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STUDY OF BLOOD COAGULATION DISORDERS IN PATIENTS OF SEPSIS AND THEIR RELATIONSHIP WITH APACHE II SCORE

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Abstract
Background- Sepsis is a severe, life-threatening condition resulting from an abnormal and uncontrolled immune response to infection, posing a significant global health challenge. Blood coagulation disorders are significant complications in sepsis, often exacerbating the severity of the condition. The APACHE II (Acute Physiology and Chronic Health Evaluation II) score is a widely used severity-of-disease classification system that provides valuable prognostic information in critically ill patients. This study aims to investigate the relationship between various blood coagulation parameters and the severity of sepsis as assessed by the APACHE II score.
Materials And Methods- A descriptive cross-sectional hospital-based study was conducted in the Department of General Medicine at Mahatma Gandhi Medical College & Hospital, Jaipur, on patients admitted to the ICU diagnosed with sepsis according to Sepsis-3 criteria. Blood coagulation parameters, including platelet count, PT, aPTT, D-dimer, and fibrinogen levels, were monitored and compared to assess the severity of sepsis using the APACHE II score.
Results- The study included 168 sepsis patients aged 18 to 65 years. The mean APACHE II score was 29.08, with a significant correlation between age and APACHE II scores ($p<0.001$). The study found 68.5% of patients in a hypo-coagulation state and 31.5% in a hyper-coagulation state. Significant correlations were observed between APACHE II scores and PT, aPTT, D-dimer, and platelet count.
Conclusions- The study highlights the critical role of blood coagulation disorders in the pathophysiology of sepsis and their correlation with disease severity as assessed by the APACHE II score. Routine monitoring of coagulation parameters in sepsis patients is essential, and incorporating these parameters into the APACHE II scoring system could provide a more comprehensive assessment of sepsis severity, aiding in better prognostication and treatment planning.

Keywords- Sepsis, Blood coagulation disorders, APACHE II score, Coagulation parameters, Platelet count, PT, aPTT, D-dimer, Fibrinogen, Sepsis severity.

INTRODUCTION

Sepsis is a life-threatening condition caused by a dysregulated host response to infection, leading to organ dysfunction.[1] It is a critical global health issue, affecting millions annually and resulting in significant morbidity and mortality. According to the Centres for Disease Control and Prevention (CDC), about 1.7 million adults in the U.S. develop sepsis each year, with around 350,000 fatalities during hospitalization.[2]In 2017, sepsis was responsible for 48.9 million cases and 11 million deaths worldwide, accounting for 20% of all global deaths.[2] The condition disproportionately affects low- and middle-income countries, where 85% of sepsis cases and fatalities occur.[3]

Sepsis triggers a systemic inflammatory response syndrome (SIRS), which can escalate to severe complications, including disseminated intravascular coagulation (DIC). DIC is characterized by widespread clotting in blood vessels, consuming platelets and coagulation factors faster than they can be replenished, leading to severe bleeding and organ damage[4].

Blood coagulation disorders are critical complications in patients with sepsis, often exacerbating the severity of the condition and contributing to higher morbidity and mortality rates. In patients with sepsis, the imbalance in clot generation (coagulation) and clot breakdown (fibrinolysis) is a pivotal response that occurs due to host defence mechanisms but is associated with the development of organ dysfunction.[5] In a study it was found in patients who hadsepsis treated in intensive care units, 29% were diagnosed with sepsis-induced coagulopathy.[5] The intricate interplay between coagulation pathways and the systemic inflammatory response in sepsis presents a significant challenge for clinicians. The APACHE II (Acute Physiology and Chronic Health Evaluation II) score, a widely used severity-of-disease classification system, provides valuable prognostic information in critically ill patients, including those with sepsis.[6]

This study aims to investigate the relationship between various blood coagulation parameters and the severity of sepsis, as assessed by the APACHE II score. By analyzing coagulation profiles in septic patients, we seek to identify specific markers that correlate with disease severity and outcomes. Understanding these correlations can enhance clinical assessment, guide therapeutic interventions, and ultimately improve patient prognosis.

