Obstetrics: *Original Research*

Association Between First-Trimester Subchorionic Hematomas and Pregnancy Loss in Singleton Pregnancies

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OBJECTIVE: To assess the association of a first-trimester subchorionic hematoma with pregnancy loss in women with singleton pregnancies.

METHODS: We conducted a retrospective cohort study of all women with singleton pregnancies presenting for prenatal care before 14 weeks of gestation over a 3-year period at a single obstetric practice. All patients had routine first-trimester ultrasound scans. We reviewed ultrasound data from the first ultrasound scan performed between 6 0/7 and 13 6/7 weeks of gestation and compared rates of pregnancy loss before 20 weeks in women with and without a subchorionic hematoma. Logistic regression analysis was used to control for potential confounding variables.

RESULTS: From January 2015 to December 2017, a total of 2,446 women met inclusion criteria, 451 (18.4%) of whom had subchorionic hematomas. Women with subchorionic hematomas had their first ultrasound scans at an earlier gestational age (8 5/7 vs 9 6/7 weeks of gestation, $P<.001$) and were more likely to have vaginal bleeding (33.3% vs 8.1%, $P<.001$). Maternal age, race, use of in vitro fertilization, body mass index, prior number of losses, and medical comorbidities did not differ between the groups. On univariable analysis, subchorionic hematoma was associated with an increased risk of pregnancy loss before 20 weeks of gestation (7.5% vs 4.9%, $P=.026$); however, after adjusting for gestational age and vaginal bleeding, this association was no longer significant (adjusted odds ratio 1.13, 95% CI 0.74–1.74). In the 451 women with subchorionic hematomas, no characteristics of the subchorionic hematoma, including size by volume, largest diameter, presence of vaginal bleeding, and presence of an additional subchorionic hematoma, were associated with pregnancy loss. Post hoc power analysis showed we had 80% power to detect an increase in pregnancy loss before 20 weeks of gestation from 4.9% in women with no subchorionic hematoma to 8.3% in women with subchorionic hematoma.

CONCLUSION: In this cohort of women with singleton pregnancies, subchorionic hematoma before 14 weeks of gestation was not independently associated with pregnancy loss before 20 weeks of gestation.

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Subchorionic hematomas are commonly observed on ultrasound scans during the first trimester, with reported incidence varying widely, from as low as 0.46% to as high as 39.5%.[1–3] Data are conflicting regarding the clinical implications of subchorionic hematomas.

One of the most reported adverse associations with subchorionic hematoma is pregnancy loss. Although a large systematic review found that subchorionic hematoma was correlated with a twofold increase in spontaneous abortion,[4] other studies have found either a lower risk of pregnancy loss[5,6] or no association between subchorionic hematoma and pregnancy loss.[7,8] Subchorionic hematomas' timing and size may also affect rates of pregnancy loss.[3,9] However, these studies are often limited by lack of important clinical information and inability to control for important covariates that may influence the pregnancy loss rate. Additionally, in many studies, the patients do not represent a general obstetrics

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population because study participants may have received an early ultrasound scan only as a result of the use of in vitro fertilization (IVF), recurrent pregnancy losses, or vaginal bleeding, for example.

Thus, the relationship between subchorionic hematoma and pregnancy loss is unclear. The objective of this study was to investigate the association between first-trimester subchorionic hematoma and pregnancy loss in unselected women with a range of comorbidities and singleton pregnancies. In addition, we sought to better understand whether any particular ultrasound or clinical features of subchorionic hematoma are associated with an increased risk of pregnancy loss to better counsel patients with this common first-trimester diagnosis.

METHODS

This was a retrospective cohort study of all women with singleton pregnancies who presented for prenatal care before 14 weeks of gestation at a single maternal–fetal medicine practice over a 3-year period between January 2015 and December 2017. In our practice, all women undergo ultrasound scans at our affiliated imaging center at or before their initial visits. All images are archived, and formal reports are generated. For each patient, we reviewed the initial ultrasound scan performed between 6 0/7 and 13 6/7 weeks of gestation. Gestational age was determined by the last menstrual period or by first-trimester ultrasound scan per standard guidelines.[10] If the pregnancy was the result of IVF, the date of embryo transfer was used to determine gestational age. We excluded pregnancies with multiple gestations, a vanishing twin, or a fetal heart rate of less than 100 beats per minute.

We reviewed each ultrasound report for the presence or absence of a subchorionic hematoma, the total number of subchorionic hematomas, the size of any subchorionic hematomas, and the presence or absence of vaginal bleeding, which are all routinely noted on the ultrasound report. Subchorionic hematoma was defined as a crescent-shaped, echo-free area between the chorionic membrane and the myometrium.[2] We also reviewed computerized medical records for each woman to obtain demographic and baseline clinical information.

