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# Disseminated intravascular coagulation in obstetric patients: maternal and fetal results

# Obstetrik hastalarda dissemine intravasküler koagulasyon: maternal ve fetal sonuçları

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## ÖZ

**Amaç:** Çalışmamızda obstetrik nedenlerle dissemine intravasküler koagulasyon (DİK) gelişen hastaların, antepartum değerlendirilmesi ile gelişebilecek komplikasyonların önceden önlenmesi ve maternal ve fetal morbidite ve mortalitenin azaltılması yönünde yol gösterici bilgilerin elde edilmesi amaçlanmıştır.

**Gereçler ve Yöntem:** Obstetri ve perinatoloji kliniklerine yatan ve DİK gelişen obstetrik hastalar retrospektif olarak incelendi. Hastaların DİK skorlaması International Society on Thrombosis and Haemostasis (ISTH) kriterlerine göre yapıldı. Hastaların maternal ve fetal sonuçları dökümante edildi.

**Bulgular:** Verilerin incelendiği 6 yıllık süre içerisinde 108281 doğumda 57 gebede DİK geliştiği tespit edildi ve DİK insidansı %0,052 olarak bulundu. DİK öncülü gebelik komplikasyonu kategorileri: plasenta invazyon ve implantasyon anomalileri, postpartum kanama (atoni), plasenta dekolmanı, gebeliğin hipertansif hastalığı ve diğer olarak bulundu. Maternal morbidite oranı %38.6, maternal mortalite oranı 1 hastayla %1.75 olarak bulundu. Hastaların %35'ine laparotomi/re-laparotomi ve bu hastalardan %21'ne histerektomi yapıldı. Yenidoğan doğum ağırlığı ortalaması 2341.3 gramdır. Yenidoğan yoğun bakım ihtiyacı %34.5, ölü doğum oranı %25,5'tir. Neonatal ölüm oranı %3,6 olarak tespit edilmiştir .

**Sonuç:** Doğumda yönetim şemasının anahtar bir rolü vardır çünkü gebeliğin terminasyonu genellikle altta yatan obstetrik bozukluğu ortadan kaldırır. Erken tanı ve aktif tedavi protokolleri, mortalite ve morbiditeyi azaltır. Gebelikteki koagulasyon kaskadında görülen fizyolojik değişikliklerden dolayı, gebe olmayan erişkinler için geliştirilen ISTH DİK skorlaması yerine gebeliğe spesifik bir DİK skorlamasının geliştirilmesi tanı koymayı kolaylaştırabilir.

**Anahtar kelimeler:** Dik, postpartum kanama, obstetrik bozukluklar, skorlama sistemi, kan transfüzyonu

## ABSTRACT

**Aim:** In our study, it was aimed to obtain guiding information to prevent complications that may develop in advance and to decrease maternal and fetal morbidity and mortality by evaluating the antepartum of patients who developed DIC due to obstetric reasons.

**Materials and methods: O**bstetric patients who were hospitalized in obstetrics and perinatology clinics and developed disseminated intravascular coagulation (DIC) were retrospectively analyzed. DIC scoring of the patients was made according to the International Society on Thrombosis and Haemostasis (ISTH) criteria. Maternal and fetal outcomes from the patients were documented.

**Results**: During the 6-year period in which the data were analyzed, DIC was detected in 57 pregnants out of 108281 deliveries, and the incidence of DIC was found to be 0.052%. The categories of pregnancy complication preceding DIC: placental invasion and implantation anomalies, postpartum hemorrhage (atonia), placental abruption, hypertensive disease of pregnancy and others were found. Its rate in maternal morbidity was 38.6% and maternal mortality rate was 1.75% with 1 patient. 35% of the patients had laparotomy / re-laparotomy and 21% of these patients had hysterectomy. The average birth weight of the newborn is 2341.3 grams. Neonatal intensive care need is 34.5%, stillbirth rate is 25.5%. Neonatal mortality rate was determined as 3.6%.