In this paper, we will present a comprehensive analysis of blood coagulation disorders in sepsis, elucidate their impact on disease progression, and explore the potential of incorporating coagulation parameters into the APACHE II scoring system for a more refined evaluation of sepsis severity.

MATERIALS AND METHODS

A descriptive cross sectional hospital based study was done in Department of General Medicine, Mahatma Gandhi Medical College & Hospital, Jaipur on patients admitted in ICU diagnosed as sepsis according to sepsis 3 criteria as per Surviving Sepsis campaign.[45] .Due ethical clearance was taken from institutional ethical committee. Systematic Random Selection of every 3rd patient admitted in ICU and diagnosed as Sepsis within the study period was done and consent was taken. Blood coagulation parameters like platelet count, PT. aPTT, D dimer and fibrinogen level and blood coagulation parameters were monitored and compared to study the severity of sepsis using Apache II score.

RESULTS

The study included 168 sepsis patients aged 18 to 65 years, with a mean age of 40.36 years (SD 13.38). The study comprised 98 (58.3%)males and 70(41.7%)females. Maximum number of study population 42 (25%) belonged to age group 31 to 40 years followed by 11 (6.5%) of age <20, 34(20.2%) of age 21-30 years, 34 (20.2%) of age 41-50 years, 35 (20.8%) of age 51-60 years and 12 (7.1%) of age >60 years . The mean age of the study subject is 40.36 years and the SD 13.38.

Table 1 Distribution of study subject according to Blood Coagulation lab parameters (N=168)

Parameter	Platelet (Per mcL)	PT (Seconds)	aPTT (Seconds)	Fibrinogen (mg/dl)	DDimer IU/ml
Mean	47331	21.86	54.15	250.10	1.31
Std. Deviation	19581	11.39	26.26	197.97	1.58

As shown in the Table 1 the mean blood coagulation laboratory parameters as platelets count, PT, aPTT, fibrinogen level and D Dimer level is 47331/mcL (SD 19581), 21.86 seconds (SD11.39), 54.15 Seconds (SD 26.26), 250.10 mg/dl (SD 197.97) and 1.31 IU/ml (SD 1.58) respectively.

Table 2 Distribution of study subject according to APACHE Score (N=168)

Parameter	APACHE Score
Mean	29.08
Std. Deviation	13.61
Minimum	10
Maximum	60

The APACHE score of the sepsis patients is calculated (Table 2) and it is found that the mean APACHE score is 29.08 (SD 13.61) with minimum score 10 and maximum score 60.

Table 3 Distribution of study subject according coagulation state

Coagulation state	Frequency	Percent
Hypo-coagulation state	115	68.5
Hyper-coagulation state	53	31.5
Total	168	100.0

As shown in the Table 3 out of total 168 sepsis patient 115 (68.5%) are in hypo-coagulation state and rest 53 (31.5%) are in hyper-coagulation state. So, hypo coagulable states were more prevalent than hypercoagulable states in sepsis patient according our study.

Table 4 APACHE II score according to Age

Age (years)	APACHE II Score						Total
	10-14	15-19	20-24	25-29	30-34	>34	
<20	11(100%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	11 (100.0%)
21-30	9 (26.5%)	21 (61.8%)	4 (11.8%)	0(0.0%)	0(0.0%)	0(0.0%)	34 (100.0%)
31-40	0(0.0%)	3 (7.1%)	25 (59.5%)	14 (33.3%)	0(0.0%)	0(0.0%)	42 (100.0%)
41-50	0(0.0%)	0(0.0%)	3 (8.8%)	6 (17.6%)	25 (73.5%)	0(0.0%)	34 (100.0%)
51-60	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	6 (17.1%)	29 (82.9%)	35 (100.0%)
>60	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	12 (100%)	12 (100.0%)
Total	20 (11.9%)	24 (14.3%)	32 (19.0%)	20 (11.9%)	31 (18.5%)	41 (24.4%)	168 (100.0%)
p	0.000						

As shown in the Table 4, figure 1 with increasing age ApacheII score increases in sepsis patient which correlates with increasing severity of sepsis. This difference of APACHE II score in various age group is statistically significant (p<0.001).

