The Effects of First-trimester Subchorionic Hematoma on Pregnancy Outcomes:A Retrospective Cohort Study

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Abstract

Background: Although first-trimester subchorionic hematoma (SCH) always concerns expectant parents, its clinical significance remains controversial. This study aimed to examine the relationship between first-trimester SCH and its association with subsequent miscarriage and other perinatal outcomes.

Methods: We conducted a retrospective cohort study including 43,660 women who underwent routine prenatal care since the first trimester and then were followed up for maternal and neonatal outcomes. SCH was detected in the first-trimester ultrasound examinations. Robust Poisson regression was used to estimate adjusted risk associations between SCH maternal and neonatal outcomes.

Results: A total of 815 (1.87%) SCH were detected in the first-trimester ultrasound examination. The rate of miscarriage was statistically significantly higher in women with SCH than in those without [35.2% vs. 23.9%, P<0.01; adjusted relative risk (RR):1.44, 95% confidence interval (CI): 1.31-1.58]. Subgroup analysis of women with SCH showed a clear trend that the earlier SCH occurred, the higher the risk of miscarriage was [adjusted RR and 95% CI for onset at the gestational weeks of 8-9, 6- 7, and <6 vs. ≥10: 1.30 (0.69-2.46), 2.33 (1.28-4.23), and 4.18 (2.30-7.58), respectively; Ptrend<0.01]. In addition, women with SCH volume ≥1ml showed higher risk than those <1 ml [adjusted RR and 95% CI for 1-4.9 ml, and ≥5 ml vs. <1 ml: 1.36 (1.10-1.68) and 1.56 (1.18-2.07), respectively]. There was no statistically significant difference in the rates of other pregnancy outcomes between women with and without SCH.

Conclusions: First-trimester SCH might significantly increase the risk of miscarriage, particularly the one that occurs early and the one with large size. Data from this study do not suggest adverse effects of SCH on other maternal and neonatal outcomes.

Introduction

Subchorionic hematoma (SCH) is intrauterine bleeding that usually occurs in the early stage of pregnancy and is displayed in ultrasound image as hypoechoic or anechoic crescent-shaped areas between the gestational sac and uterine wall. The reported incidence of SCH varies widely from 0.46–22%[1–3], probably due to differences in study population, study design, and the route and resolution of the ultrasound equipment that was employed. Although the exact etiology is uncertain, SCH is believed to be a consequence of partial detachment of the trophoblasts from the uterine wall[4]. The clinical significance of SCH in early pregnancy remains controversial, and whether it increases the risk of adverse pregnancy outcomes is still uncertain. Some studies reported that SCH increased the risk of miscarriage[5, 6], while others reported null associations[7, 8]. Increased risks of fetal growth restriction and preterm delivery associated with SCH were also reported in some but not all studies[9, 10]. Inconsistent findings from these former studies make patient counseling rather difficult. Therefore, we reexamined the relationships between SCH and major pregnancy outcomes in an obstetric cohort or women with singleton pregnancy.

