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ROLE OF CA-125 IN PREDICTING THE OUTCOME OF THREATENED MISCARRIAGE

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ABSTRACT

Background: Cancer antigen 125 (CA-125) is a glycoprotein whose origin during pregnancy is uncertain. It emerges during the first trimester and returns to non-pregnancy levels in late pregnancy. The aim of this study was to investigate any potential correlation between CA-125 levels in threatened miscarriage during the first trimester and pregnancy outcomes. **Patients and Methods:** A prospective case-control study was conducted on 165 women, including 79 women with threatened miscarriage (group 1) and 86 healthy pregnant women (group 2). The age of participants ranged from 13 to 43 years, with a mean age of 24.96 ± 5.86 years. Venous blood samples were collected to measure CA-125 levels and compare them between the two groups. The participants were followed up until 20 weeks of pregnancy to determine the outcome. **Results:** No significant difference in CA-125 levels was observed between the cases (15.50 ± 10.93) and controls (20.47 ± 35.61), with a P-value of 0.398. However, within the cases group, there was a highly significant difference in CA-125 levels between cases that continued their pregnancies and cases that ended in miscarriage ($P < 0.001$). Similarly, within the control group, CA-125 levels were significantly higher among those whose pregnancies ended in miscarriage compared to those who continued their pregnancies, with a P-value of 0.003. **Conclusion:** Statistically significant differences, indicated by higher CA-125 readings, were observed in pregnancies that ended in miscarriage in both the threatened miscarriage and control groups. This suggests that elevated CA-125 levels may indicate underlying trophoblastic injury, potentially leading to later miscarriage in the control group.

KEYWORDS: Role, CA-125, Predicting, Outcome, Threatened, Miscarriage.

INTRODUCTION

Vaginal hemorrhage in the first half of pregnancy, when the cervix is closed and there is a viable foetus, is indicative of a threatened miscarriage. During the first two trimesters, approximately 25 percent of expectant women experience vaginal haemorrhage. Approximately fifty percent of these cases may result in a miscarriage. In a threatened miscarriage, the bleeding is typically mild to moderate and may be accompanied by lower abdominal pain or cramping.[1] Chromosomal abnormalities in the foetus are the leading cause of miscarriages, accounting for approximately half of all cases. However, maternal factors can also increase the risk of an imminent miscarriage. A higher risk of threatened miscarriage has been associated with maternal infections, chronic diseases such as diabetes and thyroid disease, extreme weight, and maternal lifestyle choices such as alcohol, tobacco, and illicit substance use.[2] Although threatened miscarriage can occur in women of all ethnicities, it is more prevalent in elderly women who conceive. Age increases a woman's likelihood of experiencing a threatened or spontaneous miscarriage. In addition, the number of previous pregnancies (parity) increases the risk of a threatened miscarriage.[3] The pathophysiology of an impending miscarriage involves disruption of the delicate balance of placental development and function. Early placental development is dependent upon the equilibrium between oxygenated maternal blood and the trophoblast's (placental tissue) capacity to process oxygen and eradicate its metabolites. Early pregnancy bleeding can contribute to adverse pregnancy outcomes such as miscarriage, preterm prelabor membrane rupture, preterm labour, foetal growth restriction, and preeclampsia.[4] A threatened miscarriage is typically treated with expectant

management until symptoms resolve. Analgesia can be used to assuage pain, and bed rest is frequently advised, although its efficacy has not been established. The progression of a threatened miscarriage to an inevitable, incomplete, or complete miscarriage should be monitored. To assess foetal viability and rule out ectopic pregnancy or retained products of conception, repeated pelvic ultrasounds are performed. Evaluation may also involve blood tests, such as beta-HCG levels, RH factor, haemoglobin, and hematocrit.[5,6] This protein, also known as cancer antigen 125, is encoded by the MUC16 gene. It is a large, highly glycosylated mucin found in various tissues, including the female reproductive tract. CA-125 is a biomarker for certain cancer types and is implicated in tumour metastasis, proliferation, and chemotherapy resistance.[7] However, the relationship between CA-125 and threatened miscarriage remains ambiguous, as studies have produced contradictory results. Some studies have discovered a positive correlation between elevated CA-125 levels and spontaneous miscarriage, while others have failed to find a consistent relationship. During pregnancy, CA-125 levels may fluctuate and be influenced by a variety of factors. Further study is required to comprehend the connection between CA-125 and threatened miscarriage.[8] The aim of study is to evaluation of any possible correlation between CA-125 level in threatened miscarriage (1st trimester) and its pregnancy outcome.

