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The significance of ultrasound features of sub-chorionic haemorrhage as a predictor of adverse perinatal outcome: A retrospective review

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ABSTRACT

Introduction: This retrospective single centre study considers the predictive value of specific ultrasound features of sub-chorionic haemorrhage (SCH) as potential indicators of adverse pregnancy outcome.

Methods: Ultrasound reports and images were reviewed for 160 participants presenting to an early pregnancy assessment unit from January 2018 to January 2019. Participants were selected based upon the presence of SCH within the first trimester. The outcome of each pregnancy and the features of SCH, including the size, location and echogenicity were recorded and multinomial logistic regression was used to establish predictive value.

Results: The majority of participants were asymptomatic and delivered healthy babies. 24% miscarried prior to delivery or had stillborn babies; the features of bleed within this group revealed an increased prevalence of adverse outcome in the presence of moderate sized haemorrhage ($p = 0.02$). 61% of miscarried pregnancies presented with “wrapping” SCH, in which haemorrhage encased the gestation sac, suggesting wrapping posed a probable risk ($p = 0.01$). 71% of miscarriages occurred within 5 + 0–10 + 0 weeks gestation. Persistent SCH was of greater incidence within those participants with adverse outcome (57%). There was no association between fetal abnormality and miscarriage. Jaundice babies and premature delivery occurred more frequently ($p = 0.001$) and may be a secondary finding following SCH.

Conclusion: There was a strong correlation between presence of SCH in early pregnancy and rate of miscarriage. Specific ultrasound features of SCH, most notably a wrapping location with moderate size, may be indicative of increased risk of miscarriage or post-natal complications. Jaundice and premature births may have an association with placental compromise.

Introduction

Subchorionic haemorrhage (SCH) is commonly identified during first trimester ultrasound (US) assessment. The true incidence of SCH is disparately reported, ranging from 1.3 to 62% [1] and varies with populations studied and date of publication [2–9].

The presence of SCH, particularly sizable haemorrhage, is noted by multiple authors as a strong indicator for several adverse pregnancy outcomes or complications such as pre-term labour, intrauterine death, or placental abruption [7]. Others determined little to no association [2]. The evidence base remains inconclusive about the clinical significance of SCH and which features of SCH may be indicators of adverse outcome. This leads to challenges in determining a clear management pathway for physicians and provides an inconsistent reporting baseline for sonographers.

In 25% of pregnancies women encounter first trimester bleeding

requiring referral for US investigations [10]. At present, there is no clear national guideline to indicate whether the presence of SCH requires subsequent review or repeat US assessment. Early pregnancy specialists must therefore make an informed but subjective judgement on patient counselling and follow up management. This study explores the features of SCH that may be used to inform clinical decision making.

Isolated sonographic features of SCH, such as volume or location of bleeding are well documented [2,3,4,5,8,9]. However few papers consider the echogenicity of the haemorrhage [6] or its resolution [3] with fewer still considering the combined impact of these features [6]. Further research on a larger scale has been proposed to determine the true association between US features of SCH and pregnancy outcome [2].

This study aimed to explore the predictive value of multiple sonographic features of SCH to identify patients at greatest risk of adverse pregnancy outcome, to inform patient management and provide clarity

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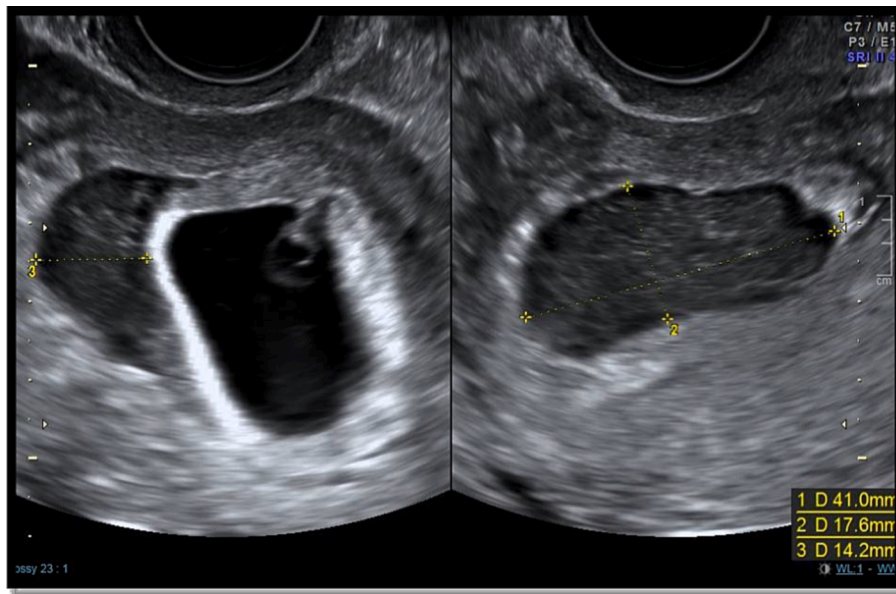


