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Original Article

The relationship between hematoma sizes and hematological parameters with miscarriage in singleton pregnancies with first trimester subchorionic hematoma

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Abstract

Objective: The aim of our study is to compare the size of hematoma in pregnant women diagnosed with subchorionic hematoma (SCH) between pregnant women with SCH who had abortion and those who did not, and to investigate the role of miscarriage risk.

Methods: Between January 2018 and December 2022, this is a retrospective cross-sectional study of women with intrauterine singleton pregnancies between 6 0/7 and 13 6/7 weeks of pregnancy at Mengücek Gazi Training and Research Hospital. Serial ultrasounds were performed on pregnant women in their first trimester to assess the presence, location, and size of any SCH. Clinical symptoms, including pelvic pain and vaginal bleeding, were recorded at each visit. Hospital records were used to obtain antenatal, birth, and neonatal outcomes.

Results: There was no discernible difference between the groups in terms of demographic or obstetric characteristics. Hemoglobin (Hb), leukocyte, neutrophil, lymphocyte, and platelet counts did not differ statistically between groups (p=0.89, 0.26, 0.16, 0.66, and 0.53 respectively). Neutrophil/lymphocyte (NLR), platelet/lymphocyte (PLR), and systemic immune inflammatory index (SII) hematological indices did not differ significantly (p=0.30, p=0.80, p=0.35). There was no discernible difference when the SCH area and volume of the two groups were compared (p=0.25; p=0.20).

Conclusion: In our study results, we showed that the hematological indices NLR, PLR, and SII are not effective in detecting the possibility of miscarriage in pregnant women with SCH. In addition, no significant correlation was found between the size of the hematoma and the probability of miscarriage. Prospective studies with larger populations, however, are required to better understand the relationship between subchorionic hematoma and miscarriage.

Keywords: Abortion, subchorionic hematoma, immune inflammatory index.

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INTRODUCTION

Abortion imminens (AI) is characterized by vaginal bleeding, abdominal cramps, occurring before the 20th week of pregnancy and is also known as threat of miscarriage. It is a common complication in the early stages of pregnancy and occurs in approximately 20% of all pregnancies. Subchorionic hematoma (SCH) is a type of uterine bleeding that occurs beneath the chorion membranes that surround the embryo. It is thought to occur due to the partial separation of the chorion membranes from the uterine wall (1). This obstetric problem usually occurs early in pregnancy in the first trimester. The patient's presenting complaint usually presents with vaginal bleeding. Subchorionic hematoma can be detected on ultrasound examination in approximately 18% of all pregnant women who apply to the hospital due to first trimester vaginal bleeding (abortus immines) (2). In the presence of a viable fetus, the most common first trimester sonographic finding is SCH, which appears as a hypoechoic or echoless crescent-shaped area between the chorion and the uterine wall (3). Since the first description of subchorionic hemorrhage in 1981, its clinical significance has been a matter of debate. Some studies have shown that a subchorionic hematoma is associated with adverse outcomes such as hypertensive disorders in pregnancy, ablatio placentae, and preterm delivery (1). On the contrary, there are studies in the literature that show that SCH has no negative pregnancy outcomes (4). It is thought that SCH may cause obstetric complications with a mechanical effect directly caused by hematoma or an indirect inflammatory response due to hematoma (5). In addition, as a result of some physiological changes in the maternal hematological system for adaptation to pregnancy, a chronic mild inflammation condition occurs (6). It is possible to detect deviations that may occur from these physiological adaptations by examining peripheral blood samples taken from expectant mothers during routine pregnancy follow-ups. In recent years, an index has been developed to show systemic inflammation using hematological parameters obtained from complete blood counts in peripheral blood. One of these indices, the neutrophil-lymphocyte ratio (NLR), is a simple and common biomarker used to detect systemic inflammation in patients (7).

