# Outcomes of in vitro fertilization pregnancies complicated by subchorionic hematoma detected on first-trimester ultrasound

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**Objective:** To estimate the association between subchorionic hematoma (SCH) on ultrasound and pregnancy outcomes in in vitro fertilization (IVF) pregnancies.
**Design:** Institutional Review Board–approved, retrospective cohort study.
**Setting:** Tertiary care university-based facility.
**Patient(s):** In this study, 1,004 patients who underwent IVF with a viable singleton pregnancy from January 1, 2009 through December 31, 2017.
**Intervention(s):** Subchorionic hematoma versus no hematoma diagnosed on first-trimester ultrasound.
**Main Outcome Measure(s):** Live birth, preterm birth, and spontaneous abortion.
**Result(s):** We found that 1,004 women met the criteria and 187 (18.6%) had an SCH. In bivariate and multivariate regression models, there were no associations between SCH and the outcomes of live birth, preterm birth, or birth weight.
**Conclusion(s):** Subchorionic hematoma detected on first-trimester ultrasound after IVF is not associated with probability of live birth, probability of preterm birth, or infant birth weight in this patient population. (Fertil Steril Rep® 2020;1:149–53. ©2020 by American Society for Reproductive Medicine.)
**Key Words:** Subchorionic hematoma, IVF, live birth



Subchorionic hematoma (SCH) was first described in 1981 as an ultrasound finding in patients with symptoms of threatened spontaneous abortion (1). Now, SCH is a common, often asymptomatic, finding on ultrasound, perhaps owing to more sensitive ultrasound technology or improved access to ultrasound. The chorionic membrane and uterine wall are approximated closely to each other in the early gestational period and SCH can cause a separation of these two structures, which can then be visualized on ultrasound. This separation could precede spontaneous abortion or lead to placental dysfunction and subsequent adverse pregnancy outcomes (2, 3).

Consistent with the proposed mechanism of SCH, a meta-analysis in 2011 concluded that, in spontaneous pregnancies, SCH is associated with an increased risk of pregnancy loss, preterm delivery, abruption, and preterm premature rupture of membranes (3). However, whether SCH is associated with adverse outcomes in in vitro fertilization (IVF) pregnancies is unclear. This is important because SCH may be identified more commonly in IVF pregnancies, in which women may undergo more ultrasound examinations. For example, a 2014 study reported that 22.4% of IVF pregnancies and 11% of non-IVF pregnancies were complicated by SCH (4). Here, we examined the association between SCH and live birth in IVF pregnancies.

## MATERIAL AND METHODS

This was a retrospective cohort study of women who underwent programmed fresh or frozen IVF at our clinic between January 1, 2009, and December

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31, 2017. Patients were included if they had a singleton viable pregnancy on first-trimester ultrasound. In our clinic, ultrasound examinations are conducted routinely on every patient between 7 and 8 weeks of gestation unless earlier ultrasound is indicated for symptoms such as pain or bleeding. Patients were excluded if they were gestational carriers, used donor eggs, had a multiple-gestation pregnancy, or had a therapeutic termination. Patients were excluded if outcome data were not available in paper charts or electronic medical records. If the patient underwent more than one IVF cycle during this time period, only the first pregnancy was included in the data. The project was approved by the Institutional Review Board at the Washington University School of Medicine.

In our clinic, American Registry for Diagnostic Medical Sonography-certified ultrasound technicians performed the ultrasounds, and all scans included a standardized check of SCH, which included a "yes or no" determination if a SCH is visualized along with its size. The technicians and nurses prospectively entered basic maternal demographics and pregnancy ultrasound data for every patient into a clinic database. Nurses collected maternal and neonatal outcomes from the patient by telephone or letter contact and entered these data into the electronic medical record and the Society for Assisted Reproductive Technology database. We used our clinic database and the electronic medical records to identify patients who met inclusion criteria and to extract outcomes data.