Fig. 1. Calliper placement used throughout the study. Author's own.

for reporting sonographers.

Methods

A retrospective audit was conducted between January 2018 and January 2019 within a single National Health Service centre. Initial participant selection was performed by an experienced independent data analyst. The analyst performed electronic searches of first trimester obstetric US reports using the key terms “haemorrhage”, “chorion” or “bleed” to identify reports with subchorionic haemorrhage. The examination codes “UPETV” and “UO1T” were used, as these represented transvaginal ultrasound scans performed in the first trimester; this resulted in 266 reports.

The researcher hand-searched the 266 reports to ensure that each met the study inclusion criteria (live pregnancy, $\leq 10/40$, with SCH). Reports were rejected where one or more exclusion criteria were evident, resulting in a final sample of $n = 106$.

(Exclusion criteria: pregnancy outcome unknown, imaging not accessible, multiple pregnancies, IVF, known risk factors, history of recurrent miscarriage, incidental complex co-existing pathologies, planned termination of pregnancy, SCH measurements not recorded.)

Data recorded were as follows:

- Reason for patient initial attendance.
- Location, size, and echogenicity of SCH.
- Persistent SCH at follow-up scans.
- Pre-natal pregnancy complications.
- Post-natal complications.

Corresponding blood tests, including serum beta-hCG and progesterone, were not recorded for this study.

Initial review of US reports was performed by the lead researcher, an experienced sonographer, and identified widely varying approaches to reporting of SCH with size, location and echogenicity of the haemorrhage frequently omitted. Missing data were retrieved through detailed review of stored images, also performed by the same researcher. Pregnancy outcomes, including complications (fetal anomalies, fetal jaundice, premature birth, or post-partum haemorrhage were noted from review of follow-up scans and maternity records.).

Results

Analysis of results, including multinomial logistic regression, was performed using SPSS software 26 [11]. A p-value of < 0.05 was considered of statistical significance with a 95% confidence interval.

Clinical indication and gestational age

Between January 2018 and 2019, 160 patients meeting the study inclusion criteria were referred through the early pregnancy assessment unit for ultrasound review. Of these pregnancies, 24% ($n = 38$) miscarried.

Of these, 71% ($n = 27$) miscarried within $5 + 0 - 10 + 0$ weeks of pregnancy, with much fewer miscarrying up to $16 + 0$ (3%, $n = 1$), $22 + 0$ (8%, $n = 3$) or to term (18%, $n = 7$).

It could be presumed that most early pregnancy patients attending for emergency scans will be symptomatic, in accordance with NICE guidelines for referral [12]. However most women who miscarried presented for asymptomatic reassurance scans (48%, $n = 18$), with the remaining women attending for pain (14%, $n = 5$), vaginal bleeding (34%, $n = 13$) or hyperemesis (4%, $n = 2$). This was statistically significant ($p = 0.002$).

Size

SCH size was categorised as “small” (6–14 mm), “moderate” (15–27 mm) and “large” (28–58 mm). These figures were adapted from Benavides-Reyes et al. [5] who considered the significance of the size of SCH, recording three calliper measurements within two image planes (Fig. 1) This was consistent with the image acquisition performed by the sonographers within the current study.

