ORIGINAL RESEARCH

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Disseminated Intravascular Coagulation in Abruptio Placenta: Who is at Risk?

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ABSTRACT Objective: This study aimed to determine the clinical risk factors of disseminated intravascular coagulation (DIC) in case of an abruptio placenta. The second objective was to evaluate the maternal and perinatal complications in the cases with DIC secondary to abruptio placenta. **Material and Methods:** This is a retrospective study conducted in pregnant women with a diagnosis of abruption at a tertiary maternity hospital. 237 patients confirmed with abruptio placenta were assigned into two groups: complicated with DIC (study group), and those who were not (control group). **Results:** 23 patients were included in the study group, and 214 patients were included in the control group. In the study group, 82.6% of the patients were admitted urgently from the emergency room with diagnosis of abruption, whereas the rate of the patients diagnosed in the emergency room was 49.1% in the control group (p=0.002). The rate of cases with a ≥50% detachment of the total placental mass was significantly higher in the DIC group (91.3% vs. 41.7%). Uterine atony, Couvelaire uterus, transfusion of blood products, intensive care unit admission were significantly higher in the DIC group. Intrauterine fetal demise, neonatal excess base deficit, neonatal intensive care unit admission were also significantly higher in the DIC group. **Conclusion:** The patients presenting with vaginal bleeding, fetal demise, those who have ≥50% of the placenta detached, and those who are diagnosed in emergency department have higher likelihood of being complicated with DIC. The patients with known risk factors for abruption and their neonates benefit from in-patient follow-up.

Keywords: Abruptio placenta; disseminated intravascular coagulation; uteroplacental insufficiency; out-patient follow-up

Abruptio placenta is partial or complete detachment of the placenta from its implantation site after 20th gestational weeks (GWs) and before the delivery of the fetus.[1] The incidence varies between 0.4-3.8% of pregnancies in different parts of the world, and it is one of the leading causes of obstetric hemorrhage, maternal and fetal morbidity, and mortality.[2] It typically presents with vaginal bleeding, uterine contractions, and fetal heart rate alterations. The placental detachment occurs due to the rupture of the uterine spiral artery, causing an expanding retroplacental hematoma leading to maternal and rarely fetal blood loss and bleeding into the decidua basalis.[3] This cascade also results in coagulation disorder via widespread microthrombi, which is associated with maternal end-organ damage, acute placental dysfunction, fetal hypoxia or even fetal demise, and postpartum hemorrhage.

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This study investigated the clinical risk factors of coagulation dysfunction in abruptio placenta. It also assessed the maternal and perinatal outcomes of abruptio placenta by comparing cases complicated with coagulation dysfunction and those not.

MATERIAL AND METHODS

After getting an approval from the ethics committee (Zeynep Kamil Women and Child Diseases Training and Research Hospital Clinical Research Ethics Committee (date:19.04.2023, no: 56) this retrospective study investigated an 8-year analysis of all abruptio placenta cases at a tertiary maternity hospital between January 2015 and February 2023. The study was conducted following the principles of the Declaration of Helsinki. An informed consent was not provided from the patients due to the retrospective study design. During the study period, 292 patients diagnosed with abruptio placenta were detected. As per routine protocol, the placentas of patients with signs of uteroplacental pathology like fetal growth restriction (FGR), oligohydramnios, vaginal bleeding, fetal distress, fetal demise, and abnormal placental apperance undergo hispotahologic evaluation. Pregnant women who delivered with clinical/sonographic suspicion of placental abruption and the diagnoses of whom were confirmed with macroscopic and histopathologic placental evaluation after delivery were included. The patients were identified on the hospital's electronic database. Fifty-four were excluded for not being confirmed as abruptio placenta in the postpartum evaluations. One patient was excluded as she had been diagnosed after vaginal delivery. The operation notes, and computerized and manual records of the remaining patients were analyzed comprehensively. All placentas underwent histopathological examination. The patients were allocated into two groups: the study group (those who were complicated with disseminated intravascular coagulation (DIC) and the control group (those who were not complicated with DIC). DIC was diagnosed with the International Society of Thrombosis and Haemostasis criteria based on thrombocytopenia, prolonged prothrombin time, low fibrinogen, and clinical suspicion.[4] The groups were compared in terms of demographic features, co-morbidities, clinical presentation features, perioperative maternal morbidities, and perinatal fetal morbidities.

