EARLY AND LATE PREGNANCY COMPLICATIONS IN WOMEN WHO EXPERIENCE FIRST TRIMESTER VAGINAL BLEEDING AT A UNIVERSITY HOSPITAL, BENIN CITY, NIGERIA

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ABSTRACT

Background: Vaginal bleeding in pregnancy is usually an alarming experience for pregnant women and this remains one common reason for them to present to the early pregnancy assessment unit (EPAU).

Objective: We sought to document pregnancy failure and risk of placenta praevia complicating first trimester bleeding per vagina (PVB), and to examine the influence of recurrent PVB on specific materno-fetal outcomes.

Method: Early pregnancy PVB managed in the EPAU was reviewed and women who reported first trimester PVB at the time of antenatal booking were recruited along with controls. Both groups were prospectively studied until delivery. The diagnosis of placenta praevia and the development of other maternal or fetal complications were noted. The association between clinical presentation and pregnancy outcome was analyzed using cross-tabulations with SPSS.

Results: PVB was reported by 7.5% of women seen in the EPAU. At booking, 14 women with early PVB and 51 controls were recruited. The experience of PVB was associated with delivery before 34 weeks (RR 3.3 with 95%CI: 1.34-7.99; P = 0.06), birth asphyxia (RR 3.7 with 95%CI: 1.59-8.50; P = 0.01) and low birth weight (RR 7.3 with 95%CI: 3.24-16.59; P = 0.001). Recurrent PVB was associated with 85.7% risk of placenta praevia.

Conclusion: Vaginal bleeding in early pregnancy can predict placenta praevia, and is associated with preterm delivery and birth asphyxia. Early identification of women who bleed in pregnancy will be instructive in their successful monitoring and delivery. We advocate a deliberate enquiry about PVB in the booking clinic.

***Key words**: First trimester vaginal bleeding, Miscarriage, Adverse pregnancy outcomes, Placenta praevia*

INTRODUCTION

Vaginal bleeding during pregnancy evokes a sense of concern among pregnant women and their healthcare professionals alike. It is one sign of pregnancy risk that the patient observes directly. However, the outcome of bleeding per vagina (PVB) in pregnancy is often unpredictable. Whereas many cases of PVB only herald a transient event, some are a feature of early pregnancy failure while others are an indication of later pregnancy complications. It is not surprising that PVB is one of the most common reasons why women present to the emergency department in early pregnancy.[1] The incidence of bleeding in pregnancy has a wide variation depending on the stage of pregnancy. In the review work by Olugbenga and associates[2] in 2019, incidence was reported to be 12% to 40%. Other researchers have previously documented 20% to 30%[3] and 3.75% in late pregnancy,[4] with higher incidence found in earlier stages of pregnancy.[5]

The experience of PVB in pregnancy has been shown by many investigators to be associated with adverse pregnancy outcome, and the sensitivity for predicting pregnancy complications increases with recurrent PVB.[2,5,6] Early complications documented in women who report PVB include miscarriage,

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ectopic gestation and molar pregnancy.[7] PVB may initially be assumed to announce implantation in some cases, but as the pregnancy advances, it may become obvious that the bleeding is from the genital tract or a feature of systemic bleeding disorders. In some cases, the bleeding may be subtle and not paid much attention or reported by the woman. Importantly, implantation bleeding, evolving miscarriage, ectopic gestation or gestational trophoblastic disease may be difficult to differentiate at the earliest occurrence of PVB in the first trimester from genital tract lesions manifesting as PVB.[7-9]

Beyond the first trimester, PVB is often associated with the placenta, an observation that may be explained by the occurrence of chronic decidual inflammation, impaired placentation, oxidative stress, and perhaps failure of invasion by spiral arterioles. These abnormalities have been associated with miscarriages, fetal growth restriction, preterm birth, preeclampsia and other adverse outcomes.[10] Previous investigators have been consistent in suggesting a role for threatened miscarriage in the later development of antepartum haemorrhage and other forms of adverse pregnancy events.[11,12]

Furthermore, the presence of intrauterine haematoma without obvious vaginal bleeding has also been documented in pregnancies subsequently found to present with increased risk of miscarriage, preterm birth, small for gestational age fetuses and hypertensive disorders of pregnancy.[10,13,14] Earlier researchers have documented up to 50% risk of miscarriage following first trimester bleeding.[15,16] Other adverse outcomes associated with early pregnancy PVB include preterm delivery, intrauterine growth restriction (IUGR), preterm premature rupture of membranes, and perinatal morbidity and mortality.[12,17,18]

