

Risk factors and Outcomes of Pregnancies Complicated by Placenta Previa Major Among Iraqi Patients

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Original Article

ABSTRACT

Background: Placenta previa complicated pregnancy is a significant health problem and a challenge for obstetricians worldwide, due to its adverse maternal, fetal and neonatal pregnancy outcomes.

Objective: To study the risk factors and outcomes of pregnancies complicated by placenta previa major among group of Iraqi patients

Patients & Methods: A prospective study conducted during a period of 18 months (March 2018 to September 2019) included 68 pregnant women presented with placenta previa at different gestational age and admitted for management in the obstetrics and gynecology department at AL Ramady Teaching Hospital for Maternity and Children who met the inclusion criteria. Diagnosis of placenta previa was approved either by U/S confirmed at the time of CS, or by examination in the theatre with or without anesthesia for those cases. Elective CS delivery was aimed at 36 complete weeks. Cases, which presented after 32 weeks of gestation advised for hospitalization until delivery. Data analyzed using the SPSS software version 22 and appropriate statistical tests were applied.

Results: Mean maternal age was 30.4 (range : 17 - 44) years. Mean gestational age at first diagnosis of major placenta previa was 31 ± 4.2 weeks. Hemoglobin (Hb) levels revealed 3 cases had $Hb < 10$ g/dL, 38 (55.9%) with Hb of 10-12 g/dL. Time of termination of pregnancy was, 32 weeks or more. Cesarean sections was the mode of delivery in 65 cases. Intrauterine growth retardation (IUGR) reported in (13.2%), Low birth weight in 17 neonates, Congenital anomalies, anemia, low Apgar scores and admission to NICU were also reported.

Conclusions: Major placenta previa was associated with poor maternofetal and neonatal outcomes. Cesarean section was the mode of choice to save the mothers and their neonates. No difference between inpatient and outpatient expectant management in diagnosed patient.

Keywords: Placenta previa, classification , etiology, epidemiology, risk factors, outcome

1. INTRODUCTION

Placenta is formed during pregnancy and it is oval in shape and delivers oxygen and nutrients to the fetus and disposes of fetal waste into the mother's blood for disposal by the mother's body. The placenta is attached to the uterine wall and covers the upper part of the inner wall of the uterus, where the umbilical cord exits, forming an important and vital connection between the mother and the fetus (1). Abnormal implantation of placenta lead to significant problems for both mothers and their fetuses (2). Placenta previa occurs when the placenta attaches to the lower part of the uterine wall, either near the cervix, or completely or partially covering the cervix. Obstetrical hemorrhage is one of the significant health problem worldwide, it has important concerns among gynecologists and obstetricians , patients and their families due to its maternal morbidity and mortality (3,4). Placenta previa (PP) is one of the causes of these hemorrhages despite it an uncommon problem that may occur during pregnancy and lead to heavy vaginal bleeding before or after childbirth (5,6).

Definition:

Placenta previa: Is the implantation of the placenta near or over the the cervix-internal-os. Usually associated with vaginal bleeding which is painless characterized by bright red blood. That occurs after the twentieth-week-gestation. In addition to clinical, its diagnosis is made with aid of ultrasound examination; trans-vaginal sonography

Classification of placenta previa (7–11)

Grade I: Placenta implanted on the lower segment but not reach the internal cervical os (low implantation).

Grade II: Placenta dose reach the edge of the cervix but does not cover it.

Grade III : The placenta covers the internal os when it is close and is a symmetrically situated (Partial)

Grade IV: The placenta is symmetrically implanted in lower segment so that it covers the cervix at full dilatation (Complete).

Major degree placenta previa are grade III and grade IV and minor degree while minor one included grade I and II (7–11).