The systemic immune-inflammation index (SII), which is based on peripheral lymphocyte, neutrophil, and platelet counts, is widely regarded as a reliable indicator of local immune response and systemic inflammation. These indices are suitable for clinical use due to their low cost and rapid results (8). However, although there have been publications on Abortus imminens in SII in recent years (9), no study has been found showing its relation with SCH. However, a valid biomarker indicating the risk of miscarriage in pregnant women with SCH has not yet been identified. Identifying a new, cost-effective biomarker in addition to hematoma size in patients with SCH would therefore be beneficial to clinicians in terms of treatment selection and patient management.

The aim of this study was to look into the relationship between SCH size and abortion risk, as well as hematological biomarkers that can help predict the risk of miscarriage in pregnant women with subchornic hematoma.

Table 1. Comparison of demographic features, among the groups

Demographic Features	Miscarriage n=83	Control n=112	p-Values
Maternal age	30.90±6.60	29.84±5.91	0.25[a]
BMI (kg/m2)	26.66±4.93	26.97±5.33	0.67[a]
Gravida	2.90±1.77	2.78±1.50	0.62[a]
Parity	1.14±1.09	1.16±0.99	0.87[a]
Living Child	1.13±1.10	1.18±1.00	0.72[a]
Chronic disease	1 (%1.2)	7 (%6.3)	0.14[b]
Anticoagulant	17(20.5%)	23(20.5%)	0.99[b]
HT	1(1.2%)	7(6.3%)	0.80[b]
Smoking	3(3.7%)	5(4.5%)	0.99[b]
UTI	8 (9.6%)	22(19.6%)	0.56[b]
Anemia	23(27.7%)	29(25.9%)	0.77[b]

a: Independent sample student t test, b: Chi-square test, Mean ± SD.
Abbreviations: BMI: body mass index; HT: hypertension; UTI: urinary tract infection.

Table 2. Relationship between hematoma location and pregnancy outcomes

Hematoma location	Miscarriage n=83	Control n=112	p-Values
Sub Segment	2	1	0.47
Front	1	2	
GS Surroundings	63	84	
Right wall	2	5	
Left wall	1	4	
Fundus	1	2	
Back	11	9	
Cervical	2	5	

* Abbreviations: GS: Gestational sac.

Table 3. Relationship between SCH area and volume wiht predicting miscarriage

Hematoma sizes	Miscarriage n=83	Control n=112	p-Values
Area	620.58	417.47	0.25
Volume	2165.94	773.49	0.20

MATERIALS AND METHODS

The present study, which was planned in accordance with the Helsinki Declaration rules, was approved by the university clinical research ethics committee with the decision numbered 7/01 on December 18, 2022.

The present study was designed as a retrospective case study in Mengücek Gazi Training and Research Hospital (MEAH), a tertiary hospital. SCH area was observed in 328 of the pregnant women who were followed up due to abortion imminens in MEAH between December 2018 and December 2021. 195 pregnant women who met our study criteria were included in the study, and the study population was divided into two groups, 83 pregnant women with SCH who had abortion (Group 1) and 112 pregnant women with SCH who gave birth (Group 2). The inclusion criteria were as follows: Between the ages of 18-40; Pregnant women with abortus imminens between 6 0/7 and 13 6/7 gestational weeks, and those whose hemogram results were reached in the first trimester were included in the study. Live singleton pregnancies with SCH in the first trimester (6-14 weeks) were collected by scanning our hospital database. If the gestational age patient's menstruation was regular, it was calculated according to the first day of the last menstrual cycle; otherwise, the head-rump distance (CRL) measurement by ultrasonography was taken as the week of pregnancy. All pregnant women were examined by ultrasound scanning between 6-14 weeks. Gestational age was calculated according to the last menstrual period or, if unknown, according to the first trimester ultrasound scan (10). We noted the presence or absence of a routinely examined SCH in the ultrasound report by examining it for the size of any SCH and the presence or absence of vaginal bleeding. In addition, we analyzed the medical information of each pregnant woman through the hospital data processing system to obtain demographic and basic clinical information (11). Considering the shape of the hematoma as a cone when calculating the SCH sizes: Area=πr(r+√(r2+h2)), and the volume was calculated using the formula Volume=(1/3)πr2h (radius of the base circle of the cone and h height of the cone). n the last two years, patient data were gathered from hospital records. Patient files and laboratory parameters were used to collect demographic information. All patients had their CBC values determined during the first trimester (6-14 weeks). It was calculated by dividing NLR by platelet/lymphocyte, PLR by neutrophil/lymphocyte, and SII by neutrophilxplatelet/lymphocyte (9, 12). In addition, the two study groups' neutrophil counts, platelet counts, lymphocyte counts, red blood cell (RBC) counts, and hemoglobin levels were determined.

