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Intrauterine haematomas in the first trimester and pregnancy complications

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Contribution

What does this work add to what is already known?

The role of intrauterine haematoma on pregnancy outcomes remains uncertain. Some studies report an association with miscarriage, whilst others refute this. The impact on long-term outcomes is not known.

What are the clinical implications of this work?

Women with intrauterine haematoma can be informed that they are not associated with an increased risk of first trimester miscarriage. They should be counseled about their increased risk of preterm birth and possibly be offered increased surveillance during their pregnancies.

Abstract

Objectives: The role of intrauterine haematoma on pregnancy outcomes remains uncertain. Some studies report an association with miscarriage, whilst others refute this. The impact on long-term outcomes is not known. We aimed to assess if intrauterine haematomas detected using ultrasonography in the first trimester are associated with adverse pregnancy outcomes.

Methods: A prospective observational cohort study at Queen Charlotte's & Chelsea Hospital, London, was conducted between March 2014 and March 2016. Participants with intrauterine pregnancies were recruited and underwent serial ultrasound scans in the first trimester. Clinical symptoms, including pelvic pain and vaginal bleeding were recorded using validated symptom scores at each visit. The presence, location and size of any intrauterine haematoma seen on ultrasonography was noted. Pregnancy outcomes were obtained from hospital records.

Results: Of 1003 recruited participants, 268 had an intrauterine haematoma (27%). The presence of intrauterine haematoma in the first trimester was associated with preterm birth (OR 1.94; 95% CI 1.07-3.53). No association was found with miscarriage (OR 0.916; 95% CI 0.571-1.471). This was irrespective of the absolute size of the haematoma or the presence or absence of vaginal bleeding and pelvic pain. A retroplacental haematoma was associated with an increase in overall antenatal complications ($P = 0.0395$).

Conclusions: Our data demonstrates no association between the presence of intrauterine haematoma in the first trimester and first trimester miscarriage. However, a relationship with preterm birth independent of the presence of symptoms of pain and bleeding is evident. These women should be counseled about their increased risk of preterm birth and possibly be offered increased surveillance during their pregnancies.

Introduction

Intrauterine haematoma (IUH) is a term used for a sonographic diagnosis of a crescent-shaped hyperechoic or hypoechoic area between the chorionic membrane and myometrium^{1, 2} (figure 1). The reported incidence of IUH varies from 1.7% to 18.2%^{3, 4}. Such variations exist due to differences in inclusion criteria, definitions and the resolution of the ultrasound equipment used.

The role of IUH in miscarriage remains controversial. Farrell *et al* suggested that the presence of IUH with vaginal bleeding in early pregnancy is associated with a greatly increased risk of miscarriage compared with vaginal bleeding alone⁵. However, similar studies have failed to support this finding^{1, 6}. A retrospective study of 144 IUH and 144 controls concluded that IUH did not increase the risk of pregnancy loss independent of vaginal bleeding⁷.

Studies to understand how IUH might affect later pregnancy outcomes have been conflicting. Some report an association with a number of adverse pregnancy outcomes including preterm birth, preterm pre-labour rupture of membranes (PPROM), pre-eclampsia and stillbirth^{8, 9}, whilst others have not^{3, 7, 10}. A systematic review by Tuuli *et al* concluded there was an association between IUH and adverse outcomes including miscarriage, stillbirth, preterm delivery and PPRM⁹. No association was found with other outcomes such as pre-eclampsia or small for gestational age⁹. A large prospective cohort study

concluded that there was an increased risk of a number of adverse pregnancy outcomes including preterm delivery, however the location, size and presence of vaginal bleeding did not have an impact on outcomes¹¹.

These discrepant findings may be explained by the varied inclusion and exclusion criteria as well as design of these studies, with many lacking an adequate control group⁹. Few studies have taken into account the location, size and presence of symptoms associated with an IUH¹², whilst IUH volume has often been calculated differently^{11, 13-15}. A further limitation is that the majority of studies on IUH are retrospective and consist of small cohorts^{6, 8, 16}. Many of the studies in the literature were conducted many years ago with poorer quality ultrasound equipment and sometimes a transabdominal approach. The result is that current evidence is unable to provide clinicians with adequate information to best counsel women.

In this study we aimed to prospectively evaluate the impact of IUH on short and long term pregnancy outcomes. The secondary aim was to explore the size and location of an IUH as well as gestational age, presence of vaginal bleeding and pelvic pain, and their association with adverse pregnancy outcomes.

