

Overt Disseminated Intravascular Coagulation in Obstetric Patients

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Objective: To determine the incidence, etiology and outcome of treatment in obstetric patients complicated by overt disseminated intravascular coagulation (DIC).

Material and Method: Medical records of 25 obstetric patients with a diagnosis of DIC in Songklanagarind University Hospital from January 1993 to December 2005 were reviewed.

Results: The incidence of overt DIC was 1 per 1,355 deliveries. Median maternal age was 30 years (range 17-44 years). Median duration of hospital stay was 10 days (range 0-32 days). The main associated conditions included abruptio placentae in 6 patients (24%), pregnancy-induced hypertension (PIH) in 5 (20%), amniotic fluid embolism in 4 (16%), acute fatty liver of pregnancy (AFLP) in 4 (16%), and HELLP syndrome in 3 (12%). A definite diagnosis of DIC was made in 8 patients (32%) with a median DIC score of 6 (range 5-7) and the remainder were clinically diagnosed with incomplete work-up. All patients received blood component replacement. Cesarean section was performed in 10 patients (40%) and hysterectomy in 9 patients (36%). Six patients died, giving a case mortality rate of 24%. Three were associated with amniotic fluid embolism and one of each with fulminant hepatitis, ALFP and HELLP syndrome. Thirteen of 24 fetuses (54%) died, most related to abruptio placentae (6/6, 100%), PIH (4/5, 80%), and amniotic fluid embolism (2/4, 50%).

Conclusion: Various pregnancy-related conditions will predispose to DIC development. Early diagnosis with prompt treatment, including a quick decision for surgical intervention, and eradication of predisposing conditions would minimize maternal morbidity and mortality.

Keywords: Disseminated intravascular coagulation, Pregnancy, Etiology, Treatment, Outcome

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Disseminated intravascular coagulation (DIC) is characterized by the widespread activation of coagulation, which results in the intravascular formation of fibrin and ultimately thrombotic occlusion of small and midsize vessels⁽¹⁾. Intravascular coagulation can compromise the blood supply to organs and, in conjunction with hemodynamic and metabolic derangements, may contribute to failure of multiple organs. At the same time, the consumptive coagulopathy may induce severe bleeding. In a normal pregnancy, the

coagulation cascade is in an activated state. DIC may be accompanied with many obstetrical complications such as abruptio placentae, amniotic fluid embolism, endotoxin sepsis and preeclampsia with HELLP (hemolysis, elevated liver enzyme, and low platelets) syndrome. It is usually associated with high mortality and morbidity. Obstetricians often fail to search for a definite clinical cause, while putting great effort into treating DIC. Early detection of the cause is important for adequate prompt management in order to reduce mortality and morbidity both to the mother and fetus.

The objective of the present study was to determine the incidence, etiology and outcomes of treatment in obstetric patients complicated by overt disseminated intravascular coagulation.

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Material and Method

There were 33,875 deliveries during the 13-year period from January 1993 through December 2005 in the authors' institute, Songklanagarind Hospital, the only tertiary university hospital in southern Thailand. Medical records were searched for final diagnosis of DIC as coded from the International Classification of Disease; Tenth Revision (ICD-10) and then reviewed. The extracted information included demographics, associated underlying clinical conditions, clinical manifestations (hemorrhage, jaundice and hypotension), laboratory profiles [complete blood count, activated partial thromboplastin time (aPTT), prothrombin time (PT), serum fibrinogen, fibrin degradation products (FDPs) and serum creatinine], modalities of treatment, and maternal and fetal outcomes.

