Original Article

Disseminated Intravascular Coagulation in High Risk Obstetric Patients

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Objective: To determine the frequency of disseminated intravascular coagulation in high risk obstetric patients, using scoring system of international society of thrombosis and hemostasis (ISTH).

Place and Duration: The study was conducted in the Maternal and Child Health Center (Outpatient and Inpatient Department), Pakistan Institute of Medical Sciences, Islamabad. from August 2010 to August 2011.

Study Design: Descriptive case series.

Materials and Methods: It was a descriptive case series conducted at Maternal and Child Health Centre,PIMS Islamabad. A total of 97 high risk pregnancies(pre-eclampsia,eclampsia,placental abruption,PPH,in utero fetal death) presented in emergency were recruited and their ISTH score was calculated. Two groups were made, group I with ISTH score<5 and group II with ISTH score≥5 and both groups were followed for the outcome in term of development of DIC and maternal mortality associated with DIC.

Results: Out of 97 patients 25 (25.7%) in high risk obstetric patients, using scoring system of international society of thrombosis and hemostasis (ISTH)..%) patients developed disseminated intravascular coagulation on the basis of clinical findings of uterine or generalized bleeding from multiple sites. DIC remained more prevalent amongst primigravidae i-e 45%. The major predisposing cause was found to be PPH i-e 64%. The proportion of patients with DIC who had ISTH score less than 5 were significantly lesser (15% vs. 72%, P-value < 0.05) as compared with patients having ISTH score equal or more than 5. There were 5 maternal deaths, one in group I and 4 (80%) deaths in the group II. The comparison of DIC showed significant association between ISTH score and DIC.

Conclusion: Disseminated intravascular coagulation is a grave complication in obstetrical population,
PPH is the major predisposition followed by placental abruption and pre eclampsia. ISTH score equal or more than 5 in high risk obstetric patients has significant association with DIC and mortality associated with it.

Key Words: Disseminated intravascular coagulation, ISTH score, DIC, High risk pregnancies.

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Introduction

Disseminated intravascular coagulation is the widespread activation of intravascular coagulation leading to depletion of fibrin within circulation, consumption of clotting factors usually leads to a bleeding diathesis.[1] Disseminated intravascular coagulation (DIC) is a clinicopathological syndrome which complicates a range of illnesses. It is characterised by systemic activation of pathways leading to coagulation, which can result in the generation of fibrin clots that may cause organ failure with concomitant consumption of platelets and coagulation factors that may result in clinical bleeding.[2]

The incidence of DIC is 1 per 1,355 deliveries.[3] IC never occurs in isolation and recognition that a patient has a clinical disorder which may result in the development of DIC is the key to appropriate investigation and management.[4] DIC may arise in patients with a wide spectrum of disorders including sepsis, malignancy, trauma, liver disease and vascular anomalies. It is also seen when pregnancy is complicated by placental abruption, pre eclampsia, eclampsia, postpartum hemorrhage, intrauterine death of fetus and amniotic fluid embolism . All of these conditions share the ability to induce systemic activation of coagulation either by activating cytokines as part of a systemic inflammatory response or by causing the release of, or exposure to, procoagulant substances.[5]

Intrauterine foetal demise (IUD) has been classically described as frequently associated with DIC. If the fetus retains longer, up to 25% of cases develop a coagulopathy that is mediated by release of thromboplastin-like material from dead products of conception.[6]

Pre-eclampsia, its clinical severity depends on the extent to which abnormal placental sensing provokes inflammatory signals. This could potentiate platelet aggregation and utero-placental ischaemia to cause preeclampsia.[7]With placental abruption, the haemorrhage upon premature placental separation can also allow entry of placental tissue factor into the circulation to promote thrombin generation and coagulation.[8]Postpartum haemorrhage (PPH) is another cause of bleeding associated with DIC. The coagulopathy arises mainly from the excessive blood loss, consumption of clotting factors and the further effects of massive transfusion.

