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EVALUATING HEMATOLOGICAL MARKERS IN DIAGNOSING CESAREAN SCAR PREGNANCY: A PREDICTIVE APPROACH

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ABSTRACT

Background: The prevalence of Cesarean scar pregnancy (CSP) is on the rise, posing serious risks to maternal health. This study explores the potential of inflammation indicators derived from hematological parameters in detecting CSP.

Methodology: This was a cross – sectional, prospective study, conducted at a tertiary care hospital. This study involved 172 subjects, divided into two groups: CSP (84 participants) and normal pregnancy (88 participants). Initial assessments included measuring various blood parameters such as neutrophils, lymphocytes, monocytes, thrombocytes, and systemic inflammatory index (SII) (calculated as neutrophil x platelet / lymphocyte ratio), along with the neutrophil – lymphocyte ratio, monocyte – lymphocyte ratio, and platelet – lymphocyte ratio. Diagnosis of CSP and NP were confirmed via transabdominal or vaginal ultrasound. The data was analyzed using SPSS 24.0. A p-value of 0.05 was considered as statistically significant.

Results:

Significant disparities were noted between the CSP and control groups in several areas, including average age, total pregnancies, parity, number of surviving offspring, history of abortions, number of previous cesarean sections, and frequency of dilatation and curettage procedures. Additionally, values of monocytes and monocyte / lymphocyte ratio (MLR) were notable higher in the CSP group.

Conclusion: The study indicates that simple, affordable, and widely accessible hemogram parameters, particularly monocytes and MLR values, are significantly elevated in CSP vases. These findings suggest that such blood parameters could effectively complement ultrasonography in diagnosing CSP.

Keywords: Hemogram, Pregnancy, Cesarean scar pregnancy, Diagnosis, Prediction.

Introduction

Pregnancies developing in the cesarean section scar, known as Cesarean scar pregnancies (CSP), are increasingly observed worldwide. This rise is thought to be linked with the growing number of cesarean deliveries[1]. While the exact frequency of CSP is not clear, it is estimated to occur in about 1 in 1800 to 1 in 2500 of these deliveries. Notable, CSP represents about 6.1% of ectopic pregnancies in those with a history of cesarean section[2]. Growing awareness among healthcare providers has led to more frequent identification of this condition. CSP can present in various ways, and often, symptoms might not be initially apparent. Diagnosing CSP poses challenges; though ultrasound is the go-to diagnostic method, in some cases, magnetic resonance imaging proves useful. Significant diagnostic clues are the presence of a pregnancy sac in the lower section of the uterus during the first trimester and a history of cesarean delivery. CSP often serves as an early stage in the development of the placenta accreta spectrum (PAS)[3,4].

The root causes of CSP are still not completely understood. It is theorized to be associated with the lack of the nitabuch layer in the weakened decidua, which may predispose individuals to both CSP and PAS[5]. The pathophysiological processes of CSP and PAS are believed to be similar. Recent findings indicate that blood flow to the scar left by a cesarean section might promote invasion by trophoblasts, triggering an inflammatory response. Inflammatory markers like the neutrophil – lymphocyte ratio (NLR), platelet – lymphocyte ratio (PLR), and monocyte – lymphocyte ratio (MLR) have been identified as useful in this context[6]. Elevated neutrophil counts typically point to active inflammation, while lymphocyte counts help in modulating this inflammatory response. PLR, in particular, is recognized as an indicator of both thrombosis and ongoing inflammation[7].

The objective of this research is to assess the efficacy of inflammation markers found in blood tests in detecting and predicting CSP early on. Undiagnosed CSP can result in significant health risks, including severe morbidity, and mortality.

Materials and Methods

This study examined the initial trimester of Cesarean scar pregnancies (CSP) and normal pregnancies (NP), through a cross – sectional, prospective study at a tertiary care hospital. This study was conducted from March 2020 to February 2022, following approval from ethical committee of the institution. A total of 172 patients were included in this study. Following informed consent from all participants, detailed demographic and obstetric profiles of the participants were compiled. The study divided these participants into two distinct groups: those with CSP and those with NP, maintain parity in group sizes. The research focused on the first trimester, defined as 0-14 weeks of gestation, for both categories. Participants with a background of hyperemesis, impeding miscarriage, twin gestation, a history of preeclampsia in previous pregnancies, any form of maternal systemic disease including diabetes, renal complications, thyroid, cardiac, hematological disorders, chronic

hypertension, cancer or autoimmune conditions, or habits of smoking and alcohol consumption were excluded. Criteria for including in the CSP group required the pregnancy to be situated in the isthmic region of the anterior uterine wall, with an evacuated uterus and cervical canal, diminished or non-existent myometrial thickness between the bladder and the gestational sac, and visible trophoblastic blood flow near the sac. All identified CSP cases were treated with dilatation and curettage (D & C). The NP group consisted of early gestation instances showing intrauterine sacs and normal fetal heart activity, verified through first – trimester ultrasound scans. Additionally, this group included randomly chose women with previous cesarean deliveries who had experiences healthy subsequent births.