Across the full cohort of participants ($n = 160$), the size of SCH was predominantly moderate (51%, $n = 81$), with fewer presenting with larger haemorrhages (14%, $n = 22$) and 35% ($n = 56$) presenting with small haemorrhages. Smaller haemorrhages may not have been reported if deemed inconsequential by sonographers compared to larger bleeds. However, in this study, moderate SCH was more likely to result in miscarriage (46%, $n = 18$) than the larger haemorrhage (16%, $n = 6$) and small haemorrhages resulting in miscarriage in 37% ($n = 14$) of cases. This suggests that miscarriage rates may be associated with moderate size SCH ($p = 0.02$) and therefore pregnancies presenting with

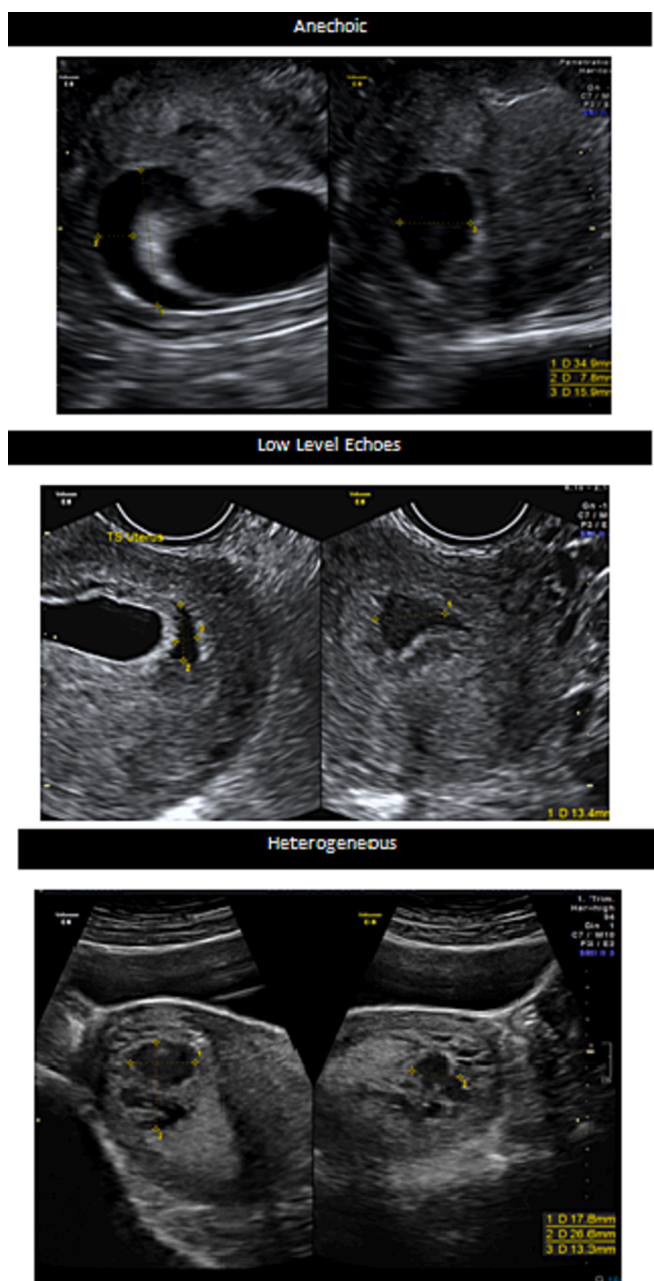


Fig. 2. The three echogenicity types described in the study. Author's own.

moderate SCH may be at greater risk.

Echogenicity and persistence

Echogenicity of SCH was graded as “anechoic”, “low-level echoes” and “heterogeneous” as these were the terms most often used within the reviewed US reports (Fig. 2).

For the full cohort of 160 participants, most frequently the SCH appeared anechoic (49%, $n = 78$) with fewer cases appearing heterogeneous (15%, $n = 24$) or containing low level echoes (36%, $n = 58$). Miscarriages ($n = 38$) most often occurred in the participants with low level echoes (40%, $n = 15$), however this showed no statistical significance ($p = 0.5$).