Materials and Methods

Study Design and Ethical Approval

This is a prospective observational cohort study based at Queen Charlotte's & Chelsea Hospital, London, between March 2014 and March 2016. The study was approved by the NHS National Research Ethics Service (NRES) Riverside Committee London (REC 14/LO/0199) and all participants provided written informed consent.

Inclusion Criteria

Women with intrauterine pregnancies in the first trimester of pregnancy were recruited between 5 weeks and 14 weeks gestational age. The first trimester was defined as <14 weeks gestation by last menstrual period (LMP) or ultrasound scan dating based on crown rump length measurements (CRL) (where the LMP was not known) ¹⁷. An intrauterine pregnancy was defined on the basis of an ultrasound scan showing an intrauterine gestation sac with or without a visible embryo and heartbeat. Women aged less than 16 and over 50 were excluded. Women were invited to participate via open advertisements (using posters) in local GP surgeries, in local hospitals and at the university where the study was being conducted (Imperial College London). The majority of women were recruited after attending the hospital Ultrasound Department or Early Pregnancy Assessment Unit.

Study Design

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All study visits were conducted at Queen Charlotte's & Chelsea Hospital, London. Demographic information, past medical, gynaecological and obstetric history were collected via a questionnaire. Pelvic pain, vaginal bleeding and nausea and vomiting were assessed using validated symptom scores. Once recruited, participants attended for an ultrasound scan and review of their symptoms every two weeks. During the study, participants were seen between two and five times in the first trimester depending on the gestational age at the time of recruitment and clinical need. The number of visits was dependent upon gestational age at recruitment. Data was collected from their routine dating (11 to 14 weeks gestation) and anomaly scans (18 to 22 weeks gestation) and participants underwent an additional ultrasound assessment of fetal growth between 31 and 36 weeks gestation. Participants were encouraged to contact the research team if they had any complications, such as vaginal bleeding, and were invited to attend for an additional ultrasound scan if deemed necessary. Pregnancy outcomes were collected from hospital medical records. The sample size was calculated using the incidence of common pregnancy complications. Using these known proportions and the predicted proportion in the cohort, an alpha of 0.05 and power of 80%, we estimated a minimum of 861 participants would need to be recruited. We set a recruitment target of 1000 participants to account for patients lost to follow-up and missing data.

Ultrasound scans and assessment of IUH

The mean gestational sac diameter (MSD), yolk sac and embryo crown rump length (CRL) were routinely measured at each visit. An intrauterine haematoma was diagnosed when a crescent-shaped hyperechoic or hypoechoic area between the chorionic membrane and myometrium was visualised. If present, it was measured in three orthogonal planes. The location of the IUH in relation to the gestational sac (anterior, posterior, above sac, below sac or surrounding the sac) was reported as well as the site of pregnancy implantation. The IUH was then classified as retroplacental or non-retroplacental. The sonographers also reported their subjective impression of the percentage of the gestational sac surrounded by the IUH. The description of the internal structure was also reported as either homogenous or heterogeneous. We also collected information on IUH persistence, which was defined as an IUH present over two ultrasound scans performed ten days apart.

Assessment of symptoms

The following validated tools were used to assess symptoms at each first trimester study visit:

Vaginal Bleeding

This was assessed using a modified pictorial blood assessment chart (PBAC) bleeding score (numerical scale 0-4) ¹⁸. The amount of vaginal bleeding experienced on the day they attended for a study visit, the worst vaginal bleeding experienced prior to their visit and the duration of bleeding in days was recorded.

Pelvic Pain

Participants were asked to rate their pain score using a Visual Analogue Score (VAS) on the day of their study visit attendance and the worst pain they had experienced until that point (scale 0-10). They were also asked to document the duration of their pain in days ¹⁹.

Main outcome measures

First trimester miscarriage:

This was defined as pregnancy loss before 14 weeks gestation and was diagnosed using criteria outlined by Abdallah *et al* ²⁰ and Preisler *et al* ²¹.

Late pregnancy outcome measures were defined as antenatal, delivery and neonatal complications.

