https://africanjournalofbiomedicalresearch.com/index.php/AJBR
Afr. J. Biomed. Res. Vol. 27 (September 2024); 812-816

Research Article

CA 125- Levels in Women Experiencing Early Pregnancy Loss versus Healthy Pregnancy. A cross sectional study.

Mahantesh B Bhutal[1,4*], Basavaraj B Devaranavadagi[2], Ashalata A Mallapur[3]

[1]*Department of Biochemistry, Shri B M Patil Medical College, BLDE (Deemed to be university), Vijayapura, Karnataka. India
[2]Department of Biochemistry, Shri B M Patil Medical College, BLDE (Deemed to be university), Vijayapura, Karnataka. India
[3]Department of OBG, SNMC & HSK Hospital, Bagalkot, Karnataka. India
[4]*Department of Biochemistry, SNMC & HSK Hospital, Bagalkot, Karnataka. India

Abstract

Background & Objective: Pregnancy loss within 20 weeks of gestation is a common entity in the reproductive age group which leads to emotional and psychological upset. Half of the losses are due to chromosomal anomalies, thyroid disorders etc. majority of others are due to unknown causes under the first trimester and goes unnoticed. The objective of this study is to determine the level of **CA- 125** in women who have early pregnancy loss and compare the result with normal pregnancy.

Materials & Methods:This case-control study was conducted at HSK Hospital in departmentof OBG, involving 20 women who had early pregnancy loss without cause before 20 weeks as the cases and 20 women age and matching gestation under 20 weeks as healthy controls. Serum was separated and **CA- 125 level** was estimated in both groups using the CLIA method.

Results: The results showed that the aborted case group had a significantly higher CA -125 level than the control group with a mean of **54.7 ± 32.9IU/ml** in cases and **15.7 ± 5.28 IU/ml with p-value <0.001**.This implies that increased CA-125 may be linked to the first-trimester miscarriage which may be an inflammatory process in the endometrium.

Conclusion: CA-125 levels were significantly high in pregnancy loss cases compared to healthy controls.This research outcome could be helpful for further investigation of the possibility of using CA -125 as the predictor for EPL and its application in the field of antenatal medicine.

Keywords:CA-125(Cancer antigen -125), Early Pregnancy Loss (EPL), Biomarker, Pregnancy Complications, antenatal, CLIA (chemiluminescence immunoassay).

**Author for correspondence: Email: drmonty105@gmail.com*

Receiving Date: 10/07/2024 Acceptance Date: 20/08/2024

DOI: https://doi.org/10.53555/AJBR.v27i1S.1288

INTRODUCTION

Early pregnancy loss or abortion is defined as pregnancy loss occurring before twenty weeks of gestation or fetus weighing less than 500 grams prior to the age of viability [1]. It affects 5% of pregnant women and can have physical and psychological consequences for women and their families. Half of these are associated with a genetic abnormality, infections, or other identifiable uterine causes, the other 50% often lack the clear cause **[2,3].** Early gestational sac physiological hypoxia protects the growing fetus against the deleterious and teratogenic effects of O2 free radicals (OFRs). In miscarriage, development of the placento-decidual interface development is severely impaired resulting in early and widespread onset of maternal blood flow and major oxidative degeneration. **[4]**.

A glycoprotein known as cancer antigen-125 has been found to be expressed in significant amounts by fetal chorion, maternal deciduas, and amniotic fluid **[5].** Any normal discrepancy or damage of the deciduas or fetal membranes would result in elevation of maternal serum CA-125 levels**[6]**. This study was conducted to estimate CA125 and use it as a biomarker for the prediction of pregnancy loss.

Significance of the Study

EPL is a normal part of women's reproductive lives but is associated with physical and psychological morbidity. The discovery of biomarkers that can be used in the prediction and diagnosis of EPL can be very useful in prenatal care because it provides information for early management of the condition. In this regard, the findings of this present study that associates high CA 125 levels with EPL may assist in the development of new diagnostic approaches and the improvement of the practices of prenatal medicine. Furthermore, the detection of CA 125 in EPL could be useful in the elucidation of the mechanisms of early pregnancy loss and its prevention and treatment.

Materials and Methods

This case-control study aimed at comparing the serum CA 125 levels in women with EPL and those with normal pregnancies. The present study was conducted on the cases and controls attending the OBG department of HSK Hospital, Bagalkote, Karnataka. The duration of the study was from January 2023 to November 2023. The case group included 20 women who had a miscarriage before the 20th week of pregnancy. The participants were selected based on their medical history, and the diagnosis of miscarriage of an unknown cause. 20 healthy pregnant women under 20 weeks of pregnancy who were matched for age and sex made up the control group. The controls were chosen based on the gestational age to make it easier to compare the groups of cases.