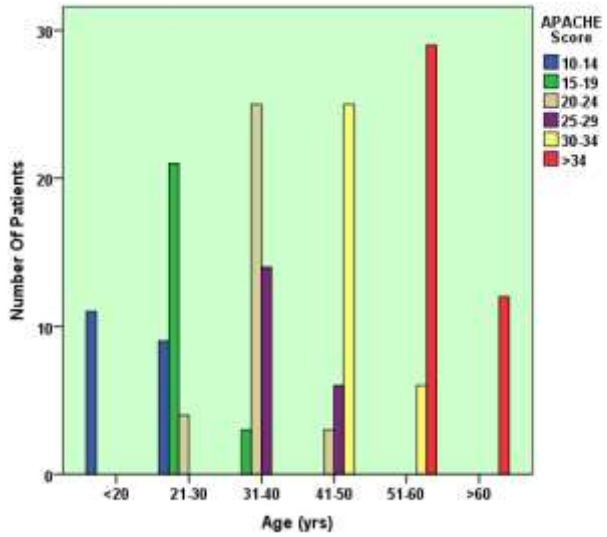

Figure 1 Relationship between APACHE II score and Age

Table 5 Correlation between APACHE score and blood coagulation parameters

APACHE Score VS Blood Coagulation Parameter	Platelet	PT	aPTT	Fibrinogen	D Dimer
Pearson Correlation	-0.223	0.449	0.306	-0.093	0.463
p	0.004	0.000	0.000	0.232	0.000

As shown in the Table 5 the APACHE score is positively correlated with PT, aPTT and D Dimer with r value 0.449, 0.306 and 0.463 respectively and p value 0.000, so as Apache II score increases PT, aPTT, D Dimer also increases. APACHE score is negatively correlated with platelet count with r value -0.223 and p value 0.004. APACHE score is negatively correlated with fibrinogen with r value -0.093 though not statistically significant and p value 0.232. We also correlated Apache II score according to gender, coagulation status according to Gender, coagulation status according to Age but all these were statistically not significant with p value being more than >0.5.

DISCUSSION

This study signifies the complex relationship between blood coagulation parameters and the severity of sepsis as assessed by the APACHE II score. Our findings reveal significant correlations that provide deeper insights into the pathophysiological mechanisms at play in septic patients, emphasizing the critical role of coagulation disorders in the progression and severity of sepsis.

Our cohort consisted of 168 sepsis patients aged between 18 and 65 years, with a mean age of 40.36 years. The demographic distribution, with a slightly higher proportion of males (58.3%), aligns with existing epidemiological data indicating that sepsis incidence does not significantly favor one gender over the other but often reflects the population structure of hospital admissions. The age distribution, peaking in the 31–40-year group, suggests a significant impact of sepsis on the working-age population, which could have socio-economic implications.

The mean platelet count in our study was 47,331/mcL, which is significantly lower than normal reference ranges, indicating a prevalent state of thrombocytopenia among the septic patients. This is consistent with the pathophysiology of sepsis, where platelet consumption and destruction are heightened due to the systemic inflammatory response and endothelial damage. Prothrombin time (PT) and activated partial thromboplastin time (aPTT) were markedly elevated, with means of 21.86 seconds and 54.15 seconds, respectively. These prolonged clotting times reflect the consumption coagulopathy and impaired coagulation factor synthesis seen in severe sepsis and DIC.

D-dimer levels, a marker of fibrinolysis, were elevated (mean 1.31 IU/ml), reinforcing the presence of ongoing coagulation and fibrinolysis. Elevated fibrinogen levels, although seemingly contradictory, can be explained by its role as an acute-phase reactant, where initial elevation might occur before consumption overtakes production in the coagulation cascade.