Table 4. Comparison of laboratory test results between miscarriage and control groups

Laboratory Parameters	Miscarriage n=83	Control n=112	p-Values
Hb (g/dL)	12.60±1.23	12.58±1.09	0.89
Leukocyte (10^3/µL)	8.84±2.36	9.23±2.47	0.26
Neutrophil (10^3 /µL)	5.94±2.07	6.36±2.15	0.16
Lymphocyte (10^3 /µL)	2.07±0.52	2.11±0.73	0.66
Platelet (10^3 /µL)	247.939±57.65	242.553±60.15	0.53
Neutrophil/lymphocyte	3.12±2.12	3.48±2.84	0.30
Platelet /lymphocyte	125.88±40.20	127.86±65.49	0.80
SII (10^9 /L)	757.53±446.14	833.61±681.82	0.35

Note: Data given as median (interquartile range), mean ± SD Abbreviations: Hb: hemoglobin; SII, systemic immune inflammation index. NLR: Neutrophil/Lymphocyte, PLR: Platelet /Lymphocyte.

Statistical analysis

The obtained data was statistically evaluated using the SPSS for Windows 22.0 package program. The distribution of hematological parameters was determined using the Kolmogorov-Smirnov normality test. In addition, the Levene statistical test was used to determine variance homogeneity. To compare normally distributed variables, an independent sample student's t test was used. Chi-square test was used for categorical variables. The standard deviation (SD) mean was used to represent the results for normally distributed variables. To compare normally unreliable hematological parameters, the Mann-Whitney U test was used, and the results were expressed as median (minimum-maximum) values. A p value of 0.05 was considered statistically significant in our current study.

RESULTS

Patients diagnosed with SCH, who were followed up in Mengücek Gazi Training and Research Hospital between December 2018 and December 2022, were included in the study by examining their files retrospectively. The demographic characteristics of the pregnant women included in the study are shown in **Table 1.** Accordingly, there was no statistically significant difference between the ages and BMIs of the low group (MG) and control group (CG) of the cases included in the study (p=0.051, p=0.99, respectively). Although gravida was 2.90±1.77 in MG and 2.78±1.50 in CG, the CG group was higher in terms of parity number, but these differences were not statistically significant (p=0.62, p=0.87, respectively). In terms of the number of living children, it was 1.13±1.10 in MG and 1.18±1.00 in CG, which was not statistically significant (p=0.72). In addition, there was no statistical difference between the groups in terms of maternal chronic diseases, anticoagulant use, hypertension, cigarette smoking, urinary tract infection, and maternal anemia (p=0.14, p=0.99, p=0.80, p=0.99, p=0.56, p=0.77, respectively).). When **Table 2** was examined, no statistically significant result was found between SCH location and miscarriage risk (p=0.47). **Table 3** shows the relationship between SCH area and volume and the risk of miscarriage. Between SCH area and miscarriage risk, 620.58 in the MG group and 417.47 in the CG group, the difference between the two groups was not statistically significant (P=0.25). The difference between SCH volume and miscarriage risk between MG group 2165.94 and CG 773.49 was also not statistically significant (p=0.20). Laboratory test results are compared between the abortion group and control groups in **Table 4**. When the hematological parameters in the first trimester, such as Hb, leukocyte, neutrophil, lymphocyte and platelet counts, were compared between the groups, no statistically significant difference was found. (p=0.89, p=0.26, p=0.16, p=0.66 and p=0.53, respectively). There was no statistically significant difference between the groups in terms of NLR, PLR and SII values, which are also hematological indices measured in the first trimester. (p=0.30, p=0.80, p=0.35, respectively).

