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## Impact of Early pregnancy bleeding on maternal and fetal outcome

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### Highlights

- A descriptive cross-sectional study, on impact early pregnancy bleeding
- Assess the effect of EPB on maternal outcome
- Assess the effect of EPB on fetal outcome
- Close monitoring and proper management among EPB women is advised

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### ABSTRACT

**Background:** Vaginal bleeding is a common event at all stages of pregnancy, and early pregnancy bleeding during the first and second trimester (EPB) is a common symptom during pregnancy. EPB could have adverse effects on pregnancy and neonate. **Objective:** Is to assess the effects of early pregnancy bleeding on both mother and fetus. **Patients and methods:** A descriptive, cross-sectional study was conducted at Benghazi medical center (BMC); all the eligible women attended the obstetric ward for delivery in the period between the 1<sup>st</sup> of August and 31<sup>st</sup> of December 2016 were included. Data collected by direct interview and from medical records. Data analyzed using SPSS ver. 23. Descriptive statistics were obtained, and means, standard deviation, and frequency distribution were calculated. Chi square test was used,  $P < 0.05$  considered as statistically significant. **Results:** Out of the 1404 women, 125 (9%) women had a history of early pregnancy bleeding (EPB). Pregnancy-induced hypertension, pre-eclampsia, antepartum hemorrhage, preterm labor, and premature rupture of the membrane were significantly ( $P < 0.05$ ) more frequent among women with a history of early bleeding. Ninety-four (3.5%) women had a history of antepartum hemorrhage, for 27 (1.9%) of them, the cause was due to placenta abruption, while for 22 (1.6%) women the cause was placenta previa. The occurrence of both placenta previa and placenta abruption was significantly ( $P < 0.05$ ) more among women with a history of EPB. Fetal health problems and early neonatal death were significantly ( $P < 0.05$ ) more among mothers with EPB. **Conclusion:** Serious maternal morbidities are significantly associated with EPB as PET, APH, and PROM. Also prematurity, IUGR, low birth weight, increase risk of neonatal ward admission and perinatal mortality are significantly more among women EPB. **Recommendation:** Proper antenatal care for early diagnosis, close follow up, and proper management of women with early pregnancy bleeding strongly recommended.

### 1. Introduction

Vaginal bleeding is a common complaint at all stages of pregnancy, and early pregnancy bleeding (EPB) is a common symptom during pregnancy complicating 16% – 25 % of all pregnancy (Farrell & Owen, 1996). EPB can be a normal sign of implantation of the pregnancy but may herald the initiation of spontaneous miscarriage. Four major sources of bleeding in early pregnancy are ectopic pregnancy, miscarriage (threatened, inevitable, incomplete, complete), molar pregnancy, and local pathology (Speert & Guttmacher, 1954). The woman with EPB requires assessment to identify normal or abnormal development of the pregnancy or a local pathologic condition that requires intervention (Snell, 2009).

About half of the women with threatened miscarriage diagnosed based on documented fetal cardiac activity on ultrasound with a history of vaginal bleeding in the presence of a closed cervix, (Dogra *et al.*, 2005; Sara *et al.*, 2010). Those women will end in miscarriage within the first 20 weeks of gestation and the other will continue the pregnancy. There are many risk factors for threatened miscarriage such as high maternal and /or paternal age (Hossain *et al.*, 2006; Andersen *et al.*, 2000). History of previous miscarriage (de la Rochebrochard & Thonneau, 2002), history of infertility (Regan

*et al.*, 1989), extremes of BMI (body mass index), and uterine malformations (Axmon & Hagmar, 2005). The mechanism of this bleeding, in many studies considered as Luteal phase deficiency. Luteal phase deficiency is the most frequent cause of (EPB), and loss, which is related to the insufficiency of progesterone secretion by corpus luteum, this deficiency is known to be predictive for gestational pathology in the first trimester (Maconochie *et al.*, 2007). Thrombosis of the uteroplacental vasculature caused by antiphospholipid antibodies is an important mechanism of miscarriage and early pregnancy bleeding, where women with APS have a miscarriage rate as high as 90% (Rai *et al.*, 1995). Immune dysfunction is another mechanism of early pregnancy bleeding, as in pregnancy there is a conflict between the semi- allogenic fetus and the mother in which fetal survival is dependent on suppression of the maternal immune response (Wilson *et al.*, 2001).

