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Hemostatic Alterations and Sepsis-Induced Coagulopathy: Epidemiology, Complications, and Mortality Risk Factors

Said Khiar[1*], *and* Ammar Taleb[1]

[1] *Department of Intensive Care, CHU Tizi Ouzou, Algeria*

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CORRESPONDING AUTHOR

khiar.said

EMAIL CORRESPONDING AUTHOR:

khiar.said@hotmail.com

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A B S T R A C T

Contexte : Le sepsis s'accompagne de perturbations majeures de l'hémostase, conduisant fréquemment à une coagulation intravasculaire disséminée (CIVD) et à une augmentation de la mortalité. Cette étude visait à évaluer les modifications hémostatiques, la survenue de la CIVD, les complications hémorragiques et thrombo-ischémiques, ainsi que les facteurs influençant la mortalité chez les patients septiques.

Méthodes :Une étude observationnelle prospective a été menée auprès de patients septiques admis en unité de soins intensifs. Les paramètres hémostatiques évalués comprenaient le taux de plaquettes, le temps de prothrombine (TP), le temps de céphaline activée (TCA), le fibrinogène et les D-dimères. La CIVD a été évaluée selon les scores ISTH, JAAM et SIC. Les complications et la mortalité ont été enregistrées, et des analyses statistiques ont été réalisées afin d'identifier les facteurs de risque associés.

Résultats :Des perturbations de l'hémostase ont été observées chez près de 95 % des patients. Une thrombopénie (<150 000/µL) était présente chez 37 %, avec une numération plaquettaire moyenne de 195 232 ± 114 298/µL. Le TP et le TCA étaient anormaux dans respectivement 34 % et 27 % des cas. Les D-dimères étaient élevés chez 95 % des patients, tandis que le fibrinogène était augmenté dans 76 % des cas. Une CIVD a été retrouvée chez 21 % des patients selon les critères ISTH, 35 % selon JAAM et 45 % selon SIC. Des complications hémorragiques ont été observées chez 8,5 % des patients, et des événements thrombo-ischémiques chez 13 %. Des scores ISTH, JAAM et SIC plus élevés à l'admission étaient significativement associés à une mortalité accrue, avec des odds ratios respectifs de 1,62, 1,47 et 1,43.

Conclusion :Les troubles de l'hémostase sont fréquents au cours du sepsis, et une proportion importante de patients développe une CIVD. Les complications, qu'elles soient hémorragiques ou thrombo-ischémiques, contribuent à la mortalité. Une reconnaissance précoce à l'aide de scores tels que ISTH, JAAM et SIC permet d'identifier les patients à haut risque et d'orienter les stratégies de prise en charge.

1. Introduction

Sepsis is frequently accompanied by disturbances in coagulation, which may progress to sepsis-induced coagulopathy and disseminated intravascular coagulation (DIC). These alterations contribute to organ dysfunction, hemorrhagic events, thrombo-embolic complications, and increased mortality (1–6). Several scoring systems, including ISTH, JAAM, and SIC, have been proposed to detect DIC and predict outcomes in septic patients.

2. Methods Study Design and Population

A prospective observational study was conducted in the intensive care unit of CHU Tizi Ouzou, Algeria. Adult patients with confirmed sepsis were included. Hemostatic parameters were measured upon admission, including platelet count, PT, aPTT, fibrinogen, and D-dimers. DIC diagnosis was performed using ISTH, JAAM, and SIC scores. Hemorrhagic and thrombo-ischemic complications were recorded. Mortality at 28 days was assessed.

Statistical Analysis Continuous variables were presented as mean ± standard deviation or median [IQR]. Categorical variables were expressed as percentages. Univariate and multivariate logistic regression analyses were performed to identify factors associated with mortality. A p-value <0.05 was considered statistically significant.

3. Results

Hemostatic Alterations Nearly 95% of patients had at least one abnormal hemostatic parameter. Thrombocytopenia (<150,000/µL) was present in 37%, with a mean of 195,232 ± 114,298/µL and median of 202,000 [95,250; 280,750]. PT and aPTT abnormalities were observed in 34% and 27% of patients, respectively, with median PT 69.0% [52.2; 87.2] and aPTT 35.4 sec [27.2; 40.0]. D-dimers were elevated in 95% of patients (mean 4,191 ± 3,467 mg/mL, median 2,710 [1,470; 7,847]), while fibrinogen was high in 76% (median 5.15 g/L [4.10; 6.80], mean 5.40 ± 2.16 g/L.