Materials And Methods

We conducted a retrospective, hospital-based cohort study at Guangzhou Women and Children's Medical Center, a tertiary referral hospital in South China. The study protocol was approved by the ethics committee of the institute (2020–15001). In the cohort women who paid their first-trimester antenatal care visits with ultrasound-confirmed singleton pregnancy between January 2016 and January 2020 were included. All the women underwent ultrasound scan before 12 gestational weeks, which was performed by ultrasonographers with a specialty in obstetrics and gynecology using a 5–7 HMz transvaginal probe (Resona 8, Mindray Co., Ltd. China). Patients with uterine malformation or scar pregnancy and patients choosing induced abortion were excluded. Gestational age was determined based on the last menstrual period or first-trimester ultrasound scan result according to the standard guideline[11]. The presence of subchorionic hematoma on the ultrasound was defined as a crescent-shaped echo-free or hypoechoic region between the chorionic membrane and myometrium. Antero-posterior, longitudinal and height diameters were recorded to calculated the size of the hematoma. All pregnant women were followed up throughout their pregnancy course during which miscarriage (unexpected pregnancy loss within 24 gestational weeks)[12], stillbirth (intrauterine fetal death after 24 gestational weeks), and other maternal and neonatal outcomes were documented. Demographic and baseline clinical characteristics, such as maternal age, presence of vaginal bleeding in first trimester and pre-pregnancy comorbidities, were obtained from the clinical records. The volume of SCH was calculated as 0.52 times the product of the antero-posterior, longitudinal, and height diameters[13]. Gestational age at the time of SCH diagnosis was also based on the last menstrual period or ultrasound scan. The maternal and neonatal outcomes under investigation included miscarriage, mid-term induced abortion, stillbirth, hypertensive disorders of pregnancy, cesarean section, preterm delivery, placental abruption, premature rupture of membrane, birth weight, Apgar scale and congenital anomalies. Among the women with SCH, we also assessed whether the volume of the hematoma and the gestational age at hematoma diagnosis are associated with miscarriage and whether vaginal bleeding in early pregnancy is an extra independent risk factor.

Statistical Analysis

Continuous variables were summarized with mean and range and compared between the subchorionic hematoma and non-subchorionic hematoma groups with a two-sample t-test. Frequencies were calculated for categorical variables, and whether there was statistically significantly different between the subchorionic hematoma and non-subchorionic hematoma groups were examined using Pearson's chi-square test or Fisher's exact test in case of small counts. For any specific maternal or fetal outcome, the relative risk (RR) and 95% confidence interval (CI) for subchorionic hematoma vs. non-subchorionic hematoma, were estimated by fitting a robust Poisson regression model that adjusted for potential confounding factors such as maternal age, vaginal bleeding, and pre-existing diabetes. Robust Poisson regression, in contrast to logistic regression, directly estimates relative risk and thus avoids the considerable overestimation of relative risk for a common event such as miscarriage. We further limited the analysis to women with diagnosis of subchorionic hematoma to identify factors that might contribute to the subsequent occurrence of miscarriage using a multivariable robust Poisson regression model that

included the following factors: maternal age, gestational age at subchorionic hematoma diagnosis, volume of subchorionic hematoma, and vaginal bleeding. All the statistical tests were two-sided with $P < 0.05$ considered statistically significant. The R software (version 4.0.2, R foundation, Vienna, Austria) was used to perform the statistical analysis.

Results

During the study period, 43,660 pregnant women with singleton pregnancy presented for routine prenatal care before 12 gestational weeks and were followed up since then throughout the entire pregnancy course. Of them, 815 (1.87%) women were diagnosed with SCH through ultrasound scan (median gestational age:7 weeks; range: 4-13^{+6} weeks). Baseline characteristics of the women with and without SCH are showed in Table 1. There were no differences between the two groups as for maternal age, leiomyomas, pre-pregnancy diabetes and chronic hypertension. However, women with SCH were more likely to have first-trimester vaginal bleeding than those without (21.7% *vs.* 18.0%, P <0.01). No maternal death occurred in this cohort.

A total of 10538 women ended up with miscarriage (median gestational age: 8 weeks; range: 5-23^{+6}weeks), the rate of miscarriage was significantly higher among women with subchorionic hematoma (35.2% versus 23.9%, p <0.01) (Table 2). Furthermore 1385 women ended up with stillbirth; the rate of stillbirth was not different between women with and without SCH (3.6% versus 3.2%, p =0.59). Among the women who maintained their pregnancy (499 with hematoma and 31,178 without subchorionic hematoma), no statistically significant difference was observed between the two groups for the mean gestational age at delivery, the rate of cesarean section, the rate of preterm delivery, the incidence of hypertensive disorders of pregnancy, and the incidences of placental abruption and premature rupture of membrane, after control for maternal age, vaginal bleeding and pre-existing diabetes (Table 2). Low birth weight (< 2500 g), macrosomia (≥ 4000 g), Apgar scale and congenital anomalies between the two groups also showed no statistically significant difference (Table 3).

