ORIGINAL ARTICLE

The Effect of Sepsis and Septic Shock on the Viscoelastic Properties of Clot Quality and Mass Using Thromboelastometry: A Prospective Observational Study

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Abstract

Background: Sepsis is associated with wide variable coagulation abnormalities. Thromboelastography (TEG) effectively measures the viscoelastic properties of the clots. This study aims to illustrate the viscoelastic properties of clot quality and mass in sepsis and septic shock patients using TEG, as an effective tool over standard coagulation tests.

Materials and methods: A single-center, prospective observational study was conducted. 50 patients each meeting the criteria for sepsis and septic shock, and a healthy group of 30 patients was included in the study. Blood samples were obtained and analyzed for standard coagulation tests, platelet count, fibrinogen, and TEG study.

Results: A total of 130 patients were included. Septic shock patients had a higher sequential (sepsis-related) organ failure score. Prothrombin time (PT) and activated partial thromboplastin time (aPTT) were increased significantly as compared to the sepsis and control groups. TEG markers such as alpha angle, and maximum amplitude (MA) were significantly prolonged while reaction time (R time), was significantly shortened in the sepsis group as compared to the healthy group, suggestive of a hypercoagulable state in sepsis patients. While in septic shock patients, MA and Lysis Index 30 (LY 30) were significantly prolonged and, R time was significantly shortened compared to all other groups. Even though LY30 in sepsis patients was found to be within the normal range ($p < 0.001$), 18% of patients had prolonged LY30 indicating a hypercoagulable state with impaired fibrinolysis.

Conclusion: Thromboelastography, as a point-of-care test combined with conventional coagulation tests can provide additional, clinically relevant information on coagulopathy, and outcome, and thus help guide treatment modality in sepsis and septic shock-induced coagulopathy.

Keywords: Biomarkers, Coagulation tests, Coagulopathy, fibrinolysis, Hypercoagulable state, Observational studies as topic, Sepsis, Septic shock, Severity, Systemic inflammatory response syndrome.

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Highlights

Sepsis is a life-threatening response to infection and is associated with wide variable coagulation abnormalities. Viscoelastic tests can allow dynamic measurement of clot quality and mass and can prove to be an effective point-of-care tool for the management of sepsis-induced coagulopathy.

Introduction

Sepsis is a clinical syndrome that has physiologic, biologic, and biochemical abnormalities caused by a dysregulated host response to infection. Sepsis severity can progress ranging from infection, bacteremia to sepsis and septic shock and ultimately leading to multiple organ dysfunction syndrome (MODS) and death. The definitions of sepsis have evolved over the years as sepsis pathobiology has yet to be understood fully.[1]

The 2016 Society of Critical Care Medicine (SCCM)/European Society of Intensive Critical Medicine (ESICM) has described quick sequential organ failure assessment (qSOFA), a modified version of Sequential (sepsis-related) organ failure (SOFA) for assessment. The task committee believed that patients who meet the positive qSOFA criteria should additionally be evaluated for potential infections. A score of ≥2 is associated with poor outcomes and has a predictive value for sepsis.[2,3] The SOFA score is an organ dysfunction score in patients who are critically ill (ICU) and includes measurements from respiratory, cardiovascular, hepatic, coagulation, neurologic, and renal systems. The task force suggested using qSOFA in non-ICU settings to explore the likelihood of sepsis and using a SOFA score as a criterion for sepsis patients in contact with the infection.[2]

The coagulation disturbances in sepsis range from mild disorders to fulminant disseminated intravascular coagulation (DIC) manifested clinically by bleeding or thrombosis. These changes are not always

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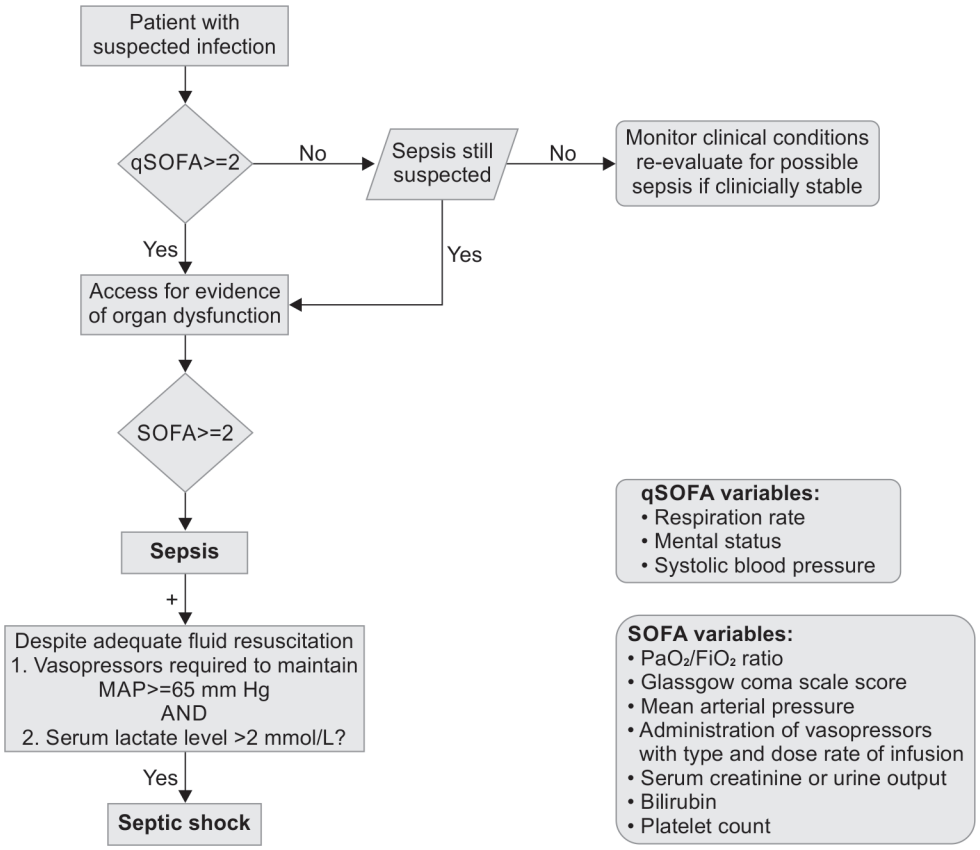