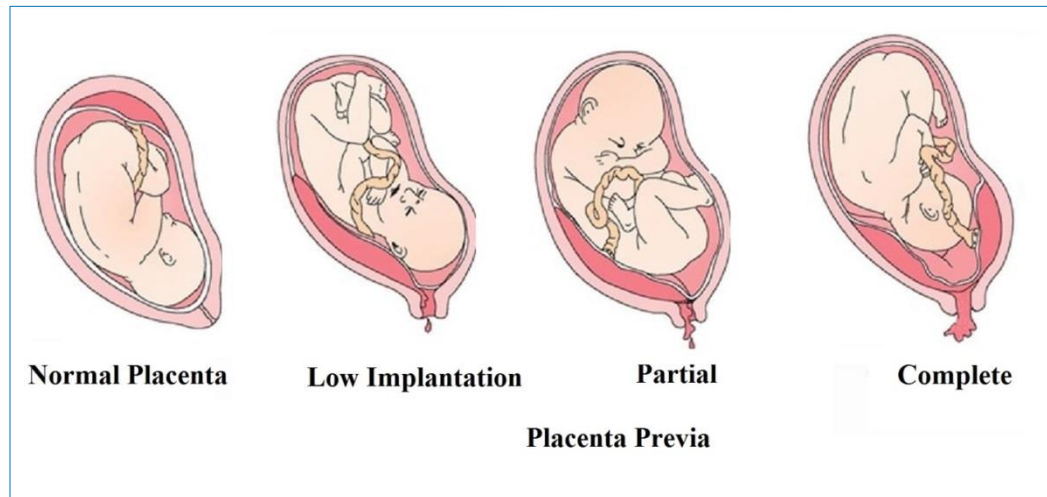


Figure 1. Schematic for Normal placenta and grades of placenta previa (7)

Epidemiology:

The frequency and incidence of PP varies from one country to other depending on the distribution of risk factors in the population , nature and ethnicity. So as the clinical practice, term of pregnancy, mode of clinical diagnosis and ultrasonography facilities. According to previous literatures and text books, there is a variation in the frequency of PP of 1% - 5%. Earlier studies referred that PP occurred in almost 2 to 6 per 1000 pregnancies and contributed to almost 5% of all perinatal maternal deaths. (12,13)

Risk factors:

- Multiparity: the phenomenon for it to occur is because when the placenta is inserted into the uterine wall it persistently alters its structure, and when a next pregnancy occurs it is more possible that it will be implanted in a different place.
- Age ≥ 35 years(14).
- Multiple pregnancy and parity (15,16).
- Anemia.(17)
- Previous uterine scar(18).
- History of placenta previa (17).
- Smoking (19)
- Use of cocaine(17) .
- Post-caesarean section intergenetic space <12 months (18).
- In vitro fertilization (20)

Etiology:

The definite etiology of placenta previa is unknown, but there are some

Associated factors such as : older age women, previous uterine scare due to previous cesarean section (CS); The risk increase with the number of prior

cesarean delivery single CS increase the risk by 0.65%, three CSs, by 2.2% and four CSs by 10%. Multiparity and multiple pregnancies als increase the risk of PP. Among other factors are, Defective decidual vascularization, smoking and use of cocaine. Furthermore, pregnant women with male fetuses, those with history of previous PP have higher risk of PP. Also African , American and Asian are more likely to have PP. Other factors such as anemia and assisted conception are also implicated (17,19,21–23).

Adverse effect of Placenta Previa:

Maternal Risks: Maternal mortality due to hemorrhage, postpartum hemorrhage, Disseminated intra vascular coagulation, surgical complications, anesthetic complications, air embolism, placenta accreta, increta and percreta, infection and sepsis and recurrence

Fetal risks: Preterm birth, perinatal mortality, intrauterine growth retardation, congenital malformations and intrauterine death (24–27).

Clinical presentation:

Placenta previa could be asymptomatic and incidentally diagnosed during routine follow up of pregnant women. However, the most common presentations of PP is painless vaginal bleeding, initiated by sexual intercourse, occur at the end of second trimester . Threatened miscarriage in the second trimester may precede PP. Persistence malpresentation is another presentation of PP; high head, oblique lie and unstable lie are evident (28,29).

Diagnosis:

In addition to history , presentations and clinical examination, ultrasound is the golden standard diagnostic method for PP, as it is simple non-invasive and highly accurate; trans - abdominal ultrasound, it is almost performed in all pregnant women before 20 week-gestation. Ultrasound can detect PP and its grade. Additionally, vaginal ultra sonography have shown as highly sensitive and specific tool for accurate detection of placental location when placenta previa is suspected especially during the second trimester. Magnetic resonance image (MRI) is highly sensitive and specific methods but high cost and limited availability make it unlikely to replace ultrasonography scanning for routine evaluation. (30–33)

Management:

Generally, all antepartum hemorrhage management measures should be followed in the hospital, where there are facilities for blood transfusion, cesarean section and neonatal care unit. The initial assessment includes maternal and fetal conditions, ability of neonatal unit (34,35). Immediate management includes insertion of intravenous lines, investigations for hemoglobin, hematocrit, blood count, blood group coagulation profile and other necessary investigations. Urinary catheter should be set, intravenous fluids, blood transfusion (8,36,37). Specific measures in treatment of placenta previa depend on gestational age, severity of hemorrhage, state of cervix, and degree of placenta previa, so the management either according to aforementioned conditions immediate delivery may be indicated (38). In some cases, conservative management in order to reduce perinatal mortality which is directly related to gestational age (39). The standard recommendation used to deliver the patient once advanced to 38 weeks or the first hemorrhage accrued at that time. Delivery before 36 weeks of gestation mainly for maternal reason, after this time pregnancy should be terminated even when there are no maternal complications. In cases with major PP (grade III and IV), delivery by CS (8,36,37,40).

