Type of the Paper (Article)

Evaluation of the role of maternal serum high sensitivity C- reactive protein correlation with total and differential leucocytic count in predicting outcome in threatened abortion

Abd Elsamie A. Abd Elsamie[1], Rehab A. El-Sheshtawy[1], Hazem G. Abdel-Hameed[1], Tarek S. Ahmed[1*]

1 Department of obstetrics and gynecology, Faculty of Medicine, Fayoum University, Fayoum, Egypt.

* Correspondence: Tarek S. Ahmed, tareksayed7754@yahoo.com; Tel.: (002) 01288585747.

Abstract

Introduction: Miscarriage is a common complication of pregnancy occurring in 15% to 20% of all clinically recognized pregnancies. In many cases, the cause of miscarriage cannot be identified; however, among the recognized risk factors of miscarriage are maternal age over 34 years and paternal age over 40 years, previous history of two or more miscarriages, and maternal autoimmune factors.

Aim of the study: Maternal serum differential leucocytic count and high-sensitivity C-reactive protein (HSCRP) were evaluated in predicting spontaneous abortion in spontaneous pregnancies presenting with threatened spontaneous abortion.

Subjects and methods: 100 pregnant women were divided into two equal groups: the threatened abortion group and the control group.

Results: The mean values of WBCs, neutrophils, monocytes, and lymphocytes were significantly higher in the study group. Comparing the level of High sensitivity CRP among the studied groups showed the higher significant mean values of the high sensitivity- CRP in the sera of the study group than in the control group.

Conclusion: The current study recommends that increased serum levels of total and differential leucocytic count and serum levels of High sensitivity- CRP are the possible mechanisms involved in the first trimester threatened miscarriage

Keywords: Miscarriage; differential leucocytic count; HSCRP; threatened abortion.

1. Introduction

Vaginal bleeding is a commonly experienced disorder in pregnant women in the first trimester. It is related to ectopic pregnancy and miscarriage. Miscarriage is the most common complication of early pregnancy and occurs with decreasing frequency with increasing gestational age. Its incidence in clinical pregnancies varies from 8% to 20% during the first half of pregnancy [1].

First-trimester pregnancy complications are common, where the differential diagnosis includes life-threatening conditions such as miscarriage. In addition to miscarriage, vaginal bleeding can be associated with ectopic pregnancy,

trophoblastic disease, or cervical bleeding from causes unrelated to pregnancy, or bleeding may occur in pregnancies that proceed without further complications [2].

Recurrent pregnancy loss is a serious growing problem among young couples. Despite various clinical and experimental tests, there is no accurate and efficient diagnostic method during the early stages of pregnancy in cases without any known cause. Therefore, it is required to determine targeted genomic methods, besides karyotyping, clinical, and pathological examination [3].

Miscarriage can manifest clinically in several different ways. Most commonly, vaginal bleeding and cramping are present. But occasionally, regression of pregnancy symptoms or lack of Doppler-detected fetal heart tones by 10 to 12 weeks gestation is the first clinical sign. Miscarriage may also be discovered incidentally when asymptomatic patients undergo early ultrasound examinations for other reasons such as pregnancy dating or genetic screening [2].

Early pregnancy complications can be very upsetting. In patients with early pregnancy loss, there is a need to improve the reliability of diagnostic tests to allow prompt commencement of management options. These attempts can reduce the psychological burden of early pregnancy loss and morbidity and mortality [4].

Although transvaginal ultrasonography and serum human chorionic gonadotropin assays after pelvic examination are generally performed in the initial evaluation of patients with early pregnancy bleeding, the differential diagnosis of ectopic pregnancy and miscarriage may be challenging and can take one to two weeks. Several biomarkers were studied to date in an attempt to ease the prompt diagnosis of early pregnancy loss; however, none of the studied biomarkers has been deemed acceptable for clinical use [5].

A healthy pregnancy requires tightly coordinated immune responses. Investigating how different immune signaling pathways impact pregnancy and fetal development could provide important insights into congenital disorders and possible therapeutics to prevent pregnancy complications [6].

High sensitivity C- reactive protein (HS-CRP) is a diagnostic marker, while its increase above 8 mg/L indicates the risk of pregnancy loss. Systemic inflammatory response during physiological pregnancy is caused by the genetic “foreignness” of the fetus; however, the reason for pathologic pregnancy is the decompensation of systems that regulate systemic inflammatory response [7].