We compared baseline characteristics between the women with and without subchorionic hematomas using χ^2 and t tests as appropriate. Our primary outcome was pregnancy loss before 20 weeks of gestation, and we compared this outcome between women with and without subchorionic hematomas. Multivariable logistic regression was used to control for differences in baseline characteristics between the two groups that were significant in the univariable analysis ($P<.05$). Adjusted odds ratios with 95% CIs were estimated from the regression analysis. For the subgroup of women with subchorionic hematomas, we also assessed whether the subchorionic hematomas' largest diameter, volume (length × width × height), or number was associated with pregnancy loss. Lastly, we assessed whether vaginal bleeding increased the risk of pregnancy loss among women with subchorionic hematomas.

This project was approved by the Biomedical Research Alliance of New York Institutional Review Board. There was no funding for this study.

RESULTS

A total of 2,586 women presented for prenatal care before 14 weeks of gestation with singleton gestations over the course of the study period. We excluded 30 women for fetal heart rate less than 100 beats per minute and 39 women for the presence of a vanished twin, leaving 2,517 women eligible for inclusion, 468 (18.6%) of whom had a subchorionic hematoma. There were a total of 71 women (2.7%) without outcome data because they left our practice before 20 weeks of gestation, and this rate did not differ between the subchorionic hematoma and non–subchorionic hematoma groups (3.6% vs 2.6%, $P=.24$). Therefore, a total of 2,446 women were included in the final analysis, 451 (18.4%) of whom had subchorionic hematomas and 1,995 (81.6%) of whom did not have subchorionic hematomas.

Women with a subchorionic hematomas presented at earlier gestational ages and were more likely to have vaginal bleeding. There were no differences in any other measured baseline characteristics, including maternal age, race, body mass index (BMI, calculated as weight in kilograms divided by height in meters squared), use of IVF, prior pregnancy losses, uterine anomalies, leiomyomas, cervical excisional procedures, prior preterm birth, and medical comorbidities (Table 1).

On univariable analysis, subchorionic hematoma was associated with an increased risk of pregnancy loss before 20 weeks of gestation (7.5% vs 4.9%, $P=.026$). However, after adjusting for gestational age at ultrasound scan and presence of vaginal bleeding, this association was no longer significant (adjusted odds ratio 1.13, 95% CI 0.74–1.74) (Table 2). Post hoc power analysis showed we had 80% power (alpha error of 5%) to detect an increase in pregnancy loss before 20 weeks of gestation from 4.9% in women

Table 1. Baseline Maternal Characteristics Based on the Presence or Absence of a Subchorionic Hematoma Before 14 Weeks of Gestation

Characteristic	Subchorionic Hematoma (n=451)	No Subchorionic Hematoma (n=1,995)	P*
Maternal age (y)	32.7±5.9	33.1±5.8	.204
Advanced maternal age (35 y or older)	157 (34.8)	765 (38.3)	.162
Gestational age at ultrasound scan (wk)	8.5±1.7	9.6±2.2	<.001
Gestational age (wk)			<.001
6 0/7–6 6/7	84 (18.6)	268 (13.4)	
7 0/7–7 6/7	113 (25.1)	303 (15.2)	
8 0/7–8 6/7	96 (21.3)	292 (14.6)	
9 0/7–9 6/7	62 (13.7)	282 (14.1)	
10 0/7–10 6/7	52 (11.5)	224 (11.2)	
11 0/7–11 6/7	29 (6.4)	198 (9.9)	
12 0/7–12 6/7	10 (2.2)	317 (15.9)	
13 0/7–13 6/7	5 (1.1)	111 (5.6)	
In vitro fertilization	60 (13.3)	289 (14.5)	.517
Vaginal bleeding at time of ultrasound scan	150 (33.3)	162 (8.1)	<.001
Race			.076
White	396 (87.8)	1,686 (84.5)	
Nonwhite	55 (12.2)	309 (15.5)	
Uterine anomaly	24 (5.3)	76 (3.8)	.143
Prior cervical excision procedure	18 (4.0)	75 (3.8)	.813
No. of prior miscarriages			.903
0	271 (60.1)	1,230 (61.7)	
1	96 (21.3)	421 (21.1)	
2	44 (9.8)	183 (9.2)	
3 or more	40 (8.9)	161 (8.1)	
Prior preterm birth	66 (14.6)	288 (14.4)	.914
Leiomyomas	36 (8.0)	135 (6.8)	.361
Prepregnancy diabetes	7 (1.6)	20 (1.0)	.313
Chronic hypertension	13 (2.9)	57 (2.9)	.977
Maternal cardiac disease	5 (1.1)	13 (0.7)	.305
Thrombophilia	28 (6.2)	97 (4.9)	.241
Systemic lupus erythematosus	2 (0.4)	14 (0.7)	.539
BMI (kg/m^2)	24.3±4.8	24.0±4.8	.300
BMI category			.524
Less than 18.5	16 (3.6)	102 (5.1)	
18.5–24.9	274 (60.8)	1,239 (62.1)	
25–29.9	100 (22.2)	415 (20.8)	
30 or greater	55 (12.2)	211 (10.6)	
No BMI data available	6 (1.3)	28 (1.4)	