Fig. 1: Flow diagram for patient selection method

reflected by standard coagulation tests.[4,5] Global coagulation markers used clinically, like Activated Partial Thromboplastin Time (aPTT) and Prothrombin time (PT), reflect only a part of the coagulation system and do not provide full information regarding the balance between coagulation and anticoagulation pathways. Standard laboratory clotting tests are static (quantitative result) and detect only the initiation phase of initial fibrin clot formation, not the propagation phase of clotting. It is performed in platelet-poor plasma.[6] Studies have questioned their ability to reflect in vivo hypercoagulability. Due to these and many more limitations, there is a need for early diagnosis and a sensitive marker of coagulation.[5,7] Viscoelastic tests such as Thromboelastometry (TEG) and Rotational Thromboelastometry (ROTEM) are point-of-care coagulation tests, which sum the effects of coagulation factors, natural anticoagulants, fibrinogen, and activated platelets. TEG measures the global viscoelastic properties of whole blood clot formation under low shear stress.[8–10] In contrast to static conventional coagulation tests (PT, aPTT, INR, Fibrinogen level, and fibrin degradation products), TEG allows dynamic measurement of clot development, stabilization, and dissolution in near real-time from the whole blood sample.

Recent studies have used TEG as a more accurate way to determine how sepsis progression affects coagulation at different stages of severity.[8,11] The graphic interpretation of thromboelastography (TEG), helps assessment of clot quality, quantity, and associated coagulopathies (thrombocytopenia, factor deficiency, heparin effect, hypofibrinogenemia, and hyperfibrinolysis).[9,11]

The whole process from the beginning of coagulation to the dissolution of blood clots is predicted through R time (Reaction time), K time, Alpha Angle, MA (Maximum amplitude), and LY30 (Lysis index 30).[8,10,12–14] Studies have confirmed that the MA predicts the quantity and function of fibrinogen (FIB) and platelets involved in blood clot formation as well as the functional status of platelets. Both the α-angle and K-time are indicators of FIB function.[14,15]

Several studies have reported existing DIC scores like the International Society of Thrombosis and Haemostasis (ISTH) and the Japanese Association for Acute Medicine (JAAM) to delay the diagnosis of sepsis-induced coagulopathy and so for diagnosis, Sepsis-induced Coagulopathy score (SIC score) has been advised by ISTH.[16]

This study investigated the viscoelastic properties of clot quality and mass in patients with sepsis and septic shock using the Thromboelastogram (TEG), along with the consecutive changes seen in standard conventional coagulation tests.

Materials and Methods

After being approved by the Institutional Ethics Committee (IEC-1027/IGIMS/2019) and registered with the Clinical Trials Registry of India (CTRI; Trial No. CTRI/2020/01/022775), this prospective observational study was conducted in the emergency and medical Intensive Care Unit (ICU) of a Tertiary Care Hospital from January 2020 to December 2021. Written and informed consent was obtained and the study included those patients who were admitted to the hospital, fulfilling sepsis and septic shock criteria within 24 hours and from the age group of 18–65 years. Exclusion criteria were patients who refused, aged <18 years and >65 years, on anticoagulant therapy, chronic liver, and renal disease, malignancy, and impending death. qSOFA and SOFA scores were considered for better assessment and patients were selected as per Figure 1.

Table 1: Baseline characteristics of healthy control, sepsis, and septic shock cases

Parameters	*Control*	*Sepsis*	*Septic shock*	*p1*	*p2*	*p3*
Age	50.83 ± 13.83	50.98 ± 16.31	50.42 ± 15.78	0.966	0.902	0.862
Gender (F/M)	14/16	25/25	25/25	0.773	0.773	1
qSOFA Score	0.47 ± 0.57	2.14 ± 0.61	2.6 ± 20.49	<0.001	<0.001	<0.001
SOFA score	1.53 ± 1.59	7.04 ± 2.32	10.92 ± 2.73	<0.001	<0.001	<0.001

Table 2: Changes in standard markers of coagulation across control, sepsis, and septic shock cases

Parameters	*Control*	*Sepsis*	*Septic shock*	*p1*	*p2*	*p3*
PT	14.94 ± 3.06	17.07 ± 3.72	20.53 ± 3.72	0.007	<0.001	<0.001
INR	1.28 ± 0.31	1.45 ± 0.44	2.28 ± 0.57	0.046	0.009	0.029
aPTT	34.39 ± 4.32	38.56 ± 7.24	50.52 ± 7.59	0.002	<0.001	<0.001
HB	10.73 ± 1.55	10.14 ± 1.72	9.32 ± 1.64	0.118	<0.001	0.015
Platelet count (in lakhs)	2.01 ± 0.63	1.42 ± 7.72	1.01 ± 0.47	0.611	0.006	<0.001

A healthy group of patients was selected from the hospital and matched for age and sex, without any symptoms or signs of sepsis clinically as well as through laboratory tests.