We, therefore, hypothesized that HSCRP might be involved in early pregnancy loss. Early detection of threatened abortion remains a challenge in the clinic. There is a serious need to identify accurate biomarkers that help in understanding the exact pathogenesis and early detection of threatened abortion. The present study aimed to assess the diagnostic value of maternal serum HS-CRP and DLC in threatened abortion.

2. Subjects and methods

2.1.Subjects

In the current study, 100 pregnant women were recruited. The procedures that were set out in the study protocol, pertaining to the conduct, evaluation, and all of the study documentation were approved by ethical and research Committee of the Council of OB\GYN Department, Fayoum University. After enrollment, written informed consent was taken after explanation of the aim of the study. Participants were divided into two groups as follows:

1- Study group: That included 50 healthy women presenting with threatened miscarriage.

2- Control group: That included 50 healthy women with an uncomplicated single pregnancy.

2.2.Inclusion criteria

All cases were pregnant women in the 1st trimester and presented with vaginal bleeding

2.3.Exclusion criteria

Pregnant patients with associated medical disorders, history of recurrent abortion, or any other risk factors that increased abortion rate were excluded.

2.4.Methodology

The current study aimed to assess the accuracy of HS-CRP and total differential leucocytic count in predicting pregnancy outcome in women presenting with threatened miscarriage in the first trimester. Full history, clinical examination, ultrasound examination, and laboratory investigations were done for each patient.

2.5.Statistical analysis

Patients' data were recorded in spread sheet Microsoft office excel 2010. The statistical tests were performed using SPSS Inc., Chicago, Version 16. We used the one-way ANOVA test to analyze continuous variables. The Chi square x2 test was used to analyze categorical variables. $P<0.05$ was considered statistically significant. Quantitative data were described using mean and standard deviation for normally distributed data while abnormally distributed data was expressed using median, minimum and maximum. For normally distributed data, comparison between two independent population were done using independent t test.

3. Results

When comparing the level of High sensitivity- CRP among the studied groups, the result of the present work showed that the mean values of HS-CRP showed a highly significant increase in the study group, when compared to the control group, as shown in **Table (1)** and **Figure (1)**.

Table 1: Comparison of serum HS-CRP levels among groups.

	Control group (n=50)	Study group (n=50)	*P-value*	% Change
HS – CRP (mg/dl)	5.17±2.04	8.73±1.55	<0.001*	+ 68.86%

n: number. Values are presented as mean ± SD, * statistically significant.

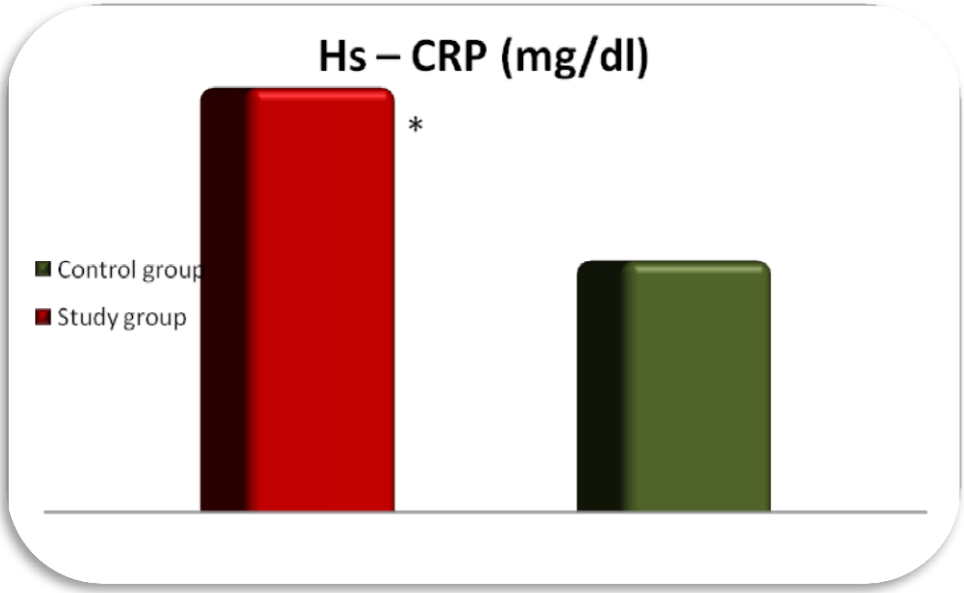


Figure 1: Comparison of Serum HS-CRP level among groups. '*' denotes statistically significant values at *P<0.001*.