1. Antenatal Complications

Hypertensive disorders of pregnancy

Pre-eclampsia (PET) was defined as raised blood pressure $\geq 140/90$ mmHg on two occasions four hours apart at >20 weeks gestation in a woman with previously normal blood pressure, with proteinuria, quantified using the urine protein creatinine ratio (UPCR >0.3 mg/dL) or by 24 hour urine collection (>3 g/24 hours) ²². A diagnosis of pre-eclampsia was also given if pregnancy induced hypertension (PIH) (no proteinuria) occurred with fetal growth restriction, in the case of eclampsia, or in the case of PIH with deranged blood tests (thrombocytopenia $<100 \times 10^9$ /L, serum creatinine concentrations greater than 1.1 mg/dL or a doubling of this in the absence of renal disease, or elevated liver transaminases to twice normal concentration) ²². Pregnancy induced hypertension (PIH) was defined as raised blood

pressure $\geq 140/90$ mmHg without proteinuria, growth restriction and abnormal blood tests²². Gestational proteinuria was defined as UPCR >0.3 mg/dL or a 24 hour urine collection protein level >3 g in the absence of hypertension²².

Gestational diabetes (GDM)

Gestational diabetes was diagnosed if fasting plasma glucose levels were >5.6 mmol/l or if a 2-hour plasma glucose level was >7.8 mmol/l after an oral glucose tolerance test (OGTT)²³.

Antepartum haemorrhage (APH)

Antepartum haemorrhage described when vaginal bleeding occurred after >24 weeks gestation and before delivery²⁴.

Placental abruption

Placenta abruption was a clinical diagnosis defined as when the placenta shears away from the uterine lining and may occur antenatally or during delivery²⁴.

Second Trimester Miscarriage

Miscarriage >14 weeks and <23 completed weeks of gestation as defined by the 11 to 14 weeks dating scan²⁵.

Preterm Birth, Preterm Delivery and Preterm pre-labour rupture of membranes

Preterm birth described any delivery >24 weeks and <37 completed weeks gestation, which included both iatrogenic preterm delivery and spontaneous preterm labour. Preterm delivery (PTD) was defined as iatrogenic delivery before 37 weeks completed gestation (as dated by routine dating scan)²⁶. Preterm labour (PTL) was defined as the spontaneous onset of labour before 37 weeks gestation (as dated by a routine dating scan)²⁶. Preterm pre-

labour rupture of membranes (PPROM) was defined as rupture of membranes before 37 weeks gestation (as defined by a routine dating scan) occurring more than 24 hours before delivery²⁶.

Fetal Growth Restriction and low birth weight

Fetal growth restriction (FGR) was a term used to describe an ultrasound based antenatal diagnosis where the estimated fetal weight was less than the 10th centile for gestational age with abnormal umbilical artery Doppler results (pulsatility index >95th percentile with or without reversed or absent end diastolic flow)²⁷. Low birth weight (LBW) was defined in accordance with WHO criteria and WHO centiles as delivery weight <10th percentile for gestational age, where the final gestational age was estimated using the dating scan (performed at 11-14 weeks gestation) as a reference²⁸.

Stillbirth

Intrauterine death or stillbirth described when there was intrauterine fetal demise and the fetus was born dead after 24 weeks gestation²⁹.

2. Delivery Complications

Delivery details were collected including date of delivery (from which gestational age can be calculated), mode of delivery and any complications. Mode of delivery included spontaneous vaginal delivery (SVD), elective and emergency caesarean section and instrumental delivery (forceps and ventouse delivery). Information as to the indication for delivery was collected including failure to progress, fetal distress or maternal exhaustion.

Meconium staining of liquor and a diagnosis of sepsis in labour were also noted. This was defined in accordance with the NICE intra-partum guideline ³⁰.

The amount of bleeding at delivery was recorded. For a vaginal delivery (including SVD, forceps and ventouse delivery), an estimated blood loss of greater than 500ml was classified as a “post-partum haemorrhage” (PPH). At Caesarean section (emergency and elective), an estimated blood loss >1000ml was recorded as PPH. Any delivery with estimated blood loss >1500ml was characterised as a massive obstetric haemorrhage (MOH) ³¹. The cause of bleeding was noted as either due to atony, trauma, retained placenta or morbidly adherent placenta. Manual removal of placenta (MROP) was defined as where traditional controlled cord traction was insufficient to complete the third stage of labour and additional manual manoeuvres were required to achieve delivery of the placenta.

3. Neonatal complications

The following neonatal complications were recorded: admission to neonatal unit and low one minute Apgar score of <7 and low five minute Apgar score of <7.

Statistical Analysis

Python 3.6.2 (Python Software Foundation, Delaware, USA) was used for statistical analysis.

Comparison of the cohort characteristics with regard to the presence or absence of IUH during the first trimester was performed using chi-squared test, Student's t-test or Mann-Whitney *U* test where appropriate.