There is evidence to show that low birth weight complicates second trimester PVB.[19,20] Similarly, threatened miscarriage is documented to have a relationship with preterm delivery, IUGR and perinatal mortality.[12] Increased interventions with induction of labour and Caesarean section are also found to be associated with PVB in the second half of pregnancy.[2] Furthermore, placental disorders associated with PVB such as placenta praevia and abruptio placentae are known to increase the risk of Caesarean section.[21]

Placenta praevia is a major contributor to adverse maternal and perinatal outcomes. The role of PVB in early pregnancy in predicting the diagnosis of pregnancy complications has been studied extensively elsewhere.[10,12,16,18-20] The need to examine the role of early PVB in the development of complications like placenta praevia in our environment remains relevant. Considering the important role of obstetric haemorrhage in maternal health and perinatal outcome, early detection of placenta praevia will be useful in mitigating the toll on maternal and perinatal health due to bleeding placenta praevia, such as maternal anemia, blood transfusion, preterm delivery and maternal and perinatal mortality. The present study was designed to determine the clinical utility of PVB in the first trimester in predicting the development of pregnancy complications like placenta praevia. The findings of the study may be imperative to defining a clinical tool that is predictive of adverse outcomes like placenta praevia in women who have PVB.

Methodology

Study setting

The University of Benin Teaching Hospital (UBTH) is a multi-specialty facility located in Benin City, Edo State, South-South region of Nigeria. The hospital has antenatal attendance rate of between 120 and 180 new patients per week and between 250 and 500 follow-up patients per week. The delivery rate in the hospital in the last five years has been about 3000 per year. The hospital has a total antenatal and postnatal bed capacity of 82 spaces, and 8 functioning delivery rooms in the labour ward. There are 4 operating theatres attached to the labour ward.

Study design

A prospective case control study of antenatal patients managed for bleeding in early pregnancy at the Department of Obstetrics and Gynaecology, UBTH, between January and April 2019 (both inclusive) was

conducted with the approval of the Research and Ethics Committee of the hospital. Inclusion criteria were: informed consent to participate and booking before 20 weeks gestation. Women who had cervical cerclage inserted were excluded from analysis.

PATIENT SELECTION

Women who were managed for PVB in the first trimester and booked for antenatal care before 14 weeks gestation were approached and those who agreed to participate and gave informed consent were recruited. They were followed up till delivery. Information regarding the experience of bleeding was documented and relevant data on sociodemographic characteristics and clinical management was extracted. Appropriate care was offered until decision for delivery was taken. The study was terminated for each woman at the time of decision for delivery either on the basis of any of the outcome measures or when pregnancy progressed to term.

At the time of recruitment of any woman with PVB, 3 others who did not experience bleeding and were matched for maternal age, parity and gestational age at the time of the experience of PVB in the cases were taken as controls, and they were also followed up till delivery.

CLINICAL MANAGEMENT

Following booking for antenatal care, the women were followed up 4-weekly until 28 weeks, 2-weekly until 36 weeks, and thereafter, weekly till delivery. For women who presented with PVB, the clinical evaluation involved confirming fetal viability, excluding obvious causes, and planning further management. Women who had miscarriage were managed appropriately, while those with ongoing pregnancies either had in-hospital care or were managed on out-patient basis depending on their individual attributes. Basic investigations including full blood count, E&U, urinalysis and blood sugar were prescribed, the presence of anemia necessitated blood transfusion, while ultrasound scan was done to confirm fetal viability, document retro-placental hematoma and exclude gross fetal anomaly. In particular, ultrasound scans were scheduled at predetermined intervals for anatomical survey around 20 weeks, growth monitoring around 28 weeks and 34 weeks as well as for placental localization to exclude placenta praevia. During follow-up visits, repeat PVB was noted and when a diagnosis of placenta praevia was confirmed beyond 34 weeks of gestation, especially in women with further episodes of bleeding, in-hospital management was instituted.

DATA MANAGEMENT

The primary outcome measure was the diagnosis of placenta praevia. Other outcome measures included preterm delivery, diagnosis of abruptio placentae and premature rupture of membrane as well as intrauterine growth restriction (IUGR) and preeclampsia.

Information retrieved from the women was used to generate a database for analysis. Categorical variables were analyzed with Chi-squared test or Fisher's exact test as appropriate, while continuous variables were analyzed using student's t test. Association between PVB in early pregnancy and adverse pregnancy events like placenta praevia was conducted by cross-tabulations with the results expressed as risk ratio (RR). Statistical significance was defined as P value of <0.05. The analysis was carried out with SPSS version 20 (SPSS Inc., Chicago IL).

RESULTS

Of the 1,445 women seen in the early pregnancy assessment unit of the department over the study period, 7.5% (109/1,445) reported first trimester PVB. Threatened miscarriage was the diagnosis in 44% (48/109), 8.3% (9/109) had complete miscarriage and the others had incomplete or missed miscarriage. (Table 1) Evacuation of retained products of conception was necessary in 35.8% (39/109) of the women.