The underlying clinical diagnosis was based on the clinical findings and laboratory results. Abruptio placentae was diagnosed by clinical bleeding and abdominal pain with the finding of a blood clot at the placental surface after delivery. Amniotic fluid embolism was diagnosed according to the following criteria: acute hypotension or cardiac arrest, acute hypoxia and coagulopathy with onset during labor or the cesarean section or within 30 minutes of delivery with no other clinical condition or potential explanation for the symptoms and signs. Patients with HELLP syndrome had the clinical diagnosis of preeclampsia and evidence of the following laboratory abnormalities: (1) *hemolysis*, (2) *elevated liver enzymes*, and (3) *low platelets*. Patients with AFLP had clinical symptoms, and labora-

tory evidence of acute hepatic dysfunction, notably increased serum transaminase (SGOT < 500 IU/L). Patients with acute fulminant viral hepatitis had high fever, malaise, jaundice, rapid deterioration with encephalopathy and high SGOT (> 5,000 IU/L).

The diagnostic criteria of DIC proposed by the Scientific Subcommittee on Disseminated Intravascular Coagulation of the International Society on Thrombosis and Haemostasis (ISTH) was used, as shown in Table 1⁽²⁾. The patients must have an underlying clinical disorder known to be associated with overt DIC before using this scoring system. A diagnosis of overt DIC can be made if the total score reaches 5 points.

Data are expressed as number (percentage), mean with standard deviation and median with range.

Results

During the study period, of 33,875 deliveries in the authors' institute, 25 cases of DIC were diagnosed, including 2 abortions and one twin pregnancy, giving a prevalence of 1 per 1,355 deliveries. The median maternal age was 30 years (range 17-44 years) and the median gestational age was 34 weeks (range 14-41 weeks). The DIC scoring was completed in 8 cases (32%) with a median DIC score of 6 (range 5-7). The common lacking data from the laboratory profiles were serum fibrinogen and FDPs. Eight cases (32%) had had antenatal care at the authors' hospital and 17 cases (68%) had been referred from other provinces in southern Thailand. The median duration of maternal

Table 1. Criteria for the diagnosis of overt DIC⁽²⁾

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1. Risk assessment: Does the patient have an underlying disorder known to be associated with overt DIC?
If yes: proceed; if no: do not use this algorithm:
 2. Order global coagulation tests (platelet count, prothrombin time (PT), fibrinogen, soluble fibrin monomers or fibrin degradation products)
 3. Score global coagulation test results
platelet count (> 100 = 0; < 100 = 1; < 50 = 2)
elevated fibrin-related marker (e.g. soluble fibrin monomers./fibrin degradation products)
(no increase: 0; moderate increase: 2; strong increase: 3)
prolonged prothrombin time
(< 3 sec. = 0; > 3 sec. but < 6 sec. = 1; > 6 sec. = 2)
fibrinogen level
(> 1.0 gram / l = 0; < 1.0 gram / l = 1)
 4. Calculate score
 5. If ≥ 5 : compatible with overt DIC; repeat scoring daily
If < 5: suggestive (not affirmative) for non-overt DIC; repeat next 1-2 days;

Sensitivity 91%, Specificity 97%

hospital stay was 10 days (range 0-32 days) and median birth weight was 2,180 gram (range 700-4,000 grams).

Maternal and Fetal Outcomes

The maternal and fetal outcomes are shown in Table 2. Abruptio placentae was the most common cause, followed by pregnancy induced hypertension (PIH), acute fatty liver of pregnancy and amniotic fluid embolism. Six patients died, giving a case mortality rate of 24%. Amniotic fluid embolism was the most common cause of maternal death (3 cases), and each one in AFLP, HELLP syndrome and acute fulminant herpes simplex hepatitis. The patients with amniotic fluid embolism rapidly worsened and most died within a few hours (only one survived). The other two maternal deaths were caused by liver failure. Maternal mortality from AFLP was associated with multiple organ failure. The case fatality rates of amniotic fluid embolism, AFLP and HELLP syndromes were 75%, 25% and 33% respectively. No maternal death occurred in the cases with abruptio placentae and PIH. Thirteen of 24 fetuses (54%) died. Fetal mortality rate was very high in abruption placenta (100%) and PIH (80%). Severe preeclampsia and eclampsia were complicated by abruptio placentae in 4 out of 5 cases. Two fetal deaths in the amniotic fluid embolism group occurred in the intrapartum period. One fetal death occurred in a case of maternal infection from acute fulminant viral hepatitis. Another cause of maternal infection was from a septic criminal preterm birth. Almost all patients had clinical hemorrhage except one with a septic criminal preterm birth. Hypotension was presented in 19/25; the 6 exceptions were 2 cases with acute fatty liver of pregnancy (AFLP), 2 cases with severe preeclampsia, one with eclampsia, and one with HELLP syndrome. All patients received blood component transfusion for treatment of hypovolemia, anemia or coagulopathy. Jaundice occurred in 7 cases, 4 cases with AFLP, 2 cases with HELLP syndrome and one case with acute viral hepatitis. One patient with abruptio placentae was complicated by renal insufficiency. The case of septic criminal preterm birth, complicated by acute renal failure and acute respiratory distress syndrome, required ventilatory support and hemodialysis. Antibiotics were used in all except three cases, two with amniotic fluid embolism and one with abruptio placentae.

