COAGULOPATHY IN CRITICALLY ILL PATIENTS

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ABSTRACT

BACKGROUND

Bleeding diathesis and coagulopathies are common in critically ill patients. Patients may have clinical bleeding or only laboratory abnormalities in haemostatic tests.

Aims- To determine the incidence and types of bleeding diathesis that commonly occur in our medical ICU.

Settings and Design- 50 patients were studied who were admitted in IMCU, IIM, RGGGH.

Study Design- Observational study.

MATERIALS AND METHODS

The patients included in this study were those with any medical illness admitted to the ICU for > 48 hours, who had no primary haematological disease at the time of admission. Patients have their history taken and subjected to clinical examination and investigations. The following tests of haemostasis are done only once: Platelet count and peripheral smear, PT (Prothrombin time), aPTT (activated Partial Thromboplastin Time), Fibrinogen and D-dimer. The results were tabulated and analysed.

RESULTS

Thrombocytopenia was the most common coagulation abnormality seen in 46% of the study population. More than half of the patients who had abnormal coagulation parameters had clinical bleeding. Melena was the most common bleeding manifestation. No patient had life-threatening bleeding; 10 out of 50 patients studied had aPTT prolongation with 2 patients having combined PT and aPTT prolongation. No patient had hypofibrinogenaemia, but 17 patients had hyperfibrinogenaemia. Sepsis ranks first in causing coagulopathy, followed by liver failure and antithrombotic drugs.

CONCLUSION

A rationale approach must be developed in treating critical care patients with abnormal coagulation parameters. Too much aggressive transfusions can do more harm than good. A good clinical judgement is required along with the current knowledge for treating such patients.

KEYWORDS

Coagulopathy, Critical Care, Sepsis.

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BACKGROUND

Bleeding diathesis and coagulopathies are common in critically ill patients. Patients may have clinical bleeding or only laboratory abnormalities in haemostatic tests. Thrombocytopenia, prolongation of PT or aPTT or both, low fibrinogen and increased fibrin degradation products are the usual abnormalities. The mortality is higher in ICU patients with bleeding tendency. These abnormalities can be independent predictors of survival.

Our study aimed at determining the incidence and types of bleeding diathesis that commonly occur in our medical ICU. Patients were screened for bleeding diathesis by the following tests- platelet count, peripheral smear, PT, aPTT, D-dimer and Fibrinogen irrespective of the presence of clinical bleeding. The incidence and the type of abnormality in the

haemostatic tests and the underlying probable causes for the bleeding tendency were identified in this study.

MATERIALS AND METHODS

The study was conducted in Intensive Medical Care Unit (IMCU), Institute of Internal Medicine, Madras Medical College, Rajiv Gandhi Government General Hospital, Chennai-600003 during the period between March 2014 and August 2014. The laboratory work was done with the help of the Haematology Department, MMC and RGGGH.

50 patients were studied who were admitted in IMCU, IIM, RGGGH. A patient is said to have a coagulopathy if he/she has either one or more combination of following abnormalities- Thrombocytopenia (less than 1 lakh cells/cu.mm), Prolonged PT and Prolonged aPTT.

Inclusion Criteria

1. Patients with any medical illness admitted to ICU who do not have primary haematological disease at the time of admission.
2. Patient should have been in ICU for a minimum of 48 hours.

Exclusion Criteria

1. Patients who have already known haematological disease.
2. Surgical ICU patients (e.g. trauma patients).

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RESULTS

The highest number of critical care patients (21) were in the age group of 13 to 39 years. There were 18 and 11 patients in the age groups 40 - 59 and 60 - 89 years respectively. Total number of patients studied were 50. All the patients were admitted in medical ICU. Majority of the patients in our study were males (31). Females were 19 in number.

Coagulation abnormality was considered as either decrease in platelet count or increase in PT or aPTT in our study. D-dimer and fibrinogen can be elevated non-specifically in sepsis and other critical conditions. Majority of haemostatic abnormalities occurred in the largest group, i.e. 13 - 39 years.

Serum creatinine of more than 1.5 was considered as renal failure for the study purpose. 30 percent of ICU patients in our study had renal failure.

Out of 15 patients with renal failure, 7 people had abnormal coagulation parameters.

Out of 50 study patients, 43 patients had normal liver function test parameters and 7 had deranged LFT. The coagulation abnormality was seen in almost all patients with deranged LFT. Commonest bleeding was in the form of melena followed by haematemesis and oral cavity bleed in our study.

Anaemia was based on peripheral smear, which showed microcytic hypochromic anaemia in 36 out of 50 patients. Remaining 14 patients showed normal study.

Thrombocytopenia was the most common coagulation abnormality in ICU patients. In our study, 46% of study population were found to have thrombocytopenia. In critically ill patients, cut-off value of 1,00,000 cells/cu.mm can be used instead of the usual 1,50,000, as there is no significant bleeding tendency to occur between these cut-off values.

Majority of patients (13) had platelet counts between 80,000 and 1 lakh, which may not cause major bleeding per se. Three patients had platelet count between 20,000 and 49,000 cells/cu.mm. Only one patient had platelet count less than 20,000 cells/cu.mm. More than half of the patients who had abnormal coagulation parameters had clinical bleeding. Melena was the most common bleeding manifestation followed by skin bleed. No patient in our study had life-threatening bleeding episode.

