Disseminated intravascular coagulation and massive obstetric hemorrhage

Management dilemma

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ABSTRACT

Objective: The objective of this retrospective study is to reflect on our experience on an optimal management for major postpartum hemorrhage, which would prevent the occurrence and complications of disseminated intravascular coagulation and minimize maternal mortality and morbidity

Methods: Ten cases out of the 30,000 of total deliveries of severe obstetric hemorrhage associated with disseminated intravascular coagulation were studied. This study was carried out over a 7 year period, October 1988 through to September 1995, at the Obstetric Unit, King Khalid University Teaching Hospital, Riyadh, Kingdom of Saudi Arabia.

Results: All of the 10 women received packed red blood cells, 8 had fresh frozen plasma, and 6 received platelet transfusion. The 10 cases developed disseminated intravascular coagulation following medical and surgical management, all women needed hysterectomy, 4 subtotal, 6 total, and 5 women had relaparotomy and pelvic packing. Two had bladder injuries. There was no maternal death.

Conclusion: An early resort to hysterectomy when conservative measures fail, will minimize maternal morbidity and mortality. In case of continuous bleeding after hysterectomy, pelvic packing proved to be effective.

Keywords: Disseminated intravascular coagulation, major obstetric hemorrhage, relaparotomy, interventional radiology guided techniques.

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Severe postpartum hemorrhage (PPH) is defined as blood loss of more than 1000 ml. Since blood loss after delivery of the baby is difficult to measure accurately, major PPH may best be defined by a fall in hematocrit (Hct) or by the need for blood transfusion.[1] Postpartum hemorrhage accounts for 28% of maternal deaths in developing countries, around 125,000 deaths each year, as there are 125,000,000 births annually in the developing world, the risk of maternal death from PPH is approximately one in 1000 deliveries.[2-4] In the Kingdom of Saudi Arabia (KSA), PPH accounts for 20% of direct maternal deaths. Hemorrhage is the 4th leading cause of death in the United Kingdom. Eight deaths out of the 15 hemorrhage deaths were attributed directly to PPH alone and the risk of death from obstetric hemorrhage is 1:100,000 deliveries.[5] The present report concerns 10 cases of major obstetric hemorrhage with disseminated intravascular coagulation (DIC), as evidenced by low platelet count prolongation of the coagulation screening tests, low fibrinogen level, and the presence of fibrin degradation product (FDP). The management in the face of a life-threatening obstetric hemorrhage with

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DIC, unfortunately, is not always evidence-based. When faced with such an emergency, obstetricians tend to give whatever is available at hand hoping to save the life of the mother. The aim of this retrospective study is to reflect on our experience on an optimal and cost-effective management protocol, which would prevent the occurrence and complications of DIC and minimize maternal mortality and morbidity.

Methods. Ten cases of severe obstetric hemorrhage that progressed to DIC were studied retrospectively over a 7 year period, October 1988 through to September 1995, in the Obstetric Unit, King Khalid University Teaching Hospital, Riyadh, KSA. Information was retrieved from the medical records regarding age and parity, detailed obstetric history illustrating the number of previous lower segment cesarian section (LSCS), placental localization, mode of delivery, blood loss, and clinical and laboratory evidence of disseminated intravascular coagulation (DIC). The available pre-hemorrhage, intra-hemorrhage, and post-replacement laboratory parameters were recorded. Replacement therapy in the form of crystalloid, colloid, blood and various blood components (platelets, fresh frozen plasma, and cryoprecipitate) was used. Conservative medical therapy includes various oxytoxic drugs, ranging from ergometrine, oxytocin and prostaglandin, administered via different routes. The antifibrinolytic agent tranexamic acid was used in some patients. Conservative surgical measures used in this study included uterine massage, suturing of placental bed, uterine packing, uterine and internal iliac artery ligation. Hysterectomy, total or subtotal was resorted to when conservative surgical attempts were not successful.