Surgical Treatment

Twenty patients (80%) had undergone surgical

Table 2. Causes, maternal and fetal outcomes, and types of surgical treatment in DIC patients (n = 25)

Cause	N (%)	Maternal Death N (%)	Fetal Death N (%)	Types of surgical treatment (n = 20)					Hypogastric artery ligation
				Cesarean section	Hysterectomy	Hysterotomy	Re-exploratory	Drainage of hematoma	
Abruptio placentae	6 (24)	0	6 (46)	-	1	2	1	-	-
Pregnancy-induced hypertension	5 (20)	0	4 (31)	3	2	-	-	1	-
Acute fatty liver of pregnancy	4 (16)	1 (16)	0	3	1	-	-	-	1
Amniotic fluid embolism	4 (16)	3 (50)	2 (15)	1	3	-	-	1	-
HELLP syndrome	3 (12)	1 (16)	0	3	-	-	1	-	-
Infection	2 (8)	1 (16)	1 (8)	-	1	-	-	-	-
Missed abortion	1 (4)	0	0	-	1	-	-	-	-
Total	25	6	13	10	9	2	2	2	1

Some patients had more than one surgical treatment (total 6 cases)

One patient with second surgical treatment

Table 3. Summary of clinical data in maternal deaths (n = 6)

Causes	GA (wk)	Clinical presentation	Laboratory findings	DIC score	Surgical intervention	Fetal outcome
Amniotic fluid embolism						
1	37	PPH, ARDS	Plt 70,000 VCT > 2 hours	-	No	Good
2	39	PPH	Plt 67,000 aPTT > 100 sec PT > 100 sec Fibrinogen 11.25 mg/dL FDPs 10.0 µg/mL	5	TAH with Rt SO	Good
3	41	Fetal distress, PPH	Plt 79,000	-	CS and TAH	Good
Acute fatty liver of pregnancy	33	Jaundice, fetal distress, PPH, acute renal failure, liver failure	Plt 38,000 aPTT > 100 sec PT 22.8 sec	5	TAH with Lt SO	Good
HELLP syndrome	36	Hypertension, hemorrhage, liver failure	Plt 34,000 aPTT > 100 sec PT 34 sec Fibrinogen 119.6 mg/dL FDPs 40 µg/mL	6	CS, Re-exploratory	Good
Fulminant herpes simplex hepatitis	24	High fever, jaundice, hemorrhage, hypotension, loss of consciousness, liver failure	Plt 11,000 aPTT 91 sec PT 39.9 sec Fibrinogen 60.75 mg/dL	5	No	Death fetus in utero