It is important to note that the stage in which the haemorrhage was imaged may impact upon its sonographic appearance, with acute haemorrhage appearing anechoic and chronic haemorrhage more likely to appear heterogeneous [5]. This may suggest that those pregnancies

presenting with heterogeneous bleeds are resolving. Equally, haemorrhage which resolved in this study appeared half as likely to miscarry (39%, $n = 15$) than those with unresolved bleeds (61%, $n = 23$) at follow-up scan, suggesting prolonged presence of haemorrhage may contribute to adverse outcome. However, again this showed no statistical significance within this sample ($p = 0.1$).

Location

SCH location was described as, “superior”, “inferior”, “lateral” or, “wrapping”. The term, “wrapping” was used to describe areas of haemorrhage adjacent to two or more walls of the gestation sac, spanning a larger surface area, and as such appeared to be wrapping around the sac. Wrapping haemorrhage was not always retroplacental, but instead is proposed as a descriptive, reporting tool to describe this appearance (Fig. 3).

With reference to all participants ($n = 160$), haemorrhage was most often visualised inferior to the gestation sac (33%, $n = 53$), closely followed by a superior position (29%, $n = 46$). Lateral appearances were fewer (22%, $n = 35$) with wrapping the least prevalent (16%, $n = 26$). The incidence of miscarriage was relatively low for inferior (18%, $n = 7$), superior (5%, $n = 2$) and lateral (16%, $n = 6$) haemorrhage. However, in 61% of the pregnancies resulting in miscarriage, the SCH was described as wrapping ($n = 23$, $p = 0.01$) (Fig. 4).

Multinomial logistic regression was used to evaluate additional features of SCH alongside wrapping as a predictor of poor pregnancy outcome.

The echogenicity of bleed appeared to be proportionate to the incidence of miscarriage. In the presence of wrapping ($n = 23$), greater numbers of participants miscarried with heterogeneous bleed and wrapping (41%, $n = 9$) than with anechoic bleeds (23%, $n = 5$). However, this did not reach statistical significance ($p = 0.2$).

Moderate sized SCH was present in 52% ($n = 12$) of cases who miscarried with wrapping haemorrhage, with larger bleeds (17%, $n = 4$) and smaller bleeds (30%, $n = 7$) having less prevalence (Fig. 5). This suggests that moderate haemorrhage in a wrapping location is likely to be present in women who miscarry ($p = 0.05$).

Gestational age was also considered, and in 86% ($n = 20$) of cases that miscarried, this occurred in the presence of wrapping at 5 + 0 – 10 + 0 weeks (Fig. 6). Of those participants who went on to miscarry with wrapping ($n = 23$), 55% ($n = 13$) were asymptomatic, suggesting that wrapping and miscarriage is likely to occur in asymptomatic populations, in earlier gestations and in the presence of moderate size bleeds ($p = 0.003$).

Other pregnancy complications

Of the 160 participants presenting with SCH, additional complications were noted. Premature delivery (7%, $n = 11$), jaundice (6%, $n = 10$), growth restriction (1%, $n = 2$), fetal abnormalities (heart defects and talipes) (6%, $n = 10$), post-partum haemorrhage (1%, $n = 2$) and polyhydramnios (1%, $n = 2$) were noted ($p = 0.02$).

Discussion

Within this study, 24% ($n = 38$) of participants with reported SCH miscarried. This was consistent with previous studies [13], suggesting that the sample was representative.

The presence of wrapping in such a high proportion of participants who later went on to miscarry was a notable finding (61%, $n = 23$) with the majority of those participants also presenting with moderate haemorrhage (52%, $n = 12$). Previous studies suggest a number of potential explanations for such a relationship between volume of bleed and pregnancy loss including increased pressure, inflammatory response or separation of the leading edge of the placenta [5,8,14,15]. It is reasonable to assume that there is potential for the increased surface area of