In our study, six patients were on antithrombotics. Out of six, four patients developed clinical bleeding. Heparin was the frequent drug that was used. Out of fifty patients studied, 3 patients had PT prolongation. Out of fifty patients studied, 10 patients had aPTT prolongation. None of the study patient had hypo-fibrinogenaemia. 17 patients had hyper-fibrinogenaemia, i.e. fibrinogen levels > 450 mg/dL. Out of fifty patients, only 2 patients had combined PT and aPTT prolongation. Almost majority of patients (43) had D-dimer positivity. Like fibrinogen D-dimer results should always be

interpreted along with other coagulation tests. Only one patient had thrombocytopenia + PT and aPTT prolongation + D-dimer positivity. That patient had developed DIC secondary to Sepsis.

As in any other ICU patients, sepsis ranks first in causing coagulopathy followed by liver failure and antithrombotic drugs and renal failure. We did not have any case of immune-mediated thrombocytopenia.

Age (in Years)	Total No. of Patients in each Age Group	No. of Patients with Coagulation Abnormality	(%)
13 - 39	21	13	62
40 - 59	18	9	50
60 - 89	11	4	36

Table 1

Coagulation Abnormality	N = 50
Thrombocytopenia	23
PT-INR prolongation	3
aPTT prolongation	10
Both PT and aPTT prolongation	2
D-dimer elevation	43
Hyperfibrinogenaemia	17
Thrombocytopenia + PT and aPTT prolongation + D-dimer positivity	1

Table 2

Aetiology of Coagulopathy	No. of Patients
DIC	1
Sepsis	8
Liver disease	4
Renal disease	3
Antithrombotic drug induced	4
Immunological thrombocytopenia	0
Others	6

Table 3

DISCUSSION

Coagulopathy is common in critically ill patients. The spectrum varies from mild abnormality in coagulation parameters to life-threatening bleeding. Almost half the patients had coagulopathy in our study. The incidence was higher in the younger age group, as they form the majority.

Thrombocytopenia

It is the most common coagulation abnormality that occurs in critically ill patients.¹ Thrombocytopenia can be due to decreased production or increased destruction or sequestration. Platelets are the first line of defence when endothelium is breached. Highest incidence occurs in cases of sepsis. First and foremost problem is spurious thrombocytopenia, which should be ruled out before evaluating any patient with thrombocytopenia. We should always confirm thrombocytopenia by looking at the peripheral smear.

ICU patients with thrombocytopenia have poor prognosis when compared with patients who have normal platelet counts.² It is not necessary to treat all patients with thrombocytopenia. At the same time, we should not miss serious conditions like heparin-induced thrombocytopenia and thrombotic microangiopathy. Each condition needs different treatment modalities.

Current studies state that if patient is haemostatically stable and has thrombocytopaenia, platelet transfusion can be withheld till the count drops less than 10,000 cells/cu.mm.³ If the patient is actively bleeding, platelet count should be maintained above 50,000 cells/cu.mm. For neurosurgical procedures, count should be maintained above 1,00,000 cells/cu.mm.⁴

Nearly, half the study population exhibited thrombocytopaenia and majority of them had their platelet counts between 80,000 and 1,00,000 cells/cu.mm, which is less likely to cause major bleeding episode. This study confirms with previous studies that thrombocytopaenia is the most common coagulation abnormality.

Sepsis Related Coagulopathy

Sepsis related coagulopathy can vary from mild laboratory abnormality in the coagulation parameters to Disseminated Intravascular Coagulation (DIC). There is a complex interplay between haemostatic mechanisms that can either lead to a bleeding tendency or can also present with thrombosis. Development of DIC is a poor outcome predictor of sepsis.⁵ Dysfunctional anticoagulant pathway and fibrinolytic system and platelet activation are responsible for sepsis related coagulopathy.

Liver Disease and Coagulopathy

Decompensated chronic liver disease is usually thought as a Haemorrhagic coagulopathy. Coagulation system in liver disease is complex. It is a dynamic process of haemostasis. There is decreased production of factors II, V, VI, IX, X, XI, XIII, fibrinogen, protein C, protein S and vitamin K.

Hence, there is a decrease in both procoagulant and anticoagulant proteins. It is also a hyperfibrinolytic state. Increased FDP and thrombocytopaenia occur. Test results may be suggestive of a bleeding tendency. The haemostatic balance can be tipped off either way by precipitating factors like renal failure, infections, etc. 10 mg parenteral vitamin K can be given for 3 days for DCLD patients routinely. FFP should not be given routinely to DCLD patients who have abnormal coagulation parameters in the absence of clinical bleeding. Melena was the most common clinical bleed that we noted. Almost all patients with chronic liver failure in our study had bleeding diathesis.

