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CA-125 in normal pregnancy and threatened abortion

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Abstract:

Background: CA-125 is a glycoprotein and its origin is uncertain during pregnancy. It arises during the first trimester and return to a non-pregnancy range in late pregnancy.

Objective: The aim of this study was to compare CA-125 level in threatened abortion and normal pregnancy less than 20 weeks of pregnancy.

Materials and Methods: This was a prospective case study carried out on 50 healthy pregnant (group 1) and 50 threatened abortion women (group 2). We compared the levels of CA-125 in these groups and followed them to be informed of the outcome of pregnancy.

Results: Fifty percent of women were in 20-24 years old group, primigravida and in the first trimester of pregnancy. The mean level of CA-125 in group 1 was 26.2 ± 3.25 IU/ml and in group 2 was 37.44 ± 2.72 IU/ml. The mean level of CA-125 in finally aborted patients was 58.17±7.25 IU/ml and in normal pregnant women, who continue to term, was 26.61±1.76 IU/ml. The CA-125 level in threatened women,whose pregnancy continued and did not abort, was 30.89 IU/ml. There was statistically significant difference between mean serum CA-125 levels of two groups ($p < 0.05$), while there was no statistically significant difference between these levels in the patients of both groups who continued pregnancies ($p > 0.1$). In group 2, there was a statistically significant difference in the level of CA-125 between those who developed abortion and those whose pregnancy continued but not aborted ($p < 0.05$).

Conclusion: Measurement of serum CA-125 may be an inexpensive, easily available, sensitive and specific predictor of outcome in threatened abortion, which results the loss of pregnancy.

Keywords: *CA-125, Pregnancy, Abortion, Threatened abortion.*

Introduction

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 (1). An increased CA-125 level is due to genital or non-genital origins. Non-genital causes include hepatic diseases, peritonitis, renal failure, breast, colon and lung cancer, and tuberculosis. Genital causes include; pelvic inflammatory diseases, endometriosis, adenomyosis, leiomioma, ectopic pregnancy, endometrial and ovarian cancer. In pregnancy, CA-125 increases in the first trimester (2, 3). Regarding the level of CA-125 in pregnancy, conflicting results have been reported. In a study by Check et al (1990), a positive correlation has been found between CA-125 levels elevated 18-22 days after conception and spontaneous abortion, while repeated measurements at 6 weeks of gestation did not correlate with the outcome (4).

One study showed that the serum CA-125 level is higher in normal pregnancy compared to ectopic pregnancy (EP) 2-4 weeks after a missed menses, whereas another study found higher CA-125 level for EP compared with normal pregnancies (5,6).

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We hypothesized that there is a correlation between high serum CA-125 levels and adverse pregnancy outcome in threatened abortion. Therefore, we aimed to research, whether or not; the measurement of CA-125 level could be used as a predictor of outcome in threatened abortion compared to the normal pregnancy.

Materials and methods

This was a prospective case control study on 50 normal pregnant women less than 20 weeks of gestational age and also 50 threatened abortion cases (vaginal bleeding with closed cervix) that referred to maternity clinic of Ghaem Hospital in Mashhad during the year 2005. All of the patients had single pregnancy. The control groups were selected as normal pregnant women with gestational and maternal age, who were matched with case group. Blood samples were collected for each patient. Those who had a history of maternal disease, which would cause an increase in CA-125 level, were not included in this study. These diseases include chronic pelvic infection, endometriosis, myoma uteri, endometrioma, and lung, kidney and hepatic disease.

The patients were chosen by a simple selection according to the subjective and then there was a questionnaire for each patient, which evaluated many of dependent variables such as patients' age, gestational age, vaginal bleeding and abortion history, and at last a dependent variable, which was CA-125 group.

Serum CA-125 level was measured with radio-immunoassay (RIA) method using CA-125 Roche E-170 kit (Roche diagnostic cooperation, Indiana polis, USA).

Statistical analysis was performed by using student's *t*- test, χ^2 test and analysis of variance (ANOVA) with "SPSS ver; 11.5 for Windows" software.

Results

Regarding the age, 50% of the patients in both groups were 20-24 years old, 13% were under 20 years of age and 38% were over 24 years old. Mean age in normal pregnant group was 23.06 ± 3.24 years and in threatened abortion group was 25.24 ± 4.12 years.

Mean age in threatened abortion group was significantly more than that seen for the normal pregnant group ($p = 0.026$). Seventy three patients were in gestational age of 12 weeks (GA) and 27 in more than 12 weeks of GA. Overall, 26 normal pregnant women were in 5-12 weeks of GA and 47 threatened abortion cases were in 5-12 weeks of GA. Three cases were admitted after 12 weeks. The patients, who had vaginal bleeding, were advised to consult sooner than the others.

The number of threatened abortion cases decreased after 12 weeks of gestational age. There was no significant correlation between serum CA-125 and maternal age or previous abortions but there was a correlation between serum CA-125 level and specific gravidity ($p > 0.1$).

CA-125 in 85% of normal patients and 60% of threatened abortion cases was less than 40 IU/ml. Mean serum CA-125 in normal pregnant group was 26.2 ± 2.72 IU/ml and in threatened abortion group was 37.44 ± 3.25 IU/ml. Therefore, there was a significant difference between these two groups ($p = 0.009$).

In the assessment of pregnancy outcomes after 20 weeks of gestation, there was an on-going pregnancy in 84% of cases, and the pregnancy was terminated before 20 weeks in 12% of the patients; while, the outcome of pregnancy was unknown in 4% of the cases because the patients were not available.