**Conclusion:** The management scheme plays a key role in delivery because termination of pregnancy often eliminates the underlying obstetric disorder. Early diagnosis and active treatment protocols reduce mortality and morbidity. Because of the physiological changes seen in the coagulation cascade during pregnancy, using a pregnancy-specific DIC score instead of the ISTH DIC score developed for non-pregnant adults may facilitate diagnosis.

**Keywords** Dic, postpartum hemorrhage, obstetric disorder, scoring system, blood transfusion

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## INTRODUCTION

Disseminated intravascular coagulation (DIC) is an acquired hemostasis disorder. It develops due to uncontrollable activation of coagulation, insufficiency of natural anticoagulant mechanisms and out of control of fibrinolysis(1). DIC is not a disease on its own, but always develops secondary to an underlying disease. It occurs especially after sepsis, infections, malignancy, obstetric complications, trauma, toxic and immunological reactions(2). Uncontrolled peripartum hemorrhage, resulting in consumption coagulopathy and disseminated intravascular coagulation (DIC), is one of the leading causes for maternal mortality worldwide(3). Tissue factor secreted from monocytes triggers the coagulation system(4). It is known that the placenta plays the greatest role in the release of tissue factor into the blood in obstetric patients(5). There is no laboratory test that alone confirms or excludes the diagnosis of DIC. The International Society on Thrombosis and Haemostasis (ISTH) proposed a diagnostic scoring system for DIC in 2001(6). The parameters evaluated in this scoring system are platelet count, D-dimer and fibrin degradation products, prolongation of prothrombin time and fibrinogen. Patients with a high probability of DIC based on their ISTH score are categorized as overt DIC and there is a good correlation between these patients and the development of DIC.

Although DIC due to obstetric causes is rare, its morbidity and mortality are quite high(7). It is often associated with adverse maternal outcomes, which can result in massive blood transfusion, hysterectomy and even death(8). Obstetric causes associated with DIC include amniotic fluid embolism, placental abruption, placenta previa, severe preeclampsia/eclampsia, HELLP syndrome, dead fetus, delayed abortion, septicemia, and acute fatty liver of pregnancy(9). The prevalence of DIC was found to be between 0.03% and 0.35% in obstetric patients(10,11). In one study, DIC was found to be the second most common cause of serious maternal morbidity after blood transfusion, with a rate of 32 cases per 10,000 births in the United States(12). The most important steps in the effective treatment of DIC are early diagnosis and treatment of the underlying disease.

In this study, it was aimed to retrospectively examine obstetric patients who developed DIC, to predict the complications that may develop and to emphasize the key points in the treatment for reducing maternal/fetal morbidity and mortality.

## MATERIAL AND METHODS

In our study, the files of obstetric patients who were admitted to the perinatology and obstetrics clinics of Dr Zekai Tahir Burak Women's Health Training and Research Hospital, Ankara, between 01/01/2010 and 31/12/2015 and who developed disseminated intravascular coagulation (DIC) were retrospectively analyzed. The files of 251 patients who were likely to have DIC were reviewed, 132 patients were excluded from the study due to deficiencies in laboratory values. DIC scoring of the patients was performed according to the International Society on Thrombosis and Haemostasis (ISTH) criteria. Patients with a score of 5 and above in the ISTH scoring were considered to be overt DIC. Sixty-two patients with a DIC score of less than 5 were excluded from the study, and 57 patients with a DIC score of 5 and above were included in the study. Obstetric complications leading to DIC were divided into 5 categories: hypertensive diseases of pregnancy, postpartum hemorrhages (atonia), placental abruption, placental invasion and implantation anomalies, and others.

Demographic data of patients (age, gravida, parity, abortions, previous D/C, gestational week, presence of chronic disease), hospitalization duration, diagnoses, ultrasonographic measurements, mode of delivery (cesarean section or normal vaginal delivery), intraoperative complications, additional surgical methods (bakri balloon, hemostatic sutures, uterine artery ligation, hypogastric artery ligation), hysterectomy, laparotomy, pregnancy complication categories, laboratory values, transfusions (erythrocyte suspension, fresh frozen plasma, whole blood, platelet suspension, fibrinogen, albumin), disseminated intravascular coagulation (DIC) score, developing maternal complications, maternal death and referral rates, infant birth weight, 1st and 5th minute APGAR scores, and newborn intensive care admission need data were obtained.