EPB could have adverse effects on pregnancy and perinatal outcomes. The women have an increased risk of developing complications later in pregnancy (Koopman *et al.*, 2003; Everett, 1997; Hasan *et al.*, 2009; Van Oppenraaij *et al.*, 2009). Many studies have revealed an association between EPB and an unfavorable outcome (Johns J, Hyett J and Jauniaux E. 2003; Strobino & Pantel-Silverman,

1989). Most of the maternal outcomes are serious and carries significant morbidity and sometimes mortality if not predicted, early diagnosed, and timely managed, these complications include, preeclampsia/ eclampsia or pregnancy-induced hypertension (PIH) (Williams et al., 1991) antepartum hemorrhage (APH); placenta Previa abruption placenta, and other APH (Dogra et al. 2005; Keith Edmonds, 2007). Another complication is the preterm prelabour rupture of membranes PPRM (Dogra et al., 2005), preterm labor PTL (Lykke et al., 2010), and postpartum hemorrhage (PPH). Early pregnancy bleeding may also affect the mode of delivery (Hosseini & Yaghoubipour, 2013; Saraswat et al., 2010; Rozina et al., 2016 study done in Pakistan). According to several studies, there are also a number of adverse fetal and neonatal outcomes of EPB including; mainly prematurity (Lykke et al., 2010; Berkowitz et al., 1983), low birth weight, intrauterine growth restriction (IUGR) (Dogra et al., 2005), and perinatal mortality (Williams et al., 1991). Indicators of perinatal morbidity such as Apgar scores, neonatal unit admission, and presence of congenital malformations were significantly more among women with EPB (Dogra et al., 2005; Batzofin et al., 1984; Dadkah, 2010).

Threatened miscarriage is an important event to predicate both maternal and fetal outcomes in late pregnancy, therefore it is essential to consider these pregnancies as a high-risk group and provide careful antenatal care. Several studies have sought to identify adverse fetal outcomes, but very few have commented on maternal complications and there is no clear evidence regarding the effect on mode of delivery. Up to our knowledge, in Benghazi, there were no previous studies to investigate this problem; consequently, this study was conducted to assess the impact of (EPB) on maternal and fetal outcome.

## 2. Subjects and method

A descriptive, cross-sectional study was conducted at Benghazi Medical Center. All women who attend the obstetric ward for delivery in the period between 1<sup>st</sup> of August and 31<sup>th</sup> of December were included in this study; women residents outside Benghazi, non-Libyan, and/or with multiple pregnancies were excluded. Data collected by direct interviews with every woman, some data collected from their medical records. Data analyzed using SPSS ver. 23. Descriptive statistics were obtained, and means, standard deviation, and frequency distribution were calculated. Chi square test was used,  $P < 0.05$  considered as statistically significant.

## 3. Results

One thousand four hundred and four Libyan women were included in this study, the ages of the women ranged from 16-48 years; the mean age was 30.8 years  $\pm$ SD 6.3 years. The vast majority of them, their ages ranged from 21-40 years, Fig. 1.

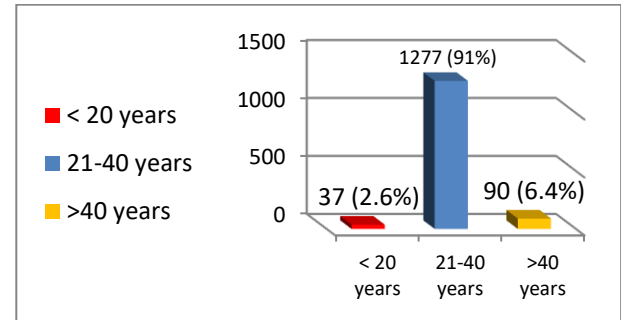


Fig. 1. Distribution of the women according to the age groups.

Out of the 1404 women, 125 (9%) women had a history of early bleeding (during the first and second trimester), Fig. 2.

