

Prospective Observational Assessment of the Role of Serum CA125 Levels in Predicting the Outcome of Threatened Abortion

Anjana¹, Rupesh Kumar², Binod Kumar³

¹Tutor, Department of Pathology, Sheikh Bhikhari Medical College, Hazaribagh, Jharkhand, India

²Associate Professor, Department of Orthopaedics, Sheikh Bhikhari Medical College, Hazaribagh, Jharkhand, India

³Associate Professor and HOD, Department of Pathology, Sheikh Bhikhari Medical College, Hazaribagh, Jharkhand, India

Received: 03-11-2021 / Revised: 23-11-2021 / Accepted: 24-12-2021

Corresponding author: Dr. Rupesh Kumar

Conflict of interest: Nil

Abstract

Aim: To evaluate the role of serum CA125 levels in predicting the outcome of threatened abortion.

Material and Methods: This prospective observational study was carried out in the Department of Pathology, Sheikh Bhikhari Medical College, Hazaribagh, Jharkhand, India for 6 months. Total 70 patients having complained of vaginal bleeding with gestation age between 7 to 14 weeks were included in this study. Their blood samples were taken and sent for Complete blood count, liver function test, renal function test, ABO Rh, viral markers, serum CA 125 levels. All participants were subjected to sonographic examination to confirm gestational age, fetal viability, and intrauterine single gestation.

Results: The ROC graphs gives us the cut off level of 60 IU/ ml in predicting the risk of abortion, with the sensitivity of 85%, specificity of 90%, PPV of 82.5%, NPV of 92 and accuracy of 88. Thus making CA 125 clinically important in predicting the outcome of patients with threatened abortion at an early stage of gestation. 71.43% of patients of threatened abortion with maternal serum CA 125 level of more than 60 IU/ml aborted while 28.57% of patients of threatened abortion with maternal serum CA125 level of more than 60 IU/ml continued to the period of viability. Among patients of threatened abortion with serum CA 125 level lesser than or equal to 60 IU/ml, 16% of patients aborted while 84% of patients continued to the period of viability. Statistically the difference was significant with p value of <0.001.

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.

This is an Open Access article that uses a fund-ing model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Spontaneous abortion is one of most common complication of pregnancy. The diagnosis of spontaneous abortion currently

depends on a combination of ultrasonography and nine hormonal methods (serum human chorionic gonadotropin (HCG), estradiol (E2),

estrone, estriol, progesterone, human placental lactogen, cortisol, urine HCG and urine estrogen.¹ Another parameter used as a predictive marker for a spontaneous abortion or subsequent outcome of pregnancy is Cancer Antigen-125 (CA-125). This antigen is a cell surface high molecular weight glycoprotein; synthesis is not restricted to malignant transformation and ovarian tumors.^{2,3} It is also expressed in normal tissues such as endometrium, endocervix, fallopian tubes, and mesothelial cells lining adult pleura, pericardium and peritoneum.⁴ 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 secretory function of these organs.⁵ 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, leiomyoma, ectopic pregnancy, endometrial and ovarian cancer. In pregnancy, CA125 increases in the first trimester.^{6,7} 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.⁸ 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

.^{9,10} Therefore the elevated serum CA 125 levels in women with threatened abortion implicate poor outcome in future. This test is rather sensitive in determining the progression to the pregnancy loss.

Material and Methods

This prospective observational study was carried out in the Department of Pathology, Sheikh Bhikhari Medical College, Hazaribagh, Jharkhand, India for 6 months. We included 70 patients complaining of bleeding per vaginum.

Methodology

The women of age group between 18-40 years with gestation age ranging from 7 to 14 weeks. The patients with singleton pregnancy and presenting with vaginal bleeding or spotting with ultrasonography signs of viable pregnancy were included in this study. Pregnant women with past history of medical disorders in pregnancy, gynecological disease, uterine malformations, history of recurrent miscarriages, chronic pelvic infection and endometriosis Conception by assisted reproductive techniques were excluded from this study.

Total 70 patients having complained of vaginal bleeding with gestation age between 7 to 14 weeks and satisfying the inclusion criteria. An informed written consent was obtained from the participants.

The characteristics of all the patients related to their age, gravidity, period of Gestation, Ultrasonographic results were determined and data were collected. They were subjected to detailed history taking, complete general physical examination, systemic examination and obstetric examination. Their blood samples were taken and sent for Complete blood count, liver function test, renal function test, ABO Rh, viral markers, serum CA 125 levels. All participants were subjected to sonographic examination to confirm gestational age, fetal viability, intrauterine single gestation.

All women in the study group were followed prospectively from their first appointment upto 20 weeks of gestation and patients were subdivided into 2 groups Group (A): continued their pregnancy Group (B):those who aborted.

Sampling methods

5 ml of venous blood was collected from each patient for measuring CA-125 serum level. After clotting of the blood sample the serum was separated from the cells by centrifugation within 1 hour of collection and removed using sterile pipette. All samples were stored refrigerated at 2-8 °C. Serum levels of CA- 125 were assayed by chemiluminescent immunometric method using ADVIA Centaur.