Subchorionic hematoma was defined as fluid collection between the uterine wall and gestational sac detected on ultrasound. Diagnosis was made, and the size of the SCH was measured, at the time of ultrasound. Measurement of SCH was calculated by visualizing the maximum diameter of the length, width, and height of the bleed with longitudinal and transverse images. A viable pregnancy was defined as the presence of a fetal pole with a heartbeat on ultrasound. We excluded women who had a viable pregnancy and no SCH on one ultrasound but had no fetal heartbeat and a SCH on a subsequent ultrasound. We did so because, in these cases, it was not possible to determine whether the SCH occurred before or after fetal demise. We defined short-interval pregnancy as less than 18 months between the delivery date of the preceding live birth and the conception date of the index birth (5).

We compared the maternal demographic information and pregnancy outcomes between the women who did and did not have a SCH. The primary outcome for this study was live birth. Secondary outcomes included spontaneous abortion, preterm delivery (at less than 37 weeks' gestation), and birth weight at delivery.

The Student *t* test was used to compare baseline continuous variables that were distributed normally, and the Mann-Whitney *U* test was used for nonparametric variables, which included maternal age and size of the SCH. Chi-square or Fisher exact tests were used for categorical variables. Unadjusted odds ratios and 95% confidence intervals were calculated for the primary outcome and each of the secondary outcomes. Multivariate logistic regression including all biologically plausible variables (age, race, body mass index, smoking status, short-interval pregnancy, and prior live birth) was used to determine the association between SCH and pregnancy outcomes after adjusting for significant variables from bivariate analysis and factors known to affect pregnancy outcomes. SPSS software (version 25) was used for all statistical analyses.

## RESULTS

Of the 1,004 women with a viable singleton pregnancy, 184 (18.3%) had a SCH during their first-trimester ultrasound examination, and, of those, 161 (87.5%) had a live birth (Fig. 1). Of the 817 (81.3%) women without a SCH in the first trimester, 737 (90.2%) had a live birth. Baseline demographics (e.g., age, body mass index, race, smoking status, fresh versus frozen embryo transfer, and day of transfer) were similar between groups. All ultrasounds were done at a gestational age (GA) between 5 weeks 5 days and 11 weeks 1 day and the median GA at diagnosis of SCH was 7 weeks 0 days for both fresh and frozen embryo transfers. Women with a SCH were more likely than those without a SCH to have a short-interval pregnancy, but this difference was not statistically significant (Table 1). Symptomatic bleeding was only collected in the patient populations with SCH, and just over half (54.7%) of those with SCH in our cohort had symptomatic vaginal bleeding with live birth rates being 91% in the SCH without bleeding and 82% in those with bleeding ($P=.105$).

The rate of live birth did not significantly differ between those with and without SCH. Additionally, in a multivariate logistic regression adjusted for all biologically plausible risk factors associated with decreased chance of live birth or full-term delivery, patients with and without SCH had similar rates of live birth (Table 2).

Subchorionic hematoma was not associated with decreased birth weight (SCH, 3,334 g $\pm$ 627 g; no SCH, 3,269 g $\pm$ 606 g; $P=.22$). SCH had no significant association with preterm birth or spontaneous abortion. In multivariate logistic regression, SCH was not significantly associated with preterm birth or spontaneous abortion (Table 2).