For the women with SCH, higher hematoma volume (≥1 ml) was statistically significantly associated with a higher risk of miscarriage than volume□1 ml (RR for 1-4.9 ml vs. <1 ml: 1.36, 95% CI 1.10-1.68; RR for ≥5 ml vs. <1 ml: 1.56, 95% CI 1.18-2.07; P_{trend}=0.10 Table 4). With respect to gestational age at SCH diagnosis, women with SCH diagnosed before 6 gestational weeks had the highest rate of miscarriage (64.4%), there was a statistically significant trend showing the earlier the was diagnosed, the higher the risk of miscarriage was [adjusted RR and 95% CI for onset at the gestational weeks of 8-9, 6-7, and <6 vs. ≥10: 1.30 (0.69-2.46), 2.33 (1.28-4.23), and 4.18 (2.30-7.58), respectively; P_{trend}<0.01, Table 4). There was no statistically significant association between vaginal bleeding and miscarriage risk (35.6% *vs.* 33.6%; RR: 1.07, 95% CI 0.79-1.44).

Table 1

Baseline maternal characteristics

	SCH (n=815)	Without SCH (n=42845)	p
Maternal age, yrs, mean (range)	31.0 (19.6-45.4)	30.8 (15.2-51.0)	0.30
Vaginal bleeding, n (%)	177 (21.7)	7704 (18.0)	<0.01
Leiomyomas, n (%)	25 (3.1)	1168 (2.7)	0.63
Pre-pregnancy diabetes, n (%)	13 (1.6)	389 (0.9)	0.06
Chronic hypertension, n (%)	2 (0.2)	186 (0.4)	0.45
SCH: subchorionic hemorrhage			

Table 2

Association between subchorionic hemorrhage and maternal complications

	SCH (n=815)	Without SCH (n = 42845)	p	RR (95% CI)
Miscarriage (<24 wk) ‡	287 (35.2)	10251 (23.9)	<0.01	1.44 (1.31-1.58)
Mid-term induced abortion, n (%)	0 (0)	50 (0.1)	0.63	NA
Stillbirth (≥ 24wk), n (%)	29 (3.6)	1356 (3.2)	0.59	1.10 (0.76, 1.57)
Hypertensive disorders of pregnancy	12 (1.5)	641 (1.5)	1.00	0.98 (0.56-1.73)
Cesarean section*‡, n (%)	135 (27.0)	9353 (30.0)	0.17	0.90 (0.78-1.04)
Preterm delivery*‡, n (%)	18 (3.6)	1223 (3.9)	0.81	0.88 (0.56, 1.40)
Placental abruption*‡, n (%)	8 (1.6)	369 (1.2)	0.52	1.31 (0.66-2.62)
Premature rupture of membrane*‡, n (%)	94 (18.8)	6894 (22.1)	0.09	0.85 (0.71-1.02)
Fetal distress, n (%)	7 (1.4)	561 (1.8)	0.67	0.81 (0.39-1.70)

SCH: subchorionic hemorrhage

*n=31687 (including 499 SCHs and 31188 non-SCHs) after exclusion of subsequent pregnancy losses

‡Adjusted for maternal age, vaginal bleeding, and pre-existing diabetes.

Table 3

Association between subchorionic hemorrhage and neonatal outcomes

Outcome	SCH (n = 499)	Without SCH (n = 31178)	p	RR (95% CI)
Newborn birth weight ≥ 4000 g: yes, n (%)	13 (2.6)	792 (2.5)	1.00	1.04 (0.60, 1.78)
Newborn birth weight < 2500 g: yes, n (%)	25 (50.1)	1398 (44.8)	0.60	1.09 (0.74, 1.60)
Apgar < 7 at 1 min, n (%)	1 (0.20)	174 (0.56)	0.25	NA
Apgar < 7 at 5 min, n (%)	0 (0)	51 (0.16)	0.24	NA
Apgar < 7 at 10 min, n (%)	0 (0)	27 (0.08)	0.37	NA
Fetal distress, n (%)	7 (1.4)	546 (1.8)	0.68	0.81 (0.39, 1.70)
Congenital anomalies, n (%)	0 (0)	77 (0.25)	0.42	NA
Adjusted for maternal age, vaginal bleeding, and pre-existing diabetes.				