Statistical analysis

Continuous variable will be summarized as mean and standard deviation whereas nominal/categorical variables as proportion (%). Unpaired t test, one way ANOVA test and tukey HSD test will be used for comparison of continuous variables while chi square test/fissure exact test will be used for nominal/categorical values. P value less than 0.05 will be taken as significant.

Result

On evaluating, the population constituted 70 patients with complain of bleeding per vagina. On assessing the outcome at 20 weeks of pregnancy, 20 of 70 (28.57%) pregnancies ended up in abortion, whereas 50 (71.43%) participants continued their pregnancy. Mean age of the total study population was 25.87 ± 3.58 years which is the peak reproductive age group. There was not much significant difference between the patients who aborted and who continued the pregnancy on the basis of age and residence. Maximum number of patients in were primigravida (45%). Out of the 20 aborted patient, 9 (45%) were primigravida and 11 (55%) were multigravida. The patient who continued the pregnancy also had similar distribution, 60% were primigravida and rest 40% were multigravida. There was no statistical difference in distribution of patients based on parity and gestational weeks. (Table 1) Among patients of threatened abortion who aborted, mean maternal serum CA 125 level was 50.11 IU/ml and patients of threatened abortion who progressed normally to the period of viability had mean maternal serum CA 125 level of 118.06 IU/ml. Statistically the difference was significant with the p value of <0.0001 .

Table 1: Distribution of study population

		Continued=50	Aborted=20	P value
Age (years)		25.94±3.48	25.88±3.21	0.64 NS
GA (weeks)		9.94±1.47	9.75±1.41	0.22 NS
Gravidity	1	30(60%)	9(45%)	0.68
	2	12(24%)	6(30%)	
	>=3	8(16%)	5(25%)	
Parity*	P0	32 (64%)	8 (40%)	0.16NS
	P1	10 (20%)	8 (40%)	
	P2	8 (16%)	4 (20%)	
Hormonal levels	CA.125(IU/ml)	50.11±37.26	118.06±80.33	< 0.0001 S

Data are presented as mean ± S NS - not significant

The ROC graphs gives us the cut off level of 60 IU/ ml in predicting the risk of abortion, with the sensitivity of 85%, specificity of 90%, PPV of 82.5%, NPV of 92 and accuracy of 88. Thus

making CA 125 clinically important in predicting the outcome of patients with threatened abortion at an early stage of gestation.

Table 2: Distribution of study population according to maternal CA 125 levels

CA 125 (in IU / ml)	Result		Total
	Aborted	Continued	
> 60	12	8	20
	60%	40%	100.0%
≤60	8	42	50
	16%	84%	100.0%
Total	20	50	100
	28.57%	71.43%	100.0%

Chi-Square = 21.71, p = 0.000

As shown in Table 2, taking 60 IU/ml as cut off limit. 71.43% of patients of threatened abortion with maternal serum CA 125 level of more than 60 IU/ml aborted while 28.57% of patients of threatened abortion with maternal serum CA125 level of more than 60 IU/ml continued to the period of viability. Among patients of threatened abortion with serum CA 125 level lesser than or equal to 60 IU/ml, 16% of patients aborted while 84% of patients continued to the period of viability. Statistically the difference was significant with p value of <0.001.

Discussion

In this prospective study, we have focused on a very specific group of patients, those with complain of threatened abortion. Namely, those who had uterine bleeding in the presence of sonographically visible fetal heartbeat. In the present work, we found statistically significant increase of CA125 in aborted patients when compared to patients that continued their pregnancy after 20 weeks (50.11±37.26 and 118.06±80.33 respectively). In addition, the sensitivity of CA125 in prediction of abortion in studied females was 85% and specificity was 90% at a cut off value of > 60 IU/ml. Our study can be compared with the work of Abd-Elrau of M Oun et al (2018).¹¹ Their study included 110 women with manifestations of first trimester threatened miscarriage. CA 125 levels

ranged from 8 to 77 IU/ml, and there was statistically significant decrease of CA125 in group (A) (continued) when compared to group (B) (aborted) (19.45±5.57 vs 53.83±9.48 respectively). As regard to sensitivity of different studied variable in prediction of threatened abortion, the best was CA125, with a sensitivity of 100% and specificity of 98.8% at cut-off value > 35 IU/ml. Concluding CA125 as a good screening tool in patients with threatened miscarriage to predict pregnancies who developed to complete abortion. It had the advantage of being available and cheap test that can be used in screening and follow up of management in patients with threatened abortion. In agreement with the results of the present work, Al Mohamedy et al. (2016)¹² reported that, the level of serum CA-125 for the threatened miscarriage (miscarried) group was 54.28±11.4 IU/ml; while for the threatened miscarriage (continued) group it was 18.81 ± 8.02 IU/ml. The difference was statistically significant (P<0.001). They added, using a ROC curve for CA-125 in predicting the outcome of pregnancy in threatened miscarriage cases, the cut-off limit of 31.2 IU/ml of CA-125 level achieved sensitivity of 96.2% and specificity of 100%. CA-125 level above 31.2 IU/ml predicted occurrence of miscarriage with an overall accuracy of 99.4% Furthermore, results of the present work are comparable to those

reported by Mohamed S. Sweed (2016)¹³ who assessed the predictive value of single measurement of maternal serum CA-125 for pregnancy outcome in threatened miscarriage. Using Receiver-operating characteristic (ROC) curve analysis, optimal cut-off criteria of CA-125 > 58 IU/ml for prediction of occurrence of miscarriage in patients with threatened miscarriage was established with sensitivity of 78% and specificity 97%.