A failure to anticipate or detect early stages of DIC in such high-risk pregnancies is cited as a major deficiency in the care of women who die from obstetric hemorrhage and despite advances in obstetric care and hematological services, hemorrhage with associated DIC remains the major cause of maternal morbidity and mortality.[9]

There is no single laboratory test that can establish or rule out the diagnosis of disseminated intravascular coagulation. Thus, it is of utmost importance to assess the whole clinical picture, taking into account the clinical condition of the patient, the diagnosis, and all available laboratory results. DIC is an extremely dynamic situation, and there is no gold standard for diagnosis is available, so it is important to establish a criteria to diagnose a hemostatic system which is under stress but still able to compensate i-e non-overt DIC before it progresses to overt-DIC, which has an override of the regulatory factors and degradation of endothelial regulatory network.[10]

This concept has been taken into consideration by the International Society of Thrombosis and Haemostasis (ISTH) recommended the use of a scoring system for DIC. [11]

The ISTH criteria proposes a 5-step diagnostic algorithm to calculate a DIC score, utilizing simple laboratory tests that are available in almost all hospital laboratories (platelet count, fibrin marker, PT and serum fibrinogen)The presence of an underlying disorder known to be associated with DIC is a prerequisite for the use of the algorithm. For overt DIC, a cumulative score of 5 or more from prolonged PT, reduced platelets and fibrinogen, and elevated fibrin-related markers (e.g. D-dimer or FDP) was proposed. The scoring system pertains to conditions which are associated with both acute onset DIC, and chronic DIC.

The ISTH overt DIC score has been shown to be sensitive to DIC of infective and non-infective aetiologies.[12, 13] The sensitivity of the ISTH overt DIC score was found to be 91% with a specificity of 97%.[14.] strong correlation between an increasing DIC score and mortality has been demonstrated by several studies, For each DIC point, increases in the odds of mortality of 1.25 -1.29 have been demonstrated. The mortality associated with overt DIC (score>5) and non-overt DIC(score<5) was found to be 56% and 26%.

Since these obstetrical conditions may predispose the mother to development of disseminated intravascular coagulation, it is important to find the frequency of DIC in high risk pregnancies so that one can anticipate the disease in patients presenting with clinical situations, considered as high risk conditions .with calculation of score of patients developing fatal DIC, based on scoring system of International Society Of Thrombosis and Hemostasis, a diagnostic criteria can be established. If this scoring is found useful in diagnosis of DIC and its severity, regarding the outcome in our setup, it would help us making a quick decision for early intervention and eradication of predisposing condition which could minimize maternal morbidity and mortality in obstetrics related to obstetric hemorrhage with DIC.

Materials and Methods

The study was conducted in the Maternal and Child Health Center (Outpatient and Inpatient Department), Pakistan Institute of Medical Sciences, Islamabad. from August 2010 to August 2011. A total of 97 high risk patients were taken and were categorized according to their ISTH score with score < 5 or score $\geq$ 5

Inclusion Criteria: Patients presenting with

- Placental abruption
- IUD
- Pre-eclampsia/eclampsia
- PPH

Exclusion Criteria: patients with non obstetric causes of DIC

- Severe infections(pneumonia0
- Trauma
- Organ dysfunction(severe panreatitis)
- Malignancy
- Severe hepatic failure
- Severe toxic or immunological reactions

Data collection procedure: After approval from hospital ethical committee, Patients were selected according to inclusion criteria, who presented in emergency, informed consent was taken.

All investigations included in ISTH scoring system (platelet count, serum FDPs, PT and serum fibrinogen) for all the selected patients were sent at the time of admission to hospital laboratory and got it reported by the pathologists. The ISTH score was calculated after collection of those investigations, following which they were divided into two groups, either with ISTH score less than 5 or ISTH score equal /more than 5.These patients were followed. Data was analyzed by using SPSS version

10.For continuous variables (age) mean+ S.D was calculated, while for categorical variables (ISTH score, development of DIC, maternal mortality) frequencies and percentages were calculated. Chi square was applied to find the association of ISTH score at the time of admission with maternal mortality value<0.05 was considered significant.