Results. Out of the 30,000 total deliveries during the 7 years study period, 735 patients developed postpartum hemorrhage of more than 500 ml blood loss giving an incidence of 2.5%. Severe postpartum hemorrhage of more than 1000 ml blood loss occurred in 84 patients giving an incidence of 0.5%. Ten cases of the severe PPH progressed to DIC giving an incidence of 0.03%. The age of the 10 patients ranged between 25 years - 40 years (mean = 36.1 years); nine patients were 35 years and above. Four patients were of high parity (6 and above), 4 were para 3, and 2 were para 2+0. Six patients had repeat LSCS for all their previous deliveries, and 3 patients had one previous cesarean section. The patient who did not have previous cesarean section had spontaneous vertex delivery at 30 weeks gestation, following a history of prolonged premature rupture of the membranes, and was admitted 12 days later with secondary PPH. Eight cases had previous cesarean section as well as anterior placenta previa; in 3 of these placenta accreta (cases number 6 and 7), or increta (case number 4) was demonstrated on histopathology, while case number 2 had syncitial endometritis and case number 5 had leiomyoma and adenomyosis. Blood loss ranged between 1.5-11 litres with a mean of 4.4 litres **(Table 1)**.

Ten of the 84 cases with major PPH showed evidence of DIC of varying severity. Low platelet

Table 1 - Patient age, parity, number of previous lower segment cesarean sections, placental localization, mode of delivery, estimated blood loss, and uteroplacental histopathology results.

Age	Parity	N of previous LSCS	Anterior low lying placenta	Histopathological results	Mode of delivery	Blood loss (litres)
36	P3+0	3	Yes	None	Em.LSCS	3.5
35	P3+0	3	Yes	Syncitial endometritis	Em.LSCS	1.5
36	P7+0	3	Yes	None	Em.LSCS	5
35	P3+0	3	Yes	Placenta increta	ELSCS	6
25	P2+1	1	No	Leiomyoma/adenomyosis	SVD	3.5
40	P8+0	2	Yes	Placenta accreta	ELSCS	6
40	P6+0	No	Yes	Placenta accreta	Em.LSCS	10
36	P7+0	1	Yes	None	Em.LSCS + BTL	4.5
38	P2+0	1	Yes	None	Em.LSCS	11
40	P3+0	3	No	None	ELSCS + BTL	4

N - number, LSCS - lower segment cesarean section, BTL - bilateral tubal ligation, ELSCS - elective lower segment cesarean section, Em.LSCS - emergency lower segment cesarean section, SVD - spontaneous vaginal delivery

Table 2 - Pre- and intra-hemorrhage and post-replacement hematological parameters.

Hemoglobin (g/dl)			Platelets NR=(140-400 x 10^9/L)			Prothrombin time NR=(9.5-15.3 sec)			Activated partial thromboplastin time (26-39 sec)			Fibrinogen NR=(2-4 g/L)			FDP N (<10 μg/ml)			D. Dimer		
Pre	**Intra**	**Post**	**Pre**	**Intra**	**Post**	**Pre**	**Intra**	**Post**	**Pre**	**Intra**	**Post**	**Pre**	**Intra**	**Post**	**Pre**	**Intra**	**Post**	**Pre**	**Intra**	**Post**
8.1	6.7	11.9	250	99	190	19	59	18	36	>120	41	-	49	30	<10	60	-	-	+	-
11.2	5	12	300	27	73	14	59	18	32	>120	41	-	50	185	<10	20	-		+	
9.8	8	8.7	164	64	224	11	24	14	28	>120	35	376	105	665	<10	40	-		+	-
10	6.7	12.3	350	44	137	17	25	19	29	78	32	420	130	350	<10	40	40	-	+	-
9.4	7.1	8.5	304	88	200	16	40	15	34	85	30	460	98	423	-	80	-	-	+	-
11.7	4.4	12.3	221	62	195	15	29	16	30	72	30	231	80	401	-	120	-	-	+	-
10.5	6.4	9.4	300	150	350	12	23	17	34	>120	32	-	80	658	-	-	-	-	-	-
9.7	4.7	10.1	308	80	122	16	20	15	30	31	-	-	130	450	-	-	-	-	-	-
11	4	10.4	304	64	97	13	12	13	32	31	30	-	206	455	-	-	-	-	-	-
13.6	8.7	11.7	260	64	98	15	19	14	29	58	58	-	122	133	-	20	-	-	+	-

NR - normal range, N - normal, FDP - fibrin degradation product, D.dimer - Dis alphabet

Table 3 - Conservative and definitive surgical measures.

