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Research article

INTERNATIONAL SOCIETY ON THROMBOSIS AND HAEMOSTASIS DISSEMINATED INTRAVASCULAR COAGULATION SCORING SYSTEM: IS IT A GOOD PROGNOSTIC INDICATOR IN DIC

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ABSTRACT

Background: Disseminated intravascular coagulation is an acquired disorder characterized by intravascular activation of coagulation due to variety of causes. There is excessive thrombin formation leading to fibrin deposition in microcirculation and consequent ischemic organ damage. The diagnosis is essentially clinical supported by laboratory parameters and a scoring system based on these. The mainstay of treatment is correction of underlying cause and haemostatic support with replacement of coagulation factors. **Aim:** To evaluate the use of ISTH DIC scoring system in patients of clinically suspected Disseminated Intravascular Coagulation. **Methods:** 60 cases were studied over a period of one year. Patients were selected with a clinical suspicion of DIC who are having an underlying predisposing condition. Clinical signs and symptoms were recorded. Routine investigations and the tests necessary to calculate the ISTH score i.e. platelet count, Prothrombin time; D-dimer and Fibrinogen were done. The scoring criteria of ISTH were applied in these cases. Chi square and Fisher's exact tests were used for analysis of the data. **Results:** The commonest cause of the underlying disorder in our study was found to be Sepsis (66.7%) followed by trauma (10%), obstetric causes (8.3%) and solid malignancy (6.7%). There was a significant association of ISTH score with outcome of the patients (P value <0.05). Raised APTT and presence of schistocytes also had a significant association with a high ISTH score. **Conclusion:** ISTH DIC scoring criteria more precisely define clinical and laboratory parameters of DIC. Its clinical utility will improve the timely diagnosis, prediction of severity and will also aid in improving prognosis of DIC patients.

Keywords: Disseminated Intravascular Coagulation, International Society on Thrombosis and Haemostasis, Disseminated Intravascular Coagulation scoring system, Schistocytes, Prothrombin time, Activated Partial Thromboplastin Time

INTRODUCTION

Disseminated Intravascular Coagulopathy (DIC) is a consumptive syndrome that is characterized by simultaneous widespread microvascular thrombosis and profuse bleeding from various sites. It is described as the combination of thrombocytopenia, decreased coagulation factors V and X causing prolonged prothrombin time, together with decreased fibrinogen and increased D-dimer levels. [1] The normal haemostatic balance is disturbed in DIC. There is excessive thrombin formation leading to fibrin deposition in microcirculation and consequent ischemic organ damage. The etiology is multifactorial. A number of medical, surgical, oncological and obstetrical conditions can cause DIC. The diagnosis is essentially clinical supported by laboratory parameters and a scoring system based on

these. The mainstay of treatment is correction of underlying cause and haemostatic support with replacement of coagulation factors. [2] Although hemorrhagic manifestations are more common in DIC, yet it is the diffuse thrombosis that leads to end-organ damage and is associated for most of its morbidity and mortality. DIC is thus a thrombohemorrhagic disorder characterized by procoagulant activation, fibrinolytic activation, inhibitor consumption and biochemical evidence of end organ damage or failure. [3] DIC is divided into overt DIC and non-overt DIC. In overt DIC, the haemostatic system is in decompensated state, and in non-overt DIC, it is in compensated state. [4] There is no single laboratory test that can establish or rule out diagnosis of DIC. A diagnosis of DIC should be made based on appropriate clinical suspicion supported by relevant laboratory tests. Although the general concept of DIC is known to most of the clinicians, a uniform definition of the syndrome and straightforward diagnostic criteria have never been defined. A combination of tests when repeated in a patient with clinically suspected DIC can be used to diagnose the disorder with reasonable certainty in most of the cases. This concept has been taken into consideration by International Society of Thrombosis and Haemostasis (ISTH). [5] The ISTH scoring criteria takes into account Platelet count, Prothrombin time (PT), D-dimer and Fibrinogen while calculating the score. [6] The present study was aimed at evaluating the usefulness of this scoring system for patients with underlying disorder predisposing to DIC as a prognostic indicator.