Next blood sample was collected in sodium citrate (3.2%; BD vacutainer) vial and EDTA (k3 EDTA 7.2 mg; Levram Lifesciences Silvassa, India) vial to measure the Standard Coagulation markers (PT, aPTT, INR, Fibrinogen) and Hemoglobin, Platelet count respectively. Standard Coagulation markers were assessed using Stago fully Automated Coagulation analyzer, HB using Siemens Advia 2120 I (6th part), and Platelet count in Sysmex XT 1800i.

Thromboelastography was performed in the hospital setting using the MultiTEMA-Automated version by Hemologix with database QC B-00145. It was turned on earlier for rewarming the channel. A blood sample for TEG was collected *via* venepuncture from the antecubital fossa or the central venous catheter in a non-heparinized syringe with full aseptic measures. Precautions were taken to keep the sample heparin free and the first few drops of the collected sample were discarded. 1 mL sample was transferred to Kaolin containing vial/container (40 microliter Kaolin; Biogen laboratories I Pvt. Ltd.) without causing bubbles and was rolled 5–6 times slowly. After 3–4 minutes, 360 microliters of blood were pipetted (Vertex 100–1000 microliter) into neutral disposable cups (Framar Hemologix s.r.l.) and placed in TEMA-A activated channel, covered with a plastic pin, and proceeded for analysis. TEMA-A was allowed to run for 60 minutes. The cup slowly oscillated around the pin, to mimic natural blood flow *in vivo* (the clotting cascade activated). Clot formation was initiated and as the clot formed, the transducer transmitted a signal, and a graph was formed. Kinetic changes in clot formation and clot dissolution were measured for 30 minutes. Thromboelastography parameters such as Reaction time (R), clot strength by K-value and Alpha angle, Maximum Amplitude (MA), and Lysis Index at 30 minutes (LY 30) were recorded to assess the kinetic, structural, and fibrinolytic aspects of clot development.

Sample Size

In this study, a total of 130 patients were included, 50 individuals were allocated to both the sepsis and septic shock groups, while an additional 30 patients were assigned to a healthy control group. The control group was carefully matched for age and gender.

Statistical Analysis

The Microsoft Excel spreadsheet was used for all data entering, and statistical analysis was carried out on Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, version 25.0.

Quantitative data was presented with the help of frequency and percentage and Qualitative data was presented in the form of mean and standard deviations. A comparison between control, sepsis, and septic shock was done with the help of an unpaired *t*-test. Spearman ranks the correlation coefficient (ρ) was used for correlation of quantitative parameters while the receiver operating characteristic (ROC) curve was used to assess cut off point, sensitivity, specificity, positive predictive value, and negative predictive value of PT, INR, platelet count, and aPTT for predicting hypocoagulability. Sensitivity, specificity, positive predictive value, and negative predictive value of TEG in predicting hypocoagulability in the shock group were calculated.

The $p < 0.05$ was considered to be statistically significant and a $p < 0.001$ was highly significant.

Results

The study includes 50 patients with sepsis and 50 patients with septic shock. A total of 30 healthy patients matched for age and gender were also recruited as a healthy control group.

- P1 represents the *p*-value for the comparison of control with sepsis cases.
- P2 represents the *p*-value for the comparison of control with septic shock cases.
- P3 represents the *p*-value for the comparison of sepsis with septic shock cases.

Demographics of the patients with sepsis and septic shock on admission and healthy controls are summarized in Table 1. The average age observed in control and sepsis cases and control and septic shock cases was significantly similar to each other (*p*-value 0.966 and *p*-value 0.902 respectively).

qSOFA score in control cases was 0.47 ± 0.57, in sepsis cases were 2.14 0.61, and in septic shock, cases was 2.62 ± 0.49. A prolongation of the qSOFA score was found in the septic shock group ($p < 0.001$).

SOFA score in control cases was 1.53 ± 1.59, in sepsis cases was 7.04 ± 2.32, and in septic shock, cases was 10.92 ± 2.73. With increasing illness severity, the SOFA score considerably increased ($p < 0.001$).

Conventional coagulation markers and TEG results in each group are summarized in Tables 2–4 respectively.

Table 3: Changes in fibrinogen level across control, sepsis, and septic shock

Fibrinogen	298.48 ± 36.99	315.52 ± 26.06	419.92 ± 31.19	<0.001	<0.001	<0.001

A significantly prolonged fibrinogen level was found in septic shock patients ($p < 0.001$)

Table 4: Changes in TEG Parameters across control, sepsis, and septic shock cases

Parameters	*Control*	*Sepsis*	*Septic shock*	*p1*	*p2*	*p3*
R (Reaction time)	5.65 ± 1.56	3.28 ± 2.19	8.12 ± 1.17	<0.001	<0.001	<0.001
K time	3.19 ± 1.01	2.29 ± 1.79	3.15 ± 1.78	0.005	0.901	0.018
Angle	57.92 ± 8.13	73.36 ± 6.82	44.81 ± 8.43	<0.001	<0.001	<0.001
MA (Maximum Amplitude)	60.76 ± 9.85	89.79 ± 8.01	49.26 ± 9.52	<0.001	<0.001	<0.001
LY 30	2.32 ± 1.83	5.04 ± 6.31	12.16 ± 5.26	0.006	<0.001	<0.001

Table 5: Percentage of prolonged fibrinolysis among sepsis patients

	Sepsis				
	Groups	*N (%)*	*Mean*	*SD*	*p-value*
LY30	<7.5	36 (72%)	2.118	1.722	<0.001
	>7.5	14 (18%)	12.552	7.615	

In septic shock, conventional coagulation markers PT, INR, and aPTT were prolonged with a reduced platelet count ($p < 0.01$). Similarly a significantly reduced HB was observed in patients with septic shock ($p < 0.05$).

