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The Study of Coagulation Parameters in Polytrauma Patients and Their Effects on Outcome

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Abstract

Background: Mortality from trauma remains a major public health issue as it is the leading cause of death in persons aged 5 - 44 years. There is a dearth of information on polytrauma from developing countries such as ours. Hence, this topic was studied at our institute. The objective is to study the coagulation parameters in polytrauma patients at our institute and to correlate the findings with the prognosis.

Methods: A prospective study was carried out in the department of pathology in a tertiary care center, during a period of 20 months from December 2012 to July 2014. All the polytrauma patients (injury severity score (ISS) ≥ 15) with injuries to head and neck, face, thorax, abdomen, extremities and external (skin) were included. Sampling was done within 20 min of arrival during primary survey of the patient. Screening tests like bleeding time (BT) and clotting time (CT) were carried out bedside. Other tests carried out were complete blood count (CBC), prothrombin time (PT), activated thromboplastin time (aPTT), thrombin time (TT) and D-dimer assay. Tests were carried out on fresh samples within 2 h of collection.

Results: The incidence of coagulopathy was 59.86%. There was significant prolongation of PT, aPTT and TT in those patients who developed coagulopathy. PT was found to be a stronger predictor of mortality among polytrauma patients.

Conclusion: A significant proportion of polytrauma patients were coagulopathic. Initial coagulation profile is very useful in predicting outcomes for major polytrauma patients. This study emphasizes the importance of early suspicion and basic screening for coagulopathy in polytrauma patients in developing countries.

Keywords: Polytrauma; Coagulopathy; Prognosis

Introduction

Trauma is a serious global health problem, accounting for approximately 1 in 10 deaths worldwide [1]. Recent reports suggest that injuries contribute to 13-18% of total deaths in India [2]. It is very important to know and keep in mind that the basic aim of total trauma care concept is "to get the patient to the right hospital at the right time". Shock, hemorrhage and associated injuries are the usual complications which accompany trauma [3]. Patients, who arrive in the emergency department with a coagulopathy, are three to four times more likely to die and eight times more likely to die within the first 24 h. Coagulopathy on admission is not restricted to mortality only, but also associated with other poor outcomes of trauma like acute renal injury, acute lung injury, increased transfusion requirements and long hospital stays [4]. These clinical observations together with recent research resulted in a new appreciation of the central role of coagulopathy in acute trauma care. Even then, coagulation profiles are not routinely done among trauma patients in resource-limited settings and there is a paucity of data regarding this. The study is carried out keeping in mind the dearth of information on polytrauma from developing countries and with the objective to study its association with outcome.

Materials and Methods

Study design

The present study is a prospective study carried out in the department of pathology in a tertiary care center, during a period of 20 months from December 2012 to July 2014. Ethical clearance was obtained prior to commencing the study.

Study setting

On arrival in the casualty, all major trauma patients were triaged and immediately transferred to examination rooms where they were attended by doctors who instituted management in trauma care unit after history taking and examination. Polytrauma or multisystem trauma is defined as severe injury to more than one physical region or organ system, one of which will be life-threatening [5]. Abbreviated injury score (AIS90/ISS) was used to score the severity of injuries of the trauma patients with multiple injuries and were classified as polytrauma patients having at-least two body regional injuries with injury severity score (ISS) ≥ 15. Detailed history, important clinical

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findings and relevant investigations were noted as per case proforma.

Eligibility criteria

All the polytrauma patients (ISS ≥ 15) with injuries to head and neck, face, thorax, abdomen, extremities and external (skin) were included. Exclusion criteria were: patients with prior history of bleeding or coagulation abnormalities, history of intake of drugs like warfarin, epinephrine or any drug-inducing coagulopathy, patients with known systemic disorders causing coagulopathy like systemic lupus erythematosus, etc., history of liver disease (like cirrhosis) or any renal impairment, history of solid or hematological malignancies, patients who have already received blood transfusion or > 2 L of intravenous fluid administration after trauma and before sampling, and patients admitted for obstetric causes or elective surgeries. Trauma scoring systems like ISS and Glasgow coma scale (GCS) were used to define the severity of trauma and the extent of severity of head injury, respectively. The outcome in terms of survival at the time of discharge was measured in the form of patients who survived and who expired. Thus, the relationship of coagulopathy with indicators of morbidity and mortality was studied.

Procedures

Sampling was done within 20 min of arrival during primary survey of the patient. Screening tests like bleeding time (BT) and clotting time (CT) were carried out bedside. Other tests carried out were complete blood count (CBC), prothrombin time (PT), activated thromboplastin time (aPTT), thrombin time (TT) and D-dimer assay. Tests were carried out on fresh samples within 2 h of collection.