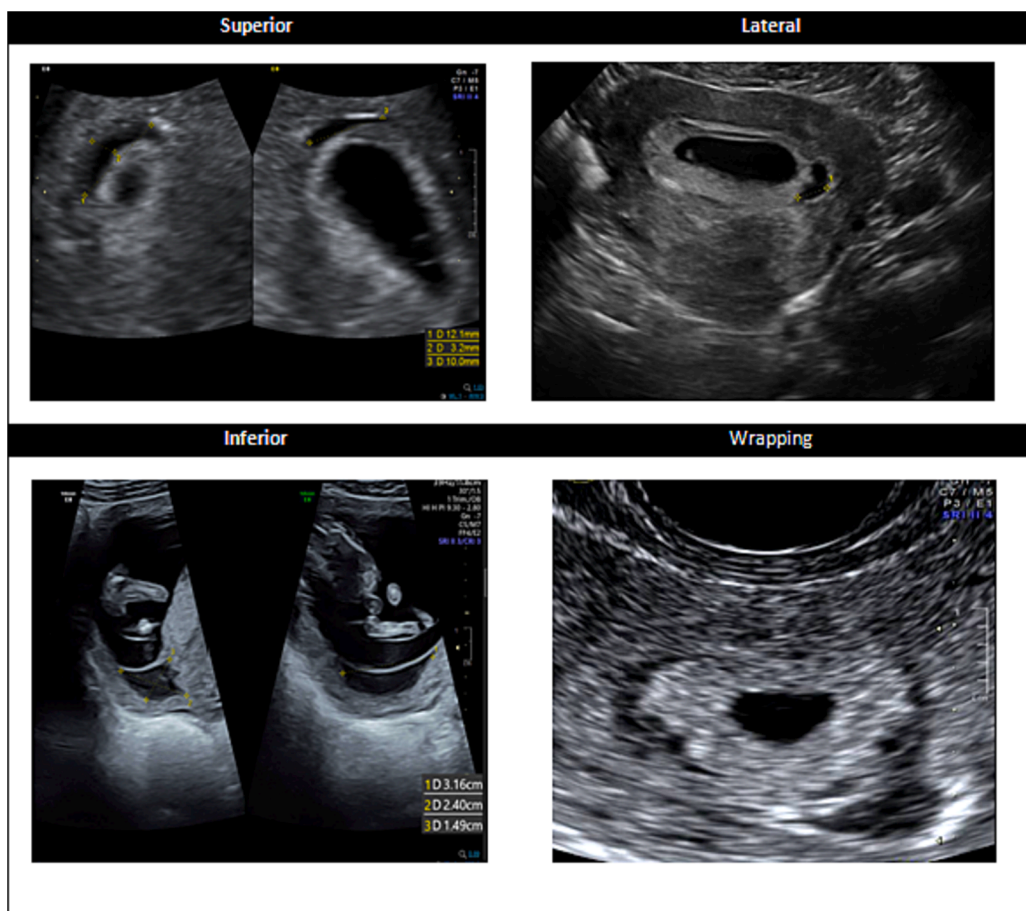


Fig. 3. The four positions of sub-chorionic haemorrhage described in this study. Author’s own.

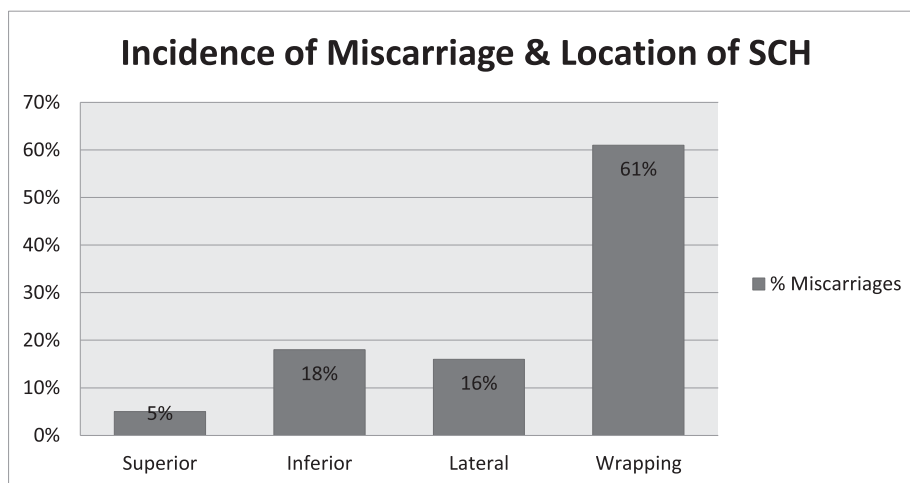


Fig. 4. Incidence of miscarriage and location of sub-chorionic haemorrhage.

haemorrhage to interfere with perfusion to, and function of, the placenta. Whilst no direct relationship between a “wrapping” appearance alongside volume has yet been considered, it could be inferred that the surface area of a “wrapping” haemorrhage that interacts with multiple points around the gestation sac, is larger and therefore also likely to compromise the placenta in a similar way.