Serum CA-125 level in the patients, whose pregnancy was terminated before 20th week of gestation, was 58.7 ± 7.25 IU/ml and in on-going pregnancy group was 26.61 ± 1.76 IU/ml. Therefore, there was a significant difference between these two groups according to the statistical analysis ($p = 0.000$).

In threatened abortion group, the final mean serum CA-125 level in aborted cases (12 cases) was 58.17 ± 7.25 IU/ml and in those with on-going pregnancy after 20th weeks of gestation (38 cases), was 30.89 ± 2.93 IU/ml (Table 1). Therefore, there was a significant difference between these two groups as well ($p < 0.01$).

Table I- Comparison of mean CA-125 level in threatened abortion group in relation to pregnancy outcome

Threatened abortion	*No of patients*	Mean CA-125 (IU/ml)	S.D	P-Value
Ongoing pregnancy	38	30.89±2.93	2.93	0.01
Abortion	12	58.17±7.52	7.25	

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Discussion

Loss of pregnancy is a distressing problem for both the patient and physician. Not all conceptions result in live birth of the infant and most of pregnancy losses are not diagnosed (2).

The clinical diagnosis of threatened abortion is presumed when any bloody vaginal discharge or bleeding appears during the first half of pregnancy. Of these women who bleed in early pregnancy; approximately half will abort (3).

Occasionally, bleeding may persist for weeks, and then it becomes essential to decide whether there is any possibility of continuation of the pregnancy or not. Vaginal sonography, serial serum quantities, human chorionic gonadotropin (hCG) levels and serum progesterone values, measured alone or in various combinations have proven helpful in ascertaining if a live intrauterine pregnancy is present.

The CA-125 tumor marker is a cell-surface antigen, derived from the surface coelomic epithelium, including the mucosa of the entire female genital tract and the germinal epithelium of the ovaries (5). The fetal chorion, amniotic fluid and maternal decidua have also been shown to contain significant amounts of CA-125 protein (7).

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 (8). A significant increase in serum CA-125 levels was also reported in a group of patients with vaginal bleeding and impending spontaneous abortion (9, 10). 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, but this has not been supported by other studies (6, 11).

A connection between serum CA-125 levels and abnormal early intra-uterine pregnancies has been investigated to determine whether it might be useful in the assessment of threatened abortion or not. It was believed that the destruction of fetal tissues and deciduas would yield different serum CA-125 values in patients with threatened abortion, compared with the patients with normal intrauterine pregnancies. One of the cross-sectional studies has reported the significantly lowered serum CA-125 concentrations in women with ectopic pregnancies (6). The low CA-125 levels were explained by the impaired interaction between the fetal trophoblast and tubal mucosa (9).

Schmidt *et al* (2001) showed that single serum measurements of CA-125 in symptomatic first trimester pregnancy patients failed to discriminate the spontaneous abortion, ectopic or normal pregnancies (9). They stated that the sequential determinations of maternal CA-125 measurements appear to be a highly sensitive prognostic marker in the patients with viable pregnancy at an abortion risk. Kobayashi *et al* (1989) stated that the serum CA-125 levels are high in the women with normal early pregnancy, spontaneous abortion and hydatiform mole but the same levels are low in the women with tubal pregnancy, especially if there had been no uterine bleeding (8). They reported that a transient elevation of the CA-125 level occur in maternal serum during early pregnancy and just after delivery, and they thought that the destruction of decidual tissues may cause this transient elevation of CA-125(12). Brumsted *et al* (1990) found elevated serum CA-125 levels in a majority of women with normal intrauterine pregnancies (13). They found lower levels of CA125 in the women with abnormal pregnancies, in which there should be an increased incidence of bleeding. Correction of this clinical finding would potentially increase the differences noted between normal and abnormal pregnancies. Moreover, they reported that as the significant differences exist in the maternal serum CA125 levels between early, normal and ectopic gestations, CA-125 may prove to be clinically useful in early pregnancy monitoring.

In our study, the median CA-125 level in the normal pregnancy was less than threatened abortion group who aborted with the same gestational weeks ($P < 0.001$).Moreover, the median values and dispersion rations of CA-125 levels of the REP group showed a similarity with in the NIUP group ($P > 0.05$). We think that such situation can be explained with the disruption of decidual tissue, resulting from an inevitable abortion.

The results of our study are in line with the results of several studies in terms of the high levels of CA-125 in early intra-uterine pregnancy (14-16). Nevertheless, our findings, with regards to the CA-125 levels in ectopic pregnancy, have shown a partial contradiction, or resemblance with the findings of published studies.

According to these findings, it can be stated that the test is rather sensitive to differentiate the normal pregnancy and threatened abortion. There was not a significant correlation between CA-125 levels and gestational weeks in two groups. Therefore, an increase in serial CA 125

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measurements in the follow-up of pregnancies with vaginal bleeding could be an early signal in determining the progression to the pregnancy loss. Fiegler *et al* (2003) revealed that all the women with symptoms of imminent abortion, who have a CA-125 level of > or = 43.IU/ml, should be considered at a greater risk of miscarriage (17).

Conclusion

Our findings showed that the serum CA-125 level determination is valuable in the women with symptoms of threatened abortion and it may be a cheap, sensitive and specific prediction in the cases of threatened abortion and pregnancy loss.

However, further detailed studies are needed to study this subject in the patients from larger populations.

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