BMI, body mass index.
Data are mean±SD or n (%) unless otherwise specified.
* Chi-square or Student *t* test.

with no subchorionic hematomas to 8.3% in women with subchorionic hematomas.

We performed a subanalysis of the 451 women with subchorionic hematomas. We compared subchorionic hematoma features between women who did and did not ultimately have pregnancy loss at less than 20 weeks of gestation (Table 3). We found no associations between subchorionic hematoma volume, subchorionic hematoma diameter, vaginal bleeding, or number of subchorionic hematomas and pregnancy loss before 20 weeks of gestation; however, owing to sample size, we were likely underpowered for some of these associations, particularly the association between number of subchorionic hematomas and pregnancy loss.

DISCUSSION

Our data suggest that the presence of a first-trimester subchorionic hematoma in singleton pregnancies is not independently associated with pregnancy loss before 20 weeks of gestation. Though subchorionic hematomas were more common in women with earlier ultrasound scans, we found that earlier ultrasound scan, but not subchorionic hematoma, was

Table 2. Adjusted Risk of Pregnancy Loss Before 20 Weeks of Gestation

Risk Factor	Rate of Pregnancy Loss at Less Than 20 wk	Unadjusted OR (95% CI)	Adjusted OR (95% CI)*
Subchorionic hematoma		1.58 (1.05–2.37)	1.13 (0.74–1.74)
Yes	34/451 (7.5)		
No	98/1,995 (4.9)		
Vaginal bleeding		1.83 (1.18–2.85)	1.39 (0.87–2.21)
Yes	27/312 (8.7)		
No	105/2,134 (4.9)		
Gestational age (wk)		0.73 (0.66–0.81)	0.74 (0.67–0.82)
6 0/7–6 6/7	44/352 (12.5)		
7 0/7–7 6/7	34/416 (8.2)		
8 0/7–8 6/7	14/388 (3.6)		
9 0/7–9 6/7	11/344 (3.2)		
10 0/7–10 6/7	14/276 (5.1)		
11 0/7–11 6/7	6/227 (2.6)		
12 0/7–12 6/7	8/327 (2.4)		
13 0/7–13 6/7	1/117 (0.9)		

Data are n/N (%) unless otherwise specified.
* Final regression model included subchorionic hematoma, vaginal bleeding, and gestational age in weeks.

independently associated with pregnancy loss. This relationship is plausible because it is well-known that the risk of pregnancy loss decreases with advancing gestational age.[11,12] In addition, we did not find any specific characteristics of subchorionic hematomas to be predictive of pregnancy loss when a subchorionic hematoma was noted. Therefore, women diagnosed with a subchorionic hematoma before 14 weeks of gestation should be reassured that their rate of pregnancy loss is not affected by the presence of the subchorionic hematoma, regardless of the subchorionic hematoma's size or the presence of bleeding. This is important information for counseling patients because subchorionic hematoma diagnoses can cause significant concern among expectant parents.

Although several previous studies found an increased rate of pregnancy loss among women with subchorionic hematomas,[4,13–15] there are several others that, consistent with our findings, did not find an increased rate of loss.[7,8] There could be many factors contributing to this inconsistency, such as differing abilities to control for important covariates that affect rates of pregnancy loss. For example, a 2011 meta-analysis by Tuuli et al showed an increased risk of pregnancy loss in women with subchorionic hematomas (17.6% vs 8.9%).[4] In that meta-analysis, there were five studies included in the analysis of subchorionic hematoma and pregnancy loss, and the results were driven by the three largest studies, which all showed a significantly increased risk of pregnancy loss in women with subchorionic hematomas.[13–15] However, these three studies all had significant limitations. The first of these studies, by Borlum et al, was a study from Denmark in 1989 that included women with "symptoms of inevitable abortion in the first or second trimester" and did not control for any covariates, including gestational age, bleeding, maternal age, pregnancy history, and BMI.[13] The second study, by