2. PATIENTS AND METHODS

This was a prospective study conducted during a period of 18 months (March 2018 to September 2019) included 68 pregnant women presented with PP and admitted for management in the obstetrics and gynecology department at AL Ramady Teaching Hospital for Maternity and Children who met the inclusion criteria.

Sample size and Sampling technique:

The required sample size was calculated according to standard equations for medical studies, the required sample was calculated using the Open Epi® online software (41), with a precision of 5%; $\alpha = 5\%$ and estimating a loss of 10%, a sample of at least 80 patients would be required, however, 12 patients were excluded from the study due to their emergency status, hence, the net sample was 68 women and were selected by simple random sampling technique.

Data collection:

Data collected using a pre-constructed data collection form , including socio-demographic characteristics of the patients, gestational age, medical history, surgical history, mode of presentation, date of diagnosis of PP, clinical findings on examination, ultrasound findings, grade of PP, investigations, mode of delivery, gestational age at labour fetal characteristics and status , pre and postoperative hemoglobin level, amount of blood transfused. complications during CS and maternal outcome.

Study protocol:

For purpose of this study, *Major placenta previa* was defined as placenta that covering the internal cervical OS partially or completely (grade III and IV).

Anemia was defined as hemoglobin of less than 10 gm/dl or hematocrit less than 30%, corrected by blood transfusion when it was needed.

Good antenatal care defined as patients have at least 3 visits and at least 2 U/S examination, poor antenatal care when there is one visit with one U/S examination. Accepted ANC is defined by 2 visits and at least one diagnostic U/S.

Diagnosis of placenta previa was approved either by U/S confirmed at the time of CS, or by examination in the theatre with or without anesthesia for those cases

who have no or poor antenatal care and confirmed during CS, also cases who were asymptomatic but admitted for CS due to other indications, and incidentally diagnosed to have PP.

Elective CS delivery was aimed at 36 complete weeks. Earlier intervention for those cases with repeated significant vaginal bleeding, two episodes or more which leading to change in vital signs or decrease hemoglobin 1 gm/dl or more , or starting of regular uterine contraction.

Normal vaginal delivery after examination in theatre without anesthesia by acceleration of labour with Oxytocin and artificial rupture of membrane was indicated for termination of pregnancy for two cases of major placenta previa, with dead fetuses in the second trimester(26-27weeks) . Tocolytics was used in some cases to suppress mild to moderate uterine contraction. Dexamethasone 24 mg daily in two divided doses ,12 hour apart was used intramuscularly and repeated weekly from a gestational age of 24 - 34 weeks. Double set up examination in the theatre was done for all cases which firstly presented as emergency

and for those managed at home after diagnosis . Emergent U/S examination was available for some emergent cases.

Fetal follow up through intrauterine U/S assessment for gestational age, congenital anomalies and growth comparing it with gestational age at delivery, weight, neonatal admission , complications and fetal outcome .

Management Protocol:

For these cases included routine U/S examination at 18-20 weeks of gestation when diagnosis of placenta previa occur, patient advice to stay home after being cautioned , repeated U/S at 28 - 30 weeks of gestation to confirm major degree placenta previa or even earlier in cases with bleeding per vagina , these patients either confined to the hospital management until delivery or to continue follow up weekly at home according to the general condition of the patients , fetus and severity of vaginal bleeding . Cases, which presented after 32 weeks of gestation advised for hospitalization until delivery.

Patients who presented as emergency case for severe vaginal bleeding or persistent abnormal presentation like transverse lie or frequent increasing uterine contraction treated by immediate management and CS after U/S examination if possible or /and examination in the theatre with or without anesthesia, however, these cases were excluded from the study.

All CS was performed through supra-pubic skin incision and lower segment uterine incision and localization of placenta were recorded. Any intraoperative complications like bleeding from placental bed or associated accreta or abruption were recorded. Cross matched blood of at least four units prepared , auto transfusion of the blood not under taken. Vaginal ultrasonography was not performed for any patients. General anesthesia were used for all CS.

Statistical analysis

All statistical procedures, data management and analysis were performed using the statistical package for social sciences (SPSS) version 25. The descriptive statistics for each of the qualitative variables were the percentage and number of samples of each of the classes within a given variable. For the quantitative variables, the mean \pm standard deviation was calculated. Appropriate statistical tests used accordingly.