Suturing	Packing (uterine)	Subtotal hysterectomy	Total hysterectomy	Packing (pelvic)
Positive	Positive	Positive	Negative	Negative
Positive	Positive	Positive	Negative	Negative
Positive	Positive	Negative	Positive	Positive
Positive	Positive	Positive	Negative	Negative
Positive	Positive	Negative	Positive	Positive
Positive	Positive	Negative	Positive	Negative
Positive	Positive	Negative	Positive	Positive
Positive	Positive	Positive	Negative	Positive
Positive	Positive	Negative	Positive	Negative
Positive	Positive	Negative	Positive	Positive

count was noted in 9 women, 9 had prolonged prothrombin time (PT), while 8 had prolonged partial thromboplastin time (APTT). Low plasma fibrinogen was evident in 9 cases, whereas a high FDP as well as positive D-dimer test was noted in 8 cases **(Table 2)**.

All the 10 women with DIC received 2 to 35 units of packed red blood transfusion (mean=12 units). Eight patients had received 4 to 20 units of fresh frozen plasma (mean=7.8 units). Six patients received platelets transfusion 4 to 12 units (mean=7.3 units) and 5 patients had cryoprecipitate ranging from 4 to 19 units. Case number 4 went into severe hemorrhagic shock and was given 6 uncross matched group specific packed red blood cells, followed by 6 units of cross-matched packed cells. All 10 patients had suturing of the placental bed and uterine packing; 6 patients had total hysterectomy, and 4 patients had subtotal hysterectomy. Five patients ultimately needed pelvic packing, 4 following total, and one following subtotal hysterectomy **(Table 3)**.

Discussion. Blood loss in obstetric patients, especially postpartum is one of the major causes of maternal death. Postpartum hemorrhage accounted for 28% of maternal deaths in 11 population-based studies from 8 developing countries and for 20% of direct maternal deaths in KSA. Postpartum hemorrhage is frequently associated with the following risk factors: maternal obesity, large baby, multifetal gestation, severe pre-eclampsia, magnesium sulfate therapy, operative delivery, and chorioamnionitis.[6,7] Other known risk factors include antepartum hemorrhage, increased maternal age, and prolonged labor. In addition, there is a well-known association of LSCS and anterior low-lying placenta.[6,7,8] The above risk factors with this association are relevant to the place of delivery and the need for the increase of vigilance. In patients presented in this review, there is a strong association between major PPH and age, since 9 of the 10 cases were 35 years of age and above. There was also significant association between PPH and grand multiparity in the present study; 4 women were of parity 6 and above. Only one patient was young and of low parity, but this patient had prolonged preterm rupture of the fetal membranes as well as a uterine fibroid. The same patient presented with secondary PPH, 12 days after delivery. In contrast, other studies did not establish an association between grand multiparity and PPH.[6] Nine patients had past history of previous LSCS, of these, 8 had a combination of anterior low-lying placenta and previous LSCS. We have observed a strong association between prolonged massive obstetric hemorrhage and the development of DIC. This necessitated the rapid intervention with blood and its derivatives in order to avoid the occurrence and the complication of DIC. In the 10 cases of severe postpartum hemorrhage that progressed to DIC, internal iliac and uterine artery ligation was unsuccessful in 2 cases.

