Is a first-trimester subchorionic hematoma and its size a risk for preterm premature rupture of membranes?

Mefkure Eraslan Sahin, Mehmet Mete Kirlangic, Ilknur Col Madendag, Mehmet Ak

Kayseri City Hospital, Department of Obstetrics and Gynecology, Kayseri, Turkey
Tuzla Government Hospital, Department of Obstetrics and Gynecology, Istanbul, Turkey

ARTICLE INFO
Keywords:
Preterm prelabor rupture of membranes
PPROM
Subchorionic hematoma
SCH

Received: Sep 20, 2021
Accepted: Dec 20, 2021
Available Online: May XX, 2022

Abstract
Aim: To assess the relationship between first-trimester subchorionic hematoma (SCH) size and preterm premature rupture of membranes (PPROM).

Materials and Methods: In this retrospective study, we included patients with a singleton intrauterine pregnancy between 5 and 14 gestational weeks. After analyzing the 1,440 pregnant women who applied for inclusion in the study based on vaginal bleeding during their first trimester, we found that 228 had SCH. After excluding those who had miscarried before viability and who had complicated pregnancies, 186 remained who were included in the final analysis. The SCH group was subdivided into three groups according to hematoma size as follows: mild (n: 62), moderate (n: 56), and severe SCH (n: 68). The severity of SCH was calculated according to the ratio of the gestational sac length to the linear length of the bleeding area.

Results: Maternal demographic characteristics were similar among the groups. The gestational age at delivery was significantly lower in the severe SCH group than in the other groups. The fetal birth weight was significantly lower in the severe SCH group than in the other groups. PPROM rates were significantly higher in the severe SCH compared to mild SCH, moderate SCH and control group.

Conclusion: Our data suggest that the presence of a first-trimester mild or moderate SCH in singleton pregnancies is not associated PPROM, but that severe SCH is associated with PPROM.

Introduction
Vaginal bleeding, with an incidence rate of 16–25%, is a frequent complication of first trimester and can cause maternal anxiety [1]. Vaginal bleeding within the first trimester can result in a subchorionic hematoma (SCH) between 1.3 and 40% of the incidence [2], which has been related with intrauterine growth restriction, miscarriage, preeclampsia, placental abruption, and preterm delivery [3-7] and hematoma size had clinical importance in terms of adverse pregnancy outcomes [8-10]. In the presence of vaginal bleeding without SCH adverse perinatal outcomes are observed less frequently, but presence of SCH is always a cause of high anxiety due to and higher complication rates for both the patients and their obstetricians because of the only treatment was expectant management.

Preterm prelabor rupture of membranes (PPROM) is defined as a rupture of membrane without signs of delivery before 37 weeks of gestation that complicates 3–4% of pregnancies. PPROM is related with preterm delivery and a major cause of adverse maternal and fetal outcomes [11]. In literature it is reported that adverse perinatal outcomes from SCH were associated to underlying placental dysfunction [12]. It is well documented that decidual hemorrhage is that which originates from damaged decidual blood vessels and presents as vaginal bleeding or retroplacental hematoma formation [13]. PPROM may be related to increased expressions of the decidual cells to help maintain hemostasis. After intrauterine hemorrhage, thrombin is generated after the decidual tissue factor combines with factor VIIa to activate factor Xa, which combines with co-factor Va. Thrombin binds to decidual protease-activated receptors (PAR1 and 3) that upregulate protease expression, such as matrix metalloproteinases (MMPs) [14]. Considering the effects of SCH on decidual cells and thrombin secretion, we aimed to evaluate the relationship between SCH, with special regard to size, within the first trimester of pregnancy and PPROM.

Copyright © 2022 The author(s) - Available online at www.annalsmedres.org. This is an Open Access article distributed under the terms of Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.
Materials and Methods

This retrospective cohort study was conducted at Kayseri City Hospital and approved by the Erciyes University Ethics Committee (approved number:2019/726) Ethics Committee and in accordance with the Declaration of Helsinki. Informed consent form was not obtained because it was a retrospective study.

Study population

The 1,440 pregnant women who applied for inclusion in the study were complicated with vaginal bleeding within the first trimester and visited the urgent obstetrics clinic between January 2010 and January 2021. The inclusion criteria were those patients who were at least 18 years old, singleton pregnancy and between 5 and 14 weeks of gestation. An intrauterine pregnancy was determined that showed an intrauterine gestation sac with or without a visible embryo and heart beat. SCH on the ultrasound was a retroplacental, hypoechoic region that was determined by an obstetric sonologist. The exclusion criteria were as follows: multiple pregnancies, patient’s ≥ 40 years old, the presence of fetal chromosomal or congenital anomalies, miscarriage before viability (24 weeks’ gestation), cervical cerclage or uterine anomaly, gestational diabetes mellitus, polyhydramnios, macrosomia, preeclampsia, placenta previa, or placental invasion anomalies during pregnancy followup.