The APACHE II score, with a mean of 29.08, is indicative of high severity among the studied patients. This score, designed to predict hospital mortality, was significantly correlated with several coagulation parameters. PT, aPTT, and D-dimer levels showed positive correlations with APACHE II scores ($r = 0.449$, 0.306, and 0.463, respectively; $p < 0.001$). These findings underscore the contribution of coagulation abnormalities to sepsis severity and the potential of these parameters to serve as markers for prognosis.

Conversely, platelet count demonstrated a negative correlation with the APACHE II score ($r = -0.223$, $p = 0.004$), reinforcing the concept that thrombocytopenia is a marker of severe disease in sepsis. The negative, albeit non-significant, correlation between fibrinogen levels and APACHE II score ($r = -0.093$, $p = 0.232$) might reflect the complex dynamics of fibrinogen in sepsis, where initial increases due to inflammation may be followed by consumption in severe stages.

A notable finding was the prevalence of hypo-coagulable states (68.5%) over hyper-coagulable states (31.5%) among the septic patients. This distribution is significant as it highlights the dominant presence of consumption coagulopathy and bleeding risks in sepsis, challenging the traditional view that hypercoagulability predominates. This insight calls for nuanced clinical management strategies that balance the risks of thrombosis and bleeding.

Age was found to significantly affect the APACHE II scores, with older patients exhibiting higher scores ($p < 0.001$). This age-related increase in severity underscores the vulnerability of older adults to the adverse outcomes of sepsis, likely due to an age-associated decline in immune function and comorbidities. However, gender did not significantly impact APACHE II scores or coagulation status, indicating that the pathophysiological processes in sepsis-related coagulation disturbances are not markedly different between males and females.

Comparative analysis with previous studies, such as those by **Kim et al. (2020)** and **Zhou et al. (2019)**, highlighted similarities and differences in patient demographics and coagulation profiles. For instance, **Kim et al**. reported a higher mean age of 65.6 years and a similar male predominance (58.6%)[7], while **Zhou et al**. found an average age of 59.14 years with 64.2% males.[8] These variations may be attributed to differences in study populations and sepsis definitions, emphasizing the need for standardized criteria in sepsis research. **Patel et al. in 2022** found that maximum patients (29%) had APACHE II scores between 15 and 19 followed by 20–24 (22%), Mortality increased with increasing APACHE II scores, and 100.0% mortality was observed with a score >34.[9] **Mumtaz et al. in 2023** in a study found mean APACHE II score to be 31.7 ± 17.94 (mean ± SD). In that

study 93 belonged to score 31-40, 135 belonged to 21-30, 123 belonged to 11-20 and 201 belonged to 3-10 APACHE score group.[10]

LIMITATIONS AND FUTURE DIRECTIONS

Despite the valuable insights provided by this study, several limitations must be acknowledged. The single-centre design may limit the generalizability of the findings to other settings. Additionally, the cross-sectional nature of the study precludes the assessment of temporal changes in coagulation parameters and their impact on long-term outcomes.

CONCLUSION

The findings of this study have several clinical implications. First, the significant correlation between coagulation parameters and sepsis severity underscores the importance of routine monitoring of these parameters in sepsis patients. Second, the prevalence of hypo-coagulable states suggests that interventions aimed at managing DIC and other coagulation abnormalities could improve patient outcomes. Third, incorporating coagulation parameters into the APACHE II scoring system may provide a more comprehensive assessment of sepsis severity, aiding in better prognostication and treatment planning. The age-related increase in sepsis severity reinforces the need for heightened vigilance and aggressive management in older patients. This study underscores the critical importance of coagulation parameters in understanding and managing sepsis. By integrating these parameters into severity scoring systems like APACHE II, clinicians can achieve more accurate prognostic assessments, guidingtherapeutic decisions and ultimately improving patient care in sepsis.

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