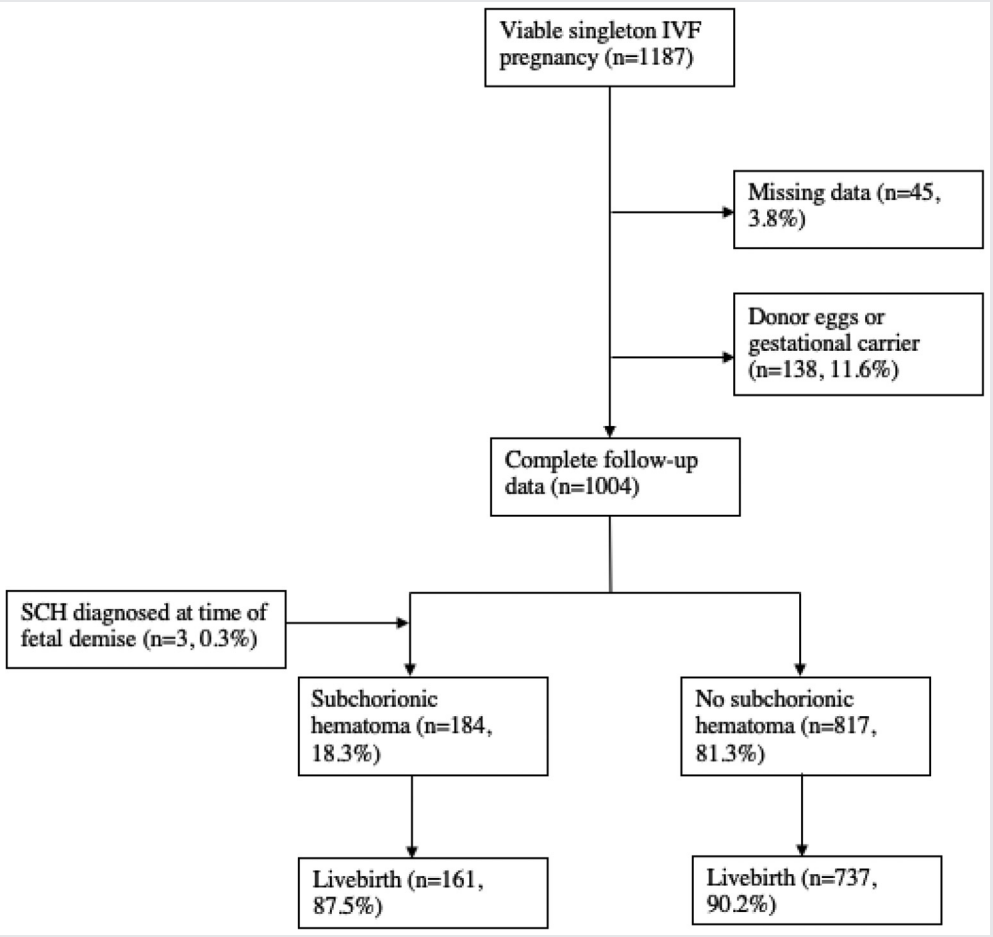
The only variable significantly associated with live birth was age (Table 3). Live birth rates were associated significantly with lower maternal age but not with body mass index. In those with a documented SCH, size of that SCH and its association with live birth also was analyzed (Table 3). Patients without a live birth had larger SCHs than those with a live birth, but the difference was not significant. Because the SCH sizes were variable (between 0.08 mL and 97.01 mL, quartiles 25th = 0.56, 50th = 1.52, 75th = 4.5), we removed patients with SCHs greater than the 90th percentile (23.76) for this cohort, but the difference in SCH size in the two groups remained statistically insignificant (2.4 $\pm$ 2.7 mL in no live birth group vs. 2.0 $\pm$ 2.1 in live birth group; $P=.55$; Table 3).

Despite having a large population, given the overall high incidence of live birth in those with and without SCH, we did not have adequate power to determine a difference between the two groups for our primary outcome (post hoc power, 20.9%).

## DISCUSSION

In our cohort of IVF pregnancies, SCH detected using ultrasound in the first trimester was not significantly associated

FIGURE 1




Study participants. IVF = in vitro fertilization; SCH = subchorionic hematoma.

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with rates of spontaneous abortion, preterm birth, or live birth, nor was it associated with birth weight at delivery. These data could be reassuring to patients who have undergone IVF and who have a SCH found incidentally on ultrasound.

In our cohort of patients who have undergone IVF, 18.6% experienced a SCH, which is at the high end of the range (0.5%–22%) reported in spontaneous pregnancies, but is consistent with a recently published 2019 study of spontaneous pregnancies (3, 6). However, SCH may occur with similar frequency in patients who have undergone IVF and spontaneous pregnancy patients but may be detected more frequently in patients who have undergone IVF because they tend to undergo ultrasound examinations at earlier GAs. Alternatively, some suggest IVF pregnancies have a higher incidence of abnormal placentation, and, therefore, blood vessels may be more likely to rupture during invasion into the endometrium (7, 8). This is debated with animal and human data supporting that placentation is similar in IVF and naturally conceived pregnancies (9, 10).

