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## The Predictive Role of Bleeding in Early Pregnancy in the Development of Antepartum Haemorrhage

Running title: Bleeding during early pregnancy and its outcome

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### Abstract

Abstract: The first trimester of pregnancy is a dynamic period during which vaginal bleeding may occur in about 20% of clinically diagnosed pregnancies, which causes considerable anxiety to the woman and her family. It is hypothesized that first-trimester bleeding may indicate an underlying placental dysfunction which may manifest later in pregnancy with an increased risk of preterm delivery, preterm prelabour rupture of membranes (PPROM), placental abruption and intrauterine growth restriction (IUGR).

Materials and methods: A total of 300 women attending gynecology department, within 14 weeks of pregnancy were recruited. Group A comprised of 150 women with threatened miscarriage and meeting inclusion criteria. Group B comprised of 150 women as age and parity matched controls without any such history. All these women were managed as per hospital protocol and were followed up till delivery.

Results: In our study a statistically significant incidence of retroplacental clot(37.3%), low lying placenta(33.3%), abruption placenta(10%), antepartum haemorrhage(20.7%), preterm birth(28%) and incidence of Caesarean section(29>3%) was found in women in later part of pregnancy who had presented with bleeding in early pregnancy

**Keywords:** Bleeding, antepartum haemorrhage

## Introduction

The first trimester of pregnancy is a dynamic period during which changes occur in fetal development at a more rapid rate than any other time during human life. Vaginal bleeding occurs in about 20% of clinically diagnosed pregnancies, which causes considerable anxiety to the woman & her partner<sup>1</sup>. It is hypothesised that first-trimester bleeding may indicate an underlying placental dysfunction with separation of the chorionic membrane from the underlying uterine wall, which may manifest later in pregnancy as adverse outcomes such as pre-eclampsia, preterm delivery, preterm prelabour rupture of membranes (PPROM), placental abruption and intrauterine growth restriction (IUGR).<sup>2,6</sup> There might be minimal or no disruption to uteroplacental development but there develops a chronic inflammatory reaction within the decidua and placental membranes, with weakening and eventual rupture of the membranes or resulting in myometrial activity,<sup>3,7</sup> development of subchorionic hematoma which is associated with 4-33% rate of miscarriage<sup>4,10</sup>. Complete miscarriage is 2.6 times as likely in cases of threatened abortions and 17% of cases are expected to develop complications later in pregnancy.<sup>5,6,8,11</sup>

Threatened abortion is rarely mentioned as a predictive factor for development of abruption or placenta praevia in literature. There is very sparse and unsystematic retrograde data available from our country for understanding maternal & fetal outcome in pregnancies complicated by bleeding at an early stage. In this study we have evaluated cases right from the time of presentation until the final outcome.

**Materials and method:** It was a prospective cohort study conducted in the department of Obstetrics and Gynecology, Vardhman Mahavir Medical College and Safdarjang Hospital, New Delhi, from May 2011 to April 2013. A total of 300 women were recruited and divided in two groups of 150 each as study cases and 150 as controls. The study group had women presenting with symptoms of threatened miscarriage at or below 14 weeks of gestation after ruling out the exclusion criteria of bleeding per vaginum due to causes other than threatened miscarriage like complete or incomplete miscarriage, ectopic pregnancy, molar pregnancy, multiple pregnancy and any medical disorder. The diagnostic criteria for threatened miscarriage was based on ultrasound report with a history of vaginal bleeding in the presence of a closed cervix and gestational age at 14 weeks or less. All women were subjected to detailed history and general physical and local examination, routine antenatal investigations like haemogram, blood group, urine examination, viral markers, blood sugar and coagulation profile.

The data was analyzed by using SPSS 17.0 software. Chi square test was used to compare different parameters by converting them into categories. Student t-test to compare mean levels of parameters between the groups. Continuous variables were expressed as mean  $\pm$  S.D. To determine the statistical significance under each group of different parameters from baseline to different points of time, paired t-test. was used. It was considered statistically significant if the p value came out  $<0.05$ .