Out of 405 women booked for antenatal care during the study period, 135 were in their first trimester and 106 of them agreed to participate in the study. Of the 106 women, 61.3% (65/106) were retained in the study and followed up till delivery. Of the 65 women, 14

(13.2%) made up the cases with PVB in early pregnancy while 51 were in the control group. The mean age of the whole group was 30.4 ±5.13 years and the median parity was para 2. Just over half of the women (33/65) had tertiary education. The cases and controls did not differ significantly in terms of maternal age (P=0.2), parity (P=0.6) and gestational age (P=0.5).

Table 2 reveals the pregnancy outcomes for the cases and controls. IUGR was 7.1% more likely with PVB group than controls (7.1% vs 0%, RR 4.9 with 95%CI: 3.03-7.99; P = 0.2). The experience of PVB increased the risk of delivery before 34 weeks by 17.5% (21.4% vs 3.9%, RR 3.3 with 95%CI: 1.34-7.99; P = 0.06). The chance of low birth weight babies in 8 out of 14 women with PVB was 53.2% higher than that in 4 out of 51 women in the control group (57.1% vs 3.9%, RR 7.3 with 95%CI: 3.24-16.59; P = 0.001). Birth asphyxia was 33.1% more likely in the women who bled than the women without PVB (42.9% vs 9.8%, RR 3.7 with 95%CI: 1.59-8.50; P = 0.01).

Table 3 gives a summary of the clinical progression of women with PVB. Of the 14 women who experienced PVB, 71.4% (10/14) had repeat bleeding beyond 26 weeks gestation, and 28.6% (4/14) had need for blood transfusion on one or more occasions. Most (78.5%) of the women with PVB had Caesarean delivery. The majority (85.7%) of women who had early pregnancy PVB were subsequently diagnosed to have placenta praevia with ultrasound scan.

Table 1

Early complications of first trimester bleeding per vagina

Complication	Number	%
Threatened miscarriage	48	44.0
Incomplete miscarriage	28	25.7
Missed miscarriage	24	22.0
Complete miscarriage	9	8.3

Table 2
Pregnancy outcome with respect to the experience of bleeding per vagina

Outcome	Bleeding in pregnancy Number (%)	No bleeding in pregnancy N umber (%)	P value
GA at delivery (week)			
<34	3(21.4)	2(3.9)	0.06
≥34	11(78.6)	49(96.1)	
IUGR			
Yes	1(7.1)	0(0)	0.2
No	13(92.9)	51(100)	
Birth asphyxia			
Yes	6(42.9)	5(9.8)	<0.01
No	8(57.1)	46(90.2)	
Birth weight (Kg)			
<2.5	8(57.1)	2(3.9)	<0.001
≥2.5	6(42.9)	49(96.1)	

GA: gestational age, **IUGR**: intrauterine growth restriction

Table 3
Clinical trend in women with bleeding per vagina in early pregnancy

Outcome	Number of events	%
Bleeding episode		
Single	2	14.3
Multiple	12	85.7
Need for transfusion		
Yes	6	42.9
No	8	57.1
Clinical diagnosis		
Placenta praevia	12	85.7
Abruptio placentae	2	14.3
IUGR	1	7.1
Mode of delivery		
Vaginal	3	21.4
Caesarean	11	78.6

IUGR: intrauterine growth restriction

The experience of multiple bleeding episodes was strongly associated with a diagnosis of placenta praevia (100%). Early PVB was also associated with the development of abruptio placentae (14.3%) and IUGR (7.2%).

Discussion

PVB in early pregnancy has been associated with adverse pregnancy outcomes especially when recurrent, and when repeat episodes of bleeding occur in the second and third trimesters of pregnancy.[2,5,6] The commonest causes of PVB in the second half of pregnancy are known to be placenta praevia and abruptio placentae.[22] In the present study, PVB in early pregnancy that did not result in failed pregnancy was found to be associated with increased risk of preterm birth, IUGR, low birth weight and birth asphyxia. Recurrent PVB was strongly predictive of placenta praevia, and women who experienced bleeding were also more likely to receive blood transfusion and deliver by Caesarean section.

The frequency of first trimester PVB was found to be 7.5% and 13.2% in our study, a proportion which is much lower than the reported incidence of 20% to 30% documented by Koifman et al [5] in their review. Our finding is also lower than the 12% to 40% reported by Olugbenga and colleagues.[2] Among the women who reported PVB at the time of antenatal booking in the present study, a majority developed complications. Most women who report bleeding in early pregnancy do not develop antepartum haemorrhage (APH) but many women with a diagnosis of APH in late pregnancy often report earlier events of bleeding. What is likely is that many of those with early pregnancy complications often progress to miscarriage, while others continue to develop normally, whereas the subset that will eventually develop late pregnancy complications are probably more likely to experience repeat PVB. Perhaps the low incidence of bleeding in early pregnancy in the present study is partly due to women who might not present to the hospital if they considered their PVB as mild and innocuous.