Disseminated Intravascular Coagulation DIC prevalence varied according to scoring systems: 21% by ISTH, 35% by JAAM, and 45% by SIC. ISTH score at admission averaged 3.3 points in DIC-positive patients. JAAM and SIC scores were 3.23 ± 1.70 and 3.44 ± 1.39, respectively. JAAM appeared more sensitive for early detection compared to ISTH ($p < 0.001$)

Complications Hemorrhagic complications occurred in 8.5% of patients, with severe bleeding in those with specific infections (meningococcal, leptospirosis) and those receiving prophylactic anticoagulation (5/75; 6.7%). Thrombo-ischemic events were observed in 13%, (table 1)

Mortality and Risk Factors Higher ISTH, JAAM, and SIC scores at admission were significantly associated with 28-day mortality. Univariate logistic regression showed odds ratios of 1.62 [1.14–2.41] (ISTH), 1.47 [1.09–2.09] (JAAM), and 1.43 [1.02–2.06] (SIC), (table2, 3)

4. Discussion

Coagulation abnormalities are ubiquitous in septic shock and contribute substantially to organ dysfunction and mortality. In our cohort, more than 90% of patients presented at least one hemostatic abnormality, a finding consistent with previous large-scale studies (1–6). These alterations reflect the complex interplay between inflammation and coagulation, which characterizes the pathophysiology of sepsis.

Thrombocytopenia occurred in 37% of patients, closely matching the prevalence reported in the POWERSS study (7). Multiple mechanisms have been implicated, including impaired bone marrow production, increased peripheral consumption, splenic sequestration, and hemophagocytic activity (8,9). Sustained thrombin generation appears to be the predominant driver of platelet consumption and endothelial destruction. Given its strong prognostic significance, platelet count remains a critical biomarker for early risk stratification in septic shock.

Prolongation of PT and aPTT was common in our cohort, in line with findings from large septic shock populations (4–6, 10). PT prolongation, described in up to 90% of severe sepsis cases (4), reflects consumptive coagulopathy and may precede the first signs of organ dysfunction (11–13). Although conventional coagulation assays lack specificity for diagnosing DIC, early abnormalities should prompt clinicians to consider evolving coagulopathy and to closely monitor for progression to overt DIC.

Almost all patients demonstrated markedly elevated D-dimer levels, confirming the intense activation of coagulation and secondary fibrinolysis characteristic of septic shock (4–6,14). Fibrinogen, a major acute-phase reactant, was increased in the majority of cases, as typically observed in early sepsis (15–17). Only a minority exhibited hypofibrinogenemia, which more likely reflects advanced consumptive coagulopathy. These findings support the exclusion of fibrinogen from sepsis-specific DIC scores such as JAAM and SIC.

The prevalence of DIC varied substantially according to the scoring system used. Using the ISTH criteria, 21% of patients met the definition of overt DIC, a rate comparable to multicenter studies such as PROWESS and JSEPTIC-DIC (4,6,18).

The JAAM criteria identified a higher proportion (35%), consistent with its well-known sensitivity in early sepsis-related coagulopathy (20,21). The SIC score classified 45% of patients as having sepsis-induced coagulopathy, in keeping with previously reported rates (5,24–26). Because it integrates both organ dysfunction (SOFA) and coagulation abnormalities, the SIC score appears particularly relevant for early risk stratification.

Our findings reinforce the central role of dysregulated immunothrombosis in septic shock. Pro-inflammatory cytokines trigger widespread thrombin generation, endothelial activation, microvascular thrombosis, consumption of coagulation factors, and inhibition of fibrinolysis (28,29). Despite extensive research, no single biomarker reliably identifies DIC in sepsis; hence, validated scoring systems remain indispensable tools for diagnosis and clinical decision-making.

Severe bleeding was observed in 8.5% of patients, a rate comparable to previous reports (6,25,31,32) once hemorrhagic etiologies such as meningococcemia or leptospirosis were excluded. Thromboembolic events occurred in 13% of patients, higher than previously reported (31), likely due to systematic Doppler screening in our cohort. These findings highlight the prothrombotic nature of septic shock, mediated by profound impairment of endogenous anticoagulant pathways and marked suppression of fibrinolysis (37).

All three scoring systems—ISTH, JAAM and SIC—were independently associated with mortality, confirming the results of previous studies (5,16,19,20,25). Higher scores likely reflect the combined effects of systemic inflammation, endothelial dysfunction, microvascular thrombosis, and multiorgan failure. Their integration into early clinical evaluation may help identify high-risk phenotypes of septic shock and support enrollment in future interventional trials targeting sepsis-associated coagulopathy.