MATERIAL AND METHODS

Study design: This was a prospective study carried out in tertiary care hospital.

Inclusion criteria: Both paediatric and adult patients were selected with an age range from new born to 80 years and included 35 male and 25 female patients who had a clinical suspicion of DIC and having an underlying condition associated with DIC.

Exclusion criteria: Patients with other hemolytic anaemias such as Hemolytic Uremic Syndrome (HUS) and Thrombotic Thrombocytopenic Purpura (TTP) were excluded from this study.

Study period: 60 cases were studied over a period of 1 year. Ethics committee approval was done as per the protocol and informed consent was taken from the patients. In paediatric patients; consent from the parents was taken.

Methodology: Clinical signs and symptoms of predisposing condition were recorded which is suspected to be leading to DIC i.e. fever, bleeding and/or thrombosis, symptoms and signs of organ failure etc. Along with the routine investigations the tests necessary to calculate the ISTH score i.e. platelet count, Prothrombin time (PT) [7], D-dimer[8] and Fibrinogen[9] were done. The scoring criteria of ISTH were applied in these cases. [6] Apart from these tests, other investigations, such as Activated Partial Thromboplastin Time (APTT) levels, Peripheral Blood Smear for presence of schistocytes were also assessed in these cases.

Blood samples were collected in 3.2 gm% trisodium citrate as anticoagulant (9 : 1 ratio) and immediately centrifuged at 3000 rpm for fifteen minutes in a temperature controlled centrifuge (eppendorf centrifuge 5804 R) at 4^0 C. The Prothrombin Time (Recombiplastin 2G, HemosIL), Activated Partial Thromboplastin Time (SynthASil, HemosIL), fibrinogen (PT derived fibrinogen), and d-dimer (D-Dimer, HemosIL) were evaluated on the ACL Elite Pro analyzer. Platelet counts were obtained on the Coulter LH750 fully automated cell counter using EDTA anticoagulated samples. In house prepared Pooled Normal Plasma (PNP) from 20 healthy individuals (equal number of males and females) as well as commercially available controls were used daily as internal quality control. A DIC score [6] was calculated using the ISTH scoring system. Platelet count more than 100000 per cumm was given a score of 0, between 50000–100000 per cumm score of 1 and less than 50000 per cumm a score of 2. Elevated D-dimer was given the score 0 if there is no increase, 2 if there is moderate increase (400-800 ng/ml), and 3 if there is strong increase (more than 800 ng/ml).

A prolonged PT with respect to daily control of less than 3 seconds was given a score of 0, more than 3 and less than 6 seconds was given a score of 1, and more than 6 seconds was given a score of 2. Fibrinogen level above 100 mg/dl was given a score of 0, and level below 100 mg/dl was given a score of 1. The DIC score was calculated by adding scores for all the four parameters. [6] **Statistical analysis:** Chi square and Fisher's exact tests were used for analysis of the data.

RESULTS

This was a prospective study carried out in Bharati Vidyapeeth Deemed Univerisity Medical College, Pune for a period of one year.

Bleeding (60.0%) was the main clinical feature observed. It was in the form of either mucocutaneous bruising, petechiae or purpura. In obstetric complications, prolonged per vaginal bleeding was observed post delivery. The cases of hematological malignancy presented with gum bleeding. Though the bleeding was the commonest presentation, other presentations like shock (13.3%), end organ failure in the form of renal failure (8.3%), hepatic derangement (8.3%) and respiratory symptoms (6.7%) were also observed in few cases. CNS (1.7%) and embolism (1.7%) were rare manifestations. One case of ovarian malignancy presented with thrombosis.