Logistic regression (LR) and chi-squared test were used to evaluate the association between IUH features and adverse pregnancy outcomes. Pregnancy outcomes were assessed individually as well as being divided into antenatal, delivery and neonatal complications. In addition, antenatal complications of similar aetiology were grouped together, for example preterm birth and preterm pre-labour rupture of membranes. Odds ratios (OR) are reported with a 95% confidence interval. All OR analyses were first adjusted for maternal age and compared with further adjustment for the presence of vaginal bleeding or the presence of pelvic pain during the first trimester. Additional adjustment with the worst bleeding score and the total number of bleeding days recorded during the first trimester as potential confounders did not significantly affect the OR and are therefore not reported.

The main variable was defined as the presence or absence of an IUH at any point during the first trimester. Secondary features were used to assess the potential impact of the size, content, location and persistence of the IUH.

The impact of the absolute IUH size was performed using three different quantifications: the maximum IUH diameter measured during the first trimester, the maximal product of the three orthogonal diameters of the IUH recorded during the first trimester and a scaled version of this product obtained by taking its cube root which relates to the original unit of measurement. Note that the aim was not to precisely measure the volume of the IUH but to

develop a proxy measurement, potentially useful for further assessment. For that reason, we did not use the scaling factor derived from ³², which is a simple linear constant that would only affect the scale of the OR.

An additional variable was also created to explore the relative size of the IUH compared to the gestational sac. To this end, we examined the ratio of the maximum diameter of the IUH divided by the MSD measured at the corresponding scan. When assessing the impact of IUH on first trimester miscarriages, only the first available scan was used to avoid introducing a selection bias, since some of these women progressively drop out of the study during the first trimester as they miscarry. The IUH content (homogeneous or heterogeneous) and location in relation to the gestational sac were also evaluated using the first ultrasound scan when the IUH was diagnosed.

Finally, the persistence of an IUH was also explored for overall antenatal, delivery and neonatal complications. We defined an IUH to be persistent if it was still present on ultrasound more than ten days after the previous scan.

The potential association of the IUH content, the IUH localisation and the persistence of an IUH with adverse outcomes was tested with a chi-squared test. Retroplacental versus non-retroplacental location of an IUH was analysed in relation to overall antenatal, delivery and neonatal complications (chi-squared).

All analyses were performed on complete cases only. The proportion of missing values among IUH variables were: presence/absence of IUH 0% ($n=0$); maximum IUH diameter: 1.8% ($n=5$); product of three diameters: 1.8% ($n=5$), IUH location at first scan: 8.5% ($n=23$);

IUH content at first scan: 18.2% ($n=49$), the ratio IUH diameter/MSD: 7.0% ($n=19$) and for placental location 7.4% ($n=18$) and retroplacental status 12.0% ($n=29$). The later proportion is mostly explained by the absence of available MSD measurements.

The majority of outcomes also had no missing values except: LBW <3% of missing values ($n=21$), mostly due to the babies birth weight not being available), PPH and MOH <5% ($n=37$) due to the absence of blood loss quantification, meconium <1% ($n=6$) and Apgar score <2% ($n=16$).

The antenatal complications analyses were performed on all pregnancies that remained viable at the end of the first trimester. Delivery and neonatal complications analyses were performed on pregnancies resulting in live births. Analysis of PPH and MOH were performed on a subset of patients excluding patients with traumatic PPH ($n=53$) and MOH ($n=10$). Results were not corrected for multiple comparison due to the exploratory setting of this study.

Results

1242 consecutive women were screened and 1003 participants were recruited (figure 2). Those who underwent termination of pregnancy ($n=20$) were excluded from the study ($n=5$), as were those that were lost to follow up ($n=32$) (figure 2). 946 women were included in the final analysis. Of these, 268 (28%) had an IUH in the first trimester (figure 2). Table 1 shows the patient characteristics of our cohort. Participants with an IUH were more likely to have experienced vaginal bleeding (P value <0.0001) and have higher bleeding scores (P value <0.0001) (table 1). However, there was no difference in the presence of pelvic pain (P value $=0.896$) and maximum pain scores (P value $=0.826$) between the two groups (table 1). The absolute numbers and percentages of each adverse outcome assessed in those with and without IUH are shown in table 2.