Two mechanisms have been proposed to explain the adverse outcomes of SCH in spontaneous pregnancies. First, SCH occurring before placentation could lead to fetal oxidative stress (11). Second, inadequate trophoblast invasion into the uterus could impair angiogenesis and thus harm the fetus (12). Nonetheless, in our cohort of IVF pregnancies, SCH was not associated with increased risk of adverse outcomes. This may be because, although every patient who has undergone IVF in our clinic undergoes ultrasound at least once in the first trimester, only 54.7% of cohort patients with SCH had symptomatic vaginal bleeding. In contrast, in spontaneous pregnancies, early ultrasounds that detect SCH are often only done because the patient has vaginal bleeding or other symptoms and the frequency of those ultrasounds are less than in the IVF population.

Our findings are somewhat inconsistent with prior studies that have evaluated outcomes of IVF pregnancies with SCH. For example, Zhou et al. (13) reported no association with pregnancy loss but found that birth weight was lower in singleton pregnancies with SCH than in singleton

## TABLE 1

**Baseline characteristics for patients with and without subchorionic hematoma.**

| Characteristic | No SCH (n = 817) | SCH (n = 184) | *P* value |
|---|---|---|---|
| Age (y) | | | .737 |
| <35 | 527 (64.6) | 126 (68.5) | |
| 35–37 | 169 (20.7) | 33 (17.9) | |
| 38–40 | 97 (11.9) | 18 (9.8) | |
| 41–42 | 20 (2.5) | 6 (3.3) | |
| >42 | 3 (0.4) | 1 (0.5) | |
| BMI (kg/m$^2$) | | | .273 |
| <18.5 | 19 (2.3) | 3 (1.6) | |
| 18.5–25 | 365 (44.8) | 94 (51.4) | |
| 25–30 | 224 (27.5) | 39 (21.3) | |
| >30 | 206 (25.3) | 47 (25.7) | |
| Race | | | .354 |
| White | 692 (84.7) | 164 (87.7) | |
| Black | 34 (4.2) | 5 (2.7) | |
| Asian | 50 (6.1) | 10 (5.3) | |
| Hispanic | 9 (1.1) | 3 (1.6) | |
| Other | 16 (2) | 5 (2.7) | |
| Unknown | 16 (2) | 0 (0) | |
| IVF method | | | .338 |
| Fresh embryo transfer | 649 (79.4) | 142 (75.9) | |
| Frozen embryo transfer | 168 (20.6) | 45 (24.1) | |
| Prior live birth | | | .388 |
| No | 606 (74.2) | 145 (77.5) | |
| Yes | 211 (25.8) | 42 (22.5) | |
| Prior pregnancy | | | .811 |
| No | 430 (52.6) | 96 (51.3) | |
| Yes | 387 (47.4) | 91 (48.7) | |
| Smoker | | | .394 |
| No | 796 (97.7) | 179 (96.2) | |
| Yes | 19 (2.3) | 7 (3.8) | |
| Short-interval pregnancy[a] | | | .068 |
| No | 784 (98.2) | 179 (95.7) | |
| Yes | 14 (1.8) | 8 (4.3) | |
| Day of embryo transfer | | | .681 |
| Day 3 | 392 (48) | 86 (46) | |
| Day 5 | 425 (52) | 101 (54) | |
| No. of embryos transferred | | | .487 |
| 1 | 187 (22.9) | 34 (18.2) | |
| 2 | 505 (61.8) | 127 (67.9) | |
| 3 | 96 (11.8) | 17 (9.1) | |
| 4 | 21 (2.6) | 7 (3.7) | |
| 5 | 7 (0.9) | 2 (1.1) | |
| 6 | 1 (0.1) | 0 (0) | |
| Congenital or genetic defects | | | 1.00 |
| No | 730 (96.1) | 165 (95.9) | |
| Yes | 30 (3.9) | 7 (4.1) | |

*Note:* Data presented as n (%), unless specified otherwise. BMI = body mass index; IVF = in vitro fertilization; SCH = subchorionic hematoma.
[a] Defined as less than 18 months between the delivery date of the preceding live birth and the conception date of the index birth.