When comparing the pregnancy outcome among the studied groups, the result of the present work showed that the mean values of continued pregnancy were significantly lower in study group than the control group. While, the mean values of miscarriage were highly significant in study group when compared to control group, as shown in **Table (3)** and **Figures (2-3).**

Table 2: Comparison of Pregnancy outcome among groups.

	Control group (n=50)	Study group (n=50)	*P-value*	% Change
Continue Pregnancy	30	45	<0.001*	-33.33%
Miscarriage	20	5	<0.001*	-300%

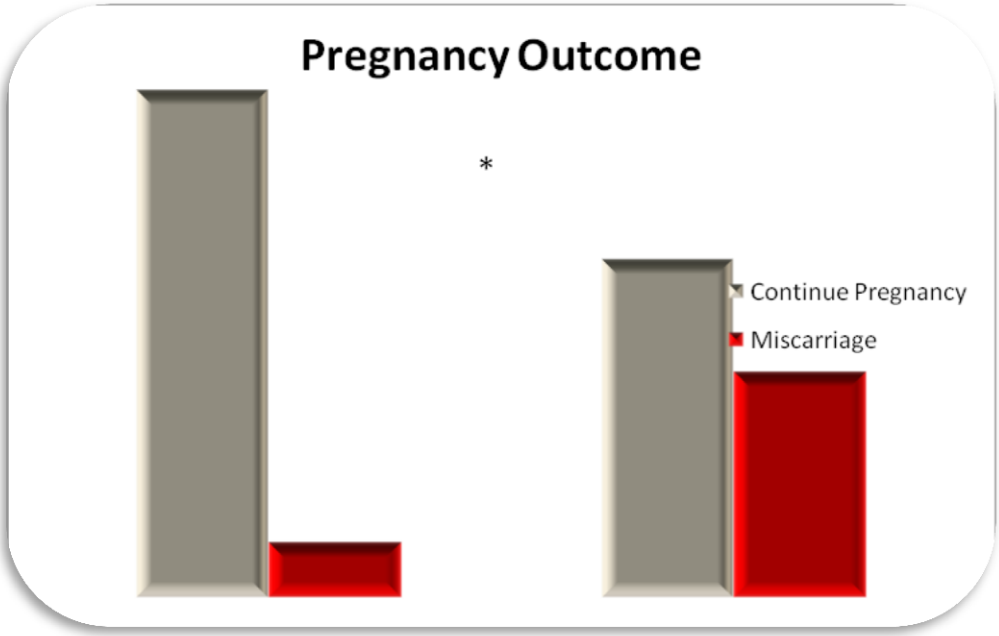
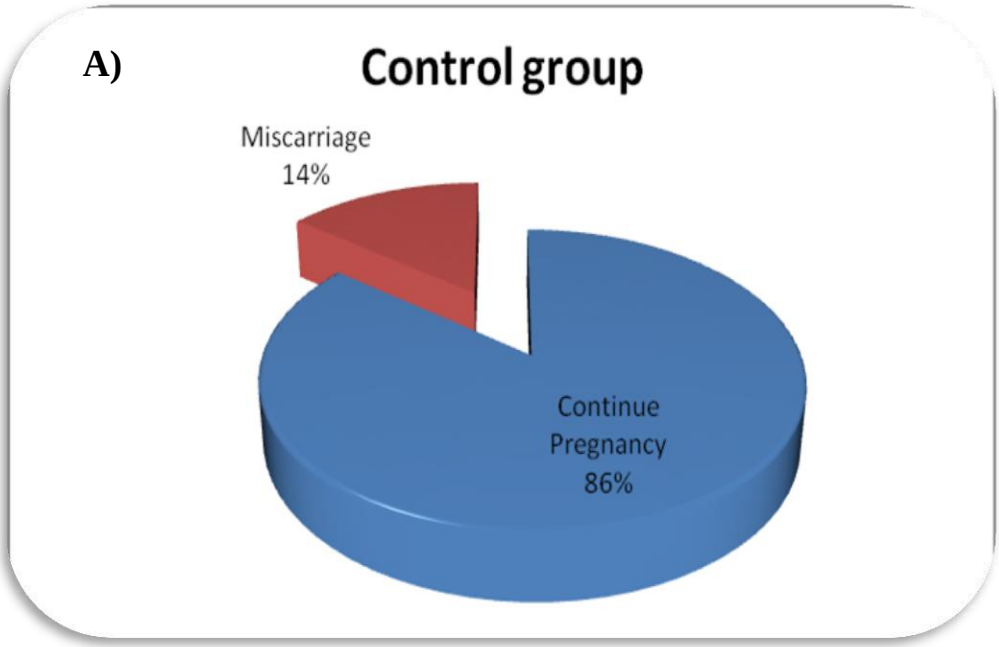


