



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

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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

DOI:

[10.5455/annalsmedres.2021.09.545](https://doi.org/10.5455/annalsmedres.2021.09.545)

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. PPRM 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 PPRM, but that severe SCH is associated with PPRM.



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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. PPRM 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]. PPRM 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 PPRM.

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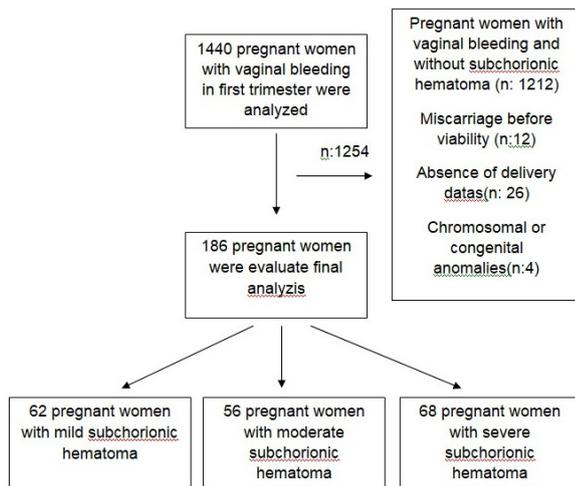


Figure 1. Study population

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), nuliparity, 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 ≥ 500 g. 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].

Statistical analyses

The data were analyzed in SPSS 22.0 program. The distribution of the data was evaluated with the Kolmogorov-Smirnov test. Descriptive statistics are shown as numbers, percentages, mean, standard deviation, minimum and maximum values in data that are in accordance with normal distribution, and median and interquartile range (IQR) values in those that do not comply with normal distribution. Pearson Chi Square test was used for categorical variables. One Way Anova and Kruskal Wallis tests were used to evaluate the relationship between independent groups in continuous variables. $p < 0.05$ was accepted for statistical significance.

Results

Table 1 illustrated a comparison of maternal demographic characteristics among the groups. Maternal age, BMI (kg/m²), nuliparity, 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 the 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.

Table 1. Comparison of maternal demographic characteristics among groups.

	Mild SCH (n = 62)	Moderate SCH (n = 56)	Severe SCH (n = 68)	Control (n = 980)	P value
Maternal age (years)	27.2±3.0	27.1±2.8	27.5±3.6	27.0±3.3	0.740
BMI (kg/m ²)	25.2±2.0	26.3±2.1	25.8±1.9	25.9±1.7	0.280
Nuliparity (n%)	13 (20.9)	13 (23.2)	14 (20.5)	223 (22.7)	0.910
Ethnicity Caucasian (n%)	53 (85.4)	50 (89.2)	58 (85.2)	847 (86.4)	0.640
Gestational age at ultrasound examination (weeks)	9 (7–10)	9 (7–11)	9(7–11)	9 (7–11)	0.440
Previous dilation and curettage (D&C) (n%)	4 (6.4)	3 (5.3)	4 (5.8)	50 (5.1)	0.930
Previous cesarian section (n%)	16 (25.8)	14 (25.0)	18 (26.4)	261 (26.6)	0.470
Previous spontaneous abortion (n%)	6 (9.6)	5 (8.9)	7 (10.2)	89 (9.1)	0.980
Previous preterm delivery (n%)	3 (4.8)	3 (5.3)	4 (5.8)	44 (4.4)	0.960

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.

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

Notes: SCH, subchorionic hematoma; PPRM, preterm prelabour rupture of membranes. Values are expressed as the mean ± standard deviation or n%. Different super scripts means statistically difference.

SCH is resulted from a collection of blood between the chorion and the underlying decidua. Although it is frequently diagnosed by ultrasound during the first trimester and because of its association with adverse pregnancy outcomes, SCH etiology and pathogenesis remain unclear. There are conflicting results in the literature on SCH and its adverse perinatal outcomes. Although previous studies have found increased rates of preterm delivery, PPRM, placental abruption and stillbirth [3-7], more recent studies have suggested that there is no association between SCH and adverse pregnancy outcomes [15, 16]. Naert et al. [15] have suggested that neither a first-trimester SCH nor hematoma size in singleton pregnancies is associated with adverse pregnancy outcomes. In addition, they found that most of these SCH resolved themselves by the second trimester. Another study has shown that first-trimester SCH is not related with pregnancy loss at < 20 weeks' gestation [16].

Despite these conflicting results, we found that first-trimester mild or moderate SCH was not associated with PPRM, but that severe SCH was associated with PPRM. These results could be based on decidual damage 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 PPRM and preterm delivery. In addition, thrombin in-

duces interleukin-8 in decidual cells, which accounts for infiltration of densely populated neutrophils in abruption-associated PPRM 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 PPRM. 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 (TAT) 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