3. RESULTS

A total of 68 cases of placenta previa were recruited in this study the mean maternal age was 30.4 (range : 17 - 44) years. Among the studied group, 11 (16.2%) were nulliparous, 41.2% were 1-2 parities, 27.9% had 3-4 parities and 14.7% with more than 4 parities. Previous cesarean sections (CSs) reported by 28 women, however, 6 cases had 4 and one case had 5 CSs. Five cases were smoker, 25 cases (36.8%) had history of pregnancy complicated by PP, 30 cases (44.1%) had history of curettage, and 9 cases had gestational diseases complicated by major degree PP; 7 with hypertension and 2 with DM, ([Table 1](#)).

Poor ANC was reported in 38 cases (55.9%), accepted ANC was seen in 17 case (25%), Good ANC was seen in 12 cases (17.6%), and only one case with no ANC visits and one case without ANC. Maternal age ranged between 17-44 years with a mean of 29.7 years. More than half, (51.5%), of the patients aged 21-30 years followed by those aged 31-40 who contributed for 38.2%, ([Figure 1](#)). Mean gestational age at first diagnosis of major placenta previa was 31 ± 4.2 weeks, furthermore, 8 cases were diagnosed with PP major at 16-24 week gestation, while 54.5% at gestational age of 31 week to 38 week. Regarding the gestational age at first episodes of bleeding, 4 cases, had no bleeding episodes while 64 have did, however, 36.8% of cases had their first episode of bleeding at the gestational week 16-28, 39.7% at 29-34 weeks while 17.6% at 35-38 week gestation. On the other hand, majority (84.3%) of these cases reported 1-4 bleeding episodes, and 10 (15.7%) had five or more episodes. Furthermore, severe vaginal bleeding episode occurred in 14 cases, moderate in 20, mild in 30 cases ([Table 2 and Figure 2](#)). The investigation about antenatal hemoglobin (Hb) levels revealed that 3 cases had Hb < 10 g/dL, 38 (55.9%) with Hb of 10-12 g/dL and the remaining 27 cases (39.7%) with Hb level of > 12 g/dL, ([Table 3](#)).

From other point of view, 3 units of blood transfusion needed in 11 cases (16.2%), Two units in 52 (76.5%) and only one unit of blood transfused in the rest 5 cases (7.4%), ([Figure 3](#)). Regarding the time of termination of pregnancy, it was < 28 week gestation 4 cases (5.9%), 28 – 31 weeks in 16 (23.5%) cases, 32 – 35 weeks in 27 cases and 36 weeks or more in 21 cases (30.9%), ([Table 4](#)).

Postpartum hemorrhage was severe in 30.9% of cases, moderate in 27.9% and mild in 41.2%, ([Figure 4](#)). The amount of blood transfused at postoperative period was 1-4 units in 75% of cases, more than 4 units in 8.8% of cases while 16.2% of cases did not need blood

transfusion including the cases delivered vaginally, (**Figure 5**).

Among the 68 PP cases, only 3 cases (4.4%), delivered vaginally while 65 with CS represented (65.6%), among CSs deliveries, 16 (24.6%), were elective , the remaining 49 cases (75.4%), delivered by emergency CS. 14 emergency CSs were due to severe vaginal bleeding during hospitalization and other 5 cases also had severe vaginal bleeding at home , therefore emergency CS was indicated (**Figure 6**)

Fetal and neonatal outcomes of PP cases are shown in (Table 5), Intrauterine growth retardation (IUGR) reported in 9 cases (13.2%), birth weight was up to 200 gram in 17 neonates, 2001 to 2500 gram in 34% of cases, 2501 to 3000 gram in 22.6% of cases, 30001-3500 in 10 cases (15.1%) and more than 3500 in 3 cases (3.8%), (**Table 5**)

Table 1. Demographic characteristics of the studied group (N = 68)

Variable		No. of patients	%
Maternal Age (year)	< 20	5	7.4
	21-30	35	51.5
	31-40	26	38.2
	>40	2	2.9
Mean age (range)	30.4 (17-44)	-	-
Parity	Nulliparous	11	16.2
	1 - 2	28	41.2
	3 - 4	19	27.9
	> 4	10	14.7
Previous cesarean sections	None	40	58.8
	1	14	20.6
	2	4	5.9
	3	3	4.4
	4	6	8.8
	5	1	1.5
Smoking		5	7.4
History placenta previa		25	36.8
History of Curettage		30	44.1
Gestational diseases	Hypertension	7	10.3
	DM	2	4.9