After analyzing the 1,440 pregnant women we found that 228 of them had SCH. After excluded complicated pregnancies 186 patients were included in the final analysis. The SCH group was subdivided into three groups according to hematoma size as follows: mild (n: 62), moderate (n: 56), and severe SCH (n: 68). During the period of the study, 980 healthy pregnant women who didn’t complicated with vaginal bleeding and SCH in the first trimester, meet the inclusion exclusion criteria and whose delivery data were accessed were included as the control group.

Figure 1 provides a flow chart of the study population.

Maternal age, body mass index (BMI), multiparity, ethnicity, gestational age at ultrasound evaluation, history of previous cesarean sections, spontaneous abortion, dilation and curettage (D&C), and preterm delivery were recorded. In addition, the delivery outcomes, such as gestational age at delivery, fetal birth weight, male newborn, spontaneous vaginal delivery rates and the presence of PPROM were recorded. PPROM defined as a spontaneous membrane rupture before 37 weeks’ gestation [8]. Fetal viability is the gestational age ≥ 24 weeks or ultrasonographic fetal weight ≥ 500g. SCH severity was calculated according to the ratio of the gestational sac length to the linear length within the bleeding area, as previously reported in the literature. This ratio was classified as mild if it was < 20%, moderate if between 20 and 50%, and severe if > 50% [7].

Results

Table 1 illustrated a comparison of maternal demographic characteristics among the groups. Maternal age, BMI (kg/m2), multiparity, ethnicity, mean gestational age at ultrasound evaluation, previous D&C, previous cesarean section rates, history of spontaneous abortion, and previous preterm delivery rates were similar among the groups. (p: 0.740, p: 0.280, p: 0.910, p: 0.640, p: 0.440, p: 0.930, p: 0.470, p: 0.980 and p: 0.960 respectively.)

Table 2 provides a comparison of delivery characteristics and perinatal outcomes among the groups. Vaginal delivery rates, male newborns and Apgar score < 7 at 5 min were similar among the groups (p: 0.780, p: 0.670 and p: 0.950 respectively). The gestational ages at delivery were significantly lower in the severe SCH group than in the other groups (p: 0.001). Fetal birth weights were significantly lower in the severe SCH group than in the other groups (p < 0.001). PPROM rates were significantly higher in the severe SCH group than in other groups (p < 0.001).

Discussion

First-trimester bleeding during pregnancy can be complicated with SCH and is always a cause of high anxiety for both the patients and their obstetricians because of the only treatment was expectant management. Our results indicated that the presence of a first-trimester mild or moderate SCH was not associated with PPROM, but that severe SCH was related with PPROM. This finding is critical to help counsel patients because of significant concerns among the expectant parents.
PPROM and preterm delivery. In addition, thrombin in the inflammatory process is reinforced, which leads to hemoglobin chains and a mechanism is created by which innate immunity is activated by these proteases and free [17]. Proteomic studies have provided evidence that inhibitory process is common after abruption without infection [17]. The inflammatory severity and, more importantly, the inflammatory process in the absence of infection [17]. The inflammatory process is common after abruption without infection [17]. Proteomic studies have provided evidence that innate immunity is activated by these proteases and free hemoglobin chains and a mechanism is created by which the inflammatory process is reinforced, which leads to PPROM and preterm delivery. In addition, thrombin induces interleukin-8 in decidual cells, which accounts for infiltration of densely populated neutrophils in abruption-associated PPROM without infection [18]. The interactive effects of thrombin-enhanced MMPs and the neutrophil-derived proteases degrade the extracellular matrix of the fetal membrane, often resulting in PPROM. Decidual hemorrhage generates large quantities of thrombin. One study has observed that a small amount of thrombin produced during coagulation increases the frequency, intensity, and tone of myometrial contractions, an effect that is suppressed by thrombin inhibitors in the blood [19]. The main effect of thrombin generated by decidual hemorrhage is to maintain hemostasis, not stimulate uterine contractions [20]. One study has noted that thrombin activation as measured by serum thrombin–antithrombin complex levels [20] was observed in women with preterm labor and in asymptomatic women who subsequently delivered preterm [21].

There were some clinic importance and limitations to our study. First, our study comprised detailed clinical information, large sample size, and a low percentage of patients lost to followup. Second, the analysis of SCH size provided important clinic information to our study. Third, we evaluated all patients with SCH and didn’t restrict our study population to only patients with vaginal bleeding. Our control group was recruited from the general population of pregnant women who were undergoing a first-trimester sonogram.