Thromboelastography markers Alpha angle (73.36 ± 6.82, $p < 0.001$) and Maximum Amplitude (MA) (89.79 ± 8.01, $p < 0.001$) were significantly prolonged in the sepsis group demonstrating a relative hypercoagulable state compared to the healthy group while R time (3.28 ± 2.19, $p < 0.001$) and K time (2.29 ± 1.79, $p < 0.05$) were shortened significantly.

Patients with septic shock showed a significantly decreased alpha angle (44.818.43, $p < 0.001$), maximum amplitude (49.269.52, $p < 0.001$), and significantly longer R time (8.121.17, $p < 0.001$) when compared to all other groups, demonstrating a hypocoagulable state. In the patients with septic shock, the LY 30 ($p < 0.001$) was similarly considerably prolonged, indicating poor fibrinolysis (Table 5).

Even though LY30 in sepsis patients was found to be within the normal range ($p < 0.001$), 18% of patients had prolonged LY30 indicating a hypercoagulable stage with first-stage fibrinolysis.

Further analysis was done and Reciever operating characteristic (ROC) curves were derived to know how accurately conventional coagulation makers were able to detect hypocoagulability, as determined from TEG parameters. (Table 6, and Figs 2–5).

Analyses revealed that conventional coagulation markers were able to predict hypocoagulability at PT >16.6s (Sensitivity 78.57%, Specificity 65.61%, PPV 52.4%, NPV 86.6%, and AUC 0.776), INR >1.4 (Sensitivity 92.86%, Specificity 59.09%, PPV 52%, NPV 94.5% and AUC 0.791), aPTT >42.5s (Sensitivity 85.71%, Specificity 82.95%, PPV 70.6%, NPV 92.4% and AUC 0.889), Platelet count <137000/cumm (Sensitivity 85.71%, Specificity 54.55%, PPV 47.4%, NPV 88.9% and AUC 0.753).

The correlation between TEG and conventional coagulation markers was assessed and it included a correlation between coagulation initiation, clot formation, and clot strength. Spearman rank correlation coefficient (ρ) was determined between TEG R time and PT, INR, and aPTT; TEG MA and platelet count, fibrinogen; TEG alpha angle and fibrinogen.

A significant positive correlation was demonstrated between TEG R time and conventional coagulation markers-INR (ρ: 0.422, p-value < 0.0001), aPTT (ρ: 0.422, p-value < 0.0001) (Table 7, Figs 6A and B). A positive correlation was also found between TEG R time and PT (ρ: 0.370, p-value < 0.0001) as seen in Figure 6A.

A significant negative correlation was found between TEG MA and conventional coagulation marker fibrinogen (ρ: –0.515, p-value < 0.0001) (Table 8, Fig. 7). Similarly negative correlation between the TEG alpha angle and conventional coagulation marker fibrinogen (ρ: –0.498, p-value < 0.0001) (Table 9, Fig. 8).

However, there was no strong association between TEG markers and platelet count.

Thromboelastography markers showed to be more specific (89.35–99.95%) with a 95% confidence interval (CI) in detecting hypocoagulability as seen in Table 10.

Discussion

Sepsis remains the leading cause of death in critically ill patients worldwide. Sepsis is a syndromic response to infection that can be acquired both in the community as well as in health care facilities. The pathogenesis of sepsis is a complex process that is still being studied. Early recognition of signs, diagnosis, and treatment can directly affect mortality. Studies have demonstrated the coagulation system's role and dysfunction in the development of sepsis.[2,4,17,18]

Sepsis-induced coagulopathy can range from subtle changes in coagulation such as microvascular thrombosis, and hypoperfusion to much more severe changes such as organ failure, DIC, and ultimately death. The mainstay of treatment remains early recognition of organ and coagulation dysfunction and initiation of tailored therapy. Therefore, for a rapid diagnosis, many conventional coagulation tests and viscoelastic assays are being used.[19] Thromboelastography reflects the changes in clotting factor, platelets, fibrin, and fibrinolysis that are involved in the coagulation process.[13]

In this study, we observed a shortened R time with a prolonged MA and alpha angle indicating an earlier clot formation with enhanced clot mass development, as compared to a normal healthy

Table 6: Receiver operating characteristic curve of PT, INR, platelet count and APTT for predicting hypocoagulability

Hypocoagulable	*PT*	*INR*	*Platelet count*	*APTT*
Area under the ROC curve (AUC)	0.776	0.791	0.753	0.889
Standard error	0.0423	0.041	0.0436	0.0287
95% Confidence interval	0.695–0.845	0.711–0.857	0.670–0.825	0.822–0.937
p-value	<0.0001	<0.0001	<0.0001	<0.0001
Cut off	>16.6	>1.4	≤137000	>42.5
Sensitivity (95% CI)	78.57% (63.2–89.7%)	92.86% (80.5–98.5%)	85.71% (71.5–94.6%)	85.71% (71.5–94.6%)
Specificity (95% CI)	65.91% (55.0–75.7%)	59.09% (48.1–69.5%)	54.55% (43.6–65.2%)	82.95% (73.4–90.1%)
PPV (95% CI)	52.4% (39.4–65.1%)	52% (40.2–63.7%)	47.4% (35.8–59.2%)	70.6% (56.2–82.5%)
NPV (95% CI)	86.6% (76.0–93.7%)	94.5% (84.9–98.9%)	88.9% (77.4–95.8%)	92.4% (84.2–97.2%)
Diagnostic accuracy	70.00%	70.00%	64.62%	83.85%