SD: standard deviation

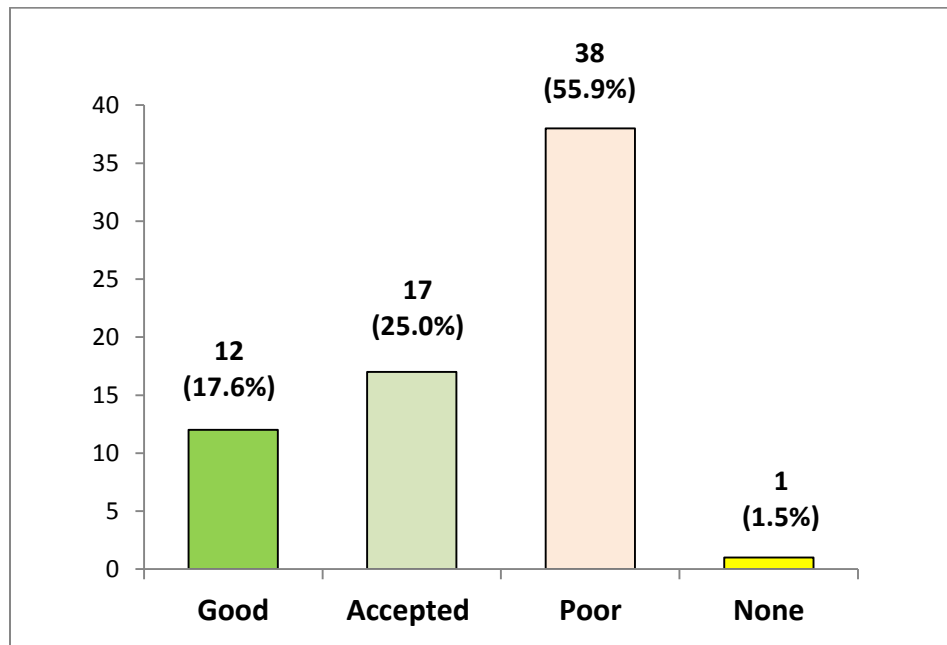


Figure 1. Distribution of 68 PP women according to their antenatal care

Table 2. Gestational age at first episode of vaginal bleeding and number of Episodes of the studied group (N = 68)

Variable		No.	%
Gestational age at first diagnosis of major placenta previa	16-24	8	11.8
	25-30	23	33.8
	31-34	15	22.1
	35-38	22	32.4
	<i>Mean ± SD*</i>	-	-
Gestational age at first episodes of bleeding (week)	16-28	25	36.8
	29-34	27	39.7
	35-38	12	17.6
	No episodes of bleeding	4	5.9
No. of episodes	1 - 4	54	84.3
	5 and more	10	15.7

SD: standard deviation

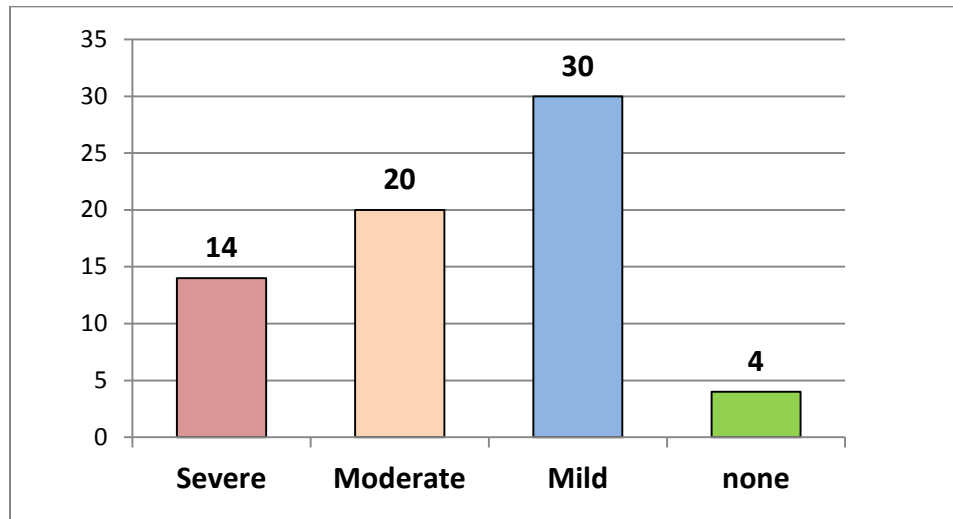


Figure 2. Distribution of cases according to severity of vaginal bleeding episodes