METHOD

This prospective case-control study was conducted at the Department of Obstetrics and Gynecology in Babylon Teaching Hospital for Maternity and Pediatrics between February 2019 and September 2019. The study received approval from the Iraqi Board of Medical Specialization, and the patients and control women provided informed consent. The study included 200 pregnant women in their first trimester of pregnancy, ranging in age from 13 to 43 years. Their parity ranged from 0 to 6, and gestational age ranged from 6 to 13 weeks. Out of the 200 participants, 100 were women with threatened miscarriage who presented to the hospital with symptoms related to threatened miscarriage, such as vaginal bleeding, lower abdominal pain, and back pain. Abdominal and transvaginal ultrasounds were performed using a Philips ultrasound machine to confirm the presence of a viable fetus. The second group consisted of 100 healthy pregnant women (control group) who were free of symptoms and signs and had confirmed fetal viability by ultrasound. During the follow-up period, some participants were lost to follow-up, resulting in a final sample size of 79 in the threatened miscarriage group and 86 in the control group. Both groups underwent history taking and physical examinations based on a specially designed questionnaire to assess risk factors. The questionnaire included information on age, last menstrual period (LMP), gravida and parity, ABO and Rh blood types, symptoms at presentation, gynecological history, past medical history, family history, and drug history. Exclusion criteria were established during the selection process and included women with conditions such as endometriosis, pelvic inflammatory disease (PID), ovarian cysts, infertility, uterine fibroids, ovarian tumors, liver cirrhosis, pancreatitis, lung and kidney diseases, diabetes mellitus, thyroid disease, previous uterine surgery, anti-phospholipid syndrome, assisted reproductive techniques, breast cancer, multiple pregnancy, ectopic pregnancy, molar pregnancy, and recurrent miscarriage. Ultrasound examinations were performed on all participants and control group by an expert radiologist. After confirming the diagnosis through history, physical examination, and ultrasound, 3 ml of venous blood was collected using a gel tube. The sample was allowed to clot at room temperature for approximately 30 minutes, and then it was centrifuged for 3 minutes at 4000 rpm. The serum sample was stored at -20°C until analysis. CA-125 levels were measured using an ELISA kit according to the manufacturer's recommendations. Statistical analysis was performed using SPSS® Software (version 23.0 for Linux®). Qualitative data were presented as numbers and percentages, while continuous numerical data were presented as mean ± standard deviation. A p-value of less than 0.05 was considered statistically significant. The chi-square test was used to compare between the groups.

RESULTS

This study included a total of (165) pregnant females, (79) cases with threatened miscarriage and (86) controls. Age of participants ranged from (13-43) years with a mean age of (24.96 ± 5.86) years. No significant difference in age was observed between cases (24.61 ± 6.00) and controls (25.29 ± 5.74), Student's t-test = 0.75, P- value = 0.456. Table (1) Show the Demographic criteria among study participant.

Table 1: Demographic criteria among study participant.

criteria	Cases means ± S/D	Controls means ± S/D	P-Value
Age (years)	6.00 ± 24.61	5.74 ± 25.29	0.456
Gestational Age (weeks)	2.20 ± 9.10	1.92 ± 9.40	0.362
Parity **Nulliparous Primipara multipara**	11 24 44	13 19 54	0.05>

Highest proportion of participants were of blood group (O+) with a proportion of (38.79%), followed by (A+) with a proportion of (33.33%) and (B+) with a proportion of (12.12%). Rh -ve participants formed only (7.27%) of total study sample. Serum CA-125 was compared between cases and controls. No significant difference in CA-125 level was observed between cases (15.50 ± 10.93) and controls (20.47 ± 35.61), P-value = 0.398 (Table 1).

Table 2: CA-125 level by study group.

Group	Mean	CA-125 level SD	Range	P-value
Case (n=79)	15.50	10.93	0–47	0.398
Control (n=86)	20.47	35.61	1.5 – 238	
Total (n=165)	18.09	26.83	0-238	

Within cases group, another comparison was performed between cases with normal outcome and cases with miscarriage regarding CA-125 level. There was a highly significant difference in CA-125 level between cases that continued her pregnancy and cases ended with miscarriage (P < 0.001), as detailed in Table (2).

Table 3: comparison of CA-125 level with cases group according to outcome.

Outcome	Mean	CA-125 level SD	Range	P-value
Normal (n=69)	13.63	9.87	0–47	**< 0.001***
miscarriage(n=10)	28.40	9.35	13-38	
Total (n=79)	15.50	10.93	0-47	

* Significant at P < 0.05

Table (4): comparison of CA-125 level with control group according to outcome.