### Statistical Analysis

The conformity of the variables in the study to the normal distribution was evaluated graphically and using the Shapiro-Wilks test. The mean ± standard deviation values were given for the age variable, which was determined to have a normal distribution. IBM SPSS Statistics 21.0 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) and MS-Excel 2007 programs were used for statistical analysis and calculations. Statistical significance level was accepted as $p<0.05$.

## RESULTS

In this study, the files of 119 patients were reviewed, and 57 patients with an ISTH DIC score of 5 and above and diagnosed with overt DIC were included in the study. The mean age of the patients was 29.4±6.3 years (min=18.0; max= 41.0). The mean hospitalization was 8.8±8.8 days. Hospitalization diagnoses of the patients are listed. It was observed that 14 (24.6%) of the 57 patients included in the study had a diagnosis of placenta previa totalis as a hospitalization diagnosis.

Gestational weeks were calculated according to the last menstrual period and the median week of gestation was 35.0 (min= 17.0; max= 40.0), and the median of gravida was 3.0 (min= 1.0; max= 12.0). Demographic characteristics and laboratory parameters of the patients were analyzed (Table 1). The ISTH DIC score parameters were evaluated and the mean platelet value was 63175/µL, the mean Inr value was 1.55 INR, the mean D-Dimer was 29.6 g/L, and the mean fibrinogen was 102.1 mg/dL. The mean creatinine of kidney function tests was 0.9 mg/dL. The creatinine value of 14 patients was found to be higher than the reference value of 1.2 mg/dL, and 4 of these patients were referred to tertiary care centers with a preliminary diagnosis of acute renal failure (ARF). The mean AST of liver function tests was 217.5 U/L. The AST value of 25 patients was found to be higher than the reference value of 35 U/L. The mean LDH value was 1249.2 U/L (Table 1).

Table 1. Demographic characteristics and laboratory parameters

| | n | median (min; max) | mean±SD |
|---|---|---|---|
| Gestational week | 55 | 35.0 (17.0; 40.0) | 33.5±5.1 |
| Gravidity | 57 | 3.0 (1.0; 12.0) | 2.9±1.9 |
| Minimum Hemoglobin | 57 | 6.0 (3.1; 13.2) | 6.5±2.1 |
| Total Hemoglobin loss | 56 | 5.0 (0.0; 9.9) | 5.0±2.3 |
| Minimum thrombocyte | 57 | 57000.0 (24000.0; 258000.0) | 63175.4±34063.6 |
| INR | 57 | 1.52 (0.87; 4.84) | 1.55±0.53 |
| D-dimer | 57 | 34.4 (2.1; 87.0) | 29.6±17.7 |
| Fibrinogen | 57 | 81.0 (23.0; 506.0) | 102.1±77.8 |
| LDH | 56 | 825.0 (318.0; 5479.0) | 1249.2±1242.7 |
| Creatin | 57 | 0.6 (0.2; 4.1) | 0.9±0.8 |
| AST | 57 | 25.0 (10.0; 3351.0) | 217.5±553.3 |

The median DIC score was 6.0 (min= 5; max=8). There were 23 (40.4%) patients with DIC score of 5 and 5 (8.8%) patients with 8. According to the analysis of pregnancy complication categories; placental invasion and implantation abnormalities in 15 patients (26.3%), postpartum hemorrhage (atony) in 13 patients (22.8%), placental abruption in 11 patients (19.3%), hypertensive disease of pregnancy in 11 patients (19.3%) and 7 patients (12.3%) were in the other category (Table 2). In the other category, there were 2 uterine ruptures and 1 each episiotomy site hematoma, HELLP syndrome, hemolytic anemia, sepsis and idiopathic DIC. While 47 (83.9%) of the patients delivered by cesarean section, 9 (16.1%) patients had normal vaginal delivery. Laparotomy was performed in 20 (35%) of the patients who developed postpartum hemorrhage, and hysterectomy was performed in 12 of these patients whose bleeding could not be stopped. The uterine bleeding of the other 8 patients was controlled with hypogastric artery ligation, B-Lynch suture or application of Bakri balloon.