Coagulopathy in Renal Disease

Platelet dysfunction in uraemia can be due to uraemic toxins, altered platelet granules, dysfunctional vWF and decreased Thromboxane. Usual clinical manifestations would be epistaxis, petechiae and bleeding from local site. Peritoneal dialysis, conjugated oestrogen, desmopressin, erythropoietin are all useful for improving bleeding time. Nearly, 50% of renal failure patients in our study had coagulopathy. 70% of patients had anaemia, which can contribute to bleeding tendency by loss of laminar blood flow.

Common Antithrombotic Drugs used in ICU

Aspirin

It is an antiplatelet drug that irreversibly inhibits cyclooxygenase enzyme. Its effect can persist up to days even

though the half-life is 20 mins. Platelet transfusion is the procedure for immediate reversal.

Clopidogrel

It is a P2Y₁₂ antagonist that is metabolised by the liver and has a half-life of six to fifteen hours. Platelet transfusion is the procedure for immediate reversal.

Unfractionated Heparin

It has indirect anti-Xa and anti-IIa effect. It also increases the action of antithrombin by a factor of 10,000. Its half-life is forty-five to ninety minutes. Protamine at a dose of 1 mg neutralises 100 units of unfractionated heparin.

Low Molecular Weight Heparin

Action is same as unfractionated heparin, but mainly Xa effect. It is cleared by the kidneys and half-life is around 4 hours. Protamine neutralises sixty percent of its effect. In case of life-threatening bleeding, use recombinant factor VII.

Vitamin K Antagonists

It reduces functional levels of vit K dependent clotting factors.⁽²⁾ It is metabolised by the liver. Antidotes are vit K parenteral and prothrombin complex concentrates. If prothrombin complex concentrates are not available use FFP.

Antithrombotic drugs were given only to 6 patients in our study, out of which 4 had clinical bleeding thus emphasising that antithrombotic drugs can create trouble when a critical care patient is planned for an invasive procedure. Melena was the commonest bleeding.

Disseminated Intravascular Coagulation

Disseminated Intravascular Coagulation (DIC) is a clinic pathologic syndrome, in which extensive intravascular coagulation occurs as a result of exposure or production of procoagulants inadequately balanced by natural anticoagulant mechanisms and intrinsic fibrinolysis. Disturbance of the endothelium in the microcirculation along with inflammatory cells and release of inflammatory cytokines play a key role in the mechanism of DIC.

Only one patient had thrombocytopaenia along with prolonged PT and aPTT who had DIC secondary to Sepsis. Such patients show dismal outcome. Nearly, 86% had D-dimer positivity. But only the patient with thrombocytopaenia and prolonged PT and aPTT was considered to have DIC. D-dimer can be elevated non-specifically in fibrinolytic conditions like liver disease, inflammation, pregnancy and trauma.

Fibrinogen was not low in any of the patient. Instead, we had elevated fibrinogen in 30% of study population which shows that fibrinogen can be elevated in conditions like chronic inflammatory states like atherosclerosis, sepsis and pregnancy. D-dimer and Fibrinogen should be interpreted only with other coagulation parameters. In our study, only one patient has significant D-dimer positivity who developed DIC secondary to sepsis.

The main aim of the study was to study the incidence and type of coagulation abnormality that occurs in critically ill patients in the ICU setup in RGGGH. We also had a secondary objective to study the common aetiologies behind these coagulopathies in ICU patients.

Melena was the most common clinical bleed that we noted. Antithrombotic drugs were given only to 6 patients in our study, out of which 4 had clinical bleeding, thus emphasising that antithrombotic drugs can create trouble when a critical care patient is planned for an invasive procedure.

Only 3 out of 50 and 10 out of 50 patients had PT and aPTT prolongation respectively. Only 2 patients had prolongation of both PT and aPTT. This shows that abnormal PT, aPTT are not so common in ICU patients.

Only one patient had thrombocytopenia along with prolonged PT and aPTT, who had DIC secondary to Sepsis. Such patients show dismal outcome. Nearly, 86% had D-dimer positivity. But only the patient with thrombocytopenia and prolonged PT and aPTT was considered to have DIC. D-dimer can be elevated non-specifically in fibrinolytic conditions like liver disease, inflammation, pregnancy and trauma.⁶

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D-dimer and Fibrinogen should be interpreted only with other coagulation parameters.⁷ In our study, only one patient has significant D-dimer positivity who developed DIC secondary to sepsis.

Regarding the aetiology behind coagulopathy sepsis was found to be the leading cause for coagulopathies, which goes along with previous studies done in critical care patients.

Renal failure and liver failure are next in line to cause coagulopathy. Use of antithrombotics is also a significant cause of bleeding tendency in our study. We did not encounter any case of immune mediated thrombocytopenia like TTP, which requires prompt recognition.

CONCLUSION

The Inferences that this Study brought

1. Coagulopathy is common in critical care patients.

2. Thrombocytopenia is the commonest abnormality in haemostatic workup.
3. Sepsis is the major cause for abnormal coagulation, which can lead to DIC in critical care patients.
4. Use of antithrombotic drugs in critical care patients can be troublesome when an invasive procedure is planned.

A rationale approach must be developed in treating critical care patients with abnormal coagulation parameters. Too much aggressive transfusions can do more harm than good. A good clinical judgement is required along with the current knowledge for treating such patients.

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