fiegler *et al*. in 2003 In which they concluded that a single serum CA-125 level determination is valuable in women with imminent abortion presenting with abdominal pain, vaginal bleeding or both (Fiegler *et al*., 2003).

Our finding was consistent with that of Sotiriadis *et al*. (2004) in which The prognostic value of maternal CA 125 level was investigated in 239 women with a first trimester intact pregnancy, imminent, incomplete, complete or missed abortion. The study showed that CA 125 levels in first trimester pregnancies tended to be higher in patients with vaginal bleedings than in patients without bleeding (40.5 U/ml +/- 55.0 vs. 28.9 U/ml

+/- 28.8 (Foth and Romer, 2000).

Our finding agreed with the finding of Ayaty *et al*. (2007) who studied the relation between CA 125 levels and abruptio placentae, they concluded that the average levels of CA 125 were higher in patients with abruptio placentae than in women with other sources of vaginal bleeding and those without bleeding (Thorneycroft *et al*., 1991). Also our result consistent with that of Yu *et al*. (2008) who proved that women with threatened miscarriage revealed higher values of serum CA125 than those in control groups, the patients who had presented the highest values of CA125 later miscarried (Kaminiski *et al*., 2002).

Bellon *et al*. (2009) found that Threatened pregnancies had statistically significantly higher CA 125 serum values than non-threatened pregnancies, especially those with a negative outcome. The CA 125 levels in the threatened pregnancies were positively correlated with the tropho-decidual hematoma volume It was concluded that the extension of decidual destruction and trophoblast separation from decidual cells was the major source of the maternal serum CA-125 elevation (Scarpellini *et al*., 1995), while Fiegler *et al*. (2003) concluded that Single serum measurements of CA 125 in symptomatic first trimester pregnant patients failed to discriminate spontaneous abortion, ectopic or normal pregnancies. However, they found that sequential determinations of maternal CA 125 measurements appear to be a highly sensitive prognostic marker in patients with viable pregnancy at risk for abortion (Schmidt *et al*., 2001). The use of CA125 as prognostic factor in threatened miscarriage not supported by Mahdi (2010); this study showed that there is a distinct pattern in CA125 level during pregnancy and puerperium. Due to the wide fluctuations in CA125 level in very early pregnancy and immediate postpartum period CA125 values during these period are not useful for clinical correlation with the pathologic condition known to be associated with elevated level of CA125 (Spizter *et al*., 1998).

Conclusions

We conclude that single measurement of serum CA-125 level determination is valuable in the women with symptoms of threatened miscarriage and it a sensitive and specific prediction in the cases of threatened miscarriage pregnancy ended with pregnancy loss.

Recommendations

However, further detailed studies are needed to study this subject in the patients from larger populations. and to use other marker as B-hCG and compare it with CA125 to conclude which more specific, sensitive and cheap in prediction the outcome of threatened miscarriage pregnancy.

Acknowledgement

We would like to express my deep respect & appreciation to Dr. Thair Wali Ali for helping us in statistical analysis of data and I express my deepest gratitude to the sonographist and biochemists for their great help.

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