Prediction of Pregnancy Outcome Using HCG, CA125 and Progesterone in Cases of Habitual Abortions

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Abstract

Background: Although CA125 is a valuable tumor marker of ovarian carcinoma but it may be have a value to assess the risk of miscarriage at the early stages of pregnancy for woman with history of recurrent pregnancy loss either alone or in combination with other biochemical marker.

Objective: To predict pregnancy outcome by studying the level of serum β HCG, progesterone and CA125 at different gestational age in the first trimester for predicting pregnancy loss.

Patient and Methods: This study was conducted in Al-Batool Teaching Hospital (in the center of Diyala governorate by studying the patient records as a prospective trail in period from Jan. 2010 to Jan. 2011. The study carried out on 90 pregnant women with a history of recurrent pregnancy loss in there first trimester of pregnancy divided in 3 groups (30 women with no history of abortion as control group, 30 women with history of recurrent pregnancy loss, 30 women who failed to complete their pregnancy in the first trimester during the study. Serial maternal B-HCG, progesterone and CA125 were determined.

Results: Serum B-HCG showed a sensitivity of 97%, a specificity of 53%, a PPV (positive predictive value) of 56% and a NPV (negative predictive value) of 97%. Serum progesterone showed a sensitivity of 27%, a specificity of 79%, a PPV of 38% and a NPV of 69%, while serum CA125 showed a sensitivity of 8%, a specificity of 60%, a PPV of 10% and a NPV of 70%.

Conclusion: the value of CA125 in recurrent abortions is still unclear and cannot be recommended on routine basis. On the other hand, β-HCG is 97% sensitive with a 53% NPV as a single serum measurement for the prediction of pregnancy outcome.

Keywords: B-HCG, CA125, progesterone, first trimester, recurrent pregnancy loss, sensitivity, specificity.

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Introduction

Early pregnancy loss, especially when recurrent, is an emotionally traumatic experience, similar to that associated with still birth or neonatal death.

Recurrent pregnancy loss (RPL) is one of the most frustrating and difficult areas in reproductive medicine because the etiology is often unknown that account for 40%-50%, 17%-20% due to endocrine factors, autoimmune factors about 20%, while 10%-15% due to anatomic factors, 0.5%-5% infections and 2%-5% genetic factors, and

there are few evidence based diagnostic and treatment strategies [1]. RPL classically refers to the occurrence of three or more consecutive losses of clinically recognized pregnancy prior to the 24th weeks of gestation (ectopic, molar, and biochemical pregnancies are not included) [1].

The American Society for Reproductive Medicine defines RPL as two more failed pregnancies (documented by ultrasound or histopathological examination) and suggests some assessments after each loss with thorough evaluation after three or more losses [2].

The rate of fetal loss in clinically evident gestations has been reported to be approximately 10-15%. The rate will be obviously higher if we consider the preclinical losses diagnosed by B-HCG level starting 3 weeks following the last menstrual period, accordingly the expected probability for a women to have three consecutive abortions should be in the range of 0.3-0.4%, the actual frequency of habitual abortion, however, is significantly higher, being in the range of 0.4-0.8% this difference suggests that not only random causes but also some specific factors must be involved in this type of reproductive failure[3].

B HCG, progesterone titers are widely used to assess the risk of miscarriage at the early stages of pregnancy [4]. Cancer Antigen-125 (CA125) is a cell surface antigen high molecular weight glycoprotein. Although CA125 is a valuable tumor marker of ovarian carcinoma but it may be have value to assess the risk of miscarriage at the early stages of pregnancy for woman with history of recurrent pregnancy loss as there is a positive correlation between CA125 level and spontaneous abortion as the distribution of CA125 during pregnancy was highest in first trimester than second and third trimester, this may be due to the secretion of CA125and placenta protein 14 by the glandular epithelium of the endometrium so by using it alone or in combination with other biochemical markers this may help prediction pregnancy losses especially for women with history of RPL[5].

Patients and Methods

This study was conducted in Al-Batool Teaching Hospital (in the center of Diyala Governorate by studying the patient records as a cohort prospective observational study with control group in period from Jan. 2010 to Jan. 2011. The study carried out on 90 pregnant women with history of recurrent pregnancy loss in their first trimester of pregnancy divided in 3 groups:-

1-The control group (Group I), comprising 30 normal pregnant women with no history of miscarriage.

2- (GroupII) the recurrent aborters group comprising 30 pregnant females with history of two or more 1st trimester pregnancy losses.

3- (Group III) group of 30 patients who failed to complete the 1st trimester of pregnancy (aborting for the first time) during the study.

All were singletons pregnancy, full history and examination done for them in order to identify the three groups Serial maternal serum levels of HCG, progesterone and CA125 were determined. Further subdivision according to the gestational age within each age group was done. (6-7 weeks group: / 8-9 weeks group: / 10-11 weeks group) all levels are tested by mini- vidas machine.

Results

Twenty-eight (90%) cases in group III were below the cutoff value for the serum B-HCG against 4 cases (13.3%) in group I with a highly statistically significant difference ($P < 0.01$) as shown in table(1). Hence, serum B-HCG showed a sensitivity of 97%, a specificity of 53%, a positive predictive value (PPV) of 56% and a negative

predictive value (NPV) of 97% and this is the median of specificity and sensitivity shown in table (4).