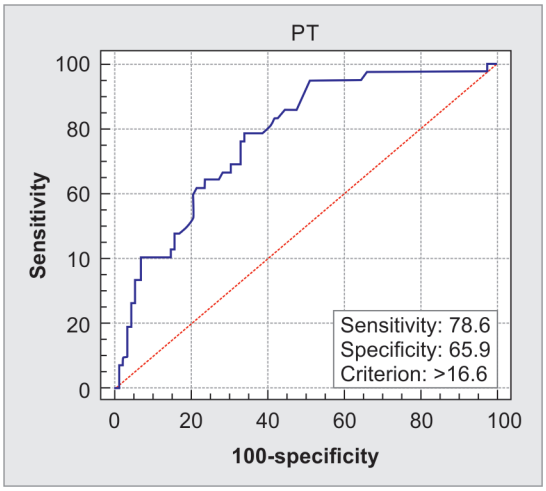


Fig. 2: Receiver operating characteristic curve of PT for predicting hypocoagulability

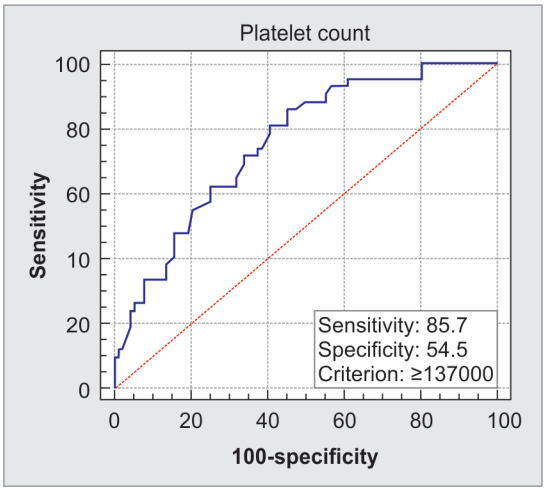


Fig. 4: Receiver operating characteristic curve of platelet count for predicting hypocoagulability

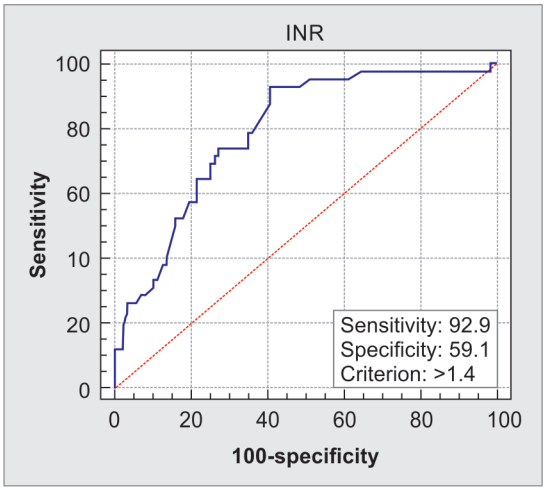


Fig. 3: Receiver operating characteristic curve of INR for predicting hypocoagulability

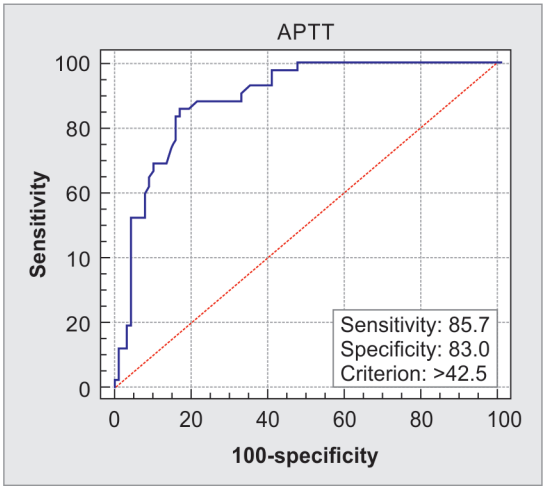


Fig. 5: Receiver operating characteristic curve of APTT for predicting hypocoagulability

control group and normal TEG ranges. Davies et al. in their study on sepsis patients found a hypercoagulable phase as evidenced by shortened clot formation time (CFT), and increased Alpha angle and viscoelasticity (MCF). However, the clotting time (CT) was within the normal range.[20]

Hence, TEG helps determine the contribution of enzymatic or platelet components to hypercoagulability and the appropriate line of treatment required. Hypercoagulable state in sepsis carries a potentially high thromboembolic risk despite thrombocytopenia, as noted in previous studies.[20–22]

Findings in the present study in sepsis patients suggest hypercoagulabity which is a coagulation dysfunction and could be due to:[20,22]