Table 3. Hemoglobin levels of studied group during antenatal period

Hb (g/dL)	No.	%
< 10	3	4.4
10 - 12	38	55.9
> 12	27	39.7
Total	68	100.0

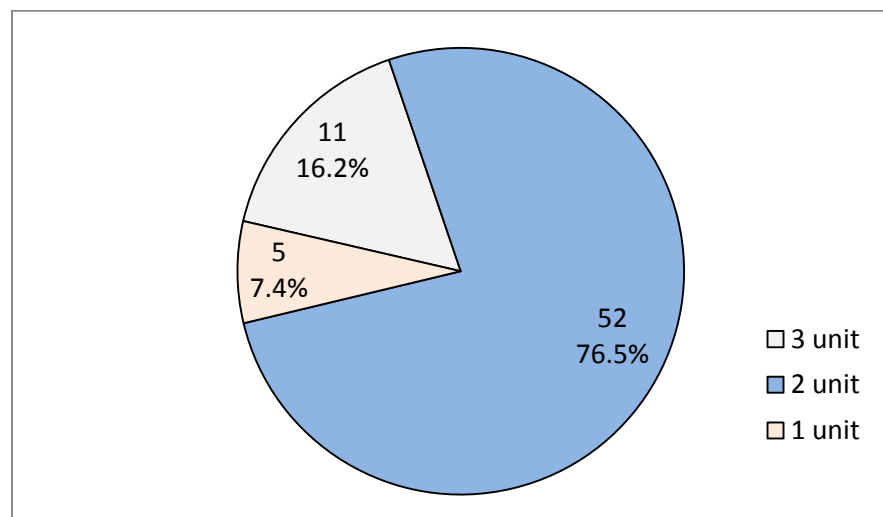


Figure 3. Amount of blood transfused during antenatal period (N = 68)

Table 4. Gestational age at the time of termination of pregnancy of the studied group (N = 68)

Gestational age	No.	%
< 28	4	5.9
28 - 31	16	23.5
32 - 35	27	39.7
36 or more	21	30.9
Total	68	100.0