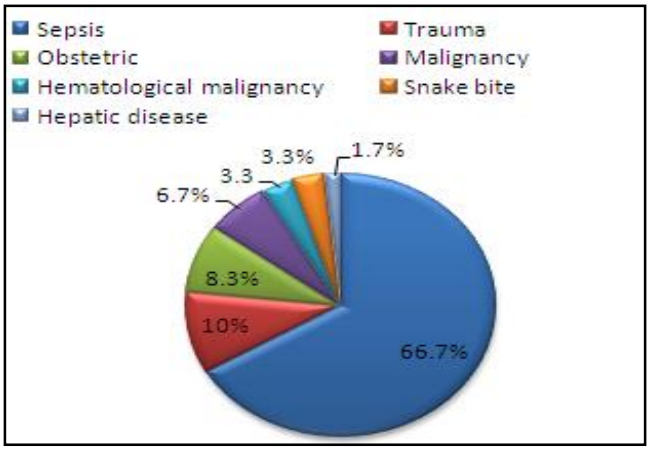

Fig 1: Cause wise distribution of cases

The commonest cause leading to DIC was found to be Sepsis (66.7%) followed by Trauma (10.0%), obstetric causes (8.3%) and malignancy (6.7%). Hematological malignancies, snake bite and other causes were rare in this study.

Out of total 60 patients; 40 (66.7%) patients were found to have an ISTH DIC score of less than 5 which were suggestive of a non-overt DIC or low grade DIC and 20 (33.3%) patients had a score of more than 5 which were consistent with an Overt DIC according to the ISTH scoring criteria.

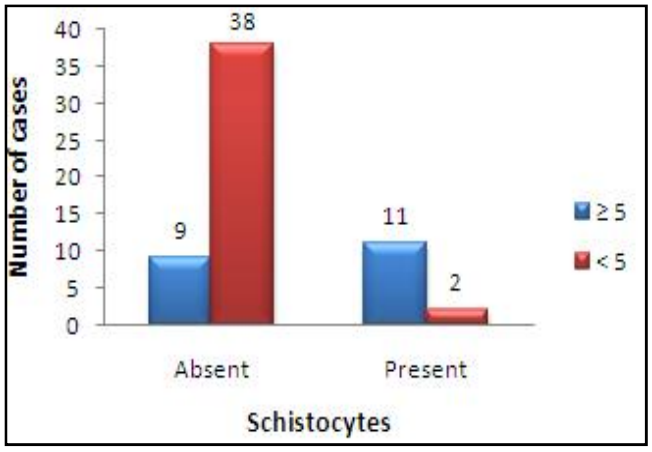

Fig 2: Schistocytes vs ISTH score

Out of 60 cases, 13 (21.7%) patients showed presence of schistocytes. Schistocytes were absent in 47 (78.3%) patients. Presence of schistocytes were seen in 11 patients with high DIC score ≥5 which is statistically significant (p value= 0.001). Schistocytes were seen in only 2 patients with a low DIC score. Schistocytes were present mainly in the cases of sepsis (9 out of 13 cases) followed by 2 cases of eclampsia and one case each of amniotic fluid embolism and Acute Promyelocytic Leukemia.

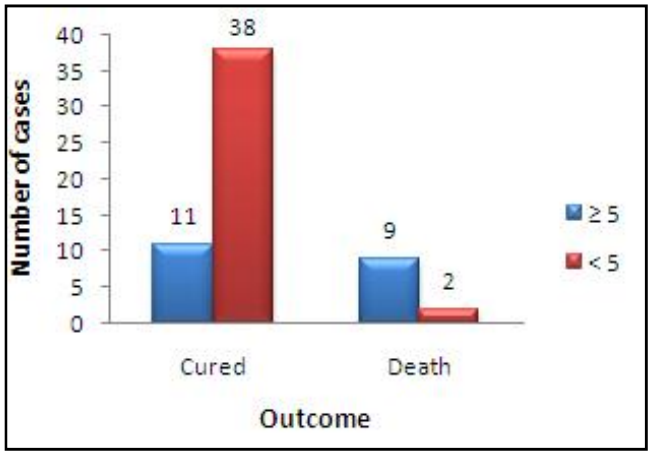

Fig 3: Outcome of patients vs ISTH score

There was a significant association of the outcome of the patients with the ISTH DIC score. A high score ≥ 5 was associated with a poor outcome in 9 patients (45%). Out of these 9 patients; five patients had underlying cause as sepsis (56%), two patients had obstetric complications and one patient each with APML and solid malignancy. Low DIC score was associated with increased chances of survival (P value= 0.001). Two out of forty patients who had a low score succumbed to the disease process itself rather than to DIC.