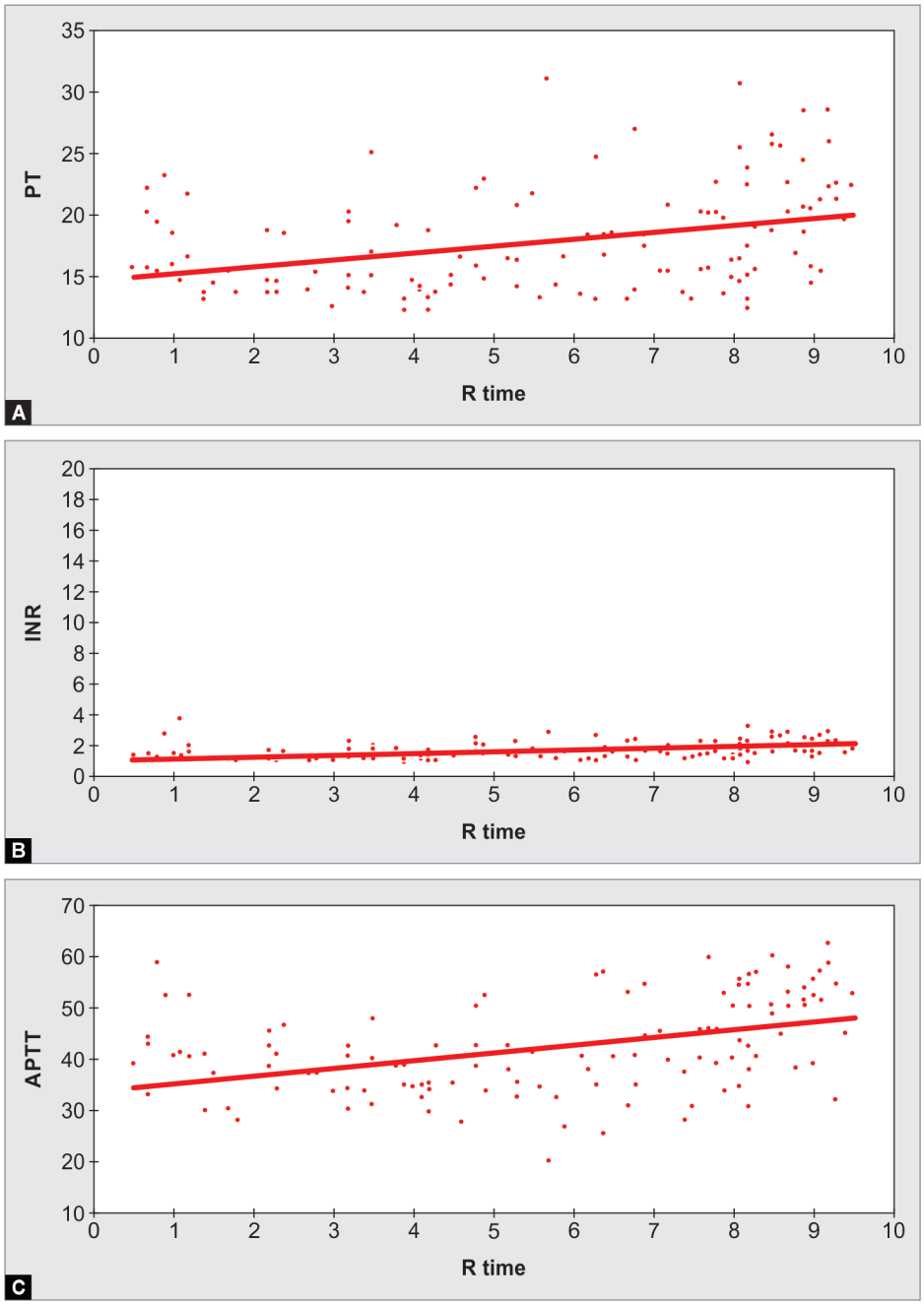
Table 7: Correlation of R time with PT, INR, and APTT

Variables	*PT*	*INR*	*APTT*
R time			
Correlation coefficient	0.370	0.422	0.450
p-value	<0.0001	<0.0001	<0.0001

Spearman rank correlation coefficient (ρ)

- Factor VIIa-TF complex activates factor X production.
- Downregulation of the physiological anticoagulation system.
- Impairment of the fibrinolytic system.

In the present study, it was observed that a certain group of septic patients developed secondary fibrinolysis along with a hypercoagulable state. This was evidenced by the prolongation of LY 30. This indicated a non-overt DIC phase in the sepsis group of patients, which was not apparent from the conventional coagulation tests.[6] Thus, TEG proves to be a superior test to the conventional coagulation tests in predicting such a state in sepsis.[24]



Figs 6A to C: (A) Correlation of R time with PT; (B) Correlation of R time with INR; (C) Correlation of R time with APTT