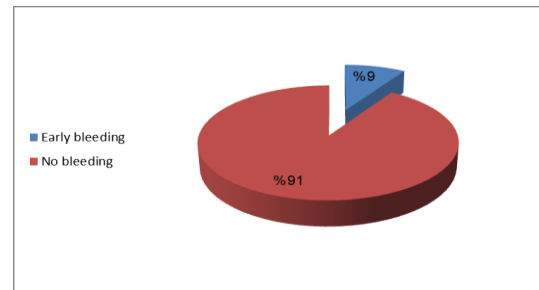


Fig. 2. Distribution of the women according to history of early bleeding.

There were no significant differences ( $P > 0.05$ ) between women regarding history of early bleeding and a history of gestational diabetes, labor induction, prolonged labor, or postpartum hemorrhage. Pregnancy-induced hypertension, pre-eclamptic toxemia, antepartum hemorrhage, preterm labor, and premature rupture of the membrane were significantly different ( $P < 0.05$ ) more frequent among women with a history of early bleeding, Table 1.

Table 1

Distribution of women by history of early bleeding and pregnancy-related complications.

Complications	Early bleeding	No bleeding	X <sup>2</sup>	P-value
Gestational diabetes:				
Yes	3 (2.4 %)	36 (2.8 %)	0.073	0.788
No	122 (97.6 %)	1243 (97.1 %)		
Total	125 (100%)	1279(100%)		
PIH_PET:				
Yes	12 (9.6%)	51(4.0%)	8.369	0.004*
No	113(90.4%)	1228(96.0%)		
Total	125 (100%)	1279(100%)		
Labor induction:				
Yes	1(0.8%)	23 (1.8%)	0.675	0.411
No	124(99.2%)	1256 (98.2%)		
Total	125 (100 %)	1279(100%)		
Prolonged labor:				
Yes	1 (0.8%)	17 (1.3%)	0.252	0.616
No	124 (99.2%)	1262 (98.7%)		
Total	125 (100%)	1279(100%)		
APH:				
Yes	18(14.4%)	31 (2.4%)	49.34	0.000*
No	107(85.6%)	1248 (97.6%)		
Total	125 (100%)	1279(100%)		
PPH:				
Yes	2 (1.6%)	22 (1.7%)	0.010	0.921
No	123 (98.4%)	1257 (98.3%)		
Total	125 (100%)	1279(100%)		
Preterm labor/PROM:				
Yes	10 (8.0%)	31 (2.4%)	12.49	0.000*
No	115(92.0%)	1248 (97.6%)		
Total	125 (100%)	1279(100%)		

\* Highly significant

Ninety-four (3.5%) women had a history of antepartum hemorrhage, 27 (1.9%) of them, the cause was due to placenta abruption, while among 22 (1.6%) women the cause was placenta previa. The occurrence of both placenta previa and placenta abruption was significantly ( $P<0.05$ ) more among women with a history of early pregnancy bleeding, Table 2. Table 3 shows the distribution of women by history of early bleeding and mode of delivery, where both elective and emergency cesarean sections significantly ( $P<0.05$ ) more frequent among women with a history of early bleeding. Table 4 shows the impact of early pregnancy bleeding on

the fetal outcome, where intrauterine growth retardation, low birth weight, low Apgar score, congenital anomalies, and admission to the neonatal ward were significantly ( $p<0.05$ ) more among infants of mothers with early pregnancy bleeding, also it shows no significant ( $P>0.05$ ) differences between them regarding occurring of fetal distress and fetal asphyxia. Early neonatal death was significantly ( $P<0.05$ ) more among infants of mothers with early pregnancy bleeding, while no significant ( $P>0.05$ ) difference between them regarding the occurrence of stillbirth and intrauterine death, Table 5.

**Table 2**

Distribution of women by the cause of antepartum hemorrhage and history of early bleeding.