Incomplete data for DIC scoring

ARDS, acute respiratory distress syndrome; CS, cesarean section; GA, gestational age; HELLP, hemolysis, elevated liver enzymes and low platelets; PPH, postpartum hemorrhage; TAH, total abdominal hysterectomy; SO, salpingo-oophorectomy; FDPs, fibrin degradation products; Plt, platelets; PT, prothrombin time; aPTT, activated partial thromboplastin time; VCT, venous clotting time

treatment during the present study period, as shown in Table 2. The most common procedures were cesarean section and hysterectomy. The indications for cesarean section were fetal distress, PIH, or other medical indications. The indication for hysterectomy was severe hemorrhage due to uterine atony. Termination of pregnancy by hysterotomy was done in 2 cases with abruptio placentae. Six patients had more than one surgical operation. Two cases after cesarean section had undergone hysterectomy (one case from PIH and one from amniotic fluid embolism). One case of cesarean section complicated with uterine atony was successfully treated by hypogastric artery ligation. A surgical procedure for hemostasis (drainage of hematoma or re-exploratory) was done in 4 cases, one of each from PIH (post normal vaginal delivery), HELLP syndrome (post cesarean section), amniotic fluid embolism (post hysterectomy with normal vaginal delivery), and abruptio placentae (post hysterectomy).

A summary of the clinical presentations and surgical treatments in maternal death are shown in Table 3.

Discussion

The incidence of DIC in the present study was 1 per 1,355 deliveries. All cases were clinically diagnosed and partially confirmed by laboratory results. Only one-third of the patients had a complete diagnosis according to the DIC score. Even with full facilities to manage these patients with prompt and appropriate surgical and medical treatment to remove the cause or stop the pathological process, the mortality was still high, especially in patients in whom the DIC was associated with amniotic fluid embolism or liver disease. The fetal death rate was high in the patients with abruptio placentae and PIH.

The present study had a higher prevalence of DIC compared with the other studies which varied between 1 per 3,000 to 5,000^(3,4). More than half of the patients had been transferred to the authors' hospital from another hospital. The prevalence may be underestimated due to partially treated with blood or blood components with severe bleeding with unknown causes. Most had been partially treated with blood or blood components and were in an emergency condition. Usually the patients had first been managed by an obstetrician. Four of the six maternal deaths had DIC scores ≥ 5 , while an other two were unable to be fully evaluated due to the rapid progress of the disease. Laboratory findings are normally of secondary importance in the diagnosis of DIC because diagnostic test

results rarely direct or redirect therapy and tests represent a static snapshot of a highly dynamic situation⁽³⁾. However, an effort should be made to evaluate the presence and severity of DIC through use of the appropriate scoring system, as such information may be of importance for clinical practice as well as clinical trials on the effect of interventions directed at pathways or components of the coagulation system to improve the situation of those who have DIC and/or the underlying disorder⁽⁵⁾. A combination of test results in a patient with a clinical condition known to be associated with DIC can be used to diagnose the disorder with reasonable certainty in most cases⁽⁶⁾.

The most common cause of DIC in the present study was abruptio placentae, which is in concurrence with previous reports^(3,7). Abruptio placentae rarely produce severe maternal complications while the fetus is alive in utero. The event of fetal death indicates a severe form of abruptio placentae and a risk that an overt coagulopathy might develop⁽⁸⁾, which was also observed in the present study. As the abruptio placentae in all of the presented cases was severe enough to cause DIC, all the fetuses died. No maternal deaths were found in the present study because the process can immediately be interrupted by termination of pregnancy. A hemorrhagic complication leading to hypovolemic shock was the cause of renal insufficiency in one patient.

DIC is a common complication of amniotic fluid embolism. Amniotic fluid has been shown to have a direct factor X activating property and thromboplastin like effect, leading to coagulation cascade and fibrinolytic system activation. The resultant hypoxia causes cardiac and hemodynamic collapse, and in most cases, maternal death. In the present study, only one patient survived with an advanced life support treatment. In management of this situation, oxygen should be administered to all patients. Optimization of preload with rapid volume infusion and during the early stages, direct acting vasopressors may be useful in restoring aortic perfusion pressure. Once this is accomplished, other inotropes such as dopamine can be added to improve myocardial function. Historically, the mortality approached to 60-80%^(9,10), which was also reflected in the present study (75%), however in more recent times with advances in technology and medical care, the mortality from this cause has declined to less than 30%⁽¹¹⁾.