Table 8: Correlation of MA with platelet count, fibrinogen

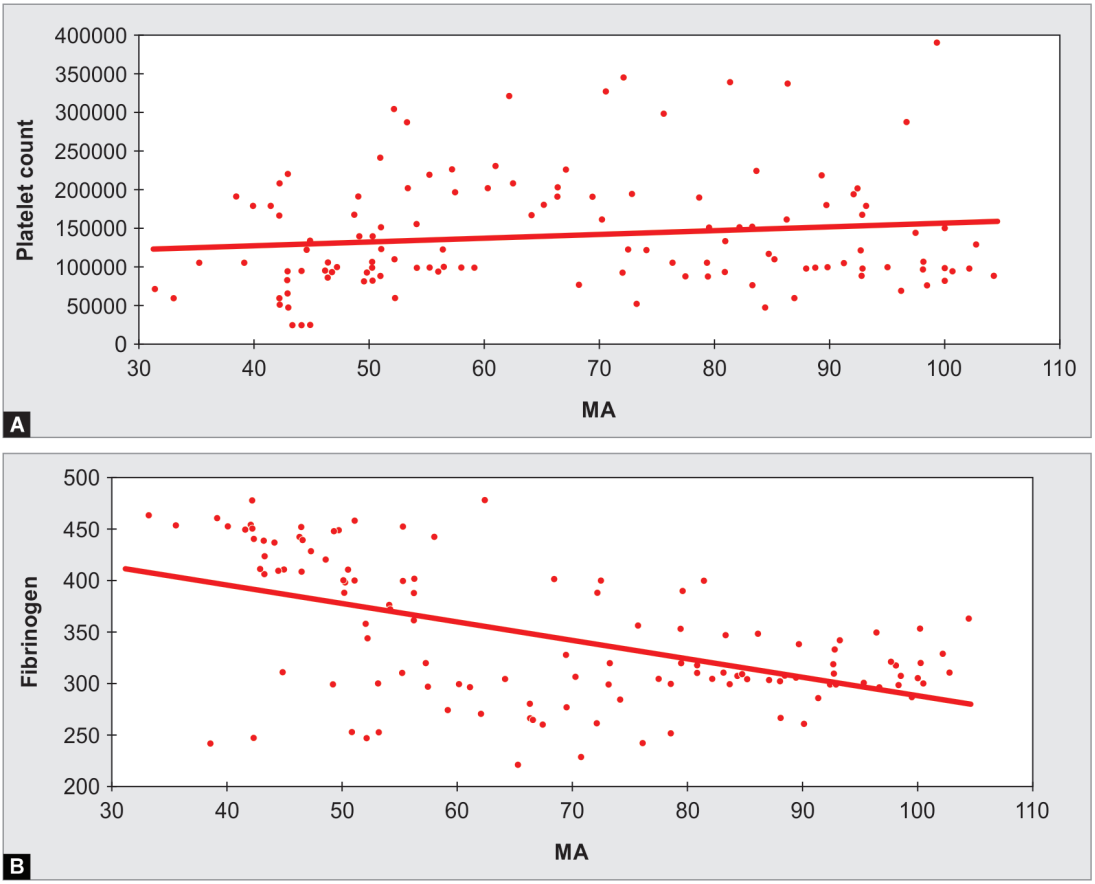
Variables	*Platelet count*	*Fibrinogen*
MA		
Correlation coefficient	0.144	–0.515
p-value	0.101	<0.0001

Spearman rank correlation coefficient

Table 9: Correlation of alpha angle with fibrinogen

Variables	*Fibrinogen*
Alpha angle	
Correlation coefficient	–0.498
p-value	<0.0001

Spearman rank correlation coefficient



Figs 7A and B: (A) Correlation of MA with platelet count and (B) Correlation of MA with fibrinogen

We found R time significantly prolonged while alpha angle and MA were significantly decreased, thereby, indicating abnormal clot formation and clot mass development. In this study, we also observed increased fibrinolysis as evidenced by prolongation of LY 30 as compared to sepsis and healthy group patients. Overall, in our study, septic shock patients exhibited a hypocoagulable state, similar to that in Davies et al. with the difference being normal Alpha angle and MCF.[15,20,22] We found that the strength of the clot drastically decreased from the sepsis to the septic shock phase, indicating a looser and weaker clot that may have been caused by a change in the cross-linked fiber.[15]

In our study, we found a positive correlation between SOFA score and the functional status of clotting factors as evidenced by TEG. Thus, the severity of the disease can be assessed by viscoelastic tools like TEG.[15]

In our study, PT aPTT and fibrinogen were significantly prolonged in association with a hypocoagulable state in septic shock patients, similar to Davies et al. study.[15,20] SangMin Kim et al. in their study on septic shock patients observed that hypercoagulability was associated with normal PT and aPTT value in non-survivors and suggested the association of hidden coagulopathy in septic patients.[25] According to Johansson et al., traditional coagulation studies revealed no differences between the groups of survivors and non-survivor groups.

In our study, conventional coagulation markers (PT, INR, aPTT, Fibrinogen, platelet count) failed to detect hypercoagulable states in the sepsis group of patients. As discussed above, sepsis-induced coagulopathy presents with a varied clinical picture and hence TEG would play an important role over conventional coagulation markers in initiating anticoagulation therapy on time to preserve homeostasis and avoid the harmful effects of coagulopathy. Previous studies were able to detect 30–100% of patients with hypocoagulability using viscoelastic tests.[26]

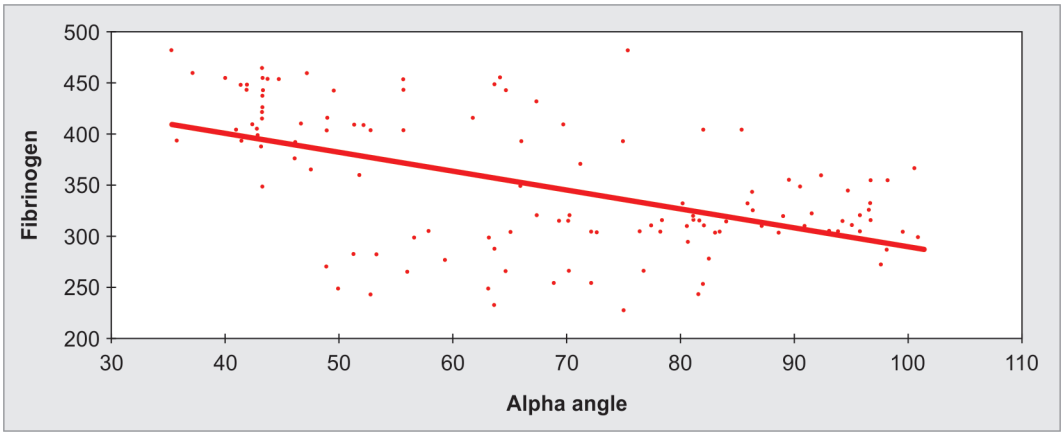


Fig. 8: Correlation of alpha angle with fibrinogen

Table 10: Sensitivity, specificity, positive predictive value and negative predictive value of TEG for predicting hypocoagulability, as defined by SIC score in shock group