We are aware that the study has some limitations. Retrospective design and single center experiences which is a

### Table 1. Comparison of maternal demographic characteristics among groups.

<table>
<thead>
<tr>
<th></th>
<th>Mild SCH (n = 62)</th>
<th>Moderate SCH (n = 56)</th>
<th>Severe SCH (n = 68)</th>
<th>Control (n = 980)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age (years)</td>
<td>27.2±3.0</td>
<td>27.1±2.8</td>
<td>27.5±3.6</td>
<td>27.0±3.3</td>
<td>0.740</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>25.2±2.0</td>
<td>26.3±2.1</td>
<td>25.8±1.9</td>
<td>25.9±1.7</td>
<td>0.280</td>
</tr>
<tr>
<td>Nulliparity (n%)</td>
<td>13 (20.9)</td>
<td>13 (23.2)</td>
<td>14 (20.5)</td>
<td>223 (22.7)</td>
<td>0.910</td>
</tr>
<tr>
<td>Ethnicity Caucasian (n%)</td>
<td>53 (85.4)</td>
<td>50 (89.2)</td>
<td>58 (85.2)</td>
<td>847 (86.4)</td>
<td>0.640</td>
</tr>
<tr>
<td>Gestational age at ultrasound examination (weeks)</td>
<td>9 (7–10)</td>
<td>9 (7–11)</td>
<td>9 (7–11)</td>
<td>9 (7–11)</td>
<td>0.440</td>
</tr>
<tr>
<td>Previous dilation and curettage (D&amp;C) (n%)</td>
<td>4 (6.4)</td>
<td>3 (5.3)</td>
<td>4 (5.8)</td>
<td>50 (5.1)</td>
<td>0.930</td>
</tr>
<tr>
<td>Previous cesarian section (n%)</td>
<td>16 (25.8)</td>
<td>14 (25.0)</td>
<td>18 (26.4)</td>
<td>261 (26.6)</td>
<td>0.470</td>
</tr>
<tr>
<td>Previous spontaneous abortion (n%)</td>
<td>6 (9.6)</td>
<td>5 (8.9)</td>
<td>7 (10.2)</td>
<td>89 (9.1)</td>
<td>0.980</td>
</tr>
<tr>
<td>Previous preterm delivery (n%)</td>
<td>3 (4.8)</td>
<td>3 (5.3)</td>
<td>4 (5.8)</td>
<td>44 (4.4)</td>
<td>0.960</td>
</tr>
</tbody>
</table>

Note: SCH, subchorionic hematoma; BMI, body mass index. Values are expressed as the mean ± standard deviation or n%.

### Table 2. Delivery characteristics and perinatal outcomes by group.

<table>
<thead>
<tr>
<th></th>
<th>Mild SCH (n = 62)</th>
<th>Moderate SCH (n = 56)</th>
<th>Severe SCH (n = 68)</th>
<th>Control (n = 980)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age at delivery (weeks)</td>
<td>39 (38–40)a</td>
<td>38 (38–40)a</td>
<td>37 (35–38)b</td>
<td>39 (38–40)a</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Vaginal deliveryrates (n%)</td>
<td>38 (61.2)</td>
<td>35 (62.5)</td>
<td>41 (60.2)</td>
<td>610 (62.2)</td>
<td>0.780</td>
</tr>
<tr>
<td>Male newborns (n%)</td>
<td>34 (54.8)</td>
<td>31 (55.3)</td>
<td>38 (55.8)</td>
<td>208 (55.9)</td>
<td>0.670</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>3150±350a</td>
<td>3200±370a</td>
<td>2850±280b</td>
<td>3210±310a</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Apgar score &lt; 7 at 5 min (n%)</td>
<td>2 (3.2)</td>
<td>1 (1.78)</td>
<td>2 (2.8)</td>
<td>8 (0.8)</td>
<td>0.950</td>
</tr>
<tr>
<td>PPROM (n%)</td>
<td>4 (6.4)a</td>
<td>4 (7.1) a</td>
<td>13 (19.1)b</td>
<td>19 (1.9)a</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Notes: SCH, subchorionic hematoma; PPROM, preterm prelabour rupture of membranes. Values are expressed as the mean ± standard deviation or n%. Different super scripts means statistically difference.
limitations of the study. In addition, it is well documented in the literature that most SCH within the first trimester resolve themselves by the second trimester [15]. Although we did not evaluate the resolution rates, we suggest that severe SCH would be resorbed much later and would cause increased noninfectious inflammation for a longer period of time than mild or moderate SCH. Thus, it would be more likely that PPROM would increase in the presence of severe SCH.

Conclusion

Our data suggest that the presence of a first-trimester mild or moderate SCH in singleton pregnancies is not associated with PPROM, but that severe SCH is associated with PPROM.

References