Eight cases (26.6%) cases in group III were below the cutoff value for the serum progesterone against 6 cases (20%) in group I with no statistically significant difference ($P > 0.05$) as shown in table (2). Hence, serum progesterone showed a sensitivity of 27%, a specificity of 79%, a PPV of 38% and a NPV

of 69% and this is the median of specificity and sensitivity shown in table (4).

four cases (13.3%) cases in group III were above the cutoff value for the serum CA125 against 5 cases (16.6%) in group I with no statistically significant difference ($P > 0.05$) as shown in table (3). Hence, serum CA125 showed a sensitivity of 12%, a specificity of 67%, a PPV of 15% and a NPV of 61% and a NPV of 69% and this is the median of specificity and sensitivity shown in table (4).

Table (1): Show two groups of patients regarding B-HCG level below the cut off value (6500 IU/L).

Groups of patients	Number	Percent %	P- value
Group I*	4	13.3%	< 0.01 significant
Group II**	25	83.3%	
Group III***	28	90%	

Number= 30, ** number=30, *** number=30

Table (2): Show two groups of patients regarding progesterone level below the cut off value (30 ng/ml).

Groups of patients	Number	Percent %	P- value
Group I*	8	26.6%	> 0.05 not significant
Group II**	4	13.3%	
Group III***	6	20%	

Number= 30, ** number=30, *** number=30

Table (3): Show two groups of patients regarding CA125 level above the cut off value (65 IU/ml).

Groups of patients	Number	Percent %	P- value
Group I*	5	16.6%	> 0.05 not significant
Group II**	3	10%	
Group III***	4	13.3%	

Number= 30, ** number=30, *** number=30

Table (4): Evaluation of serum B-HCG, Progesterone, CA125 in different gestational age groups.

B-HCG	Sensitivity	Specificity	PPV*	NPV**
6-7 Weeks	95%	50%	59%	95%
8-9 Weeks	99%	52%	50%	99%
10-11Weeks	96%	50%	30%	96%
Progesterone				
6-7 Weeks	40%	55%	35%	54%
8-9 Weeks	20%	85%	55%	65%
10-11Weeks	2%	83%	2%	83%
CA125				
6-7 Weeks	12%	45%	15%	50%
8-9 Weeks	2%	70%	2%	48%
10-11Weeks	45%	75%	27%	88%

*Positive predictive value, ** Negative predictive value

Discussion

It is clinically important to predict the outcome of patients with history of recurrent abortion at an early stage of gestation, number of biochemical markers used nowadays for prediction of pregnancy outcome. The most common of these are B-HCG, progesterone.

Several studies conclude that a single B-HCG measurement in early pregnancy can reliably predict pregnancy outcome. Other reports suggest that serial measurements of B-HCG provide means of differentiating viable from nonviable events of pregnancy, particularly when other tests such as transvaginal ultrasonography or serum progesterone concentrations provide no insight regarding viability or location of a pregnancy [4, 6].

The serum progesterone level reflects the production of progesterone by the corpus luteum that is stimulated by a viable pregnancy. During the first 8-10 weeks of gestation, serum progesterone concentrations change little; as pregnancy fails, the levels decrease [7].

Recently there is new biochemical marker become under focus to use it with others to predict spontaneous pregnancy loss especially in women of history of recurrent abortion which is CA125, tumor marker in a cell- surface antigen derived from the surface coelomic epithelium, including the mucosa of the entire female genetic tract and maternal deciduas.

Therefore extensive tissue destruction in uterine abortions has been shown the result in a significant increasing in the level of CA125 [8]. In the present study, the serum CA125 in the control group showed no significant differences between different gestational age groups, also if we consider the cut off value of CA125 used in this study (65 IU/ml), it was found that there was no significant difference between control group and group of women who aborted first time in this study and those who had previous history of recurrent abortion. Serum CA125 showed a sensitivity of 12%, a specificity of 67%, a PPV of 15% and a NPV of 61% and a NPV

of 69% this may make us to consider that CA125 marker is not predictive value to pregnancy outcome in this and study may be due to small number of patients' sample. This in agree with Batool M. study [5] who found that measurement of CA125 is not of value to predict the outcome of threatened abortion because it is secreted from different origin but not agree with Katsikis I. et al [8] who found that CA125 concentrations are significantly increased in spontaneous intrauterine abortions compared to both ectopic and intrauterine normal pregnancy.

On the other hand, in the present study, serum B-HCG showed highly statistically significant differences ($P < 0.01$) between the control group and second and third group this mean lower level of B-HCG measured in women with abortion below the cutoff value in this study (6500 IU/L) compared to control group. Serum B-HCG showed a sensitivity of 97%, a specificity of 53%, a positive predictive value (PPV) of 56% and a negative predictive value (NPV) of 97% and this matches well with Lijun D. et al [4] serum levels of B-HCG in patients with inevitable miscarriages were significantly lower than those levels in ongoing pregnancies ($P < 0.001$). A single serum determination of serum B-HCG was found to have 64.1% sensitivity and 81.4% specificity at a cutoff value of 7,236 mIU/ml in diagnosis of miscarriage.

Finally, serum progesterone showed no significant difference (P>0.05) in serum levels of women of different gestational age, also there were no significant difference between the three groups regarding number of patients who had level of progesterone below the cutoff value (30 ng/ ml). Serum progesterone showed a sensitivity of 27%, a specificity of 79%, a PPV of 38% and a NPV of 69% this may be due to that progesterone production by placenta does not significantly increase until about 10-11 weeks after

ovulation [7] and this exactly the age group that involved in the study or again may be due to small sample size. This is not in agree with Katsikis I. et al who said progesterone levels in abnormal pregnancies were significantly decreased [8].

Conclusion

The value of CA125 in recurrent abortions is still unclear and cannot be recommended on routine basis. On the other hand HCG is highly sensitive as a single serum measurement for the prediction of pregnancy outcome.

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