Continuous variables were expressed as mean± standard deviation or median (minimum-maximum). Categorical data were expressed as numbers and percentages. Normality analyses of continuous variables were performed with the Kolmogorov-Smirnov test. For comparisons between the two groups, the Student's t-test was used when the data conformed to normal distribution, and Mann-Whitney U test was used when it did not. Using possible factors identified in previous analyses, independent predictors of risk were examined using univariate logistic regression analysis. Analyzes were performed with IBM SPSS version 26.0 (IBM Corporation, Armonk, NY, USA). The statistical significance level was accepted as $p<0.05$.

RESULTS

Considering the inclusion and exclusion criteria, 237 patients were enrolled in the analysis. The mean age of the patients was 30.07±6.06, and the mean GWs was 32.22±4.84. Only 15.7% of the pregnancies were at term GWs. Forty percent of the patients (95 cases) were primigravid. Demographic features, co-morbidities, and obstetric histories of the present and prior pregnancies are shown in Table 1. Fifty-four

TABLE 1: Demographic features, co-morbidities and obstetric history of the present and prior pregnancies.

Age ($\bar{X}$±SD)	30.07±6.06
GW at diagnosis ($\bar{X}$±SD)	32.22±4.84
Gravidity [median (minimum-maximum)]	2 (1-15)
Parity [median (minimum-maximum)]	1 (0-7)
IVF n (%)	10 (3.4)
DM n (%)	2 (1.3)
HT n (%)	11 (5)
Thrombophilia n (%)	8 (2.9)
Prior preeclampsia n (%)	14 (5.9)
Prior abruptio placenta n (%)	11 (5)
GDM n (%)	34 (14.6)
Multiple pregnancy n (%)	8 (3.8)
Preeclampsia n (%)	79 (33.5)
PROM n (%)	29 (12.6)
Polyhydramnios n (%)	9 (2.8)
Oligohydramnios n (%)	35 (15.1)

SD: Standard deviation; GW: Gestational weeks; IVF: In vitro fertilization; DM: Diabetes mellitus, HT: Hypertension; GDM: Gestational diabetes mellitus; PROM: Preterm rupture of membranes.

TABLE 2: Perioperative and postoperative maternal morbidities in abruptio placenta.

Maternal morbidity	n (%)
Preeclampsia	72 (33.8)
Uterine atony	22 (9.6)
Couvelaire uterus	5 (2.5)
Transfusion	48 (20.1)
DIC	23 (9.6)
ICU admission	119 (50.2)
Re-laparotomy	7 (2.4)
Acute renal failure	2 (0.008)

DIC: Disseminated intravascular coagulation; ICU: Intensive care unit.

percent of the patients presented with vaginal bleeding, 86% of the patients presented with uterine contractions, and 15.1% of the patients had intrauterine fetal demise (IUFD) at the time of diagnosis of abruption. 10.9% of the patients had a history of vaginal bleeding in the prior weeks of the current pregnancy.

All patients had undergone a cesarean section. Perioperative and postoperative morbidities of the patients are shown in Table 2. Seven patients (2.9%) underwent re-operation secondary to complications such as ileus, incision abscess, intraabdominal hemorrhage, and hematoma. One of them required hysterectomy. More than half of the patients with abruptio placenta were admitted to the intensive care unit (ICU). 47.4% of these ICU admissions were on purpose of intensive monitoring of preeclampsia with severe features. The other main reasons for ICU admission were obstetric hemorrhage and DIC.

We evaluated the patient characteristics and comorbidities between the patients who were complicated with DIC [DIC (+)] and those who were not [DIC (-)]. Among the patients complicated with DIC, only 17.4% were diagnosed with abruptio placenta during the in-patient follow-up. 82.6% of the DIC (+) group were diagnosed with abruption in the emergency department during out-patient follow-up. On

TABLE 3: Comparison of clinical and obstetric features and known risk factors of abruptio placenta.