DISCUSSION

Based on the literature (13, 14) indicating that poor obstetric outcomes may be caused by inflammatory processes, we investigated whether there is a link between hematological parameters measured in the first trimester and SCH that may develop later in the pregnancy. To the best of our knowledge, this is the first study to compare pregnant women with SCH who had abortions and those who did not have a miscarriage in terms of systemic immune inflammation index, NLR and PLR values. In our results, no significant correlation was observed between Hb, Leukocyte, neutrophil, lymphocyte, platelet counts and NLR, PLR, SII levels, which we looked at in the first trimester, and low. Furthermore, no significant relationship was found between the size of the hematoma and the risk of miscarriage. In the literature, the role of SCH in first trimester miscarriages is debatable. According to our findings, there is no significant link between the presence of SCH and an increased risk of miscarriage. In a meta-analysis, Tuuli et al. (15) discovered that SCH increased the risk of miscarriage, whereas Naert et al. found no increased risk in another study (16). An increased risk of early pregnancy loss has been shown in the literature in pregnant women with subchorionic hematoma (SCH) (1). On the other hand, in a study conducted by Ball et al. on 238 pregnant women with ultrasonographic subchorionic hematoma, the absence of a relationship between heatoma size and abortion development was similar to our current study results (17). When the literature is examined in terms of SCH localization, there are publications showing that SCH size and localization affect the course of pregnancy and pregnancy outcomes (18). On the contrary, Nagy et al., in their study on 187 pregnant women with subchorionic hematoma, claimed that subchorionic hematoma size and localization did not show a significant relationship between pregnancy course and outcomes (19), which was similar to our current study results. In terms of hematological parameters, the lack of a significant difference in NLR between healthy pregnant women who had a live birth and pregnant women who had abortions shows parallelism with our study results (20). On the other hand, Liu D et al. in their study on 200 pregnant women with missed abortion (miscarriage),

they could not find a statistical difference between the control group and the missed abortion group in terms of NLR and PLR levels. These results are similar to our study results in terms of both NLR and PLR parameters (21).

As part of the physiological adaptation to pregnancy; There is a mild systematic inflammatory response in pregnancy. As a reflection of this, the number of leukocytes in the peripheral blood increases. There is also an increase in neutrophil and monocyte activity, as well as increased concentrations of circulating inflammatory cytokines (IL-6 and TNF-α) (22, 23). It is assumed that an increase in cytokines like IL-2 and IFN-γ released by Th1 cells, as well as cytokines like TNF-α, IL-1, and IL-6 released by activated macrophages, may increase the risk of miscarriage by influencing the circulating inflammatory state (24).

The cost and availability of many of these markers and cytokines, however, limit their clinical utility. SII is a new generation inflammation marker that is simple, inexpensive, and easy to obtain by counting platelets, neutrophils, and lymphocytes (12). According to a recent study, high SII levels in early pregnancy can be used as an additional marker to predict miscarriage in pregnant women who are at risk of miscarriage (9). In our study, no significant difference was found between SII values and miscarriage, unlike the above liatature information. We think that this is due to the fact that both the pregnant women in our control group and the pregnant women in the abortion group consisted of pregnant women with subchornic hematoma. We intend to compare future miscarriages among pregnant women with SCH to subsequent healthy pregnancies in our study.

Limitations:

This study has some restrictions. We can start by pointing out that it was intended to be a retrospective, single-center study. The small number of our patients can also be demonstrated.

CONCLUSION

In this study results, we found that the hematological indices NLR, PLR, and SII were not effective in detecting the possibility of miscarriage in pregnant women with SCH. In addition, no significant correlation was found between the size of the hematoma and the probability of miscarriage. To comprehend the connection between subchorionic hematoma and miscarriage, however, prospective studies involving larger populations are required.

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Ethical approval: The study was conducted with the conditions recommended by the Helsinki Declaration. The study was approved by the university clinical research ethics committee with the decision numbered 7/01 on December 18, 2022.
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