Impact of IUH and pregnancy Outcomes

First trimester miscarriage

There was no association between the presence of an IUH and first trimester miscarriage irrespective of its' size (OR 0.81; 95% CI 0.44-1.5) (figure 3, table 3). This finding was independent of the presence of pelvic pain or vaginal bleeding (table 3) and adjustment for gestational age (supplementary table 1). If an IUH was present, its content, absolute size and location did not impact on the risk of miscarriage (supplementary table 1).

Long-term adverse pregnancy outcomes

There was no association between the presence of an IUH in the first trimester and overall antenatal, delivery or neonatal complications (figure 4). There was a general trend towards an association with individual antenatal complications, with preterm birth reaching significance (OR 1.94; 95% CI 1.07-3.53) (figure 5). When grouped together, there was also an association between IUH and preterm birth and preterm prelabor rupture of membranes (OR 1.84; 95% CI 1.03-3.27) (table 3). This association was independent of the presence or absence of bleeding or pain (table 3).

If an IUH was present, there was no association between the size, content or location of the IUH in relation to the gestation sac and pregnancy outcome (supplementary table 2). Retroplacental haematomas were associated with a greater risk of antenatal complications ($P = 0.0395$) and not delivery or neonatal complications (supplementary table 2 and 3). Those with an IUH that persisted more than 10 days ($n=66$) were not associated with an increased risk of antenatal, delivery and neonatal complications overall (supplementary table 1 and 2). No association was seen between the presence of an IUH and individual delivery and neonatal complications (table 3).

Discussion

We have found that the presence of an IUH in the first trimester of pregnancy was associated with an increased risk of preterm birth. An IUH was not associated with an increased likelihood of first trimester miscarriage. These findings were independent of the presence or absence of bleeding or pain. In addition, the size and content of the IUH did not influence pregnancy outcomes. A retroplacental IUH appeared to be associated with an increase in overall antenatal complications. Although associations with other individual antenatal complications were observed, these did not reach significance.

The incidence of IUH in our study was greater than that previously reported^{11, 12}. This is likely the result of higher quality imaging and that recruitment was conducted in a dedicated early pregnancy assessment unit. The finding that there is an overall increased risk of preterm birth in our study is consistent with other studies¹¹, including a previous systematic review⁹. Another systematic review reported that a retroplacental location and persistent haematomas are most predictive of adverse outcomes¹². However, further stratification to assess risk including size, location, sonographic appearance and persistence of an IUH were not useful in our study. This may be due the limited number of various types of IUH and adverse outcomes.

A number of mechanisms have been proposed to explain how an IUH may cause preterm birth, for example IUH may hamper implantation and development of the placenta³³.

Another study assessed the relationship between IUH, cervical length (measured using ultrasound) and preterm birth ³⁴. This retrospective cohort study found an association between PTB and IUH even when adjusted for cervical length, the presence of vaginal bleeding and use of progesterone ³⁴. This suggests that another mechanism other than cervical shortening exists for PTB in women with an IUH. A candidate mechanism is subclinical infection. Seki *et al* found chorio-amnionitis was more common in women with a persistent IUH ³⁵.

Studies specifically assessing first trimester miscarriage have differed, some showing no increased risk of miscarriage ^{7 1}, with others showing an increased risk ^{6, 36 5}. Previous studies have also suggested that the presence of IUH before seven or eight weeks' gestational age is associated with a higher risk of miscarriage ^{37 8}. Our study did not show an increased risk of miscarriage even when adjusting for the presence of bleeding, pain or gestational age at the time of diagnosis. If present, the size, location and content of the IUH did not impact on miscarriage risk. This finding is similar to a recent meta-analysis aiming to assess predictors of miscarriage in viable pregnancy that also found IUH were not associated with miscarriage ³⁸.

The strengths of our study are the prospective design, consecutive recruitment, well-characterised patient cohort and the use of validated symptom scores. To our knowledge, this is the first study where participants were followed up intensively in the first trimester

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and symptoms were thoroughly assessed in a prospective manner. In this way, we have been able to reliably explore the association between IUH, clinical symptoms of pain and/or bleeding and pregnancy complications. However, there are limitations. Although we recruited over 1000 women, the relatively small numbers of each individual adverse outcome means that establishing statistically significant associations in relation to these was difficult. Most of our participants were recruited through the Early Pregnancy Unit, which may constitute a higher risk group. However, the incidence of preterm birth in the UK has been reported as 8% of all live births ³⁹, whereas in our population the incidence was 5.7% of all live births. During follow-up, an unavoidable bias common to all observational studies in this field is that some participants underwent treatment to prevent an adverse outcome as part of their standard clinical care. For example, cervical cerclage was carried out on 18 women in the study, which may have led to fewer preterm deliveries in our cohort and so the overall impact of IUH may have been underestimated. It is also possible that we have underestimated the prevalence of IUH. Haematomas may have developed and resolved in the time period between serial ultrasound examinations. Furthermore IUH may have been present and persisted prior to recruitment but resolved by the time of recruitment to the study.