Eight patients in the present study had severe liver diseases which caused maternal death in 3 cases (37%). Tank et al⁽¹²⁾ reported maternal mortality from

liver failure of 42%. DIC with multiple organ failure was the most common proximate cause of death. All three maternal deaths had liver failure and metabolic encephalopathy. Pregnancy affected by severe liver disease is an extremely high-risk situation requiring intensive care. An important aspect of patient care is early diagnosis⁽¹³⁾. AFLP has clinical presentation, biochemical findings and complications clearly distinguishable from HELLP syndrome, and unlike AFLP, maternal mortality in HELLP syndrome is usually low (1.1%)⁽¹⁴⁾. One maternal death in the present study was from acute fulminant herpes simplex viral (HSV) hepatitis (confirmed by autopsy). The patient had clinical symptoms of high fever, severe nausea, vomiting, malaise, jaundice, encephalopathy, and was complicated with DIC. HSV hepatitis in pregnant women is a rare condition. Primary infection in the latter part of pregnancy appears to constitute a greater risk. A high index of suspicion is necessary to diagnose and begin appropriate treatment with acyclovir⁽¹⁵⁾. Maternal and fetal mortality rates in this condition are high⁽¹⁶⁾. Though the authors began acyclovir treatment in the third day after the clinical symptoms appeared in the presented case, both patient and fetus died on day 10. One case with DIC was caused by missed abortion at the gestational age of 14 weeks. Generally, only 25% of the women with missed abortion developed a coagulopathy⁽⁷⁾. Another case was associated with septic criminal preterm birth. Unsafe abortion is one of the neglected health care problems in developing countries. In the present study, the patient was complicated by septic shock, which required intensive care and aggressive supportive treatment.

Emergency hysterectomy was the most common surgical intervention for severe postpartum hemorrhage in the present study. Maternal mortality in the present study was high with this treatment, contrary to other studies^(17,18), in which emergency peripartum hysterectomy usually results from uterine atony with no other underlying clinical condition. However, this procedure leads to significant morbidity and requires complicated supportive treatment. Alternative surgical procedures such as hypogastric artery ligation have been reported for treatment in severe postpartum hemorrhage⁽¹⁹⁾. One patient in the present study was successfully performed by this procedure.

All of the presented patients required treatment with blood components. Replacement of blood loss with packed red blood cells is the first priority in order to maintain oxygen delivery to tissue. Plasma components and platelet concentration are given to

replace the coagulation factors, antithrombin III and the platelets that are consumed in the clotting process. Cryoprecipitate may be useful in circumstances where fibrinogen is low, particularly less than 100 ng/dl, and volume overload is a concern. The therapy should be guided by the clinical condition of the patient and laboratory evidence of a coagulopathy.

The present study had several limitations, including that the data were collected retrospectively, the sample size was small, and there was selection bias because the presented setting was in a tertiary medical care center, and most of the presented severe cases had been transferred from other hospitals. Despite these limitations, the present study provides important background information about DIC in obstetric patients, especially in Thailand.

Conclusion

Removal of the triggering mechanism and supportive treatment are the key to successful management of DIC in obstetric patients and the outcome depends primarily on the ability to deal with the trigger and not on direct attempts to correct the coagulation deficit.

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ภาวะลิ่มเลือดแพร่กระจายแบบชัดเจนในผู้ป่วยสูติกรรม

อุ๋นใจ กอนันตกุล, อานภาพ เลขะกุล

วัตถุประสงค์: เพื่อศึกษาอุบัติการณ์ สาเหตุและผลของการรักษาในผู้ป่วยสูติกรรมที่มีภาวะลิ่มเลือดแพร่กระจายแบบชัดเจนแทรกซ้อน