Table 3. Subchorionic Hematoma Features in Women Who Did and Did Not Have Pregnancy Loss Before 20 Weeks of Gestation

SCH Feature	Pregnancy Loss at Less Than 20 wk (n=34)	No Pregnancy Loss at Less Than 20 wk (n=417)	*P*
Volume (cm^3)*	5.7±12.8	5.6±16.0	.965
Largest diameter (cm)	2.0±1.1	2.1±1.4	.695
More than 1 SCH	2/34 (5.9)	15/417 (3.6)	.372†
Vaginal bleeding	13/34 (38.2)	137/417 (32.9)	.522

SCH, subchorionic hematoma.
Data are mean±SD or n/N (%) unless otherwise specified.
* Measured as length × width × height.
† Nonparametric testing.

Nagy et al,[14] was a study from Hungary in 2003 whose primary analysis was the association between subchorionic hematoma and third-trimester pregnancy outcomes. They reported the rate of spontaneous abortion, but for this outcome they did not report any analysis controlling for covariates. They said the analysis of subchorionic hematoma and spontaneous abortion would be "the subject of another report," but this follow-up report could not be found on a PubMed search of each of the authors' names. Finally, a study by Ball et al[15] from Washington University in 1996 included women up to 22 weeks pregnant, 70% of whom had bleeding. When they controlled for vaginal bleeding, there was, in fact, no association between subchorionic hematoma and pregnancy loss. Therefore, the three studies driving the significant findings in the meta-analysis all have significant limitations.

In comparison, our study had more participants than any of those three studies and included ultrasound scans performed only before 14 weeks of gestation, and we were able to control for gestational age, bleeding, parity, maternal comorbidities (including leiomyomas, prepregnancy diabetes, chronic hypertension, maternal cardiac disease, thrombophilia, and systemic lupus erythematous), and history of pregnancy loss, as well as maternal age, BMI, use of IVF, uterine anomalies, and prior cervical excisional procedures. As such, we believe our results are more reliable than those included in the meta-analysis and that first-trimester subchorionic hematoma is not independently associated with an increased risk of pregnancy loss before 20 weeks of gestation.

The effect of subchorionic hematoma size on rates of pregnancy loss also varies by study. This could be a result of the difficulty in accurately measuring the size of this irregular, three-dimensional structure. In our study, similar to a study by Ben-Haroush et al,[16] subchorionic hematoma size was not associated with pregnancy loss. Another study found that size was only correlated with first-trimester loss when measured as a fraction of the gestational sac, not using the three orthogonal measurements of the hematomas.[9]

Timing has also been proposed as a predictor of pregnancy loss associated with subchorionic hematoma. One retrospective cohort study reported a first-trimester pregnancy failure rate of 12% among women with subchorionic hematomas; the rate was statistically significantly higher for women with subchorionic hematomas diagnosed before 7 weeks of gestation (19.6%) compared with those diagnosed after 8 weeks (3.6%).[9] In our study, subchorionic hematoma was more commonly observed at earlier gestational ages, and gestational age was independently associated with pregnancy loss.

The strengths of our study include the large sample size, detailed clinical information, minimal selection bias, and a low percentage of women lost to follow-up. In our practice, all ultrasound images are archived, and formal reports are generated. We have routine documentation of the presence of vaginal bleeding at the time of the ultrasound scan per protocol. In addition, all of our patients' records are on an electronic medical record system. This allows for a complete and thorough review of the patients' ultrasound reports, maternal risk factors, and pregnancy outcomes. We had a large number of low- and high-risk women with a wide range of comorbidities. This is an improvement from several prior studies that looked only at specific subsets of the obstetric population, such as patients undergoing infertility treatment.[8,17]

Our study is limited by its retrospective design. In addition, our study may be limited by using data from one obstetric practice, as opposed to a more heterogeneous population. Another limitation of this study is that ultrasonographers and physicians were not blinded to whether a patient had vaginal bleeding or not; thus, it is possible that an increased index of suspicion may have affected the detection of subchorionic hematomas in those women. Our study also only looked at subchorionic hematoma at one point in time; it is possible that persistence of subchorionic hematoma during the pregnancy, increasing size, and gestational age of the subchorionic hematoma at the time of resolution may be important predictors of pregnancy outcome. Thus, further studies should include separate analyses of persistent hematomas compared with those that resolved over time to evaluate associations with pregnancy loss and other adverse pregnancy outcomes.

In conclusion, in women with singleton pregnancies, the presence of subchorionic hematoma before 14 weeks of gestation is not independently associated with pregnancy loss before 20 weeks of gestation, regardless of the subchorionic hematoma's size and presence of vaginal bleeding.

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