Clinical/obstetric features	DIC (-) (n=214)	DIC (+) (n=23)	p value
Advanced maternal age	106 (49.5)	13 (56.5)	0.524
Gestational age <28 weeks	38 (17.8)	4 (18.2)	0.960
IVF	10 (3.8)	0 (0.0)	0.353
Multiple pregnancy	7 (3.7)	1 (4.3)	0.604
DM	2 (1.4)	0	0.570
Chronic hypertension	11 (5.6)	0	0.612
Thrombophilia	7 (2.8)	1 (4.3)	0.512
Prior preeclampsia history	11 (5.1)	3 (13.6)	0.128
Prior abruptio placenta history	10 (5.1)	1 (4.3)	0.876
GDM	32 (15.3)	2 (8.7)	0.544
Preeclampsia	72 (33.8)	7 (30.4)	0.820
PROM	29 (13.9)	0	0.089
Polyhydramnios	7 (3.3)	2 (8.7)	0.212
Oligohydramnios	33 (15.7)	2 (8.7)	0.543
Fetal growth restriction	27 (17.2)	5 (21.7)	0.571
Vaginal bleeding history during current pregnancy	23 (11.1)	2 (8.7)	0.724
Abdominal trauma during current pregnancy	1 (0.5)	1 (4.3)	0.184
IUFD	18 (5.6)	10 (43.5)	**<0.001**
Vaginal bleeding at the time of diagnosis of abruption	109 (51.4)	18 (78.3)	**0.015**
Surveillance mode at the time of diagnosis of abruption			
Out-patient/no follow-up (diagnosis at emergency room admission)	105 (49.1)	19 (82.6)	**0.002**
Diagnosis during in-patient follow-up	109 (50.9)	4 (17.4)	
Extent of ablatio ≥50 of the total placental mass	90 (41.7)	21 (91.3)	**<0.001**

Chi-square test was performed for the analysis. p<0.05 is considered significant; DIC: Disseminated intravascular coagulation; IVF: In vitro fertilization; DM: Diabetes mellitus; GDM: Gestational diabetes; PROM: Preterm rupture of membranes; IUFD: Intrauterine fetal demise.

the other hand, in the DIC (-) group, the rate of out-patient follow-up was 49.1%. The difference was statistically significant. 91.3% of the DIC (+) patients had ≥%50 of the placenta detached, whereas ≥%50 detachment was seen in only 41.7% of the DIC (-) group (p<0.001). The DIC (+) group had a rate of 43.5% for IUFD, while the DIC (-) group had a 5.6% IUFD rate (p<0.001). Uterine atony, Couvelaire uterus, postoperative obstetric hemorrhage, and ICU admission were also significantly higher in the DIC (+) group (39.1%, 78.3%, 13.0%, and 95.7%, respectively). The comparison of the clinical and obstetric features and known risk factors for abruptio placenta (5) between the groups are displayed in Table 3. The patients complicated with DIC had higher rates of Couvelaire uterus, uterine atony, transfusion of blood products and postoperative ICU admission (Table 4). Regarding the short-term neonatal outcomes, low birth weight (LBW) was detected in 69.6% of the neonates. The short-term outcomes which significantly differed between DIC (+) and DIC (-) groups were NICU admission rate (100% vs. 67.1%, respectively, p=0.006) and umbilical cord blood base excess (-6.9 vs. -3.4, respectively, p<0.036) (Table 5). Diagnosis at the emergency department during out-patient follow-up, vaginal bleeding at the time of diagnosis, IUFD, the large extent of abruption, Couvelaire uterus, and postpartum atony were identified as the clinical factors which significantly increase the likelihood of DIC (Table 6).

TABLE 4: Comparison of intraoperative and postoperative maternal complications.

Intraoperative/postoperative complications	DIC (-) (n=214)	DIC (+) (n=23)	p value
Atony n (%)	13 (6.5)	9 (39.1)	<0.001
Couvelaire uterus n (%)	2 (1.4)	3 (13.0)	0.013
Transfusion n (%)	25 (11.6)	23 (100)	<0.001
ICU admission n (%)	97 (45.4)	22 (95.7)	<0.001

Chi-square test was performed for the analysis. p<0.05 is considered significant; ICU: Intensive care unit.

DISCUSSION

In this study, we presented the clinical experience of a tertiary maternity center about the risk factors and maternal and neonatal outcomes of abruptio placenta. The risk factors of DIC in case of abruptio placenta have also been investigated.

We found out that most of our patients with abruptio placenta were at preterm GWs, contrary to most of the studies in the literature.[5-7] Preterm or "early" abruptio placenta differs from abruption at term GWs (late abruption) to some extent. Despite both presenting with bleeding in the decidual-placental interface, which subsequently leads to detachment of the placenta from its bedside, the underlying etiology, pathophysiologic cascade, and histopathologic findings may differ between the two.[7] Acute abruption can occur in early or late GWs and is mainly a result of mechanical and shearing forces to the abdomen. Abdominal trauma or a rapid

TABLE 5: Comparison of neonatal outcomes between the groups.