Inclusion Criteria: Pregnant women within the age range of 20–41 years who had unexplained early pregnancy loss (cases) and whose age, sex, and parity matched women with normal pregnancy (controls) under 20 weeks of gestation.

Exclusion Criteria: Women with thyroid disorders, antiphospholipid syndrome, Hypertension, diabetes, uterine anomalies or other systemic diseases, baby anomalies on USG, etc. Cases with known causes of early pregnancy loss were excluded to ensure a focus on unexplained miscarriage.

Approval and Consent: The research has been approved by the BLDE (Deemed to be University) institution ethics committee **(Approval no- BLDE(DU)/IEC/814/2022-23)**. Informed and written consent has been attained from all the participants before any procedure was performed on them and the patient's identity was not revealed at any time during the study. 4 ml venous blood had been gathered from the participants and serum was separated. CA 125 level in serum samples was measured by CLIA (chemiluminescence immunoassay**)[7].** Using SPSS version 21, apply the "chi-square test", and unpaired "t" test. Mean CA 125 levels were then compared between the case group and the control group using the above tests. Both the group's mean and standard deviation were calculated. It was also possible to compare the significance of the differences between groups.

Results

The mean age of the patients and gestation weeks in Table 1 of the case and control groups show no statistical difference between the two groups. Table 2 shows the CA-125 level in the case group was 54.7 ± 32.9 IU/ml, and the control group was 15.7 ± 5.28 IU/ml. The comparison of these two groups showed a highly significant ($p < 0.001$) difference, which means that high levels of CA 125 are linked to early pregnancy loss in some cases.

Table 1. Age in cases and controls (not significant)

	Cases (N=20)	Controls (N=20)	p-value
Age in years	**26.2 ± 3.9 IU/ml**	**28.4 ± 8.18 IU/ml**	**0.71**
Gestational age (weeks)	**11 (9 -18 weeks**	**12 (10 -18 weeks)**	**0.58**

Table 2. CA-125 levels in cases and controls

Test	Cases (N=20)	Controls (N=20)	p-value
CA-125 (IU/ml)	**54.7 ± 32.9 IU/ml**	**15.7 ± 5.28 IU/ml**	**<0.001****

**** Highly significant**

Figure 1. CA-125 levels in cases and controls

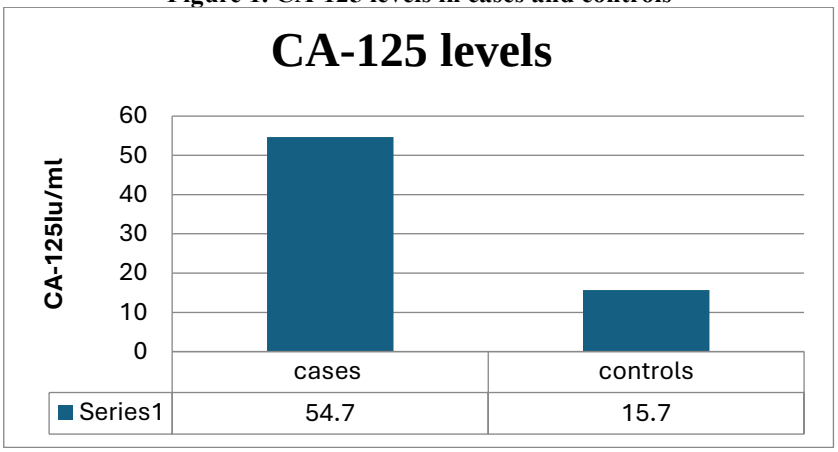


Table 3. Area Under the Curve(AUC)

Test Result Variable (CA- 125)

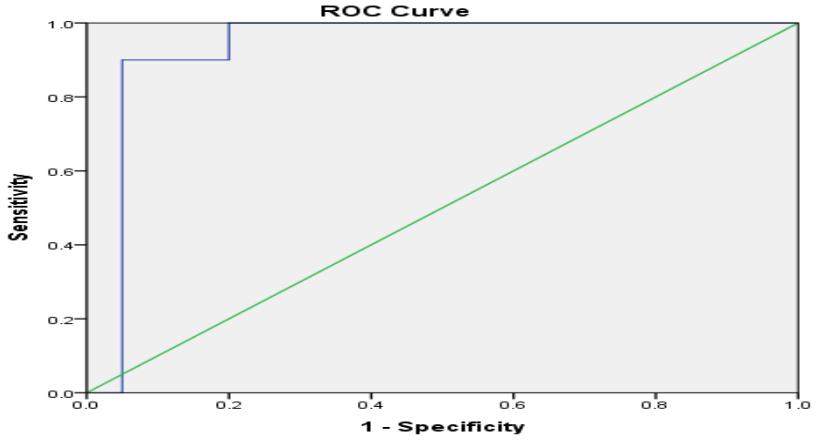
Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.935	.050	.000	.837	1.000

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

An AUC of 0.935 indicates the excellent discrimination ability of the CA-125 marker to determine abortions. A standard error of 0.05 suggests that the estimate is relatively precise. The 95% confidence interval is from 0.837 to 1.00. Since the observed change is above 0.5, it confirms that the CA-125 marker is useful in predicting the outcome, i.e., a high AUC of 0.935 has excellent discriminative power in predicting abortions. Narrow C.I. shows the performance of the test is robust and reliable, and the low standard error shows lesser variability. Thus, the CA-125 biomarker is a strong and reliable indicator for determining abortions.