Figure 2: Comparison of Pregnancy outcome among groups. '*' denotes statistically significant values at *P<0.001*.



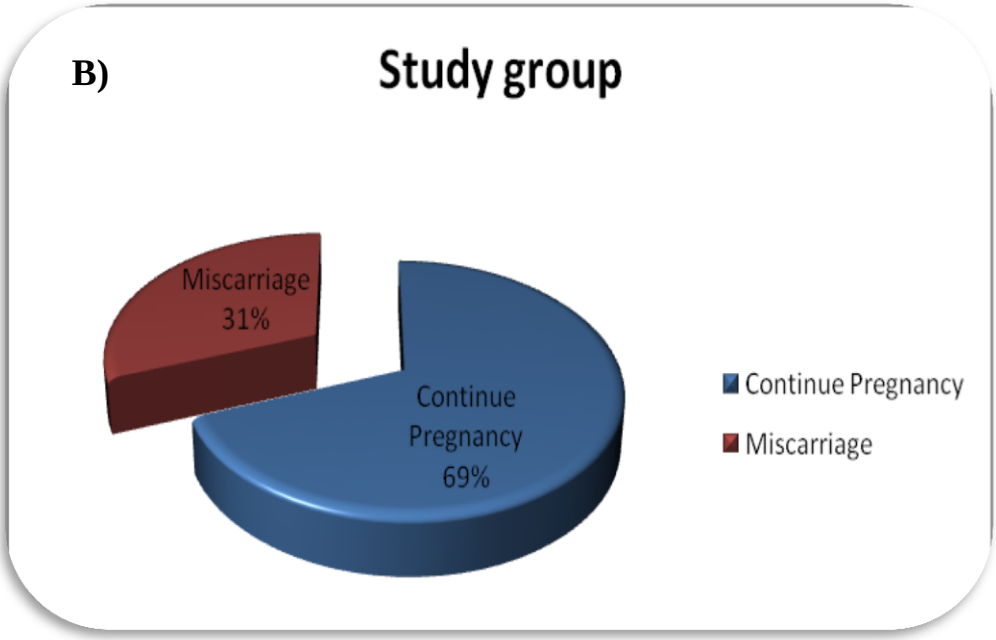


Figure 3: Pregnancy outcome in the study population. A) Control group, B) Study group.

4. Discussion

HS-CRP is an acute-phase protein secreted by the liver in response to inflammation. It is the protein that binds to the C-polysaccharide of the pneumococcal cell wall, and its levels in the serum can be detected using high-sensitivity assays [8].

Measurements of HS-CRP serum levels in reproductive medicine are limited to screening pre-eclampsia and, more recently, for screening gestational diabetes in obese women [9]. HS-CRP is a diagnostic marker, which indicates the presence of inflammatory processes in the body of pregnant women [10]. It is well-known, that HS-CRP can stimulate an inflammatory response by activating the classical complement pathway, tissue damage, and induction of pro-inflammatory cytokines in monocytes. Those factors can cause adverse pregnancy outcomes [8].

In our study, when comparing the level of HS-CRP among the studied groups, the result showed that the mean values of serum HS-CRP were significantly higher in the study group than in the control group.

That was in agreement with with the study conducted by Jauniaux *et al.* (2015), in which the particibants had high serum CRP level that resulted in pregnancy loss [10]. Also, Bondarenko *et al.* (2018) found that HS-CRP is the most sensitive and fastest indicator of tissue damage during inflammation [8]. Besides, Pregnant women with high levels of serum CRP risked preterm delivery [8].