Initially, interruption of the placenta may not appear as problematic relative to miscarriage given the process of placental formation; the placenta is not the primary source of nutrients within the first 10 weeks

of pregnancy, when risk seemed to be highest within this sample. However, the placenta begins to form within 17–22 days post conception, with continuous development of vasculature within the embryo and placenta occurring throughout this period [16]. The earliest stages of pregnancy development are of greatest risk relative to embryonic development [17]. Umbilical cord development completes its formation between the fifth and seventh week, suggesting that vascular formation is integral during this time – the time at which most pregnancies in this sample miscarried [16]. Interruption within the earliest stages of

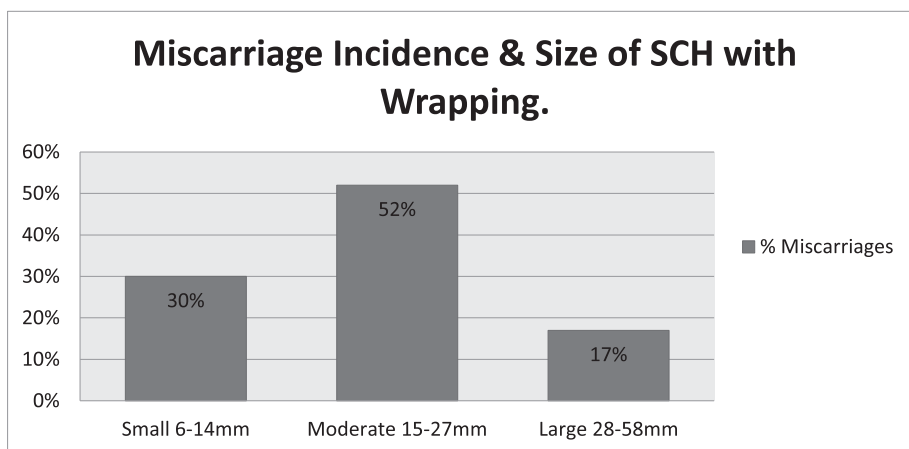


Fig. 5. Incidence of miscarriage, size of sub-chorionic haemorrhage and wrapping location.

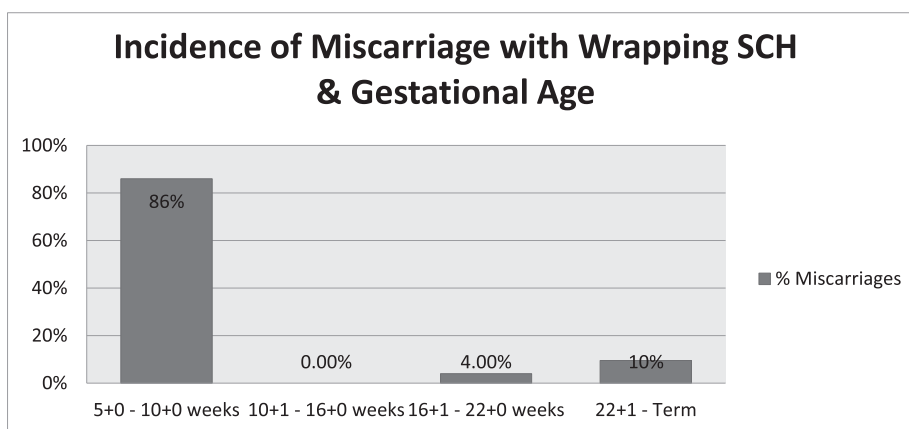


Fig. 6. Incidence of miscarriage, wrapping location of sub-chorionic haemorrhage and gestational age.

embryological and physiological development are likely to have greater impact upon placental formation and successful attachment. Further studies [1] support this explanation, indicating that prolonged presence of SCH could encourage separation of the placenta from the endometrium, further impeding placental function, leading to miscarriage.