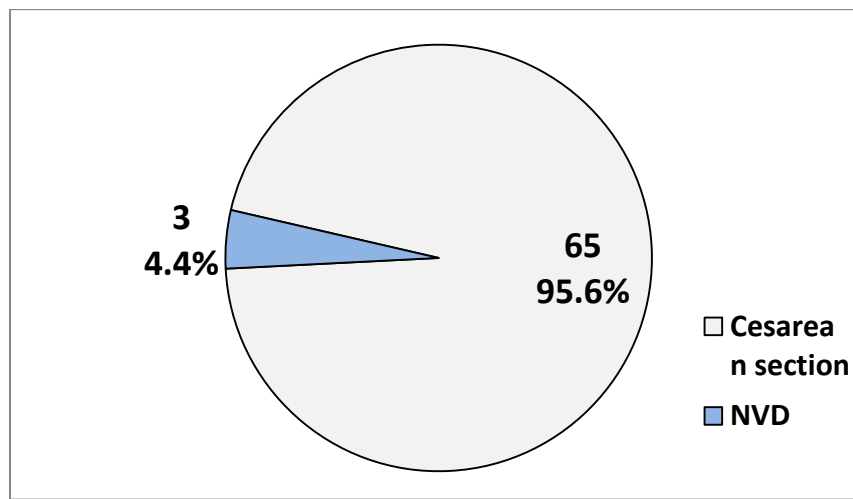


Figure 4. Mode of delivery of the studied group

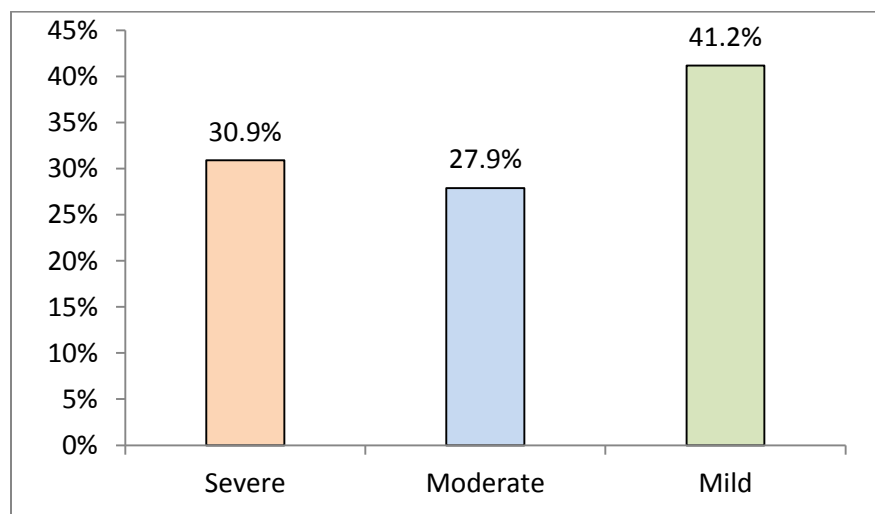


Figure 4. Severity of postpartum hemorrhage

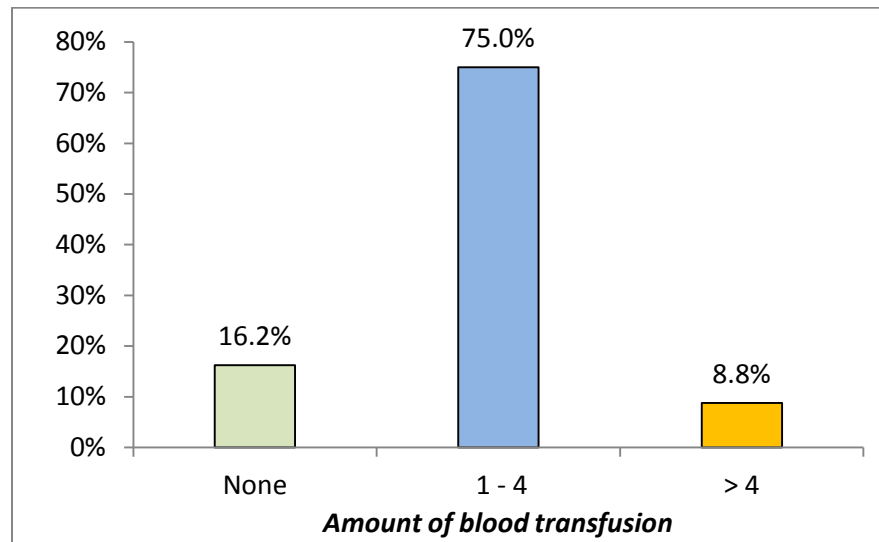


Figure 5. Amount of blood transfusion in postoperative period.

Table 5. Fetal and neonatal outcomes of the studied group (N = 68).

Variable		No.	%
IUGR		9	13.2
Birth weight	Up to 2000	17	25.0
	2001-2500	23	34.0
	2501-3000	15	22.6
	3001-3500	10	15.1
	3501 and above	3	3.8
RDS		9	13.2
Congenital anomalies		4	5.9
Anemia		6	8.8
Low ABGAR score < 7 at first minute		28	41.2

4. DISCUSSION

Placenta previa complicated pregnancy is a significant health problem and a challenge for obstetricians worldwide, due to its adverse maternal, fetal and neonatal pregnancy outcomes with high morbidity rates. Different risk factors contribute to development of PP (42). This study aimed to study the main risk factors of PP major and pregnancy outcomes among group of Iraqi women who were diagnosed with PP major and followed up until end of pregnancy. The mean age of the studied group was 30.4 (range 17-44) years which was lower than other studies, Tuzovic et al. (43) and Sheiner et al. (44). This difference could be attributed to the earlier age at marriage and conception in our country in addition to the prolonged age of fertility in our community. Multiparity is well documented to be a risk factor for the development of major degree placenta previa (16), we reported that 42.6% of our cases had multiple parity of 3 or more, this findings also supported by other studies (12,16). Increase number of parity in our community may be related to the nature of Iraqi population, with regard to the religious and social factors.

The mean gestational age at diagnosis of the major degree placenta previa was 31.0 weeks, 33.8 % of patients diagnosed between 25 - 30 weeks and 32.4% of patients at or after 35 weeks, the mean gestational age at which first attacks of bleeding found was 29.6 weeks, the majority of attacks (44.1 %) were mild vaginal bleeding, while severe in 20.6% of patients. In 84.3 % of those patients, the attacks of vaginal bleeding recurrence between 1 - 4 times, From these results we found that the time of first attack of vaginal bleeding is approximate the time of the diagnosis, and this may be a result of poor antenatal care and delay in the diagnosis of placenta previa, so the majority of cases diagnosed after starting of vaginal bleeding which necessitate shifting the patient to the hospital. In Japanese study, Onoyama et al. (45) revealed that when genital bleeding and first uterine contraction occurred at < 29 weeks, patients were at high risk for delivery at <34 weeks. The management protocol aimed to deliver the fetus beyond 36 complete weeks, this was achieved only in 33.1 % of patients, The highest proportion, 39.6%, of patients, deliver between 32-35 weeks. Which is comparable to results of, Onoyama et al. (45).

Previous cesarean sections reported in 41.2% of cases indicated the association between previous CS and PP, this finding was widely postulated and approved in previous studies that documented such relation in addition to association between higher number of CSs and higher

incidence rate of PP (13,16,26). Smoking approved as a risk factor of PP , nonetheless, only five cases of our studied group were smokers, the lower rate of smoking could be attributed to the fact that Iraqi women, even when they are smokers, deny their smoking status, from other point of view, there still some debate regarding the association between smoking and PP among different studies (13,19).