Results

This study included 97 obstetric patients who were at high risk for development of DIC. ISTH scoring of these patients was done at the time of admission and then these patients were followed for frequency of DIC and maternal mortality associated with DIC over a period of seven days.

The mean age of study population was found to be 28.12+6.12 S.D years, with a range of 18 to 45 years and the patients who developed DIC found to have mean age of 28.13±6.29 years.

Out of 97 patients 25 (25.7%) patients developed DIC on the basis of clinical findings of uterine or generalized bleeding from multiple sites. DIC remained more prevalent amongst primigravida (45%). Multiparous and grandmultiparous women made 44% and 8% respectively. Of these 25 patients, 9 patients (36%) were at term, 11 (44%) preterm and 7(28%) were postnatal.

The distribution of gestational age of the patients show that mostly patients with DIC were at term followed by postnatal patients. Similarly in patients without DIC majority had gestational age of 34 to 36 weeks followed by term patients.

Major obstetrical complications leading to disseminated intravascular coagulation in our study were PPH (64%), placental abruption (16%), pre-eclampsia (12%), in utero death of fetus (8%), while no eclamptic patient developed DIC as shown in figure 1.

Similarly in patients who did not develop DIC majority had pre-eclampsia 30 (41.7%) followed by in utero death in 18 (25%) patients According to the results of the study in patients with ISTH score less than 5 majority of the patients 31 (39.2%) had pre-eclampsia, followed by 19(24.1%) patients with in utero death of fetus and 13(16.5%) had eclampsia. In patients who had ISTH score of equal or more than 5, majority 13 (72.2%) patients had PPH and 2 (11.1%) patients had pre-eclampsia.

In our study there were 5 maternal deaths in which there was one death in group who had ISTH score of less than 5, 4 (80%) deaths in the group of ISTH score of equal or more than 5 as given in **table 1**.

The results of the study show that there was significant association between DIC and ISTH score. The proportion of patients with DIC who had ISTH score less than 5 were significantly lesser (15% vs. 72%, P-value < 0.05) as compared with patients having ISTH score equal or more than 5 as given in **table 2**.

Similarly the comparison of mortality also showed significant association between DIC and mortality. The mortality was significantly higher (100% vs. 0%, P-value < 0.05) in patients with DIC as compared with non-DIC patients as given in **table 3.**

Table 1: Frequency of Maternal Mortality in High Risk Obstetric Patients on the Basis of ISTH Scoring System

Score	Mortality	Frequency	Percent	Cumulative Percent
Less than 5	Yes	1	1.3	1.3
	No	78	98.7	100.0
	Total	79	100.0	
Equal or more than 5	Yes	4	22.2	22.2
	No	14	77.8	100.0
	Total	18	100.0	

Table 2: Comparison of ISTH score in DIC groups

		DIC		Total	P-value
		With DIC	Without DIC		
ISTH SCORE	Less than 5	12	67	79	0.000
	Equal or more than 5	13	5	18	
Total		25	72	97	

Table 3: Comparison of Maternal Mortality in DIC groups

		DIC		Total	P-value
		With DIC	Without DIC		
Mortality	yes	5	0	5	0.000
	no	20	72	92	
Total		25	72	97	

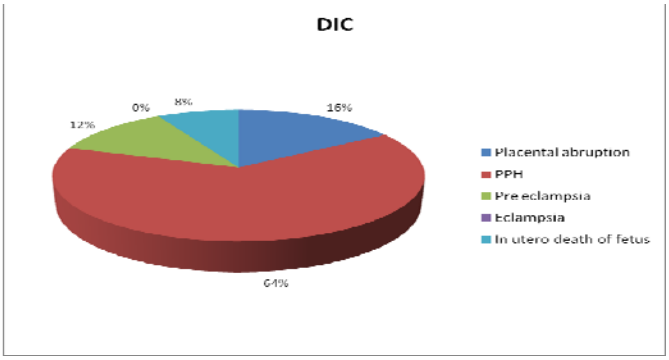

Figure 1: Frequency of DIC in High Risk Obstetric Patient (n=25)

Discussion

DIC is a clinic pathological syndrome which complicates a range of illnesses. It is usually associated with many predisposing clinical conditions. The leading predispositions to development of DIC in our subjects remained PPH followed by abruption of placenta, pre-eclampsia and intra-uterine death. In modern obstetric practice DIC remains the leading complication of PPH, abruption, intrauterine death and haemorrhagic shock with delay in resuscitation leading to endothelial damage. The diagnosis of DIC was made on clinical presentation. The coagulation studies, serial platelet counts and serum fibrin degradation products (FDPs) included in ISTH scoring system were also done.