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

- Sukur YE, Goc G, Kose O, Acmaz G, Ozmen B, Atabekoglu CS, et al. The effects of subchorionic hematoma on pregnancy outcome in patients with threatened abortion. *J Turk Ger Gynecol Assoc.* 2014;15(4):239-42.
- Nagy S, Bush M, Stone J, Lapinski RH, Gardo S. Clinical significance of subchorionic and retroplacental hematomas detected in the first trimester of pregnancy. *Obstet Gynecol.* 2003;102(1):94-100.
- Palatnik A, Grobman WA. The relationship between first-trimester subchorionic hematoma, cervical length, and preterm birth. *American journal of obstetrics and gynecology.* 2015;213(3):403. e1-. e4.
- Sharma G, Kalish RB, Chasen ST. Prognostic factors associated with antenatal subchorionic echolucencies. *Am J Obstet Gynecol.* 2003;189(4):994-6.
- Norman SM, Odibo AO, Macones GA, Dicke JM, Crane JP, Cahill AG. Ultrasound-detected subchorionic hemorrhage and the obstetric implications. *Obstet Gynecol.* 2010;116(2 Pt 1):311-5.
- Tuuli MG, Norman SM, Odibo AO, Macones GA, Cahill AG. Perinatal outcomes in women with subchorionic hematoma: a systematic review and meta-analysis. *Obstet Gynecol.* 2011;117(5):1205-12.
- ŞAHİN E, MADENDAĞ Y, AÇMAZ G, ÇÖL İ, ŞAHİN ME, KARAKILIÇ EÜ, et al. BİRİNCİ TRİMESTERDE MEYDANA GELEN SUBKORYONİK HEMATOMUN PRETERM DOĞUM VE FETAL GELİŞİM GERİLİĞİ İLE İLİŞKİSİNİN DEĞERLENDİRİLMESİ. *Bozok Tıp Dergisi.* 7(1):54-8.
- Hashem A, Sarsam SD. The impact of incidental ultrasound finding of subchorionic and retroplacental hematoma in early pregnancy. *The Journal of Obstetrics and Gynecology of India.* 2019;69(1):43-9.
- Tuuli MG, Norman SM, Odibo AO, Macones GA, Cahill AG. Perinatal outcomes in women with subchorionic hematoma: a systematic review and meta-analysis. *Obstetrics & Gynecology.* 2011;117(5):1205-12.
- Li Q, Zhu J, Hua K. Effects of subchorionic hematoma on pregnancy outcome: a meta analysis. *Zhonghua yi xue za zhi.* 2016;96(17):1383-5.
- Ekin A, Gezer C, Taner CE, Ozeren M. Perinatal outcomes in pregnancies with oligohydramnios after preterm premature rupture of membranes. *J Matern Fetal Neonatal Med.* 2015;28(16):1918-22.
- Weiss JL, Malone FD, Vidaver J, Ball RH, Nyberg DA, Comstock CH, et al. Threatened abortion: A risk factor for poor pregnancy outcome, a population-based screening study. *Am J Obstet Gynecol.* 2004;190(3):745-50.
- Buhimschi CS, Schatz F, Krikun G, Buhimschi IA, Lockwood CJ. Novel insights into molecular mechanisms of abruption-induced preterm birth. *Expert reviews in molecular medicine.* 2010;12.
- Mackenzie AP, Schatz F, Krikun G, Funai EF, Kadner S, Lockwood CJ. Mechanisms of abruption-induced premature rupture of the fetal membranes: Thrombin enhanced decidual matrix metalloproteinase-3 (stromelysin-1) expression. *American journal of obstetrics and gynecology.* 2004;191(6):1996-2001.
- Naert MN, Rodriguez AM, Khadraoui H, Naqvi M, Fox NS. Association Between First-Trimester Subchorionic Hematomas and Adverse Pregnancy Outcomes After 20 Weeks of Gestation in Singleton Pregnancies. *Obstetrics & Gynecology.* 2019;134(4):863-8.
- Naert MN, Khadraoui H, Rodriguez AM, Naqvi M, Fox NS. Association Between First-Trimester Subchorionic Hematomas and Pregnancy Loss in Singleton Pregnancies. *Obstetrics & Gynecology.* 2019;134(2):276-81.
- Buhimschi IA, Zhao G, Rosenberg VA, Abdel-Razeq S, Thung S, Buhimschi CS. Multidimensional proteomics analysis of amniotic fluid to provide insight into the mechanisms of idiopathic preterm birth. *PLoS One.* 2008;3(4):e2049.
- Lockwood CJ, Toti P, Arcuri F, Paidas M, Buchwalder L, Krikun G, et al. Mechanisms of abruption-induced premature rupture of the fetal membranes: thrombin-enhanced interleukin-8 expression in term decidua. *Am J Pathol.* 2005;167(5):1443-9.
- O'Sullivan CJ, Allen NM, O'Loughlin AJ, Friel AM, Morrison JJ. Thrombin and PAR1-activating peptide: effects on human uterine contractility in vitro. *Am J Obstet Gynecol.* 2004;190(4):1098-105.
- Norwitz ER, Snegovskikh V, Schatz F, Foyouzi N, Rahman M, Buchwalder L, et al. Progesterone inhibits and thrombin stimulates the plasminogen activator/inhibitor system in term decidual stromal cells: implications for parturition. *Am J Obstet Gynecol.* 2007;196(4):382 e1-8.
- Elovitz MA, Baron J, Phillippe M. The role of thrombin in preterm parturition. *Am J Obstet Gynecol.* 2001;185(5):1059-63.