Table 4

Association between subchorionic hemorrhage (n=629) and miscarriage

Features	Miscarriage (n=213)	Without Miscarriage (n=416)	p	P_{trend}	RR (95% CI)
Maternal age	31.6 (20.9-45.4)	30.3 (19.6, 44.1)	<0.01		1.05 (1.02-1.07)
SCH volume, n (%)					
<1 ml	74 (30.6)	168			1.00
1-4.9 ml	109 (35.6)	197			1.36 (1.10-1.68)
≥5 ml	30 (37.0)	51	0.38	0.18	1.56 (1.18-2.07)
GA at diagnosis, n (%)					
≥10 wk	9 (16.7)	45			1.00
8-9 wk	38 (20.6)	146			1.30 (0.69-2.46)
6-7 wk	110 (36.2)	194			2.33 (1.28-4.23)
< 6 wk	56 (64.4)	31	< 0.01	< 0.01	4.18 (2.30-7.58)
Vaginal bleeding, n (%)					
no	187 (35.6)	369			1.00
yes	26 (33.6)	47	0.84		1.07 (0.79-1.44)
CI, confidence interval; GA, gestational age; RR: relative risk; SCH, subchorionic hemorrhage.					

Discussion

In this cohort study, we observed an increased risk of miscarriage associated with first-trimester subchorionic hematoma in singleton pregnancies. Further analysis showed that among women with SCH, the volume of SCH is positively, while the earlier onset of SCH is negatively, associated with the occurrence of miscarriage. We observed no statistically significant associations between SCH and neonatal and other maternal outcomes.

The exact pathological mechanism of SCH is unknown, although the asynchronous development of the decidua and trophoblast and the impaired function of trophoblastic capillaries are suspected[14]. When the impaired capillaries are located in the margin of trophoblast or closed in cervix, bleeding could flow

through the cervix and could not form a hematoma, but when the impaired capillaries are located in the inner interface of the chorionic and uterine wall, the collected blood could result in partial detachment of the trophoblasts from the uterine wall. Theoretically, it is possible that the hematoma changes the local microenvironment of chorionic and might have an impact on function of trophoblast. Our results suggest that SCH occurring in the first trimester might increase the risk of miscarriage. This result is consistent with three previous studies[4, 5, 15], but inconsistent with the study of Mackenzie et al[16]. In their study, the rate of pregnancy loss before 20 weeks of gestation was 7.5% and 4.9% in women with and without SCH, respectively, which was substantially lower than the rates (15%-25%) observed in other populations[17, 18]. The higher percentage of vaginal bleeding we observed in the women with SCH is not surprising, as it has been suggested that both SCH and vaginal bleeding are very likely to concur following the bleeding in the area of the trophoblast site[19].

Prior studies concerning the effect of hematoma size on the pregnancy loss reported inconsistent findings[4, 16, 20, 21]. These studies were subject to a smaller sample size and lack of consistent methods used to assess bleeding volume. For example, Bennett et al. and Heller et al. evaluated the hematoma size using the percentage of hematoma area to gestational sac[20, 21], Naert et al. and Maso et al. in volumes[4, 16], and Lulu et al. in median centimeters[22]. The cut-off value of hematoma size also varied across studies. Our results suggest that the risk of miscarriage might be proportional to the volume of the hematoma, which however deserves a more detailed study where more women with higher volume of bleeding are included.