In our study, majority of patients were young, primigravida except with PPH which was found more common amongst multigravidae. The frequency of DIC due to PPH in our study was found to be 64%. While another study found it to be 46%. [15]

[n] H et al found it 6% in patients with PPH in a study conducted at a local hospital.[16]

In our study population second predisposing cause of DIC was placental abruption and it occurred in 16% of patients. Pitaphrom A determined in her study that DIC occurs in 5.8% of patients as result of placental abruption.[17] The difference in results could be due to non booked status of our patients who came from rural areas with no facilitation of emergency obstetric care. Intrauterine death leading to DIC occurs in (8%) of patients in our study where as it was 14% in a study done by Ansari et al.[18] This difference may be related to very short diagnosis intervention interval and avoidance of conservative approach towards majority of patients, since the triggering mechanism was removed early so less patients developed DIC.

Pre-eclampsia was a predisposition in 12% of our patients which is comparable to another local study.[19] The ISTH Sub-Committee of the Scientific and Standardization Committee (SSC) on DIC has recommended the use of a scoring system for overt DIC.[20]

ISTH scoring system was used in our study and it was calculated for all high risk patients at the time of presentation and that score was found significantly matched with outcome of the patients in term of development of DIC and maternal mortality due to DIC.

Of the high risk obstetric patients with DIC, 5(20%) had maternal mortality. Another study found 6.7% mortality due to DIC in study population. The possible reason for that high mortality rate might be because study was conducted at a tertiary care hospital which received non booked patients with no antenatal care available, lack of transport facilities, illiteracy and lack of awareness. All above mentioned factors contributed towards their late presentation at hospital and hence having their disease already at an advanced stage. There are many recent studies which have recommended that supportive measures and removal of the triggering mechanism are the key to successful management.[21]

Out of these high risk patients, 3(4.3%) with PPH,1(14.2%) with placental abruption and 1(5%) with IUD had maternal mortality due to DIC. It was found 6.2% due to DIC secondary to PPH in one of the study.[22] Ounjai Kor-anantakul mentioned no maternal mortality due to DIC secondary to placental abruption.[29]

The ISTH score at the time of admission was found equal to or more than 5 in 80%of the patients while only 20% patients had score less than 5, so a score of 5 or more was found significantly matched with the outcome in term of maternal mortality in these high risk obstetric patients. A strong correlation between an increasing DIC score and mortality has been demonstrated by several studies. For each DIC point, an increase in the odds of mortality of 1.25 -1.29 have been demonstrated. Several other studies have similarly confirmed that the presence of overt DIC by the ISTH algorithm to be independently predictive of mortality[-23]

Few limitations to our study must be acknowledged. Firstly, this is a hospital based descriptive study, where non-probability convenience sampling was adopted as a method of sampling, which has its own inherent weaknesses.

Secondly, the study was not meant to establish a cause and effect relationship. It being a descriptive study was primarily meant to describe some of the general aspects of the disease. It is definitively recommended that separate epidemiological surveys be carried out to further augment or disapprove our findings.

Conclusion

Disseminated intravascular coagulation is a grave complication in obstetrical population, which increases the maternal mortality and morbidity many folds.

PPH is the major predisposition followed by placental abruption and pre eclampsia. ISTH score equal or more than 5 in high risk obstetric patients has significant association with DIC and maternal mortality associated with it. So on the basis of ISTH score, early diagnosis

with prompt treatment, including a quick decision for surgical intervention, and eradication of predisposing conditions would minimize maternal morbidity and mortality related to DIC.

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