วัสดุและวิธีการ: ทำการศึกษาย้อนหลังในสตรีตั้งครรภ์ที่เกิดภาวะลิ่มเลือดแพร่กระจายแบบชัดเจนในโรงพยาบาลสงขลานครินทร์ ตั้งแต่เดือนมกราคม พ.ศ. 2536 ถึง ธันวาคม พ.ศ. 2548 รวมผู้ป่วยที่นำมาวิเคราะห์ 25 ราย ได้ทำการเก็บข้อมูลทั่วไปของผู้ป่วย สาเหตุ วิธีการรักษา และผลลัพธ์ที่เกิดขึ้นทั้งในมารดาและทารก

ผลการศึกษา: พบผู้ป่วยตั้งครรภ์ที่มีภาวะลิ่มเลือดแพร่กระจายแบบชัดเจนทั้งหมด 25 ราย อุบัติการณ์ 1 ต่อ 1,355 ของการคลอด ค่ามัธยฐานของอายุมารดา คือ 30 ปี (ค่าพิสัย 17-44 ปี) ค่ามัธยฐานของเวลาที่นอนโรงพยาบาล คือ 10 วัน (ค่าพิสัย 0-32 วัน) สาเหตุหลักที่ทำให้เกิดคือ รกลอกตัวก่อนกำหนด 6 ราย (ร้อยละ 24) ความดันโลหิตสูงแทรกซ้อนระหว่างตั้งครรภ์ 5 ราย (ร้อยละ 20) ภาวะน้ำคร่ำหลุดหลุดหลอดเลือด 4 ราย (ร้อยละ 16) acute fatty liver 4 ราย (ร้อยละ 16) และกลุ่มอาการ HELLP 3 ราย (ร้อยละ 12) การวินิจฉัยโดยการให้คะแนนตามผลการตรวจเลือดทางห้องปฏิบัติการ สามารถให้การวินิจฉัยภาวะลิ่มเลือดแพร่กระจายแบบชัดเจนได้เพียง 8 ราย (ร้อยละ 32) พบค่าคะแนนมัธยฐาน คือ 6 (ค่าพิสัย 5-7 คะแนน) ผู้ป่วยส่วนใหญ่ได้รับการวินิจฉัยจากลักษณะทางคลินิก และผลการตรวจเลือดทางห้องปฏิบัติการที่ไม่สมบูรณ์ ผู้ป่วยทุกคนได้รับการรักษาด้วยการให้ส่วนประกอบของเลือดผู้ป่วย 10 ราย (ร้อยละ 40) คลอดด้วยวิธีผ่าตัด ผู้ป่วย 9 ราย (ร้อยละ 36) ได้รับการรักษาด้วยการตัดมดลูก ผู้ป่วยเสียชีวิตทั้งหมด 6 ราย คิดเป็นอัตราตายร้อยละ 24 สาเหตุเกิดจากภาวะน้ำคร่ำหลุดหลุดหลอดเลือด 3 ราย สาเหตุอื่น ๆ (อย่างละ 1 ราย) เกิดจากภาวะ fulminant hepatitis, acute fatty liver และกลุ่มอาการ HELLP ทารกเสียชีวิต 13 ราย (ร้อยละ 54) สาเหตุเกิดจากภาวะรกลอกตัวก่อนกำหนด 6 ราย (6/6, ร้อยละ 100) ความดันโลหิตสูงแทรกซ้อนระหว่างตั้งครรภ์ 4 ราย (4/5, ร้อยละ 80) และภาวะน้ำคร่ำหลุดหลุดหลอดเลือด 2 ราย (2/4, ร้อยละ 50)

สรุป: ภาวะทางสูติกรรมและโรคแทรกซ้อนหลายชนิดทำให้เกิดภาวะลิ่มเลือดแพร่กระจายได้ง่ายขณะตั้งครรภ์ การวินิจฉัยภาวะนี้ได้ตั้งแต่ระยะแรก ให้การดูแลรักษาที่รวดเร็ว โดยเฉพาะการทำหัตถการต่าง ๆ เพื่อกำจัดสาเหตุที่กระตุ้นทำให้เกิดภาวะนี้จะช่วยลดภาวะทุพพลภาพและการตายของมารดาได้