Our study shows that women with IUH in the first trimester are at increased risk of preterm birth. These pregnancies should potentially be managed as high-risk pregnancies with additional antenatal surveillance. Intrauterine haematomas were not associated with an increased risk of first trimester miscarriage irrespective of location or size. Women should

therefore be counselled accordingly. Future research should focus on identifying sub-groups of women most at risk of preterm birth. In addition, further work is required to address the possible mechanisms by which IUH may cause PTB.

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Figure legends

Figure 1. Intrauterine haematoma adjacent to a viable pregnancy at 6 weeks gestation.

Figure 2. Study flowchart

Figure 3. Forest plot showing the association between IUH and first trimester miscarriage as Odds ratio, adjusted for maternal age.

Figure 4. Forest plot showing the association between first trimester IUH and antenatal, delivery and neonatal complications (adjusted Odds ratio).

Figure 5. Forest plot showing the association between individual antenatal complications and first trimester IUH (adjusted Odds ratio).

Table 1. Table showing cohort characteristics in those with and without intrauterine haematoma

Variables	With IUH (cases) N=268	Without IUH (controls) N=678	P value
Maternal Age (year) Mean (range)	32 (17-48)	33 (17-48)	0.1165
Maternal ethnicity N (%)			0.5135
White	182 (67.9)	450 (66.4)	
Asian	27 (10.1)	91 (13.4)	
Black	32 (11.9)	82 (12.1)	
Mixed	8 (3.0)	20 (2.9)	
Other	19 (7.1)	34 (5.0)	
Missing	0	1 (0.1)	
BMI (kg/m²) Median (range) Missing	23.4 (17.4-44.5) 9 (3.4%)	24.1 (15.8-53.9) 22(3.2%)	0.0218
Parity	135.0 (50.4)	350.0 (51.6)	0.0442
1	93.0 (34.7)	231.0 (34.1)	
2	34.0 (12.7)	59.0 (8.7)	
3	4.0 (1.5)	20.0 (3.0)	
4 and+	1.0 (0.4)	18.0 (2.7)	
Missing	1 (0.4)	0	
1st Trimester Miscarriage history			0.0134
0	163.0 (60.8)	346.0 (51.0)	
1	73.0 (27.2)	198.0 (29.2)	
2	24.0 (9.0)	86.0 (12.7)	
3	4.0 (1.5)	29.0 (7.1)	
4 and +	3 (1.1)	19(2.8)	
Missing	1 (0.4)	0 (0.0)	
2nd Trimester Miscarriage history			0.2835
0	261.0 (97.4)	649.0 (95.7)	
1	6.0 (2.2)	27.0 (4.0)	
1+	0 (0.0)	2.0 (0.2)	
Missing	1.0 (0.4)	0 (0.0)	
Cervical surgery			0.5404
No	255 (95.1)	654 (96.5)	
Yes	12 (4.5)	23 (3.4)	
Missing	1 (0.4)	1 (0.1)	
Smoking Status			0.8005
No	231 (86.2)	592 (87.3)	
Yes	33 (12.3)	78 (11.5)	

Missing	4 (1.5)	8 (1.2)	
Index Pregnancy outcome			0.6401
Live birth	235 (87.7)	594 (87.6)	
1st T Miscarriage	26 (9.7)	73 (10.8)	
2nd T Miscarriage	6 (2.2)	8 (1.2)	
Stillbirth	1 (0.4)	3 (0.4)	
Final GA (days)*			0.0801
Median (range)	278.0 (181-295)	276.0 (170-302)	
Missing	1.0 (0.4)	3 (0.5)	
Baby weight (g)*			0.5527
Median (range)	3340.0 (850.0 -4640.0)	3340.0 (700-4830.0)	
Missing	0 (0.0)	3.0 (0.5)	
Bleeding during 1st Trimester			
Presence	199 (74.3)	350 (51.6)	<0.0001
Absence	69 (25.7)	328 (48.4)	
Max bleeding score			<0.0001
0	67 (25.0)	323 (47.6)	
1	75 (28.0)	195 (28.8)	
2	67 (25.0)	105 (15.5)	
3	31 (11.6)	27 (4.0)	
4	27 (10.1)	24 (3.5)	
Missing	1 (0.4)	4 (0.6)	
Pain during 1st trimester			0.896
Presence	164 (61.2)	418 (61.7)	
Absence	104 (38.8)	260 (38.3)	
Max Pain Score			0.826
0	105 (39.2)	265 (39.1)	
1-2	36 (13.4)	77 (11.4)	
3-4	39 (14.6)	86 (12.7)	
5-6	38 (14.2)	103 (15.2)	
7-8	30 (11.2)	91 (13.4)	
9-10	19 (7.1)	52 (7.7)	
Missing	1 (0.4)	4 (0.6)	