Table 2. DIC causes and maternal outcomes

| Causes<br>number | Hypertensive Disease of Pregnancy<br>(11) | Postpartum Hemorrhage (atony)<br>(13) | Placental abruption<br>(11) | Placental invasion and implantation abnormalities<br>(15) | Other<br>(7) | Total<br>(57)-(%) |
|---|---|---|---|---|---|---|
| Case, % | 19.3 | 22.8 | 19.3 | 26.3 | 12.3 | 100 |
| Type of delivery | | | | | | |
| Vaginal delivery | 1 | 5 | 0 | 0 | 3 | 9 - 16.1 |
| Cesarean delivery | 10 | 8 | 10 | 15 | 4 | 47 - 83.9 |
| Massive transfusion | 1 | 3 | 0 | 7 | 0 | 11 - 19.2 |
| Hysterectomy | 0 | 8 | 0 | 4 | 0 | 12 - 21 |
| Complication | 9 | 4 | 4 | 2 | 3 | 22 - 38.6 |
| Refer | 5 | 1 | 2 | 1 | 1 | 10 - 17.5 |
| Maternal death | 0 | 0 | 0 | 0 | 1 | 1 - 1.75 |

Red blood cell suspension (RBCs), fresh frozen plasma (FFP) and fibrinogen were mostly used in blood and blood products transfusion. The median number of units of 51 patients who received RBCs was 6.0 units (min=1; max=18.0), the median amount of 53 patients who received fibrinogen was 2.0 grams (min= 1.0; max= 5.0), the median unit of 55 patients who received FFP was 5.0 (min= 1; max= 15.0) units. In addition, there were 30 patients who received platelets (min=1; max=9), 33 patients who received whole blood (min=1; max= 9), and 2 patients who received cryoprecipitate (min= 10; max= 11). The number of patients who received massive blood transfusion (≥10 U RBCs in 24 hours) was 11 (Table 2). There was 1 patient who was not transfused, and

the patient's ISTH DIC score was 5.There were 22 (38.6%) patients with maternal complications. These complications are: HELLP syndrome, ARF, pleural effusion, retinopathy, hemolytic uremic syndrome (HUS), acute respiratory distress syndrome (ARDS), pulmonary thromboembolism, hepatorenal syndrome, hemolytic anemia and thrombophlebitis (more than one complication can be found in a patient). The mean DIC score of the patients who developed complications was 6.3 (there were 7 patients with DIC score of 5; 5 patients with 6; 6 patients with 7; and 4 patients with 8). There was 1 patient with a DIC score of 8 and no complication, and 1 of the patients with a DIC score of 8 died. Maternal mortality rate was 1.75%. Ten (17.5%) patients who developed complications were referred to a tertiary center and none of these patients died.

Pregnancy complication categories leading to DIC and neonatal outcomes were compared. Neonatal outcomes of pregnant women with abruptio placentae showed that 7 out of 9 (77.7%) newborns were stillborn, and 1 out of 2 live-borns died in the neonatal period. Due to the high rate of cesarean section performed in the early weeks of pregnancy in patients diagnosed with hypertensive disease of pregnancy, the birth weights of the newborns in this group were found to be lower than the other groups (mean week of birth=31.6; min=25; max39). The mean newborn birth weight was 2341.3±1043.3 grams (median= 2455.0; min= 380.0; max= 4650). The birth weight of newborns were evaluated and 13 (24.1%) had a very low birth weight, 13 (24.1%) had a low birth weight and 28 (50.9%) had normal birth weight and there was a 1 (1.8%) non viable fetus (Table 3). Nineteen of these newborns were transferred to newborn intensive care unit (NICU), 13 newborns' Apgar scores were less than 7 at 5 minutes. Apgar score information at the 5 minute of 16 newborns could not be reached. The live birth rate was 74.5% (41/55), stillbirth rate was 25.5% (14/55) and the neonatal mortality was 4.8% (2/41).