The present study revealed that women who bled in early pregnancy had an increased risk of delivery before 34 weeks of gestation. Previous researchers have noted the association of PVB in early pregnancy with preterm delivery.[5,23] Similar to the reports of previous studies, low birth weight was found to be more associated with women who experienced PVB in early pregnancy in the present study. This is probably explained by the increased risk of preterm delivery found in this group of women which is directly associated with low birth weight. Perhaps the analysis of weight based on the expectation for specific gestation will help define an independent role for PVB in the observation of low birth weight. Furthermore, gestation-based weight classification may provide more insights into the impact of PVB on fetal weight rather than the application of a dichotomy referenced by 2.5kg.

IUGR was another pregnancy complication noted to be associated with PVB in early pregnancy in the present study. Previous studies by Saraswat et al [12] and Spinillo et al[20] also reported an observed risk of IUGR in the setting of PVB. This complication is probably due to the presence of micro-infarctions from diffuse areas of placental abruption which are not clinically or radiologically identifiable but can lead to placental insufficiency and subsequent IUGR.[6]

Birth asphyxia was also found in the present study to be associated with women who experienced bleeding in pregnancy. Koifman et al [5] had previously noted such a relationship in their study. Again, this observation may be attributed to the higher rates of preterm delivery within the PVB group, and hence the attendant increased association of perinatal morbidity and/or mortality.

Saraswat et al [12] in their study revealed that PVB in early pregnancy was associated with adverse pregnancy outcomes including placenta praevia and placental abruption. Nwafor et al [17] also noted similar findings in a study in Abakaliki, Southeastern Nigeria. However, Olugbenga et al [2] did not find any association between PVB in early pregnancy and the diagnosis of placenta praevia. In the present study, PVB in early pregnancy was significantly associated with the development of placenta praevia.

The diagnosis of early pregnancy failure and late complications like placenta praevia usually, as in the present study, require confirmation with an abdominal or transvaginal ultrasound scan. [21,24,25] Over 80% of the women with early first trimester PVB in the present study who were diagnosed to have placenta praevia later in pregnancy had recurrent PVB beyond 26 weeks gestation, with a third of them requiring blood transfusion on one or more occasions. The occurrence of PVB in early pregnancy apparently results in decrease in hematocrit level that may necessitate blood transfusion, especially when the blood loss is recurrent. Perhaps this group of women may benefit from more frequent checks of their hematocrit to determine the need for more intensive use of haematinics or early medical correction of deficit so as to reduce the need for blood transfusion.

In the present study, the rate of surgical intervention for delivery was almost 80% for women who bled in early pregnancy and later had a diagnosis of placenta praevia or abruptio placentae. This rate is similar to the 72.9% previously reported by Koifman et al.[5] The contribution of placenta praevia and abruptio placentae to Caesarean section rate is huge, especially in the setting of bleeding placenta praevia and mild abruption with a live baby. [22] Hence, the high rate of Caesarean delivery among women with PVB in the present study can be partly explained by the high rate of placenta praevia among this group of women.

The present study has shown that women who report PVB in pregnancy are at high-risk for adverse pregnancy events such as pregnancy failure, placenta praevia, preterm delivery and birth asphyxia. The prospective design employed in this study assured reliability of the data; however, a multicenter study with a larger sample size may confirm the findings of our study as well as improve the external validity of the results. Future research in this area of interest should focus on defining socio-demographic determinants of women who bleed in early pregnancy, quantify the pattern and severity of vaginal bleeding as a score, [26] and attempt to correlate these features with maternal serum markers of placental dysfunction which may also predict adverse maternal and perinatal outcome.

CONCLUSION

PVB in early pregnancy may herald pregnancy failure, is associated with pregnancy complications like placenta praevia and preterm birth, and increases the risk of Cesarean delivery. This knowledge is relevant to both the woman and the obstetrician for proper management and timely intervention to forestall adverse maternal and perinatal outcomes. We advocate the development of a bleeding score to define individual risk for adverse outcome.

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Author Contribution

N Enaruna: Project concept and design, Data collection, Data analysis, Final manuscript writing

C Anya: Data analysis and interpretation, Manuscript preparation

C Anyanwu: Project development, Data interpretation, Manuscript preparation

All authors read and approved the final manuscript

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Conflict of Interest

We declare that we have no conflict of interest.

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