Variables	*Values*
Sensitivity (95% CI)	51.25% (39.81–62.59%)
Specificity (95% CI)	98% (89.35–99.95%)
AUC (95% CI)	0.75% (0.66–0.82%)
Positive predictive value (95% CI)	97.62% (87.43–99.94%)
Negative predictive value (95% CI)	55.68% (44.70–66.27%)
Diagnostic accuracy	69.23%

Alpha angle and MA are functional markers of fibrinogen and platelet. In our study on septic shock patients, we found a decrease in Alpha angle and MA value, suggestive of a decrease in fibrinogen function. The fibrinogen level was significantly increased in these groups of patients compared to the sepsis and normal healthy group.

The results of several research support the notion that a hypocoagulable state with lower MA implies a diminished platelet function. In our study, we found a similar result along with decreased platelet count as compared to septic and normal healthy group patients.

In our study, we evaluated the relationship between TEG parameters and conventional/conventional coagulation markers. A strong relationship was found between the TEG marker of clot initiation R time and conventional coagulation marker PT, INR, and aPTT. Though we found a significant negative correlation between TEG marker MA, alpha angle, and fibrinogen; the correlation between platelet and TEG markers was poor. Overall, research revealed that in both hypocoagulable and hypercoagulable patients, only fibrinogen levels were related to clot strength. Sisse R. Ostrowski et al. in their study concluded the same.[6,25] Studies conducted by Cristina Solomon et al and Jeffrey N Harr et al. found the contribution of both platelet and fibrinogen to clot strength.[27,28] Absolute platelet count does not correlate with the viscoelastic parameters reflecting clot strength. Despite the fact that TEG results in our study demonstrated a hypercoagulable state without considerable thrombocytosis, the lack of a correlation between clot strength in hypercoagulable patients and clot strength in hypercoagulable patients may point to decreased hemostatic platelet function in the septic group of patients.[6]

Table 6 shows conventional coagulation makers were able to predict hypocoagulability at: PT > 16.6s with Sensitivity of 78.57%, Specificity 65.61%, PPV 52.4%, NPV 86.6% and AUC 0.776; INR > 1.4 with Sensitivity 92.86%, Specificity 59.09%, PPV 52%, NPV 94.5% and AUC 0.791; aPTT > 42.5s with Sensitivity 85.71%, Specificity 82.95%, PPV 70.6%, NPV 92.4% and AUC 0.889; Platelet count 13700/cumm with Sensitivity 85.71%, Specificity 54.55%, PPV 47.4%, NPV 88.9% and AUC 0.753.

We found using TEG, patients had hypercoagulability with non-overt DIC (primary fibrinolysis) and in some, patients had hypocoagulability with overt DIC. We found TEG markers to be more specific in predicting hypocoagulability in the shock group of patients and hence can be used for early detection of sepsis-induced coagulopathy in the sepsis spectrum group of patients. Thus, conventional coagulation markers alone cannot diagnose the degree of coagulopathy and TEG might add additional support.[29]

Our study suggests that further research with a larger sample size and defined duration of testing is required for a better assessment of the hypercoagulable state. Hypercoagulability can present with organ dysfunction and not necessarily with a bleeding tendency, organ dysfunction being an independent marker of disease progression.[22,25]

The result of the TEG profile in a certain group of patients such as intracerebral bleeding and pregnant patients should be interpreted with caution.

In our study we also found hemoglobin levels to be significantly reduced in septic shock patients as compared to sepsis and normal healthy group patients. Impaired fibrinolysis, hypocoaguable state, and organ dysfunction all contribute to the overt DIC phase with a high risk of bleeding.

The results presented here are subject to limitations due to the small sample size and other factors. The time between blood

sampling for TEG analysis and the beginning of symptoms was not rigorously gathered information, which may have had an impact on the TEG profile. Furthermore, continuous ICU stays in other medical centers and single-center studies all influence the result.

Conclusion

In our prospective observational study, we found a hypercoaguable state in the sepsis group of patients, and with severe disease, TEG predicted a hypocoagulable state. The traditional coagulation function test does not indicate the functional condition of platelets and fibrinogen; it simply reflects quantitative changes. TEG markers had a correlation with PT, INR, aPTT, and fibrinogen in a hypocoaguable group of patients. Our study implies TEG is superiority to other conventional coagulation tests especially in sepsis patients and a better tool for early diagnosis of sepsis-induced coagulopathy. TEG can be combined with conventional coagulation tests and provide additional, clinically relevant information on the coagulopathy, outcome, and guide treatment modality.[10,24,25] TEG can be used as a promising tool for assessing coagulation alteration in patients with sepsis and septic shock. The coagulation system is affected invariably in sepsis and septic shock patients, so using TEG as a point-of-care test may improve outcome and mortality and also prevent the aberrant use of blood products. However, our study needs validation with a larger number of patients.

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