Table 3. Neonatal outcomes

| | n (%) | | n (%) |
|---|---|---|---|
| **Neonatal outcome (n= 55)** | | **Admission to the NICU (n= 19)** | |
| Live | 41 (74.5) | No | 36 (65.5) |
| Stillbirth | 14 (25.5) | Yes | 19 (34.5) |
| **Weight grup (n= 54)** | | **Apgar score at 5 minutes (n= 41)** | |
| Very low birth weight (500 – 1499) | 13 (24.1) | ≤ 7 | 13 (31.7) |
| Low birth weight (1500 – 2499) | 13 (24.1) | > 7 | 28 (68.3) |
| Normal birth weight (≥ 2500) | 28 (50.9) | | |
| Non-viable | 1 (1.8) | | |

Between 2010 and 2015, 229 patients (0.21%) were diagnosed with placental abruption with ICD 10 code "O45" out of 108281 deliveries in our hospital. DIC occurred in 11 of these patients and the incidence of DIC in placental abruption was found to be 4.8%. In 108281 deliveries that occurred during this 6-year period, a total of 57 patients were found to have overt DIC, and the calculated incidence of DIC for the six-year study was found to be 0.052%.

## DISCUSSION

In this study, we retrospectively analyzed the maternal and fetal outcomes of 57 patients who developed DIC due to obstetric reasons. Since the total number of births in our hospital during this 6-year period was 108281, we found the incidence of DIC in our hospital as 0.052% (57/108281), and this value was similar to other rates in the literature(10,12). Since there is no specific method to diagnose DIC, we tried to gain objectivity in the diagnosis by using the DIC scoring system recommended by ISTH. The ISTH scoring system was originally designed for non-pregnant patients and its use in pregnancy is still controversial due to the physiological changes seen in the coagulation cascade during pregnancy. It is known that fibrinogen increases throughout pregnancy, especially in the third trimester(13). It has been suggested that serum fibrinogen may not be as important as other laboratory parameters in the diagnosis of DIC because only 5% of patients showed a decrease in serum fibrinogen in the validation study of the ISTH scoring system(14). However, this system has good predictive value for the diagnosis of DIC and the identification of critically ill patients. This score can be used not only for diagnostic purposes but also prognostically, therefore it is important to use a DIC score in the diagnosis of patients with DIC(11). Erez et al developed a modified DIC score in pregnancy using only three components of the ISTH DIC score (platelet count, fibrinogen concentrations, and PT difference), suggesting that physiological hemostatic changes in pregnancy limit the applicability of this scoring system(11). They stated that this scoring system had 88% sensitivity and 96% specificity when the cutoff value was ≥26. When we designed our study, we did not use the modified DIC scoring suggested by Erez et al., as the ISTH scoring system is more widely used.

In our study, obstetric precursors causing DIC were placental invasion and implantation anomalies (26.3%), postpartum atony bleeding (22.8%), placental abruption (19.3%), hypertensive