Comparison of both groups, according to the outcome of pregnancy, revealed that in the study group (n=50), the spontaneous miscarriage was 20 cases (40%), while in the control group (n=50), the spontaneous miscarriage was five cases (10%) only.

There was a statistically significant difference between the two studied groups according to the outcome of pregnancy (spontaneous miscarriage and continued pregnancy).

Our data also indicated that the role of HS-CRP is limited and didn't provide any additional information for the management of threatened spontaneous abortion in spontaneous pregnancies. That suggested that serum HS-CRP is a reliable marker for screening pregnant women through assisted reproduction techniques at risk of premature delivery after first-trimester threatened spontaneous miscarriage [10].

An increased level of the marker of systemic inflammation HS-CRP testifies to its active participation in the launch of a complex mechanism for the development of labor activity and the occurrence of fetal disorders, which was confirmed in groups of pregnant women with clinical complications in different pregnancy periods [8].

5. Conclusion

In conclusion, threatened miscarriage pregnant women (study group) showed significant increase in total leucocytic count, neutrophils, monocytes, and lymphocytes, as compared with the control group. However, eosinophils and basophils were insignificantly higher in the study group when compared with the control group. In addition, serum levels of HS-CRP significantly increased in threatened miscarriage pregnant women when compared with the control group.

Acknowledgments

Authors would like to acknowledge to all doctors and staff of Department of Obstetrics and Gynecology, Fayoum University Hospital for their sincere support and help.

Funding: This research is not funded.

Ethical Approval Statement: The study was approved by the Institutional Ethics Committee of Fayoum Faculty of Medicine, Fayoum, Egypt.

Informed Consent Statement: Written informed consents were obtained from all patients.

Conflicts of Interest: All authors declare no conflict of interest.

References

1. Norwitz ER. Overview of the etiology and evaluation of vaginal bleeding in pregnant women. In: UpToDate, Post TW, editors. Waltham, MA: UpToDate. 2014.
2. Deutchman M, Walker JE. First-Trimester Pregnancy Complications. In: Leeman L, Quinlan JD, Dreasang LT, Gregory DS (Eds.) ALSO Advanced Life Support in Obstetrics Provider Manual (8th edition). Leawood, KS: American Academy of Family Physicians 2017.

3. Moghbeli M. Genetics of recurrent pregnancy loss among Iranian population. Mol Genet Genomic Med. 2019 Sep;7(9):e891. doi: 10.1002/mgg3.891.
4. Tulandi T. Spontaneous abortion: Risk factors, etiology, clinical manifestations, and diagnostic evaluation. In: UpToDate, Post TW editors. Waltham, MA: UpToDate. 2014.
5. Shaw JL, Diamandis EP, Horne AW, Barnhart K, Bourne T, Messinis IE. Ectopic pregnancy. Clin Chem. 2012 Sep;58(9):1278-85. doi: 10.1373/clinchem.2012.184168.
6. Yockey LJ, Iwasaki A. Interferons and Proinflammatory Cytokines in Pregnancy and Fetal Development. Immunity. 2018 Sep 18;49(3):397-412. doi: 10.1016/j.immuni.2018.07.017.
7. Francis F, Bhat V, Mondal N, Adhisivam B, Jacob S, Dorairajan G, Harish BN. Fetal inflammatory response syndrome (FIRS) and outcome of preterm neonates - a prospective analytical study. J Matern Fetal Neonatal Med. 2019 Feb;32(3):488-492. doi: 10.1080/14767058.2017.1384458.
8. Bondarenko N. Evaluation of high-sensitivity c-reactive protein levels during various periods of pregnancy in woman, infected with parvovirus–B19 infection. EUREKA: Health Sciences, 2018; (2):3-8. doi: 10.21303/2504-5679.2018.00604.
9. Vashist SK, Czilwik G, van Oordt T, von Stetten F, Zengerle R, Marion Schneider E, Luong JH. One-step kinetics-based immunoassay for the highly sensitive detection of C-reactive protein in less than 30 min. Anal Biochem. 2014 Jul 1;456:32-7. doi: 10.1016/j.ab.2014.04.004.
10. Jauniaux E, Gulbis B, Jamil A, Jurkovic D. Evaluation of the role of maternal serum high-sensitivity C-reactive protein in predicting early pregnancy failure. Reprod Biomed Online. 2015 Mar;30(3):268-74. doi: 10.1016/j.rbmo.2014.11.009.