Figure 2. ROC curve for prediction of pregnancy loss based on CA-125 level.



Statistical Analysis

The difference in CA 125 levels between the case and control groups was statistically significant with p < 001. This statistical significance goes on to confirm the hypothesis that high CA 125 is a risk predictor for early pregnancy loss.

Discussion

The study's findings indicate that there is a statistically significant difference in the CA 125 level between pregnant women with EPL and those who are not. The mean of CA 125 level in the case group was **54.7 ± 32.9 IU/ml**, compared to **15.7 ±5.28 IU/ml**. A difference of this magnitude goes a long way in explaining why CA 125 is a good marker for early pregnancy loss.

Our research supports the findings of Pillai et al.'s systematic review and meta-analysis, which found that serum CA-125 had a higher predictive value for pregnancy outcome than other hormones like progesterone and beta HCG **[8]**.

Study by Novi et al. showed median MOM values of CA 125 were significantly higher in women with vaginal bleeding (1.81 MOM) as compared both to non-bleeders (0.82 MOM; p < 0.01) and to the normal pregnancies (1.01 MOM; p < 0.05)

[**9**]. Threatened pregnancies had statistically significantly higher CA 125 serum values than non-threatened pregnancies, especially those with a negative outcome ($P < 0.01$). The CA 125 levels in the threatened pregnancies were positively correlated with the tropho-decidual hematoma volume ($r=0.839$, $P < 0.0001$.)This finding lends credence to the theory that CA-125 is released as a result of decidual damage or disruption **[10-11].**

While a study by Kobayashi **[12]** and Wafaa **[13]** observed that CA-125 levels were significantly higher in healthy outcomes compared to those who aborted. Many others studies showed a CA-125 single measurement is a valuable predictive marker for abortion**[14-15]**. Simultaneously, on the other side, a single measurement of CA-125 was not reliable enough to predict the outcome of abortion. Conversely, they proved that sequential assessment of serum CA-125 was a highly sensitive marker for prognosis in these patients. The differences between the case and control groups are significant in terms of CA 125 levels, which implies that this marker may reflect inflammation or pathological changes that are related to miscarriage **[16].**

Some authors have studied the correlation between CA 125 and pregnancy, and the outcomes have been inconclusive. For instance, study by Barooti E. reveal that elevated CA 125 is associated with an increased risk of miscarriage and can be the inexpensive prognostic test to identify the threatened abortion outcome**[17]**.

The discrepancies in the results could be explained by the differences in the research design, sample and method, and approach taken; therefore, more research is required to determine the relationship between CA 125 and recurrent miscarriage. If CA-125 is proven to be a biomarker, then it can be used in clinics for diagnosing EPL and, thus, enhance the prognosis of high-risk pregnancies. This would be especially relevant in prenatal care where the potential issues may have a severe effect on the patient's health.

Conclusion

This study shows that CA 125 levels are high in women who had early pregnancy loss compared to women with a healthy pregnancy, so CA- 125 could be used to predict early pregnancy loss. If CA-125 is proven to be a biomarker, then it can be used in clinics for diagnosing EPL and thus enhance the prognosis of high-risk pregnancies. This would be especially relevant in antenatal care where the potential issues may have a severe effect on the patient's health. Hence the study offers a rationale for the use of CA 125 as a biomarker for early pregnancy loss.

Limitations of the study.

One of the study's limitations is its short duration, which means it does not cover long-term effects, and another is the small sample size of 20 women in each group. To overcome these limitations and enhance external validity, future research should involve a larger patient population and multi-center trials to validate these results. Future research should take the form of prospective studies comparing changes in CA 125 levels during pregnancy and their effects on the developing fetus. Together with CA 125, other biomarkers may also be examined in order to enhance miscarriage understanding and predictive value overall.

Acknowledgement: I thank Dr Umesh Ramadurg and Dr Satish Potdar for their contribution.