Upon admission, complete blood count tests were conducted on all the pregnant participants. These tests measured level of hemoglobin, lymphocytes, neutrophils, platelets, and monocytes. Furthermore, ratios such as the neutrophil – lymphocyte ratio (NLR), platelet – lymphocyte ratio (PLR), monocyte – lymphocyte ratio (MLR), and systemic inflammatory index (SII) (calculated as neutrophils x platelets / lymphocytes) were determined. Blood specimens were collected in tubes containing ethylenediaminetetraacetate (EDTA) and analyzed using the Mindray automated blood count analyzer.

The statistical analysis for continuous variables encompassed reporting on the mean, standard deviation, median, and the range of minimum and maximum values. The assessment of categorical variables involved determining their frequency and proportion. The evaluation of variable normality was conducted through Skewness and Kurtosis coefficients and Kolmogorov – Smirnov test. For the comparison of continuous variables, that did not exhibit normal distribution across both groups, the Mann-Whitney U test was employed. In cases where variables displayed normal distribution, the study utilized an independent sample t-test. The research also incorporated logistic regression analysis to pinpoint variables that could potentially predict the presence of scar. All these statistical analysis were carried out using SPSS 24.0. A p-value of <0.05 was considered as statistically significant.

Results

In this study, 172 participants were analyzed, with 88 (51%) assigned to the control group and 84 (49%) of the scar group. Table 1 details the comparison of these groups based on various obstetric and hematological factors. The data revealed that the scar group had significantly higher values in numerous aspects, including the average age of the patients ($p<0.001$), total number of pregnancies (gravida) ($p<0.001$), childbirths (parity) ($p<0.001$), the count of living children ($p<0.001$), incidence of miscarriage ($p<0.001$), cesarean section occurrences ($p<0.001$), instances of dilatation and curettage (D & C) ($p=0.023$), count of monocytes ($p=0.029$), and MLR ($p=0.025$). Furthermore, the duration of pregnancy (gestational week) was significantly shorter in the scar group compared to the control group (0.011) as indicated in Table 1 and 2.

To determine the factors influencing scar conditions, logistic regression analysis was employed. This analysis initially incorporated the gestational week as a variable, followed by the inclusion of monocyte count and the MLR, both of which displayed significant group differences. The results, shown in Table 3, revealed that while the duration of pregnancy significantly affected the likelihood of scar condition (p=0.013), the levels of monocytes and MLR did not significantly influence the prediction of scar status (p>0.05).

Table 1: Obstetric Parameters in Control and Patient Group (n=172)

Variables	Control Group (n=88)	Patient Group (n=84)	p-value
Age	27.31 ± 5.87	36.31 ± 4.82	<0.001
Gravida	3.19 ± 1.98	4.13 ± 2.01	<0.001
Parity	1.31 ± 1.01	2.24 ± 1.13	<0.001
Abortion	0.09 ± 0.29	0.92 ± 1.01	<0.001
Cesarean Section	0.63 ± 0.41	2.24 ± 0.73	<0.001
D&C	0.37 ± 0.54	0.71 ± 0.89	0.02
Gestational Age	7.81 ± 1.21	6.34 ± 1.48	0.11

Table 2: Hematological Parameters in Control and Patient Groups (n=172)

Variables	Control Group (n=88)	Patient Group (n=84)	p-value
Platelets	281.11 ± 61.33	293.78 ± 68.51	0.81
Neutrophils	6.72 ± 1.91	7.01 ± 2.03	0.25
Lymphocytes	2.31 ± 0.71	2.12 ± 0.77	0.59
Monocytes	0.51 ± 0.19	0.72 ± 0.32	0.02
Hemoglobin	12.91 ± 1.39	13.05 ± 1.62	0.77
NLR	3.41 ± 1.29	4.11 ± 1.98	0.24
PLR	136.40 ± 38.01	149.97 ± 53.22	0.29
MLR	0.22 ± 0.11	0.39 ± 0.61	0.02

NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; MLR, monocyte-lymphocyte ratio

Table 3: Association of Pregnancy Scar with Gestational Age, Monocytes, and MLR

	B	SE	Wald	Exp (B)	CI (95%)	p-value
Gestational age	-0.341	0.17	4.29	0.75	0.53-0.99	0.02
Monocyte	1.412	1.69	0.72	4.11	0.16-109.9	0.30
MLR	2.201	2.51	0.81	9.09	0.07-1.71	0.27

Discussion

The objective of this research was to assess the levels of inflammatory markers in the blood of patients with scar pregnancy in comparison to those with a normal pregnancy. These markers are recognized for their predictive capabilities in a range of obstetric scenarios and cancers related to gynecology. While elevated levels of neutrophils, platelets, and SII were observed in cases of scar pregnancy, these were statistically significant. On the other hand, a marked increase in M and MLR levels were noted. However, these indicators did not prove to be predictive when the age of the gestation was taken into account, thereby confirming that ultrasonography remains the primary tool for diagnosing CSP, overshadowing the utility of easily accessible and cost – effective blood markers.

For diagnosing CSP, the most reliable technique continues to be a combination of Doppler, abdominal and vaginal ultrasonography[8]. However, there are instances where the usual indicators of scar pregnancy might not be apparent in ultrasound scans, which can result in delayed or inaccurate diagnosis, particularly critical in cases of CSP that lead to placental invasion abnormalities. The most opportune time for diagnosis in between the 5th and 7th weeks of gestation; diagnosis become more challenging in later stages as the gestational sac and fetus shift towards the upper part of the uterus. This makes it essential to meticulously examine the placenta at the incision site and its vascular surroundings[9]. Differentiating CSP from inevitable miscarriages and cervical pregnancies poses difficulties. Delay in diagnosis can cause complications like uterine rupture, leading to significant maternal health risks[10]. In a survey of 751 cases of CSP, 13.6% patients ended in hysterectomy due to diagnostic errors, impacting fertility[11]. Additionally, another analysis found that 17 out of 111 CSP cases were mistakenly identified as incomplete abortions or cervical pregnancies[12]. Identifying the lower segment sacs early on is vital for CSP diagnosis in the initial and for PAS in later stages. Cases of CSP treated with an expectant approach showed a high frequency of hysterectomies, mostly associated with pervasive PAS, underlying the need for improved medical expertise in diagnosing CSP[13].

Recent research indicates that inflammatory markers in peripheral blood, specifically lymphocytes, neutrophils, monocytes, and platelets, are indicative of both local and systemic inflammatory reactions[7]. Investigations into preeclampsia have revealed that raised levels of monocytes signify chronic inflammation and that MLR is an indicator of poor health outcomes. The activation of neutrophils by microparticles from the placenta is a key factor in the systemic inflammatory response observed in preeclampsia patients[14]. Studies focusing on PAS in the third trimester, which shares pathophysiology with CSP, have shown elevated NLR in comparison to normal pregnancies, alongside higher neutrophils and PLR[15,16]. Research comparing ectopic pregnancies to normal ones recorded elevated levels of neutrophils and monocytes, but only monocyte levels showed statistically significance. Typically, ectopic pregnancies exhibit low PDW and high monocyte ratios, suggesting the involvement of monocytes in the pathophysiology of tubal ectopic pregnancies, corroborating our

findings in scar pregnancies. Increased levels of NLR and PLR were also observed in cases of ruptured ectopic pregnancies17. In our findings, despite low lymphocyte ratios and high levels of neutrophils and platelets, the results were not statistically significant. The higher monocyte and MLR values did not establish a definitive threshold, potentially affected by the avoidance of early D & C due to the risk of complicating pregnancies. Further studies indicate that lower lymphocyte ratios and higher PLR and NLR are present in patients with hyperemesis gravidarum, assisting in diagnosis18.

The limitation of our study include the challenges in early detection of scar pregnancies, the premature termination of pregnancies, the absence of an in – depth analysis of inflammatory cytokine responses, and its retrospective design. For a comprehensive investigation of cytokine responses, extensive laboratory research and larger patient cohorts are necessary.

Conclusion

Out results showed significant association of inflammatory hematological parameters in diagnosing CSP, with analysis of various parameters. Therefore, while systemic inflammatory indicators might be useful for diagnosis, they do not have predictive power. Ultrasound continues to be a vital diagnostic technique for CSP. Elevating public awareness is key to averting serious complications.

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