**Results:** Maximum number of patients(20%) presented with bleeding during 7-8 weeks of gestation. (Table 1)USG findings suggestive of retro-placental clot was found in 37.3% in group

A and 1.3% in group B. Low lying placenta within 14 weeks was found in 33.3% in group A while in 6% of group B women which was highly significant. Abruptio was present in 10% women in group A compared to 1.3% women in group B. Placenta previa was present in 8% cases in group A and 3.3% cases in group B. Although, the p value equals 0.1 making the finding insignificant the Odd's Ratio came out to be 2.522, with Confidence Interval 0.866-7.344. Antepartum haemorrhage was present in 20.7% cases in group A and 4.7% cases in group B which shows the association of APH in group A to be significant. APH of unknown origin had an incidence of 2.6% in group A and 0.6% in group B. An interesting observation was made of retained placenta which was a significant finding. Preterm birth (<37 weeks) was present in 28% cases in group A and 12% in group B, however birth of small for gestational age babies was not a significant finding in our study. Mode of delivery was operative in 29.3% cases in group A and 20.6% cases in group B (Table 2). History of prior miscarriage was present in 40.7% women in group A and in 19.4% in group B.

### Discussion:

First trimester vaginal bleeding is the most common complication of pregnancy, occurring in 14–20% of ongoing pregnancies.<sup>1</sup> Most often vaginal bleeding originates from the placenta during early pregnancy. It is thought that bleeding between the chorionic membrane and the uterine wall can result in a spectrum of effects on pregnancy development and outcome. At one end, direct pressure and disruption of the placental bed can result in miscarriage. At the other end of the spectrum in the later part of pregnancy is placental abruption, placenta praevia, preterm prelabour rupture of membranes, low birth weight, preterm delivery and fetal death, where there is minimal or no disruption to uteroplacental development but a chronic inflammatory reaction within the decidua and placental membranes, with weakening and eventual rupture of the membranes or resulting in myometrial activity.

The gestational age of the two groups is comparable with majority of the cases of bleeding being in the age group of 21-30 which is consistent with the findings of most of the studies by Sipila et al<sup>4</sup>, Weiss et al<sup>6</sup>, Bimsara et al<sup>7</sup> and Williams et al<sup>8</sup>. In both the groups majority of women were multiparous with a previous live birth, making the two groups comparable with  $p > 0.05$  which is consistent with findings of Sipila et al<sup>4</sup>, Weiss et al<sup>6</sup>. In our study the history of prior miscarriage was a statistically significant finding ( $p = 0.04$ ) and was consistent with findings of Sipila et al<sup>4</sup>, Weiss et al<sup>6</sup> and Williams et al<sup>8</sup>, suggesting prior miscarriages have a significant bearing for a risk of bleeding in present pregnancy. Period of gestation at which most of the patients reported first with complaints of bleeding was at 6-8 weeks. The timing of this peak coincides with the timing of important phases of placental development. A hormonally functional placenta is required for the luteal to placental shift in progesterone production that occurs around gestational week 7. (Table 1). Retroplacental clot was present in 37.3% women who presented with bleeding and 1.3% women who did not report bleeding as an independent finding making the p value 0.000. This is consistent with findings of Pederson et al<sup>12</sup> who reported retroplacental clots in 18–39% of the women presenting with threatened miscarriage. In a study by Sandor Nagy et al<sup>9</sup>

placental abruption abnormalities were also significantly more frequent in the hematoma group. **(Table 2)**

The incidence of abruption was statistically significant in our study which is consistent with a study by Weiss et al.<sup>6</sup>, Wijesiriwardana et al.<sup>10</sup> and Bimsara et al.<sup>7</sup> **(Table 3)**

A low lying placenta was present in 33.3% cases in group A and 6% cases in group B, within 14 weeks of pregnancy making the p value 0.000 which is clinically significant. The presence of a low lying placenta in early pregnancy can possibly contribute to low lying placenta later in pregnancy. Similar results were seen by Davari et al.<sup>11</sup> and Das et al.<sup>12</sup> with  $p < 0.001$  **(Table 4)**

Placenta previa was present in 8% cases in group A and 3.3% in group B. Although, the p value obtained is 0.1 making the finding insignificant, however in our study 18 % cases who were initially diagnosed of low lying placenta remained low lying and formed 75% cases of placenta previa with  $p < 0.05$  making it statistically significant with increase in incidence of placenta praevia from 1.0% to 2.42% with  $p < 0.005$ . The incidence of antepartum haemorrhage in group A was 20.7% and 4.7% in group B, making the p value 0.000.