Recent interventional radiology guided techniques of stenting, occlusive balloons, or embolization to the uterine, internal or common iliac arteries were not attempted. In spite of conservative medical and surgical measures in the form of oxytoxics, prostaglandins, suturing of placental bed, uterine packing, uterine and internal iliac arterty ligation, all the 10 women eventually needed hysterectomy (4 subtotal, 6 total). Pelvic packing was necessary to achieve hemostasis in 4 patients following total hysterectomy, and in one patient after subtotal hysterectomy. The use of hysterectomy followed by pelvic packing in case of continuing pelvic hemorrhage proved to be life-saving and reduced both maternal mortality and morbidity.[9] Moreover, it prevented further worsening of DIC. Given the availability of interventional radiology, training of potential radiologist and gynecologist on the interventional radiology guided techniques of stenting, occlusive balloons and or embolization of the uterine and internal iliac arteries should be encouraged. It is also worthwhile demonstrating uterine artery and internal iliac ligation, during elective abdominal hysterectomy, to young gynecologist. This will open the minds to these life-saving procedures in the face of acute life-threatening hemorrhage, and in this way preserving the patients' reproductive potential. Internal iliac artery ligation is effective in controlling bleeding in patients undergoing treatment for severe PPH and DIC, and allows for conservation of reproductive potential and avoids emergency obstetric hysterectomy. It is particularly recommended in cases where DIC does not respond to medical treatment.[10] Surgery is usually simple and does not pose any technical difficulties and can be taught during elective abdominal hysterectomy.

Selective emergency uterine arteries embolization is yet another effective means of controlling severe PPH, and it also avoids high-risk surgery and maintains reproductive ability.[11] Lastly, selective transcatheter arterial embolization was also shown to be effective in controlling severe PPH.[12] The selection of which artery to embolize is still controversial (internal iliac versus uterine). Occasionally, the determination of the bleeding vessel in massive obstetric hemorrhage may be difficult even by angiography. The results of the present study emphasized the importance of the early resort to cesarean hysterectomy, when conservative measures fail, thereby removing the cause of DIC, and avoiding the subsequent massive transfusion with its inherent risks. It may also help to minimize or eliminate the need for admission to the intensive care unit. The corner stone of the DIC management is the specific and vigorous treatment of the underlying cause. However, controlling the coagulation activation and subsequent thrombin generation is a major challenge to the successful management of DIC. At the time when the cases reported in this study were managed the administration of heparin used to be the prime anticoagulation employed in the control of DIC due to obstetric or other causes, or both. However, in the last few years a better understanding of natural anticoagulant mechanism has led to the elaboration of more effective therapies,[13-16] primarily antithrombin monotherapy, activated protein C, synthetic protease inhibitors such as gab exact mesilate, recombinant thrombomodulin (rtm), tissue factor pathway inhibitor, (TFPI) and hirudin. Nonetheless, controversies are still abound on which anticoagulant to use in specific DIC situations. This is compounded further by the lack of both the local unavailability of most of these agents, and also the local experience using some of these newly emerging novel agents.

The guiding principle of therapy in D & C is to identify and vigorously treat the underlying cause without delay. Treatment options to correct the

hemostatic defect and to dampen the intravascular clotting/fibrinolytic process include transfusion of blood products, heparin, antithrombin III, and antifibrinolytic agents. The availability of new drugs such as activated protein C, tissue factor pathway inhibitor, bureidein or synthetic serine protease inhibitors, and upcoming trials investigate the role of these and older treatment options to help us to more clearly recommend evidence based on specific therapy in acute obstetric DIC.[14] When all measures fail, then pelvic packing is the last resort and this proves to be effective as was demonstrated previously.[9] The final outcome of these measures will be: shorter hospital stay, faster postoperative recovery, reduced maternal morbidity and mortality with subsequent benefits for both the patients and the hospital.

In conclusion, in the face of massive obstetric hemorrhage and DIC, an early and appropriate evidence-based blood components and missing factor replacement will minimize the occurrence and effects of DIC. Moreover, in case of failure of conservative medical and surgical measures, prompt resort to hysterectomy will reduce maternal mortality and morbidity. In case of continuous bleeding following hysterectomy, pelvic packing proved to be effective.

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