The present study supports the existing evidence that earlier onset of SCH is particularly dangerous to maintenance of pregnancy. The study of Maso et al. showed that the risk of pregnancy loss was nearly 15 times higher for SCH diagnosed before 9 weeks of gestation than for those diagnosed after 9 weeks[4]. Likewise, Howard et al. observed that compared with women diagnosed with SCH after 8 weeks of gestation, SCH diagnosed before 8 weeks was associated with a significantly higher risk of miscarriage[21]. It is well known that over half of the early miscarriages are caused by chromosomal abnormalities such as aneuploidy[3, 23]. However, it is unclear whether women with aneuploidy pregnancies are more prone to subchorionic hematoma because of the embryonic origin of the trophoblast cells. It is suggested that presence of SCH in the early stage of pregnancy affects the normal process of trophoblast invasion, which is vital for a successful pregnancy[19, 24]. However, as the pregnancy proceeds, it is possible that the fetus would become less vulnerable to and the resulting trophoblast impairment.

Our data demonstrated no statistically significant associations between first-trimester SCH and maternal complications other than miscarriage, not fully in line with the two prior studies [9, 25], where SCH was also associated with increased risks of stillbirth and placental abruption. Of note, the two prior studies detected SCH at, on average, 18 and 10 gestational weeks, respectively, considerably later than the present study (around 7 gestational weeks), suggesting that SCH at the early stage of pregnancy has chance to dissolve spontaneously and eventually causes less harm, while persisting SCH might be more concerning and indicative of multiple maternal complications. In addition, our results also suggest that

the risks of neonatal outcomes were not increased in pregnant women with SCH in first trimester. Three recent studies also found no relationship between birth weight and SCH [8, 10, 26], but two early studies reported lower birth weight in women with SCH than in those without[9, 15]. Oxidative stress impairment and mechanical effects of the hematoma are two supposed mechanisms underlying the positive associations between SCH and adverse pregnancy outcomes [5, 27] All the cases included in our study were women with SCH detected in first trimester. If the pregnancy continued, the hematoma would probably be absorbed after several months and the mechanical effects of the hematoma in the third trimester would diminish. Prospective studies should be designed to continuously observe the hematoma during the pregnancy in order to analyze persistent hematoma compared with those absorbed over time to clarify the potentially differed associations with perinatal outcomes.

Our study has several limitations. Firstly, the data of the study were collected retrospectively. Secondly, we were unable to confirm the potential impact of the localization of the hematoma on pregnancy outcomes since the location data of SCH were not routinely collected in our institute. However, several studies have consistently shown that retroplacental hematomas are significantly associated with an increased risk of averse maternal and neonatal outcomes.[9, 10] Lastly, our study did not include information on previous miscarriage, previous premature birth, and use of in vitro fertilization for the index pregnancy, as data on these variables were largely missing.

In conclusion, SCH during the first trimester might significantly increase the risk of miscarriage in women with singleton pregnancy, particularly the one that occurs early and the one with large size. However, a diagnosed of SCH is not associated with adverse maternal complications and neonatal outcomes. Our study provides new evidence for the clinical consultant of those expected patients.

Abbreviations

SCH: subchorionic hemorrhage

Declarations

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Conflict of Interest:

All listed authors declare that they have no conflict of interest.

Ethics approval and consent to participate:

The study was approved by the Ethical Committee of the Guangzhou Women and Children's Medical Center. (2020-15001). All methods were carried out in accordance with relevant guidelines and regulations. Ethics approval and consent to participate was waived by the Ethics Committee of Guangzhou Women and Children's Medical Center due to the retrospective nature of the study.

Contribution to authorship

CG and KL drafted the manuscript. CG and YH contributed to the design of the research. KL contributed to the development of the statistical plan and statistical analysis of the data. QL contributed to the conception of the study. XL and QX contributed to data management and prepared the retrospective data for analysis. All authors reviewed, read and approved the final manuscript.

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Availability of data and materials

Datasets obtained and/or analyzed in this study are available from the corresponding author on reasonable request.

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