Data analysis

Coagulopathy was defined as PT >18 s (or INR >1.2) and/or aPTT > 36 s [4, 6, 7]. Coded data were entered in Microsoft® Office Excel 2010 and SPSS® statistical software version 21 and analyzed. Relationships between categorical variables were established using chi-square test. Relationship between quantitative variables was established using *z*-test for mean between two samples and Student's *t*-test of two samples assuming unequal variances, whichever applicable. Correlations were established using Spearman's rank correlation coefficient (r^2) and *t*-test of probability for correlation coefficient. The multiple logistic regression analysis was used to ascertain the association between the initial coagulation parameters and overall hospital mortality. The results were considered statistically significant when "P" value was ≤ 0.05.

Results

Among the total 142 polytrauma patients studied, 85 patients developed coagulopathy. The incidence of coagulopathy was 59.86% (Table 1).

In our study, the maximum number of (37) cases were from 21 - 30 years of age group (26.06%). The age range was 3 - 80 years. One hundred sixteen (81.69%) patients were male. Among the coagulopathic polytrauma patients, 65 (76.47%) were male; while among polytrauma patients who did not develop coagulopathy, 51 (89.47%) were male. Blunt injury was observed in majority of the patients. In our study, there was no significant difference in mean age of presentation, male sex predominance and the incidences of blunt injury between polytrauma patients who developed coagulopathy and those who did not.

BT was seen elevated in 8 (5.63%) patients. Four of them had coagulopathy. Thrombocytopenia was associated with six of these patients; four out of them developed coagulopathy. CT was seen elevated in 13 (9.15%) patients. All of them developed coagulopathy.

We observed that, while there was significant prolongation of PT (and INR), aPTT and TT along with significant reduction in mean platelet count in those who developed coagulopathy than those who did not, the incidence of thrombocytopenia was not significantly affected. We found that D-dimer levels were raised in 17 polytrauma patients; all of them had coagulopathy. The average value of D-dimer in coagulopathic polytrauma patients was 1,505.88 ± 992.77 ng/mL (range: 200 – 3,200 ng/mL).

Comparison of different coagulation parameters with each other among coagulopathic polytrauma patients

Among total 85 coagulopathic polytrauma patients, abnormal aPTT values were seen in 82 (96.47%) patients and abnormal PT/INR values were seen in 42 (49.41%) patients. Twenty (24.71%) patients showed elevated TT values, while raised D-dimer levels were seen in 17 (20%) patients. Out of total 85 coagulopathic polytrauma patients, 39 (45.88%) patients had both abnormal aPTT and PT values. The isolated abnormal aPTT values were seen in 43 (50.59%) patients, while isolated abnormal PT values were seen in 3 (3.53%) patients.

There was significantly higher number of coagulopathic polytrauma patients showing abnormal aPTT values than abnormal PT values ($P < 0.001$). PT had strong and positive correlation with aPTT values (Spearman's rank correlation coefficient $r^2 = 0.506$; $P < 0.001$).

Impact on prognosis

The mortality rate was significantly much higher in polytrauma patients who developed coagulopathy than who did not. We found PT, aPTT and D-dimer were independent predictors of mortality, while platelet count was not. PT was found to be a stronger predictor of mortality among polytrauma patients than aPTT and D-dimer.

While significantly longer stay in hospital, higher values of ISS and more transfusion requirement were observed in co-

Table 1. Comparison of Various Parameters Among Polytrauma Patients

Parameter	All polytrauma patients (n = 142)	Coagulopathic polytrauma patients (n = 85)	Polytrauma patients without coagulopathy (n = 57)	"P" value
Mean age of presentation (years)	38.92 ± 17.81	40.06 ± 17.22	37.21 ± 18.69	0.36
Male to female ratio	4.46:1	3.25:1	8.5:1	0.45
Incidence of blunt injury (%)	91.55	92.94	89.47	0.86
Incidence of thrombocytopenia (%)	14.79	18.82	8.77	0.18
Mean platelet count ($\times 10^3/\mu L$)	208.21 ± 116.22	191.88 ± 124.65	232.56 ± 98.47	0.02
Mean value for PT (s)	19.7 ± 10.8	24.0 ± 12.2	13.2 ± 1.0	< 0.001
Mean value for aPTT (s)	43.2 ± 15.1	53.5 ± 10.7	28.0 ± 2.4	< 0.001
Mean value for TT (s)	17.5 ± 3.9	18.4 ± 4.8	16.2 ± 1.3	< 0.001
Mortality (%)	43.66	62.35	15.79	< 0.001
Mean time delay between injury and hospital admission (h)	6.09 ± 3.53	7.34 ± 3.63	4.22 ± 2.37	< 0.001
Mean length of hospital stay (days)	6.64 ± 10.52	7.85 ± 13.08	4.84 ± 4.03	0.02
Glasgow coma scale	11.25 ± 4.69	9.68 ± 5.10	13.58 ± 2.67	< 0.001
Injury severity score	33.65 ± 14.11	40.29 ± 14.67	23.75 ± 3.47	< 0.001
Number of patients transfused (%)	42.25	26.76	15.49	0.04
Hemoglobin (g/dL)	9.56 ± 2.74	8.00 ± 1.72	11.88 ± 2.30	< 0.001
Hematocrit (%)	34.63 ± 7.54	29.43 ± 3.85	42.39 ± 4.33	< 0.001

agulopathic polytrauma patients, GCS, hemoglobin (Hb) and hematocrit (Hct) levels were significantly lower in them.