disease of pregnancy (19.3%) and other (unclassified) (12.3%) and this distribution was different from similar studies in the literature(9,11). Placental anomaly is a major risk factor for peripartum hemorrhage and can lead to morbidity and mortality of the mother and neonate(15). Uncontrolled postpartum bleeding from placenta previa can lead to overt DIC in patients and can result in blood transfusion, hysterectomy, admission to the ICU, and even death(16). Considering the hospitalization diagnoses of the patients who developed DIC in our study, the diagnosis of placenta previa totalis was prominent in 14 (24.6%) patients. All of the 15 pregnant women in our study with placental invasion and implantation anomaly delivered by cesarean section. All of these patients underwent blood transfusion due to acute postpartum hemorrhage (min=6 ES, max=18 ES), 7 of them underwent massive transfusion, and 4 of them underwent hysterectomy due to unceasing uterine bleeding, and no patient died. Similarly, in a study by Goksever et al., it was seen that 35% of 279 patients with overt DIC received more than 4 units of blood transfusion(17). As seen in our study, due to the risk of postpartum hemorrhage, in order to stabilize blood loss during delivery and reduce morbidity and mortality rates, deliveries must be planned electively in the presence of an experienced team and adequate blood preparation must be done before the operation. Since DIC occurs with uncontrollable activation of coagulation and insufficiency of anticoagulant mechanisms, supportive treatment and blood transfusion to these patients are of critical importance. Early recognition of patients with DIC and initiation of treatment are very important. In DIC secondary to obstetric causes, the diagnosis may sometimes be delayed because pregnancy itself predisposes to coagulation. Laboratory tests should be repeated every 30 minutes and transfusion should be started with a minimum of 6 U Erythrocyte, 6 U FFP and 4-6 U Platelet suspension in pregnant women with severe bleeding. Massive transfusion protocols generally recommend 1/1/1 red blood cell/FTP/platelet transfusion(18). The goal in massive obstetric hemorrhage is to keep the hemoglobin concentration above 10 g/dL because pregnant women who develop DIC continue to lose blood and this blood loss reaches its maximum at the time of delivery.

When maternal complications were evaluated, we found that the most frequently affected organ associated with obstetric DIC was the kidney. Elevated creatinine levels were detected in 14 patients (higher than the reference value of 1.2), and ARF developed in 4 (7%) patients and were referred to multidisciplinary centers. In a study by Zhao et al, ARF (16.5%) was stated as the most common type of organ failure(19). The overall ARF rate in our study (7%, 4/57) was lower than in other studies (24.1% to 61%) in developing countries(20,21). Although DIC is not directly related to morphological changes in the kidney, it is thought that DIC potentially triggers ARF by stimulating cytokine release from the endothelium, which is one of the important mechanisms of kidney damage(22).

We observed that the worst results among newborn outcomes were in the ablatio placenta group. In 9 patients, 7 of the newborns resulted in stillbirth, 2 of them resulted in live birth, while 1 of the live-borns died in the early neonatal period. While placental abruption alone can cause severe bleeding that threatens maternal and fetal life, additional DIC in these patients complicates the situation. In these patients, termination of pregnancy as soon as possible and initiation of blood transfusion reduces maternal morbidity and mortality. In hypertensive diseases of pregnancy, emergency cesarean section rates are high in the early weeks due to preeclampsia or eclampsia. Since these patients are classified in the risk group for postpartum bleeding(23), it is important to keep the amount of intraoperative bleeding to a minimum. In cases of acute bleeding, the necessary blood and blood products should be transfused immediately before the coagulation factors in the serum are depleted.

## CONCLUSION

DIC secondary to obstetric complications is a life-threatening condition(7). As we mentioned in our study, identification of the antecedent causes, early diagnosis and active treatment protocols are of critical importance in reducing maternal and fetal morbidity and mortality rates. The most important point in the treatment of DIC is the rapid elimination of the underlying disease, because delayed treatment is often associated with a poor prognosis. Delivery also plays a key role in the management scheme because termination of pregnancy usually eliminates the underlying obstetrical disorder.

Since obstetric patients who develop DIC usually have severe peripartum hemorrhage, transfusion of blood and blood products to these patients is very important in the treatment. If the hospital where the patient is located does not have sufficient blood bank reserves, if the team that can do this is inexperienced when surgical intervention is required, or if there is no neonatal intensive care unit, the patient should be referred to a multidisciplinary center quickly.

Although the ISTH DIC scoring system gives good results in non-pregnant patients, physiological changes in the coagulation cascade during pregnancy may delay the diagnosis. Although modified DIC scoring for pregnant women has been developed in some studies, there is still a need for an internationally accepted pregnancy-specific DIC scoring.

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The authors have no conflicts of interest to report.

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