Outcome	Mean	CA-125 level SD	Range	P-value
Normal (n=83)	14.20	11.71	1.5 – 49.8	**0.003***
miscarriage(n=3)	194.00	38.11	172 - 238	
Total (n=86)	20.47	35.61	1.5 - 238	

* Significant at P < 0.05

Regarding the outcome of pregnancy between the two study groups; the cases group had shown significantly higher proportion of miscarriage compared to control group, with chi-square = 4.77, P-value = 0.029. Details are provided in Table (4). Relative risk (RR) for threatened miscarriage cases to have an outcome of miscarriage was (3.63), with 95% confidence interval of (1.03 – 12.71).

Table 5: Outcome of pregnancy by study group.

Threatened miscarriage				
Outcome (Cases)	**Exposed (Controls)**	**Non-exposed**	**Total**	**P-value**
Normal	69 (87.34%)	83 (96.51%)	152 (92.12%)	**0.029***
Miscarriage	10 (12.66%)	3 (3.49%)	13 (7.88%)	
Total	79 (100%)	86 (100%)	165 (100%)	

* Significant at P < 0.05

DISCUSSION

The assessment of miscarriage risk in early pregnancy commonly involves the use of ultrasound, serum β-HCG, and progesterone levels.[9] However, these tests have limited sensitivity during the first trimester. While CA-125 levels have been helpful in diagnosing and monitoring ovarian carcinoma[10], some studies suggest its potential as a predictive marker for miscarriage risk in early pregnancy.[11] In our study, we examined the association between threatened miscarriage and CA-125 levels. We found no significant difference between CA-125 levels and the study variables such as parity, gestational age, and blood groups. This finding is consistent with previous studies by Sweed et al. (2016)

and Adeku et al. (2019).[12, 13] CA-125 may play a role in preparing the endometrium for successful implantation.[14] Higher CA-125 levels have been associated with increased trophoblastic damage.[15] It could potentially serve as a prognostic factor for pregnancy outcomes by reflecting the extent of trophoblastic destruction.[16] In our study, serum CA-125 levels differed significantly between cases that resulted in normal pregnancies and cases that ended in miscarriage, indicating its potential as a predictor of outcome in threatened miscarriage cases. These findings align with a study by Al Mohamady et al. (2016).[16] However, we did observe a significant positive correlation between CA-125 and age among cases with threatened miscarriage, which contradicts a study by Magid et al. (2013).[17] However, conflicting results exist in the literature. A study by Mahdi B. (2009) found no statistically significant difference in CA-125 levels between patients who miscarried and those who continued their pregnancies, despite higher levels.[18] Some researchers suggest that sequential measurements of CA-125 may be a more sensitive prognostic marker.[18,19] Others have found that a single measurement of serum CA-125 is valuable for women with symptoms of imminent miscarriage.[20,21] In our study, we did not observe a significant difference in CA-125 levels between cases and controls, aligning with studies by Hornstein et al. (1995) and Schmidt et al. (2001).[22,23] However, a study by Mahdi (2009) in Baghdad reported higher CA-125 levels in threatened miscarriages compared to normal pregnancies, although the difference was statistically insignificant, possibly due to the small sample size.[24] In our study, 12.5% of the threatened miscarriage cases resulted in pregnancy loss, which differs from a study by Ayaty et al. (2007) reporting a miscarriage rate of 25%. This variation may be attributed to the inclusion of ultrasound assessment of viability in our study.[25]

CONCLUSION

Statistically significant difference (higher readings of CA-125) were observed in pregnancies ended with miscarriage in both women groups (threatened and control groups) which explain that higher CA-125 level may uncover a hidden trophoblastic injury in the control group that lead them to miscarry later on. No significant difference in CA-125 levels between normal pregnancy and threatened miscarriage groups.