There was independent and strong positive correlation was seen between PT and ISS (Rs = 0.691; P < 0.001); aPTT and ISS (Rs = 0.651; P < 0.001); PT and GCS (Rs = -0.438; P < 0.001) and aPTT and GCS (Rs = -0.448; P < 0.001). The correlation between PT with ISS and aPTT with GCS was stronger.

Discussion

The incidence of coagulopathy among the 142 polytrauma patients studied by us was 59.86%. Our findings are comparable with Mujuni et al [4] who also reported more number of coagulopathic patients in their studies. Maegele et al [8], Rugeri et al [9] and Shaz et al [10] reported slightly lower incidences. This may be due to differences in the characteristics of the study population and varying severity of trauma.

Majority of the important works, tasks and travelling chores are performed by the younger population [11]. Clearly, risk-taking behavior involving transportation with/without alcohol, more prevalent in younger males, conveys a higher likelihood of injury [12]. Gender-based differential outcomes in the setting of trauma have been well documented [13]. The gender difference is probably related to both exposure and risk taking behavior. Globally, trauma is the leading cause of death in persons aged 5 - 44 years [4]. Our findings related with age and gender-based differences are consistent with the studies of MacLeod et al [14], Matar [15], Kanna et al [3], Mujuni et al [4], Shaz et al [10] and Brown et al [13].

The prognostic factors in the patients, who suffer multiple injuries, are influenced by the timely surgical interventions, specifically in patients with blunt abdomino-thoracic and head injuries [11]. Unlike penetrating, where hemorrhage may be localized and take the form of a distinct vascular damage, patients severely injured due to blunt trauma may have diffuse abdominal bleeding caused by extensive organ injuries. Majority of the patients in our study had blunt injuries, regardless of those who developed coagulopathy or not. The incidence and comparison of blunt injury in coagulopathic and non-coagulopathic groups in our study is comparable with those of Davenport et al [16], Mujuni et al [4], Mica et al [17] and Shaz et al [10].

Bleeding times are difficult to perform and not predictive of bleeding [18]. It has been hypothesized that the main reason for the lack of a relationship between the cutaneous bleeding time and surgical bleeding lies in the multiple determinants of surgical bleeding, which might obscure, by their preponderant weight, the possible predictive capacity of the bleeding time test. Both the bleeding time and the clotting time tests have gone to disrepute because of inherent fallacies in the tests [19]. Like us, Davenport et al [16] too noted no significant difference in the CT values in coagulopathic and non-coagulopathic polytrauma patients.

In trauma patients, platelet quantitative abnormality (thrombocytopenia) is seen more frequently than qualitative abnormality [20]. Infusion of large volumes of crystalloid and colloid during resuscitation reduces the concentration of platelets and coagulation factors [1]. The occurrence of thrombocytopenia during hypothermic bleeding has been known for many years. The incidence of thrombocytopenia, mean platelet count and its significant reduction in coagulopathic polytrauma patients in our study are comparable with studies by Kanna

et al [3], Davenport et al [16], Shaz et al [10], Chandler [21], Rugeri et al [9] and Sixta et al [22]. MacLeod et al [14], however, reported a lesser incidence (3%) of thrombocytopenia in their study. This difference may be due to diversity in the magnitude of injury and differences between the average times of arrival of the patients.