*live births only

IUH = intrauterine haematoma, BMI = Body Mass index, T = trimester, GA = gestational age

Table 2. Percentage of complications in cohort overall and those with and without first trimester intrauterine haematoma

	All women, % (n/N)	IUH at 1 st scan % (n/N)	No IUH at 1 st scan % (n/N)
Miscarriages (based on 1 st scan only)	10.4 (99/946)	8.9 (13/146)	10.7 (86/800)
	All women, % (n/N)	IUH 1 st Trimester % (n/N)	no IUH during 1 st T % (n/N)
Miscarriages (overall numbers at the end of the first trimester)	10.4 (99/946)	9.7 (26/268)	10.8 (73/678)
	All women, % (n/N)	IUH % (n/N)	no IUH % (n/N)
Antenatal Complications	23.7 (196/827)	26.7 (63/236)	22.5 (133/591)
APH and Abrupton	6.7 (57/847)	7.9 (19/242)	6.3 (38/605)
LBW	6.2 (51/827)	7.6 (18/236)	5.6 (33/591)
PTB	5.5 (47/847)	8.3 (20/242)	4.5 (27/605)
Gestational diabetes	5.2 (44/847)	5.4 (13/242)	5.1 (31/605)
PET	3.0 (25/847)	2.9 (7/242)	3.0 (18/605)
PPROM	2.7 (23/847)	3.7 (9/242)	2.3 (14/605)
FGR	2.5 (21/847)	4.1 (10/242)	1.8 (11/605)
PIH	1.9 (16/847)	1.7 (4/242)	2.0 (12/605)
2nd trimester miscarriage	1.7 (14/847)	2.5 (6/242)	1.3 (8/605)
Stillbirth	0.5 (4/847)	0.4 (1/242)	0.5 (3/605)
Gestational Proteinuria	0.5 (4/847)	0.0 (0/242)	0.7 (4/605)
Delivery Complications	64.9 (512/789)	63.0 (143/227)	65.7 (369/562)
Operative Delivery	49.6 (411/829)	43.0 (101/235)	52.2 (310/594)
PPH (trauma excluded)	21.9 (159/727)	21.6 (45/208)	22.0 (114/519)
OD for fetal distress	22.3 (153/685)	18.4 (36/196)	23.9 (117/489)
Meconium	11.2 (92/823)	12.0 (28/234)	10.9 (64/589)
Sepsis in labour	4.9 (41/829)	5.5 (13/235)	4.7 (28/594)
MOH (trauma excluded)	4.5 (33/727)	5.3 (11/208)	4.2 (22/519)
Neonatal Complications	9.5 (77/810)	10.9 (25/230)	9.0 (52/580)
Abnormal Apgar 1 min	7.3 (59/813)	7.8 (18/232)	7.1 (41/581)
Admission to NNU	4.5 (37/828)	5.1 (12/234)	4.2 (25/594)
Abnormal Apgar 5 min	0.9 (7/811)	0.4 (1/231)	1.0 (6/580)

N = number, *IUH*=intrauterine haematoma, *APH* = antepartum haemorrhage, *LBW* = low birth weight, *PTB* = preterm birth, *PET* = pre-eclampsia, *PPROM* = preterm prelabour rupture of membranes, *FGR* = fetal growth restriction, *PIH* = pregnancy induced hypertension, *PPH* = post-partum haemorrhage, *OD* = operative delivery, *MOH* = massive obstetric haemorrhage, *NNU* = neonatal unit

Table 3. Table showing odds ratios with 95% confidence intervals for the presence of IUH adjusted for maternal age, and presence of bleeding and pain for individual antenatal, delivery and neonatal complications and first trimester miscarriage