History of early bleeding	APH			Total
	No	Abruption placenta	Placenta previa	
Yes	107 (85.6%)	9 (7.2%)	9 (7.2%)	125 (100%)
No	1248 (97.6%)	18 (1.4%)	13 (1.0%)	1279 (100%)
Total	1355 (96.5%)	27 (1.9%)	22 (1.6%)	1404 (100%)

$X^2= 49.348$        $df=2$        $P=0.000^*$

**Table 3**

Distribution of women by history of early bleeding and mode of delivery

History of early bleeding	Mode of delivery			Total
	Normal vaginal	Elective C/S	Emergency C/S	
Yes	59 (47.2%)	22 (17.6%)	44 (35.2%)	125 (100%)
No	773 (60.4%)	191 (15.0%)	315 (24.6%)	1279 (100%)
Total	832 (59.1%)	213 (15.2%)	359 (25.6%)	1404 (100%)

$X^2=8.878$        $df=2$        $P\text{-value}= 0.012^*$

**Table 4**

Fetal & neonatal complications and history of early pregnancy bleeding

Complications	Early bleeding	No bleeding	$X^2$	P-value
IUGR				
Yes	4(3.2%)	12(0.9%)	5.171	0.023*
No	121(96.8%)	1267(99.1%)		
Total	125(100%)	1279(100%)		
Fetal distress				
Yes	12 (9.6%)	120 (9.4%)	0.006	0.937
No	113 (90.4%)	1159 (90.6%)		
Total	125(100%)	1279(100%)		
Birth asphyxia				
Yes	1(0.8%)	3 (0.2%)	1.282	0.258
No	124 (99.2%)	1276 (99.8%)		
Total	125(100%)	1279(100%)		
Birth weight				
<2.5 kg	23 (18.4%)	56 (4.4%)	42.708	0.000*
2.5-4 kg	98 (78.4%)	1125 (90.1%)		
>4 kg	4 (3.2%)	71 (5.6%)		
Total	125(100%)	1279(100%)		
Low Apgar score				
Yes	14(11.2%)	32 (2.5%)	27.185	0.000*
No	111 (88.8%)	1247 (97.5%)		
Total	125(100%)	1279(100%)		
Congenital anomalies				
Yes	4 (3.2%)	9 (0.7%)	7.735	0.005*
No	121 (96.8%)	1270 (99.3%)		
Total	125(100%)	1279(100%)		
Admission to the neonatal ward				
Yes	76 (60.8%)	550 (34.0%)	14.599	0.000*
No	49 (39.2%)	729 (56.0%)		
Total	125(100%)	1279(100%)		

\* Highly significant

**Table 5**

Fetal and neonatal death and history of early pregnancy bleeding

Complications	Early bleeding	No bleeding	X <sup>2</sup>	P-value
Stillbirth			0.762	0.383
Yes	1 (0.8%)	4(0.3%)		
No	124 (99.2%)	1275 (99.7%)		
Total	125(100%)	1279(100%)		
Neonatal death ( 1 <sup>st</sup> . day)			24.79	0.000*
Yes	4 (3.2%)	2 (0.2%)		
No	121 (96.8%)	1277 (99.2%)		
Total	125(100%)	1279(100%)		
IUFD			1.177	0.278
Yes	2 (1.6%)	9 (0.7%)		
No	123 (98.4%)	1270 (99.3%)		
Total	125(100%)	1279(100%)		

#### 4. Discussion

This study was designed to evaluate the association between EPB without miscarriage and complications later in the same pregnancy. The total number of the study population was 1404 out of these 125 cases had EPB. The prevalence of the cases with EPB was 9%. This is slightly lower than the results of other studies where it was ranging between 15-25% (Farrell, T. and Owen, 1996), which could be explained by an undocumented lesser degree of bleeding, however, it is still a significant figure that necessitates evaluation and actions to be taken for reducing further complications.

When evaluating the pregnancy outcome later that complicated by bleeding in the first and second trimester, there was an increased risk of some obstetric complications. In the EPB group, there were PIH and /or PET was significantly more among women with EPB, this result is in accordance with the results obtained by (Hosseini, S. & Yaghoubipour, 2013) where the gestational HTN and preeclampsia were found in 7.2% of the cases with EPB. In contrast with a conclusion from a systemic review conducted by (Saraswat et al., 2010), where they found the incidence of hypertensive diseases was not significantly altered by bleeding in EPB.