5. Conclusion

Sepsis frequently causes hemostatic alterations, with a considerable risk of DIC and associated complications. Higher scores on ISTH, JAAM, and SIC at admission are significant predictors of mortality. Systematic assessment of coagulation status is essential to optimize the management and outcomes of patients with severe sepsis.

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ANNEXEES:

Table 1: Demographics and clinical characteristics of study patients

	N (%)	Mean (standard deviation)
AGE (years)		60.9 (17.8)
MALE SEX	49 (60%)	
PAST MEDICAL ACTIVITIES	72 (11%)	
HTA	30 (37%)	
Diabetes	30 (37%)	
Heart disease	11 (13%)	
stroke	6 (7.3%)	
IRCT	3 (3.7%)	
COPD	5 (6.1%)	
Neuropsychiatry	25 (30%)	
Neoplasia	9 (11%)	
Others	23 (28%)	
STARTING POINT		
Pulmonary	30 (37%)	
Urinary	22 (27.2%)	
Digestive	13 (16%)	
Haematological	10 (12%)	
Meningitis	4 (4.9%)	
Cutaneous	3 (3.7%)	
BACTERIOLOGIES		
Positive	25 (31%)	
BGN	16 (20%)	
COCCI	9 (11%)	
Bilirubin		17.9 (36.5)
> 12 mg/l	23 (28%)	
Createnine		33.2 (34.2)
> 12 mg/l	53 (65%)	
P/F		223 (86.2)
PAM		61.6 (7.20)
SCG		11.6 (2.65)
SOFA		8.99 (2.74)
HEMOSTASIS		
blood platelets		195,232 (114,298)
< 150,000/µL	30 (37%)	

TP		69.0 (22.2)
TP < 60%	28 (34%)	
a PTT		35.4 (12.4)
a PPT > 40 sec	22 (27%)	
D dimer		4191 (3467)
DD <500mg/l	78 (95%)	
Fibrinogen		5.40 (2.16)
Fb < 2 g/l	5 (6%)	
CIVD		
ISTH Score		3.30 (1.45)
ISTH ≥ 5;	17 (21%)	
JAAM Score		3.23 (1.70)
JAAM ≥ 4;	29 (35%)	
Scorere SIC		3.44 (1.39)
SIC ≥4	37 (45%)	
TREATMENTS		
VM	38 (46%)	
Transfusion	16 (20%)	
RTT	8 (9.8%)	
COMPLICATIONS		
Thrombosis	11 (13%)	
TVP	8 (9.8%)	
EP	2 (2.4%)	
TVC	1 (1.2%)	
Severe hemorrhage	7 (8.5%)	
Deceased	49 (60%)	
Length of stay		6.44 (3.58)

Table 2: Correlation between profile of patients and sepsis outcome (mortality)

	Survived (n = 49)	Not Survived (n = 33)	n	p
AGE	60.7 (18.3)	61.3 (17.3)	82	0.87
P/F,	198 (87.2)	261 (70.3)	82	**<0.001**
SCG	11.0 (2.56)	12.6 (2.50)	82	**<0.01**
SOFA,	10.4 (2.47)	6.85 (1.42)	82	**<0.001**
blood platelets	185980 (124498)	208970 (97433)	82	0.35
>150,000/µL	29 (59%)	23 (70%)	52	0.33
<150,000/µL	20 (41%)	10 (30%)	30	
TP	67.5 (21.8)	71.2 (23.0)	82	0.46
TP >60%	31 (63%)	23 (70%)	54	0.55
TP <60%	18 (37%)	10 (30%)	28	-
D Dimer	4517 (3477)	3707 (3447)	82	0.3
Fibrinogen	5.44 (2.36)	5.33 (1.86)	82	0.81
ISTH	3.65 (1.32)	2.79 (1.49)	82	**<0.01**
JAAM	3.61 (1.54)	2.67 (1.80)	82	**0.016**
SIC	3.69 (1.36)	3.06 (1.37)	82	**0.043**
VM				
NO	17 (35%)	27 (82%)	44	**<0.001**
YES	32 (65%)	6 (18%)	38	-

Table 3: Regression simple logistics analysis of Relationship between mortality and DIC score

	Odds Ratio [95% CI]	p
ISTH	1.62 [1.14; 2.41]	**0.01**
JAAM	1.47 [1.09; 2.09]	**0.018**
SIC	1.43 [1.02; 2.06]	**0.046**