	DIC (-) (n=214)	DIC (+) (n=23)	p value
APGAR score 1st minute	6 (0-8)	4 (3-6)	0.102*
APGAR score 5th minute	8 (0-9)	7 (6-8)	0.088*
Birth weight (grams)	1870 (420-7309)	1572.5 (410-3080)	0.205*
Umbilical cord blood pH	7.31 (6.45-7.49)	7.24 (6.86-7.50)	0.057*
Umbilical cord blood base excess	-3.4 (-28.9-13.1)	-6.9 (-14.2-2.1)	**0.036***
Umbilical cord blood PO_2	30.1 (6.3-189)	20.3 (12.4-126)	0.097*
Umbilical cord blood PCO_2	44.7 (20.7-130.3)	47.5 (22-110)	0.384*
Umbilical cord blood HCO_3	20.8 (2.6-35)	18.6 (8.6-22.7)	0.079*
NICU admission	141 (67.1)	14 (100.0)	**0.006****
Neonatal death	27 (13.0)	3 (21.4)	0.412**
HIE	16 (12.5)	2 (20.0)	0.619**

*Mann-Whitney U test; **Chi-square test; DIC: Disseminated intravascular coagulation; NICU: Neonatal intensive care unit; HIE: Hypoxic-ischemic encephalopathy.

TABLE 6: Univariate (binary) logistic regression analysis of risk factors of DIC in abruptio placenta cases.

Clinical risk factor	LR (95% CI)	p value
Out-patient/no follow-up (first diagnosis at emergency department admission)	3.9 (1.144-13.595)	**0.030**
Abdominal trauma	9.7 (0.588-160.977)	0.112
Polyhydramnios	2.8 (0.552-14.506)	0.212
Preeclampsia	2.9 (0.755-11.469)	0.120
Extent of ablatio (≥50 of the total placental mass)	9.7 (2.101-45.589)	**0.004**
Vaginal bleeding at the time of diagnosis	3.4 (1.220-9.502)	**0.019**
IUFD	13.1 (4.766-35.877)	**<0.001**
Atony	4.9 (1.374-18.091)	**0.015**
Couvelaire uterus	10.6 (2.016-56.273)	**0.005**

DIC: Disseminated intravascular coagulation; LR: Likelihood ratio; CI: Confidence interval; IUFD: Intrauterine fetal demise.

decompression of the uterine cavity after the rupture of membranes causes vascular damage and rapid bleeding in the decidua basalis, which consequently detaches the placenta from the placental bedside. On the other hand, chronic abruption usually presents at earlier GWs. It is a consequence of uteroplacental vasculopathy triggered by impaired immune response, thrombosis, systemic inflammation, or infection.[5] These pathologies lead to vascular endothelial damage, accumulation of inflammatory response, and defective spiral artery remodeling, resulting in inadequate placentation. The placental and decidual vasculopathy leads to inflammation and dysfunction of the placental vessels, expedites low-pressured venous decidual bleeding, and gradually separates the placenta from decidua basalis, further decreasing the placental surface area for oxygen and nutrient transportation. Therefore, this pathway also ends up with chronic uteroplacental insufficiency, early-onset FGR, and preterm preeclampsia.[8] Per this pathophysiologic cascade, abruption is reported to be associated with LBW.[2] LBW can be related both to preterm delivery and early-onset FGR secondary to uteroplacental insufficiency. Preterm delivery was reported between 40-60% and FGR/SGA was reported between 2-40% in the literature.[9] Our cohort's LBW rate was much higher than previously reported (69.6%). We assume that the higher rate of preterm abruption placenta and LBW in our cohort is due to the high volume of referred cases with early-onset uteroplacental insufficiency presenting with FGR and preeclampsia. The eminent high rate of gestational hypertensive diseases (33.5%) in our cohort supports this argument. Furthermore, in our cohort, oligohydramnios, which is associated with chronic placental dysfunction, was higher than polyhydramnios, which is known to be related mostly to acute abruptio placenta (15.1% vs. 2.8%). A recent study investigating the trend of changes in risk factors of placental abruption over eight years reported that, overall, polyhydramnios was a more frequent risk factor than oligohydramnios (6.1% vs. 2.2%).[10] These results differ from the literature due to the dominance of high-risk pregnant women, including a high number of early-onset uteroplacental insufficiency at our center.