The incidence of retained placenta was 4.6% in group A and 2% in group B. The OR came out to be 2.399 with a CI(0.6-9.4). In a study by Wijesiriwardana et al.<sup>10</sup> and Davari-Tanha et al.<sup>11</sup> women presenting with threatened miscarriage were more likely to deliver prematurely, 14.7% compared with 52.9%, respectively (relative risk 3.6, 95% confidence interval [CI] 2.4-4.8),  $p < 0.001$ . Similarly, in a study by Bimsara et al.<sup>7</sup> in 2009 the incidence of preterm delivery was 10.9% in cases with threatened miscarriage and 2.3% in the control group, making the p value 0.003. L. Saraswat et al.<sup>13</sup>, in 2009 in their meta-analysis also found an increased risk of preterm delivery with OR 2.05, 95% CI (1.76, 2.4) for manual removal of placenta in cases vs. controls was 1.40 CI(1.43-1.71).

Our study reports an incidence of 28% preterm birth in group A and 12% in group B with an OR 2.85 CI(1.53-5.23), p value 0.001.

An increased incidence of caesarean section has been reported by most studies. Bimsara et al.<sup>7</sup> reported Caesarean section rate in 30 % cases and 21.4% controls with a p value of 0.084. Weiss et al.<sup>6</sup> in 2003 reported an increased frequency of caesarean with an OR of 1.4 in the subgroup with heavy bleeding. The rate of caesarean delivery in our study was 29.3% in cases and 20.6% in controls with p value 0.100, OR 1.59(0.93-2.70).

### **Conclusions:**

To conclude, bleeding in early pregnancy increases the incidence of a myriad of maternal and fetal complications arising from early placental dysfunction. In our study, a statistically significant increase in incidence of retroplacental clot, low lying placenta, abruptio placentae, antepartum haemorrhage, preterm birth and an increased incidence of Caesarean section was found. Also a statistically significant correlation was found between low lying placenta before 14

weeks and placenta previa after 28 weeks and between retroplacental clot on ultrasound before 14 weeks and development of abruption after 28 weeks. All these findings suggest that women with bleeding in early pregnancy must be treated as high-risk pregnancy and should be followed closely.

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Tables

**Table 1:** Period of gestation at the time of bleeding

POG at Bleeding ( weeks)	Group A N=150	
<5	3	(2%)
5-6	23	(15.3%)
6-7	36	(24%)
7-8	30	(20%)
8-9	16	(10.7%)
9-10	10	(6.7%)
10-11	10	(6.7%)
11-12	8	(5.3%)
12-13	8	(5.3%)
13-14	6	(4%)

**Table 2:** Comparison of observations between the two groups

Observations	GroupA (n=150)	GroupB(n=150)	P value
Retroplacental clot(upto 14 wks)	56(37.3%)	2(1.3%)	0.000
Low lying placenta(upto 14 wks)	50(33.3%)	9(6%)	0.000
Abruption	15(10%)	2(1.3%)	0.001

Placenta previa	12(8%)	5 (3.3%)	0.8
Antepartum haemorrhage	31(20.7%)	7(4.7%)	0.000
Retained placenta	16(10.7%)	3(2%)	0.002
Preterm birth	42(28%)	18(12%)	0.001
C-section	44 (29.3%)	31 (20.6%)	0.083

**Table 3** Retro placental clot and placental abruption

USG-RPC(within 14weeks)	Abruption Present	Abruption Absent
Present	12(80%)	44
Absent	3	91
p=0.000		

**Table 4** Low lying placenta and placenta previa

LLP (within 14 weeks)	PP Present	PP Absent
Present	9(75%)	41
Absent	3	97
p=0.001		