	Adj Maternal Age	Adj Maternal Age+Bleed	Adj Maternal Age + Pain
Antenatal Complications	1.27 (0.90 - 1.80)	1.19 (0.84 - 1.71)	1.27 (0.900 - 1.81)
APH and Abruption	1.27 (0.72 - 2.25)	1.36 (0.76 - 2.45)	1.28 (0.72 - 2.27)
LBW	1.42 (0.78 - 2.58)	1.38 (0.75 - 2.54)	1.42 (0.78 - 2.58)
PTB	1.94 (1.07 - 3.52)	1.93 (1.04 - 3.56)	1.95 (1.07 - 3.55)
Gestational diabetes	1.13 (0.58 - 2.2)	1.04 (0.53 - 2.07)	1.11 (0.57 - 2.17)
PET	1.00 (0.41 - 2.44)	0.91 (0.37 - 2.24)	1.00 (0.41 - 2.44)
PPROM	1.67 (0.71 - 3.91)	1.74 (0.72 - 4.18)	1.67 (0.71 - 3.92)
FGR	2.31 (0.97 - 5.52)	2.11 (0.87 - 5.13)	2.31 (0.97 - 5.52)
PIH	0.83 (0.27 - 2.60)	0.71 (0.22 - 2.24)	0.84 (0.27 - 2.63)
2nd trimester miscarriage	1.86 (0.64 - 5.42)	1.68 (0.56 - 5.02)	1.83 (0.63 - 5.35)
Gestational Proteinuria	NA	NA	NA
Stillbirth	0.84 (0.09 - 8.14)	1.59 (0.16 - 15.72)	0.85 (0.09 - 8.19)
LBW-FGR	1.63 (0.92 - 2.88)	1.57 (0.88 - 2.82)	1.63 (0.92 - 2.87)
Hypertension	0.77 (0.37 - 1.59)	0.69 (0.33 - 1.44)	0.77 (0.37 - 1.58)
PTB-PPROM	1.84 (1.03 - 3.28)	1.84 (1.02 - 3.33)	1.85 (1.04 - 3.30)
Delivery Complications	0.91 (0.66 - 1.26)	0.86 (0.62 - 1.20)	0.91 (0.66 - 1.26)
Operative Delivery	0.71 (0.52 - 0.97)	0.67 (0.49 - 0.91)	0.71 (0.52 - 0.97)
PPH (trauma excluded)	1.00 (0.67 - 1.47)	0.96 (0.64 - 1.43)	0.99 (0.67 - 1.47)
OD for fetal distress	0.73 (0.48 - 1.12)	0.69 (0.45 - 1.06)	0.74 (0.48 - 1.12)
Meconium	1.11 (0.69 - 1.78)	1.18 (0.73 - 1.92)	1.11 (0.69 - 1.78)
Sepsis in labour	1.21 (0.61 - 2.38)	1.19 (0.59 - 2.39)	1.20 (0.61 - 2.36)
MOH (trauma excluded)	1.35 (0.64 - 2.85)	1.30 (0.60 - 2.81)	1.34 (0.63 - 2.83)
Neonatal Complications	1.23 (0.74 - 2.04)	1.09 (0.65 - 1.83)	1.23 (0.74 - 2.04)
Abnormal Apgar 1 min	1.12 (0.63 - 1.99)	1.02 (0.56 - 1.83)	1.12 (0.63 - 1.99)
Admission to NNU	1.18 (0.58 - 2.41)	1.09 (0.53 - 2.25)	1.20 (0.59 - 2.45)
Abnormal Apgar 5 min	0.41 (0.05 - 3.43)	0.31 (0.04 - 2.63)	0.41 (0.05 - 3.44)
		MA + bleed at1st scan	MA + Pain at1st scan
First trimester miscarriage	0.81 (0.44-1.50)	0.81 (0.43-1.52)	0.88 (0.44-1.51)

IUH = intrauterine haematoma, Adj = adjusted, APH = antepartum haemorrhage, LBW = low birth weight, PTB = preterm birth, PET = pre-eclampsia, PPRM = preterm prelabour rupture of membranes, FGR = fetal growth restriction, PIH = pregnancy induced hypertension, PPH = post-partum haemorrhage, OD = operative delivery, MOH = massive obstetric haemorrhage, NNU = neonatal unit, MA = maternal age, 1st = first

NA : no odd ratio available because of complete separation due to small number of cases.