The pathogenesis of coagulopathy in trauma patients is complex. The causes are multifactorial. The major causes of coagulopathy in trauma patients are: blood loss, hypocalcemia, hypothermia, coagulation-compromising effect of colloids, impaired functions of platelets and coagulation factors, dilution of coagulation factors and platelets, consumption of platelets and coagulation factors [1]. The key stimulus for coagulopathy is tissue trauma. Because the liver is the source of most coagulation proteins, severe liver injury or significant shock results in failure of the body to compensate for consumption of coagulation factors [18]. Traumatic injuries vary widely in the amount of associated tissue damage. Crush or explosion injuries may carry an enormous tissue injury load, whereas lethal penetrating trauma may have very little associated tissue damage, yet coagulopathy may be a feature of both clinical pictures [23]. Trauma is associated with increased fibrinolytic activity [24]. Our findings for abnormal PT/INR and aPTT values are in accordance with studies by MacLeod et al [14], Sixta et al [22], Kanna et al [3], Shaz et al [10], Chandler et al [21] and Brown et al [13]. Slightly lower incidence of abnormal aPTT values was observed by Mujuni et al [4] and Kanna et al [3] in their studies. The differences in values might be due to diversity in selection of patients, difference in severity of injuries between these studies and ours. The lower incidences of elevated aPTT in the studies by Johanssen et al [7], MacLeod et al [14] and Sixta et al [22] might be attributed to less overall incidence of coagulopathy in them. Comparable with our study, Shaz et al [10] too noted strong and positive correlation between PT and aPTT.

Fibrin split products are detectable in 80% of trauma patients in the intensive care unit (ICU). Johanssen et al [7], Rugeri et al [9] and Davenport et al [16] reported a significant difference in D-dimer levels in coagulopathic and non-coagulopathic trauma patients which are comparable with our study. Kanna et al [3] reported much higher incidence of raised fibrin degradation product (FDP) and D-dimer levels in their study (51.79%). This may be due to different incidences of severity of injury, secondary complications in hospitalized trauma patients like deep vein thrombosis, pulmonary thromboembolism, acute cerebrovascular accident, pneumonia and so on.

Development of coagulopathy contributes significantly to morbidity and mortality in the patient with trauma. The ability to determine whether the trauma patient at admission is coagulopathic or not, is a single most important predictor of outcome [4]. In our study, the mortality was significantly more in coagulopathic group. These findings correlate with the studies of Johansson et al [7], Mujuni et al [4], Brown et al [13] and MacLeod et al [14].

We found PT, aPTT and D-dimer were independent predictors of mortality, while platelet count was not. Macleod et al [14] in their study, too, found that PT and aPTT were independent predictors of mortality. They also concluded that the prothrombin time and APACHE-II score most effectively predicted early death in polytrauma patients and platelet count was not found as the predictor for mortality. Shaz et al [10] noted that PT was significantly associated with mortality and association of aPTT and mortality was insignificant. Mujuni et al [4] found aPTT to be a stronger predictor of mortality than PT in their study.

In our study, the mean time delay between injury and hospital admission for polytrauma patients with coagulopathy was significantly higher than for those who did not develop coagulopathy ($P \leq 0.001$). In the study by Mujuni et al [4] (from Uganda), the average time from injury to admission for coagulopathic patient was 4 and 3.6 h for non-coagulopathic patients ($P = 0.05$). This time delay is likely to be far less in developed countries with better trauma infrastructure and emergency transportation services. Thus, it could possibly be a contributing factor in the increased incidence of coagulopathy in our study as compared to some others, a point concurred by Mujuni et al [4] as well.

Coagulopathy on admission is associated with longer intensive care and hospital stays [24]. We found that the coagulopathic group stayed longer in hospital than the non-coagulopathic group which is in accordance with other studies [4, 22, 23]. High ISS and low GCS values correspond to the extent of injury. ISS characterizes the severity of injury according to the anatomic region, and indirectly indicates the mass of destroyed tissue in the patient. Tissue destruction is associated with the activation of the kininogen-kallikrein system and releases Hageman factor. This systemic activation leads to the consumption of blood clotting factors which in turn leads to bleeding. This vicious cycle leads to death of the patient [17]. Unsurprisingly, patients with an acute coagulopathy have increased transfusion requirements in the first 24 h of admission [24]. Anemia is almost universal in trauma patients admitted to the ICU [25]. The decreased hematocrit values favor the development of acidosis. Acidosis itself inhibits the blood coagulation cascade and probably also the normal function of platelets. Our findings associated with these parameters are consistent with other studies [4, 7, 9, 10, 13, 22]. Turtay et al [26] noted a marked positive correlation between ISS and INR and ISS and aPTT and a marked negative relationship between GCS and INR, aPTT, which correlates with our study.

Conclusions

A significant proportion of polytrauma patients are coagulopathic. There are independent and strong correlations between coagulation parameters and indicators of mortality and morbidity. The paucity of relevant data in our region emphasizes the importance of our study for early suspicion and basic screening for coagulopathy in polytrauma patients in developing countries. Our study aims to highlight these attributes so as to ensure more effective treatment and improvement in the outcome.

Conflict of Interest

None.

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None.

Presentation at Meeting

None.

Author Contributors

GNP was responsible for concept, design, definition of intellectual content, literature search, data acquisition, data analysis, statistical analysis and manuscript preparation. TYPV and GAP were responsible for concept, design, definition of intellectual content, literature search, data analysis, statistical analysis, and manuscript editing and review.

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