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## TABLE 2

**Pregnancy outcomes for patients with and without subchorionic hematoma.**

| Characteristic | No SCH (n = 817) | SCH (n = 184) | Unadjusted OR (95% CI) | Adjusted OR (95% CI) |
|---|---|---|---|---|
| Live birth | | | 0.7 (0.5–1.1) | 0.40 (0.2–1.1) |
| No | 80 (9.8) | 23 (12.5) | | |
| Yes | 737 (90.2) | 161 (87.5) | | |
| Spontaneous abortion | | | 1.4 (0.9–2.3) | 2.6 (1.0–6.9) |
| No | 738 (90.7) | 161 (87.5) | | |
| Yes | 76 (9.3) | 23 (12.5) | | |
| Preterm | | | 0.7 (0.4–1.2) | 0.7 (0.4–1.3) |
| No | 639 (85.9) | 146 (90.1) | | |
| Yes | 105 (14.1) | 16 (9.9) | | |

*Note:* Data presented as n (%), unless specified otherwise. CI = confidence interval; OR = odds ratio; SCH = subchorionic hematoma.

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**TABLE 3**

**Characteristics of patients with and without a live birth.**

| Characteristic | No live birth | Live birth | *P* value |
|---|---|---|---|
| Age (y) | 34.7 ± 3.9 | 32.8 ± 4.0 | < .00 |
| BMI (kg/m$^2$) | 27.5 ± 6.8 | 26.8 ± 6.3 | .274 |
| Size of SCH (mL) [a] | 8.68 ± 21.7 | 3.78 ± 5.7 | .329 |

*Note:* Data presented as mean ± standard deviation, unless specified otherwise. BMI = body mass index; SCH = subchorionic hematoma.
[a] Included only patients with SCH; age and body mass index included entire cohort

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pregnancies without SCH. Eaton et al. (14) also reported no association with pregnancy loss but found that birth weight was lower in twin IVF pregnancies with SCH than in twin pregnancies without SCH. Conversely, Xiang et al. (12) found no association between SCH and birth weight but found that those with SCH had a higher rate of preterm birth than those without SCH. Our study was consistent with a retrospective cohort from 2019 including 2,446 women including spontaneous and IVF pregnancies (6, 15). In this most recent study, no independent association was found between SCH and spontaneous abortion before 20 weeks or after 20 weeks, which is consistent with our findings. However, their study included spontaneous (n = 340) and IVF pregnancies (n = 49), whereas our study was novel because it included a larger group of only patients who had undergone IVF.

Our study has several strengths, including our large sample size and the fact that we included each woman only once to decrease bias. However, despite having a large sample size compared with other studies, we still did not have adequate power to detect a difference in our primary outcome, and future studies and meta-analyses will improve the power. Additionally, we had access to data on many of the biologically plausible causes of decreased live birth, including smoking, pregnancy interval, and prior live birth, allowing us to adjust for confounders in the logistic regression.

Our study also has several limitations. First, the retrospective nature of our design increased the risk for data collection errors, confounders, and biases. Second, we were unable to know if scans were performed earlier due to bleeding, however, our protocol always includes a viability scan at 6–8 weeks GA, which should decrease selection bias, and the average GA at diagnosis of SCH was 7 weeks. Third, chart review can lead to errors during the charting or data collection. Fourth, we did not have all pregnancy outcome data, including diagnosis of pre-eclampsia or premature rupture of membranes, which would contribute to the incidence of preterm delivery. Fifth, we did not compare the SCH rate in patients who had undergone IVF with the SCH rate in spontaneous pregnancies at our institution. Finally, we did not stratify women with or without SCH according to whether or not they had vaginal bleeding because we did not have the data of those without SCH who reported vaginal bleeding during their pregnancy. This may be an important factor to consider.

In conclusion, in women who conceived using IVF and have a singleton pregnancy, SCH was not independently associated with increased risk of spontaneous abortion or preterm birth, and similar rates of live birth were noted between the two groups. Further studies with larger patient populations or meta-analyses, which can include multiple studies, will help to further evaluate these outcomes in the IVF population.

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