In the sample presenting with wrapping and moderate haemorrhage, 13% of those live births resulted in babies who were premature or had jaundice. Whilst only a small number of pregnancies had complications, there is a possibility that placental insufficiency could have been caused by reduced blood supply due to the moderate area of wrapping. This could have contributed to reduction in placental function and thus resulted in jaundice. Reduced removal of bilirubin from the fetus via the placenta would result in an increased level of bilirubin within the fetal liver, and as such a jaundice appearance would result [18]. Further studies [15] have suggested that the inflammatory reaction to SCH has the potential to degrade placental membranes, resulting in premature births and jaundice. Whilst 80% of premature babies present with jaundice within the first week of life, this is often not recorded at the time of delivery as the pregnancies in this study were; in instances in which this is recorded, a pathological cause for jaundice is more likely [19].

The presence of SCH surrounding the gestation sac and covering a larger surface area may therefore influence early pregnancy miscarriage and subsequent reduction in placental function for later gestations. This is supported by Hashem et al. [3] who determined that pregnancies with retroplacental SCH, and therefore with greater arteriole involvement, had significantly greater rates of miscarriage than those with laterally located bleeds; again, this is consistent with the data from this study.

Equally, Wang et al. [20] considered the relationship between adverse outcome and SCH size as an isolated feature suggested that an anterior placenta may offer protective benefits when SCH is present.

Identification of SCH moderate volume and large surface area, which are not necessarily the same, could reliably indicate a greater risk of miscarriage and would therefore allow for specific counselling or follow up assessment. Potential monitoring of placental function for those pregnancies with SCH meeting these criteria may also be helpful in identifying potential PPRM.

In the absence of guidelines, reporting decisions, counselling advice and referral pathways are largely reliant upon subjective professional judgement. The potential consequences are, at minimum, an inconsistent approach to patient care and management decisions. However, guidance at a national level cannot be communicated until there is a robust evidence base. The literature reviewed highlighted the lack of a large prospective study to reliably determine the relationship between multiple features of SCH and potential for pregnancy complications or loss.

Whilst there is evidence that particular features of SCH are likely to correlate with miscarriage rate [21], these are often considered in isolation, in a single centre, were often shown to have poor control of co-variants contributing to miscarriage rates, were small-scale and few in number. There is therefore a need for larger prospective studies considering multiple ultrasound features of SCH, across multiple centres.

Limitations

The small number of participants in the sample who experienced pregnancy miscarriage (24% n = 38) may have impacted upon the generalisability of this study. However, the total population studied is one of the largest to date [2–9].

Data collection was limited by variation in reporting styles. As identified in the initial hand search by the researchers, the variation in approach to reporting SCH presence means that some pregnancies may not have been identified if key terms were absent from the report. Equally, if a SCH was not reported, as presumed inconsequential by the sonographers, those pregnancies will also not have been identified.

Image review by a single researcher provided consistency in approach, however a degree of subjectivity may be expected. Ultrasound is also a dynamic assessment, and static images may not have been entirely representative of the true appearance of SCH.

Conclusion

Results of the study suggest that moderate size and wrapping of SCH between 5 + 0 – 10 + 0 weeks gestation may have good predictive value for greater risk of miscarriage, whereas echogenicity and persistence of bleed had no statistical significance. Miscarriages also most often occurred in asymptomatic populations and particularly in cases in which wrapping and moderate size were both present. At present there is no national guideline to support clinicians in the reporting of SCH or ongoing patient management. We recommend that sonographers report the size and location of haemorrhage, with follow up ultrasound surveillance for pregnancies with higher risk features of moderate or wrapping haemorrhage.

Whilst pregnancy complications demonstrated no significant correlation with SCH presence, jaundice and premature birth was present in 13% of participants; considering the size of this study and the potential implications for those pregnancies, this would benefit from further review from larger prospective studies.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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