The APTT levels were also included in this study though they were not a part of ISTH score to see their association with ISTH score. APTT levels were

raised in 40 out of total 60 cases. In 18 out of 20 patients of high (≥ 5) DIC score; APTT levels were increased which was statistically significant (p value=0.008). Raised APTT levels showed a good correlation with high DIC score (≥5) and thus patient's outcome.

DISCUSSION

The present study "International Society on Thrombosis and Haemostasis Disseminated Intravascular Scoring System: Is it a good prognostic indicator in DIC?" was carried out for a period of one year in Bharati Vidyapeeth Deemed University Medical College, Pune. No single test is sufficiently accurate to establish or rule out a diagnosis of DIC. ISTH DIC scoring system for overt DIC uses a combination of commonly done laboratory tests and can be used widely in intensive care units. Although the cases of sepsis dominated the number over all other predisposing conditions, Obstetric causes, trauma and malignancy were also seen leading to DIC. The underlying conditions predisposing to DIC are frequently unsuspected and are frequently underestimated. DIC is usually associated with several predisposing clinical conditions. In our study, Sepsis (66.7%) was found to be the main underlying cause leading to DIC. Similar incidence was observed by Siegal et al and Spero et al. Siegal et al[10] who have studied the medical records of 118 cases who met laboratory criteria of DIC. Van Bunderen et al[11] have studied the association of DIC and solid tumours. They have found that it is rare but has been known for decades.

Presence of schistocytes were seen in 11 patients with high DIC score ≥5 which is statistically significant (p value= 0.001). Schistocytes were seen in only 2 patients with a low DIC score. Schistocytes were present mainly in the cases of sepsis (9 out of 13 cases) followed by 2 cases of eclampsia and one case each of amniotic fluid embolism and Acute Promyelocytic Leukemia. In agreement with our study, schistocytes have been described in most patients with DIC after septicemia by Levi M et al. [12] However Visudhiphan et al[13] did not find any difference between patients of sepsis with or without DIC. In the present study; there was a significant association of the outcome of the patients with the ISTH DIC score (P value< 0.001). A high score ≥ 5 was associated with a poor outcome in 9 patients (45%). Out of these 9 patients; five patients had underlying cause as sepsis (56%), two patients had obstetric complications and one patient each with APML and solid malignancy. Pati et al[14] found that Survival was better in patients in whom DIC was precipitated by obstetric causes compared with those with septicemia ($P < 0.01$). Spero et al[15] had analyzed 346 cases of disseminated intravascular coagulation (DIC). They have found an overall mortality of 68% which further confirms the dismal prognosis previously associated with DIC. Bakhtiari et al[16] analyzed 660 samples from 217 consecutive patients. The prevalence of DIC was 34%. According to them, there was a strong correlation between an increasing DIC score and 28-day mortality.

Limitations of the Study: ISTH recommends daily scoring in case of overt DIC and repeat scoring 1-2 days for non overt DIC. ISTH DIC scoring system also recommends follow up scoring and use of additional tests like Protein C, Antithrombin and Thrombin anti-thrombin complexes as another algorithm for non-overt DIC when one gets a DIC score of less than 5 with the initial scoring done by using algorithm for overt DIC. These tests were not done in our study.

CONCLUSION

Disseminated intravascular coagulation is a common complication secondary to a variety of clinical conditions. Its early diagnosis is the key for better outcome of the patient. There is a significant association of a high ISTH score with the outcome of the patient. Serial monitoring of ISTH DIC score in cases of low score i.e. < 5 should be done which will help in assessing the improvement or worsening of the patient's condition. Presence of schistocytes is not a clue test for initial diagnostic workup of DIC but, it might be of clinical value to suggest an associated thrombotic microangiopathy if found in significant numbers. In order to improve the prognosis of DIC, it is important to diagnose the condition accurately and as early as possible. ISTH DIC scoring criteria more precisely define clinical and laboratory parameters of DIC and its clinical utility will help for accurate diagnosis and monitoring of the patients.

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Conflict of Interest: Nil

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