One of the serious complications associated with EPB is antepartum hemorrhage, in this study the prevalence of abruptio placenta is significantly ( $P<0.05$ ) higher in the cases with EPB, this is related also to abnormal placentation. This result is consistent with the result of (Hosseini & Yaghoubipour, 2013) where the prevalence of abruptio placenta also higher among the cases with EPB. In addition, the association of low lying placenta and bleeding in the first half of pregnancy has been reported in the same study in agreement with this study.

Preterm labour and preterm prelabour rupture of membranes (PPROM) rates increased in the cases with EPB. It hypothesized that disruption of the chorio-amniotic plate by adjacent hemorrhage may make the membranes more susceptible to rupture. This may be due to the subchorionic bleeding that occurred earlier and iron deposition which damaging the membranes or because of the chronic inflammatory reaction and thrombin formation within the decidua and placenta and membranes with weakening and rupturing them. Moreover, thrombin is an uterotonic agent that may cause preterm labour during late pregnancy (Lockwood et al., 2007). The prevalence of PPRM is significantly higher among cases with EPB in agreement with other studies conducted by (Hosseini & Yaghoubipour, 2013; Lykke et al., 2010).

The frequency of operative delivery among cases with EPB was 52.8 % (17.6% elective and 35.2% emergency), which significantly ( $p<0.05$ ) higher than that among cases without a history of EPB, this reflects the higher obstetric complications among EPB cases which seen in this study. In other study conducted in India (Hosseini & Yaghoubipour, 2013), there were no significant differences between cases with EPB and without EPB regarding the mode of delivery, while it was only 29.69% in (Naurin et al., 2016 study done in Pakistan)

By evaluating perinatal complications that can be associated with EPB. The results of the study showed that the prevalence of prematurity among the cases with EPB was about 27%, which significantly more than that among cases without EPB. Similar findings were reported by another study conducted by (William et al., 1991). Where the data analysis demonstrated that the women with EPB had double the risk of preterm infants compared with those who experienced no bleeding. This also in agreement with the results of a systemic review done by (Saraswat et al., 2010). Where they found the overall risk of preterm delivery was 2.0 (95%, CI 1.76, 2.4), while in a study conducted in (Hosseini & Yaghoubipour, 2013) there where little rise in the incidence of preterm infants in cohort group 18.6% while was 16.9% in the control group. This factor alone may be responsible for other findings including low birth weight, low Apgar score, and increased perinatal mortality.

The intrauterine growth-retarded (IUGR) was significantly higher in the EPB group if compared with infants of cases without EPB (3.2% vs. 0.9%). A similar result was observed in a systemic review done by (Saraswat et al., 2010) where the risk of IUGR in EPB is 1.54 (CI 95percentage 1.18-2.0) higher than that of the control group. In the other study conducted by (Hosseini & Yaghoubipour, 2013), the incidence of IUGR was 6.4 % in EPB while it was 2.3% in the control group, this reflects the defect in placenta and fetal growth if bleeding occurs in early pregnancy.

Low birth weight, congenital anomalies, and low Apgar score were also significantly ( $P<0.05$ ) more among infants born to cases with a history of EPB, in agreement with others studies done by (Saraswat et al., 2010; Hosseini & Yaghoubipour, 2013)

Admission to the neonatal ward was significantly more among infants born to cases with a history of EPB if compared with infants born to women without a history of EPB (60.8% and 34% respectively). This could be due to the higher rate of prematurity, IUGR, PROM, low Apgar score, and congenital anomalies among infants born to cases with EPB. These complications may also be the causes of the significant ( $P<0.05$ ) increase risk of perinatal death among the cases with a history of EPB (5.6% vs. 1.6%) and this is consistent with a systemic review done by (Saraswat et al., 2010).

#### 5. Conclusion

Serious maternal morbidities are significantly more common among women with a history of EPB. Also prematurity, IUGR, low birth weight, increase risk of neonatal ward admission and perinatal mortality are significantly more among women with a history of EPB

#### 6. Recommendation

- Proper antenatal care for early diagnosis, close follow up and proper management of women with early pregnancy bleeding recommended.



- Conducting a prospective cohort study recommended for assessing the incidence of maternal, fetal & neonatal complications. Also the occurrence of these complications in relation to the time of bleeding, severity, and recurrence.

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