REFERENCES

1. Karataşlı V, Kanmaz AG, İnan AH, Budak A, Beyan E. Maternal and neonatal outcomes of adolescent pregnancy. Journal of gynecology obstetrics and human reproduction, 2019 May 1; 48(5): 347-50.
2. Hendriks E, MacNaughton H, MacKenzie MC. First Trimester Bleeding: Evaluation and Management. American family physician, 2019 Feb 1; 99(3): 166-74.
3. Goodarzi P, Falahzadeh K, Aghayan H, Payab M, Larijani B, Alavi-Moghadam S, Tayanloo-Beik A, Adibi H, Gilany K, Arjmand B. Therapeutic abortion and ectopic pregnancy: alternative sources for fetal stem cell research and therapy in Iran as an Islamic country. Cell and tissue banking, 2019 Mar 15; 20(1): 11-24.
4. Boiko VI, Nikitina IM, Babar TV, Boiko AV. The problem of miscarriage in multiple pregnancy. Wiadomosci lekarskie (Warsaw, Poland: 1960), 2018; 71(7): 1195-9.
5. Carp HJ. Progestogens and pregnancy loss. Climacteric, 2018 Jul 4; 21(4): 380-4.
6. Wahabi HA, Fayed AA, Esmaeil SA, Bahkali KH. Progestogen for treating threatened miscarriage. Cochrane Database of Systematic Reviews, 2018; (8).
7. Pillai RN, Konje JC, Richardson M, Tincello DG, Potdar N. Prediction of miscarriage in women with viable intrauterine pregnancy—A systematic review and diagnostic accuracy meta-analysis. European Journal of Obstetrics & Gynecology and Reproductive Biology, 2018 Jan 1; 220: 122-31.
8. Kanmaz AG, Inan AH, Beyan E, Budak A. The effects of threatened abortions on pregnancy outcomes. Ginekologia Polska, 2019; 90(4): 195-200.
9. Jouppila P, Huhtaniemi I and Tapanainen J. Earlypregnancy failure, study by ultrasound and hormonalmethods. Obst. Gynea, 1980; 55: 42-47.
10. Crombach G, Scharl A, Würz H. CA 125 in normal tissues and carcinomas of the uterine cervix, endometrium and fallopian tube. Archives of gynecology and obstetrics, 1989 Jun 1; 244(2): 113-22.
11. Fiegler P, Kaminski K and Wegrzyn P. Serum levels ofCA-125 Ag during the first trimester of pregnancy complications and the risk of miscarriage. Ginekol Pol, 2003; 74: 345-9.
12. Sweed MS, Sammour HM, Bakr AA. Serum CA-125 for Early Prediction of Miscarriage. Med J Obstet Gynecol, 2016; 4(1): 1077.
13. Adeku MA, Adegbola O, Ajayi GO. The predictive value of serum cancer antigen 125 (CA125) levels on pregnancy outcome in threatened miscarriages. Journal of perinatal medicine, 2019 Sep 25; 47(7): 704-9.
14. Yu X, Cohen J, Deshmukh H, Zhang R, Shin JY, Osann K, Husain A, Kapp DS, Chen L, Chan JK. The association of serial ultrasounds and CA125 prior to diagnosis of ovarian cancer—Do they improve early detection?. Gynecologic Oncology, 2008 Nov 1; 111(2): 385-6.
15. Madendag Y, Col-Madendag I, Kanat-Pektas M, Danisman N. Predictive power of serum CA-125 and LDH in the outcome of first trimester pregnancies with human chorionic gonadotropin levels below discriminatory zone. Archives of gynecology and obstetrics, 2009 May 1; 279(5): 661-6.

16. Al Mohamady M, Fattah GA, Elkattan E, Bayoumy R, Hamed DA. 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, 2016 Jan; 9(4): 506.
17. Maged AM, Mostafa WA. Biochemical and ultrasonographic predictors of outcome in threatened abortion. Middle East Fertility Society Journal, 2013 Sep 1; 18(3): 177-81.
18. Schmidt T, Rein DT, Foth D, Eibach HW, Kurbacher CM, Mallmann P, Römer T. Prognostic value of repeated serum CA 125 measurements in first trimester pregnancy. European Journal of Obstetrics & Gynecology and Reproductive Biology, 2001 Aug 1; 97(2): 168-73.
19. Bhattacharya A, Pramanik SR, Saha R, Bhaswati das, Sen OM. Correlation of Serial Beta HCG Titre and CA125 Estimation In Predicting Early Pregnancy Failure. IOSR J of Pharm, 2015; 5: 16-20.
20. 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. The Journal of reproductive medicine, 2003 Dec; 48(12): 982-8.
21. Yamane Y, Takahashi K, Kitao M. Prognostic potential of serum CA125 and pregnant markers in threatened abortion. Nihon Sanka Fujinka Gakkai zasshi, 1989 Dec; 41(12): 1999-2004.
22. Hornstein MD, Check JH, Hill JA. Serum CA 125 levels and spontaneous abortion. American journal of obstetrics and gynecology, 1995 Feb 1; 172(2): 695-9.
23. Schmidt T, Rein DT, Foth D, Eibach HW, Kurbacher CM, Mallmann P, Römer T. Prognostic value of repeated serum CA 125 measurements in first trimester pregnancy. European Journal of Obstetrics & Gynecology and Reproductive Biology, 2001 Aug 1; 97(2): 168-73.
24. Mahdi B. Estimation of CA-125 level in first trimester threatened abortion. Internet Journal Of Gynecology And Obstetrics, 2009; 1-5.
25. Ayaty S, Vahid Roudsari F, Tavassoly F. CA-125 in normal pregnancy and threatened abortion. International Journal of Reproductive BioMedicine, 2007 Jul 10; 5(3): 57-0.