Regarding the pregnancy outcomes, there was an apparent increment in perioperative maternal morbidities in our patients complicated with abruptio placenta (Table 2). The majority of the morbidities were associated with obstetric hemorrhage. In a recent systematic review, abruptio placenta was reported to be associated with a 3.5-31.1 times increase in the risk of relaparotomy after cesarean operation.[2] The rate of relaparotomy was 2.95% in our cohort. This rate is 16 times higher than reported in the general population, and 71.4% of the relaparotomies were performed due to perioperative or postoperative hemorrhage.[11] 9.6% of the patients were complicated with DIC. DIC (+) patients had a significantly higher rate of atony, Couvelaire uterus, transfusion of blood products, and ICU admission (Table 4). Abruption causes a greater decrease in platelet and fibrinogen levels and necessitates more transfusions than the other causes of obstetrical hemorrhage.[12,13] Therefore, it is crucial to identify the patients who are prone to DIC. Among the characteristics and obstetrical risk factors associated with abruptio placenta, presentation with vaginal bleeding, detachment extending ≥50% of the total placental mass, IUFD, and diagnosis of abruption in the emergency department during out-patient follow-up were detected to increase the likelihood of DIC in regression analysis significantly. These features are more consistent with a scenario of an acute abruption with bleeding of centrally located large arteries. The abruption due to the mechanical and shear forces on the uterus usually presents with

acute vaginal bleeding and contractions. The rapid and large detachment of placental mass from its bedside leads to a catastrophic decrease in placental blood flow, which deteriorates the fetus immediately and even leads to IUFD. Along with the acute separation of the placental tissue, collagen and tissue components accumulate in circulation. Decidual bleeding triggers the release of tissue factor from the decidual cells. Increased tissue factor induces the extrinsic pathway of coagulation, leading to widespread microthrombi, which causes endothelial damage concomitant with fibrinolysis and consumption of thrombocytes and coagulation factors.[14]

Chronic abruption secondary to impaired placentation occurs gradually with concealed bleeding in the small vessels of the placental bedside and may present recurrent episodes of mild vaginal bleeding. However, chronic abruption cases are at risk of a rapid expansion of detachment in the impaired placental bedside. There is a lack of data about the optimal management and timing of the delivery in chronic abruption. In-patient or out-patient management is a debatable issue. Some authors advocate that out-patient management is acceptable for those patients who can comply with close fetal surveillance.[5] However, it was shown that fetal heart rate decelerations in cardiotocography (CTG) was an early signal of placental abruption before the onset of apparent clinical presentations like vaginal bleeding, uterine hypertonus, or associated sonographic images. Rapid intervention in case of these "early signals" improves maternal and fetal outcomes.[15] Considering the findings of our study, in-patient follow-up of high-risk patients not only reduces the risk of fetal demise, but also reduces the risk of DIC and related maternal morbidity by giving the opportunity for rapid intervention.

This study has some limitations worth mentioning. The records about the behavioral risk factors of abruptio placenta needed to be included; however, we could not report the association of DIC and behavioral risk factors due to the retrospective design. We also could not present the long-term outcomes of the babies as most patients were referrals and did not have their babies' follow-ups at our center after birth. We should have discussed the long-term outcomes of the babies as there was a large amount of preterm abruption, which would have a considerable impact on the long-term outcomes via premature birth. Nevertheless, with a relatively high number of cases from a single center, this is the only study in the literature investigating the characteristics and clinical features of the patients who are more prone to DIC when diagnosed with abruptio placenta. It also brings a different point of view to the debates on in-patient or out-patient follow-up of the patients who carry a high risk of acute abruptio placenta.

CONCLUSION

We detected that detachment of ≥50% of the total placental mass and IUFD, which are the consequences, and also late signs of abruption increase the risk of DIC. We also showed that in-patient follow-up of high-risk patients decreases the risk of DIC, most probably via the early diagnosis and rapid intervention in the early phase of detachment thanks to frequent CTG or immediate evaluation in case of a clinical manifestation like abdominal pain or mild vaginal bleeding in any patient in the ward. Therefore, we suggest those patients with known high-risk for abruptio placenta to be hospitalized in capable tertiary maternity centers.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Oya Demirci, Dilara Tuğcu;* ***Design:*** *Oya Demirci, Dilara Tuğcu;* ***Control/Supervision:*** *Dilara Tuğcu;* ***Data Collection and/or Processing:*** *Dilara Tuğcu;* ***Analysis and/or Interpretation:*** *Dilara Tuğcu;* ***Literature Review:*** *Lütfiye Uygur, Dilara Tuğcu;* ***Writing the Article:*** *Lütfiye Uygur, Dilara Tuğcu;* ***Critical Review:*** *Lütfiye Uygur;* ***References and Fundings:*** *Dilara Tuğcu;* ***Materials:*** *Dilara Tuğcu.*

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