Results of Marwa Eid et al (2017)¹⁴ also showed that women who continued their first trimester of pregnancy showed a significantly lower level of CA 125 when compared with those who aborted. (34.9±11.053 vs. 61.9±19.21 P=0.022). The sensitivity, specificity, PPV and NPV of CA 125 predicting occurrence of abortion were 80.66, 100, 100, 95.4% respectively. Concluding CA125 is a good predictor for the outcome of first trimester of pregnancy in both normal women and those with threatened abortion.

Several cut-off values were suggested in other studies in order to predict pregnancy outcome in early viable pregnancies complicated by vaginal bleeding. In this study, a cut-off limit of 60 IU/ml of CA-125 level was suggested, with a sensitivity of 85% and specificity of 90%. Fiegler et al. (2003)¹⁵ used a cut-off value of 66.5 IU/ml with a sensitivity of 55%. Schmidt et al. (2001) used 65 IU/ml as a cut-off value and reported a sensitivity of 50% for this level. Azougi et al. (1996)¹⁶ used a 125 IU/ml as a cut-off value and reported a 100% sensitivity and specificity.

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.

Reference

1. Gerhavad I and Runnebaum B. Predictive value of hormone determinations in the first half of the pregnancy. Eur. J. Obstet. Gynec. Reprod.Biol.1984.17:1-17.
2. Kabawat SE, Bast RC, Welch WR et al .Immunopathologic characterizations of a monoclonal antibody that recognizes common surface antigen of human ovarian tumors of serous , endometrioid and clear cell types. Am.J .Clin.Pathol.1983.79:98-104.
3. Yu X, Cohen J, Deshmukh H, Zhang R, Shin JY, Osann K, Husain A, Kapp DS, Chen L and Chan JK. The association of serial ultrasounds and CA-125 prior to diagnosis of ovarian cancer –Do they improve early detection. Gynecol Oncol.2008.111:385-386.
4. Zeimet AG, Offner FA, Muller-Holzner E. etal. Peritoneum and tissues of the female reproductive tract as physiological sources of Ca-125. Tumor Biol.1998.19:275-282.
5. Berek S.J “Novak’s Gynecology”, 13th Ed. Lippincott William & Wilkins; 2002:518.
6. Speroff L, FritZ M, A .Clinical Gynecology endocrinology and infertility. 7th ed., Lippincott Williams and Wilkins 2005; 11-12.
7. Cunningham F.G, “Williams’s obstetrics”, 22nd ed.USA, Appleton & Lange, 2005.
8. Check JH, Nowroozi K, Winkel CA. Serum CA125 levels in early pregnancy and subsequent spontaneous abortion. Obstet Gynecol 1990; 75:742-744.
9. Kobayashi F, Sagawa N, Nakamura K. Mechanism and clinical significance of elevated CA-125 levels in the sera of pregnant women. Am J Obstet Gynecol 1989; 160:563-566.
10. Niloff JM, Knapp RC, Schaetzl E. CA-125 antigen levels in obstetric and gynecologic patients . Obstet Gynecology 1984; 64:703-707.

11. Abd Elrau of M Oun et. al. Role of Both Serum CA125 and Ultrasound in Prediction of Pregnancy Outcome in First trimester Threatened Miscarriage. International Journal of Life Sciences. 2018; 7(2):79-84.
12. Maged AM, Mostafa W. AI, et al. "Correlation of Serum CA-125 and Progesterone Levels with Ultrasound Markers in The Prediction of Pregnancy Outcome in Threatened Miscarriage" International journal of fertility & sterility. 2015; 9(4):506-11.
13. Sweed MS, Sammour HM, Bakr AA. Serum CA-125 for Early Prediction of Miscarriage. Med J Obstet Gynecol. 2016; 4(1):1077.
14. Eid, Marwa, Abdallah Amal. Cancer antigen 125 (CA-125) and serum progesterone as predictors of fate of threatened abortion: Case control study. Evidence Based Women's Health Journal, 2018, 177-183.
15. Fiegler P, Katz M, Kaminski K, Rudol G. Clinical value of a single serum CA-125 level in women with symptoms of imminent abortion during the first trimester of pregnancy. J Reprod Med. 2003; 48:982-988.
16. Azogui G, Yaronovski A, Zohar S, Ben-Shlomo I. CA-125 is elevated in viable pregnancies destined to be miscarried: a prospective longitudinal study. Fertil Steril. 1996; 65:1059-1061