References:

Abd-Alamieer WS, Al Dulaimi SA, Al-Taai AJ. Biochemical Markers for Prediction of Pregnancy Outcome in Cases of Recurrent Pregnancy Loss. Iraq Medical Journal. 2021 Mar 26;5(1):18-21.https://doi.org/10.22317/imj.v5i1.1009

Adeku M, Adegbola O, Ajayi G. The predictive value of serum cancer antigen 125 (CA125) levels on pregnancy outcome in threatened miscarriages. Journal of Perinatal Medicine. 2019;47(7): 704-709. https://doi.org/10.1515/jpm-2019-0097

Barooti E, Fakari F, Darvish S, & Tavakoly N. The Comparison of CA-125 Levels in Normal Pregnancy and Threatened Abortion. Journal of Obstetrics Gynecology and Cancer Research.2022; 7(3): 226–229. https://doi.org/10.30699/jogcr.7.3.226

Cumming GP, Klein S, Bolsover D, Lee AJ, Alexander DA, Maclean M, Jurgens JD. The emotional burden of miscarriage for women and their partners: trajectories of anxiety and depression over 13 months. BJOG. 2007 Sep;114(9):1138-45. https://doi.org/10.1111/j.1471-0528.2007.01452.x

Gidwani C, Meena BS, Meena M, Gera R. Role of serum CA-125 in predicting the outcome of threatened abortion.International Journal of ClinicalObstetrics,and Gynaecology.2019;3(2):14-8. https://doi.org/10.33545/gynae.2019.v3.i2a.05.

Jauniaux E, Poston L, Burton GJ. Placental-related diseases of pregnancy: Involvement of oxidative stress and implications in human evolution. Hum Reprod Update. 2006 Nov-Dec;12(6):747-55. https://doi.org/10.1093/humupd/dml016

Katsikis I, Rousso D, Farmakiotis D, Kourtis A, Diamanti-Kandarakis E, Panidis D. Receiver operator characteristics and diagnostic value of progesterone and CA-125 in the prediction of ectopic and abortive intrauterine gestations. Eur J Obstet Gynecol Reprod Biol. 2006 Apr 1;125(2):226-32. https://doi.org/10.1016/j.ejogrb.2005.10.014

Kenemans P, Yedema CA, Bon GG, von Mensdorff-Pouilly S. CA 125 in gynecological pathology--a review. Eur J Obstet Gynecol Reprod Biol. 1993 Apr;49(1-2):115-24. https://doi.org/10.1016/0028-2243(93)90135-Y

Kobayashi F, Sagawa N, Nakamura K, Nonogaki M, Ban C, Fujii S, et al. Mechanism and clinical significance of elevated CA 125 levels in the sera of pregnant women. Am J Obstet Gynecol. 1989;160(3):563-6. https://doi.org/10.1016/S0002-9378(89)80027-4

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. Arch Gynecol Obstet. 2009 May;279(5):661-6.https://doi.org/10.1007/s00404-008-0798-x

Noci I, Biagiotti R, Periti E, Baronci D, Torricelli F, Cefalà L, Branconi F, Borri P. Maternal serum CA 125 levels in first trimester abortion. Eur J Obstet Gynecol Reprod Biol. 1995 May;60(1):35-6. https://doi.org/10.1016/0028-2243(95)02073-X

Osmanagaolu MA, Karahan SC, Aran T, Güven S, Turgut E, Menteşe A, Bozkaya H. The Diagnostic Value of β-Human Chorionic Gonadotropin, Progesterone, and Ischemia-Modified Albumin and Their Combined Use in the Prediction of First Trimester Abortions. International Scholarly Research Notices. 2014;2014(1):846531. https://doi.org/10.1155/2014/846531

Pillai RN, Konje JC, Tincello DG, Potdar N. Role of serum biomarkers in the prediction of outcome in women with threatened miscarriage: a systematic review and diagnostic accuracy meta-analysis. Hum Reprod Update. 2016 Mar-Apr;22(2):228-39. https://doi.org/10.1093/humupd/dmv054

Rossen LM, Ahrens KA, Branum AM. Trends in Risk of Pregnancy Loss Among US Women, 1990-2011. Paediatr Perinat Epidemiol. 2018 Jan;32(1):19-29. https://doi.org/10.1111/ppe.12417.

Scarpellini F, Mastrone M, Sbracia M, Scarpellini L. Serum CA 125 and first trimester abortion. Int J Gynaecol Obstet. 1995 Jun;49(3):259-64. https://doi.org/10.1016/0020-7292(95)02371-I

Schmidt T, Rein DT, Foth D, Eibach HW, Kurbacher CM, Mallmann P, Romer T. Prognostic value of repeated serum CA 125 measurements in first trimester pregnancy. Eur J Obstet Gynecol Reprod Biol. 2001; 97(2):168-73.https://doi.org/10.1016/S0301-2115(00)00533-9.

Yadav K, Ojha P, Chopra A. Comparison of maternal serum CA-125 and ultrasonography findings as a prognostic marker in threatened abortion. Int J Reprod Contracept Obstet Gynecol.2021 June;10(6):2253-58. https://doi.org/10.18203/2320-1770.