In the current study we found that 10.3% of cases had gestational hypertension and 4.9% with gestation diabetes which agreed findings in previous studies (46). Similarly, gestational DM was also reported to be associated with PP (47). History placenta previa is approved as a significant risk factor for PP (17,22). In our study , 36.8% of cases had history of PP which support findings of previous studies; in a 10-year retrospective cohort study conducted by Zhang et al (48) authors concluded that women with a history of placenta previa are at risk for adverse outcomes and placenta previa in the subsequent pregnancy. In contrast, Tuzovic et al. found no difference in the incidence of placenta previa between women with history of PP and those without (43). The high rate of recurrent PP in our study could be attributed to high parity, high rate of CS and uterine evacuation. In our study, at least one curettage was seen in 44.1% of patients after incomplete or missed abortion. A study conducted by Johnson et al. in 2016 documented that risk of placenta previa increased with multiple curettage in a dose response fashion (49) . This indicated a role like termination of pregnancy to be a predisposing factor for placenta previa. Despite ANC is completely free in our country so as in many countries, unfortunately, in our studied group poor ANC reported in 55.9% of cases while one case had no ANC, this indicated an association between poor ANC and incidence of PP where poor ANC is another risk factor for complicated pregnancies (50,51). *Cesarean section is the method of choice* for delivery of patient with major degree placenta previa(52,53) , in our study majority of cases delivered by CS, however, only 3 patients delivered by NVD due to their preferences, and more acceptance of NVD by the patients (54,55), NVD performed in only 3 cases with gestational age < 28 weeks and stillbirth babies, with adequate blood transfusion and closed monitoring of the patients.

Postpartum hemorrhage complicate 63.2% of patients (43/68), however, of these 43 cases, 30.9% had severe, 27.9% moderate and 41.2% mild PPH, the main cause of bleeding were atony, bleeding from placental attachment and associated accrete It is noted that blood loss in intraoperative and postoperative period were different This variation between may be explained

by the presence of large number of patients who are presented in emergency state due to vaginal bleeding and surgical interference achieved immediately after resuscitation. Ohkuchi et al. found in their study that the 19th centile value of blood loss was 615 ml and 1.531 ml for women with vaginal and cesarean deliveries respectively (56).

Adverse fetal and neonatal outcomes were more frequently reported in cases with PP major, compared to their incidence among general population, in our study IUGR (13.2%), LBW (25%), , RDS (13.2%) , Congenital anomalies (5.9%),, Anemia (8.8%)%, and Low ABGAR score < 7 at first minute (41.2%), were reported . It was expected to get such outcomes, patients with PP major are at high risk to have adverse fetal, neonatal and maternal outcomes. Poor outcomes could be also associated and shared the same risk factors of PP such as delay in diagnosis of major degree placenta previa and preterm labour , which is unavoidable , leading to prematurity and it's complications (Respiratory distress syndrome). No perinatal mortalities reported in our study. These findings were almost similar to that reported in previous studies with some variation in the incidence rates of these complications and outcomes, (9,17,21,22). The variation in the incidence rates among different studies could be attributed to the differences in the facilities, antenatal care availability, maternal characteristics and other factors, Senkoro et al. (21) found that adverse maternal and neonatal outcomes such as PPH, APH, cesarean delivery, fetal malpresentation and early neonatal death were significantly associated with PP. Gargari et al. (22) concluded that PP was associated with reduction of gestational age and low neonatal birth weight. Interestingly, there is also a variation in the outcomes according to the type of PP ; complete vs. incomplete as Feng et al. (17) concluded that cases with complete PP admitted earlier and had more adverse pregnancy outcomes. Ahmed et al. from Egypt, found that among women with major PP, 15.1% end with hysterectomies, 13.2% were delivered fresh stillbirth babies. Admission to NICU in 20% of survived babies. However, similar to our finding no maternal death reported in the Egyptian study. Our study is not free of limitations, of these the restriction in data collection and missed to follow up of some cases lead to inability to involve larger group of cases, furthermore, we were unable to include control group due to same reasons, however, we recommend to conduct further studies with larger sample size as case-control or cohort study .

5. CONCLUSIONS

Major placenta previa was associated with poor maternofetal and neonatal outcomes. Cesarean section was the mode of choice to save the mothers and their neonates. No difference between inpatient and outpatient expectant management in diagnosed patient , and our findings were comparable to other previous studies and literatures . However, further studies with larger sample size and multiple centers are highly suggested

Ethical Clearance

Ethical clearance and approval of the study are ascertained by the authors. All ethical issues and data collection were in accordance with the World Medical Association Declaration of Helsinki 2013 for ethical issues of researches involving humans, verbal and signed informed consent obtained from all patients. Data and privacy of patients were kept confidentially. .

Conflict of interest: Authors declared none

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