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(ARTICLE ORIGINAL)

Hemostatic Disorders In The Intensive Care Unit: A 12-Month Retrospective Study

Kenza Damaan[1] , Sara Haddady[2] , Mohammed amine El abidi[3] , Sabah Benhamza[4] , Mohamed Lazraq[5] , Youssef Miloudi[6] , Abdelhak Bensaid [7]

1. Anesthesia and Critical Care, 20 August Hospital 1953, University Hospital Centre IBN Rochd of Casablanca ,Hassan II University, casablanca, MAR
2. Anesthesiology and Critical Care, 20 August Hospital 1953 ,University Hospital Centre IBN Rochd/ Hassan II university, Casablanca, MAR
3. Anesthesia and Critical Care, Intensive Care Unit, 20 August 1953 Hospital, University Hospital Centre IBN Rochd, Hassan II university, CASABLANCA, MAR
4. Anesthesia and Critical Care, Anesthesia and Critical Care, Intensive Care Unit, 20 August 1953 Hospital, University Hospital Centre IBN Rochd CASABLANCA, Hassan II university,, Casablanca, MAR
5. Anesthesiology and Critical Care, Anesthesiology and critical care, Ibn Rochd University Hospital of Casablanca, Hassan II University of Casablanca, Morocco, casablanca, MAR
6. Anesthesiology and Critical Care, Intensive Care Unit, 20 August 1953 Hospital, University Hospital Centre IBN Rochd of Casablanca , Hassan II university, Casablanca, MAR
7. Department of Anesthesiology and Reanimation, Intensive Care Unit, 20 August 1953 Hospital, University Hospital Centre IBN Rochd, Hassan II University, Casablanca, MAR

Résumé

Introduction : Les troubles de l'hémostase sont fréquents en réanimation, notamment dans les contextes de sepsis, de coagulation intravasculaire disséminée (CIVD) et d'autres affections critiques. Ils sont associés à une augmentation de la morbidité et de la mortalité.

Objectif : Décrire l'incidence des troubles de l'hémostase chez les patients admis en réanimation, identifier leurs principales causes, présenter leurs caractéristiques clinico-biologiques et évaluer leur impact pronostique.

Méthodes : Nous avons réalisé une étude rétrospective au service de réanimation de l'Hôpital du 20 Août 1953 sur une période d'un an, du 1er janvier au 31 décembre 2020. Parmi 442 dossiers analysés, 80 patients présentaient des anomalies de l'hémostase. Les données ont été recueillies et analysées à l'aide de Microsoft Excel et SPSS version 22.

Résultats : Les troubles de l'hémostase ont été observés chez 18 % des patients admis en réanimation. L'âge moyen était de 43,7 ans avec une prédominance masculine (55 %). Le purpura constituait le principal signe hémorragique (33,8 %). Les anomalies biologiques les plus fréquentes étaient la thrombopénie (60 %), la diminution du taux de prothrombine (73,8 %), l'allongement du temps de céphaline activée (63,8 %) et l'hypofibrinogénémie (16,3 %). Le sepsis représentait l'étiologie la plus fréquente (22,5 %). La mortalité était significativement plus élevée chez les patients présentant un trouble de l'hémostase que chez les autres (53,8 % versus 16,6 % ; $p < 0,0005$).

Conclusion : Les troubles de l'hémostase sont fréquents en réanimation et associés à une mortalité élevée. Leur diagnostic précoce et leur prise en charge adaptée sont essentiels pour améliorer le pronostic.

Mots-clés : Trouble de la coagulation ; Troubles de l'hémostase ; Unité de réanimation ; Pronostic des patients ; Thrombopénie

* Auteur correspondant: Sara Haddady, sarahaddady8@gmail.com

1 Introduction :

Many clinical situations encountered in intensive care can lead to hemostatic disorders, one of the most serious complications of which is hemorrhage. These abnormalities can manifest as spontaneous or induced bleeding at surgical sites, mucous membranes, or other areas not typically prone to bleeding, due to impairment of the physiological mechanisms of hemostasis. Hemostatic disorders exhibit heterogeneous clinical and biological profiles, and their diagnosis relies primarily on the interpretation of standard laboratory coagulation tests [1]. Hemostasis is a complex physiological process that ensures the maintenance of vascular integrity. It enables the rapid formation of a clot to stop bleeding following vascular injury, followed by the clot's gradual dissolution once tissue repair is complete. It involves three main components: the vascular wall, platelets, and plasma coagulation factors. Any disruption of one of these mechanisms can lead to a hemorrhagic syndrome or, more rarely, a thrombotic syndrome [2]. In intensive care patients, who are already compromised by the severity of their underlying conditions, the development of hemostatic disorders is a major factor contributing to disease severity. In particular, severe or rapidly progressive thrombocytopenia is associated with an increased risk of potentially life-threatening bleeding complications. Furthermore, these abnormalities are often associated with increased mortality, making them an important prognostic factor in intensive care [3,4]. Sepsis and septic shock are major causes of hemostatic dysfunction in the intensive care unit. The systemic inflammatory response triggered by infection promotes coagulation activation through tissue factor expression while simultaneously impairing physiological anticoagulant pathways. This dysregulation results in excessive thrombin generation, microvascular thrombosis, and impaired tissue perfusion, thereby contributing to the development of multiple organ dysfunction [5]. Disseminated intravascular coagulation (DIC) represents the most severe manifestation of these abnormalities. It is characterized by diffuse and uncontrolled activation of the coagulation cascade, leading to the consumption of coagulation factors and platelets, which may result in both thrombotic events and hemorrhagic complications. The occurrence of DIC in critically ill patients is widely recognized as a marker of disease severity and is associated with poor prognosis and increased mortality [6]. The prognostic assessment of patients with hemostatic disorders relies on several clinical and laboratory parameters. Among the most commonly used tools in intensive care is the Sequential Organ Failure Assessment (SOFA) score, which was developed to quantify the extent of organ dysfunction and monitor its progression during hospitalization [7]. The objectives of this study were to assess the incidence of hemostatic disorders in intensive care patients, describe their clinical and laboratory manifestations, identify their etiologies, evaluate their management, and analyze patient outcomes.

2 Matériels et méthodes :

2.1 Study design and duration :

This retrospective study was conducted in the intensive care unit (ICU) of 20 Août 1953 Hospital, Casablanca, over a 12-month period (January 1 to December 31, 2020). Medical records of all patients admitted during this timeframe were reviewed (n = 442).

2.2 Inclusion criteria:

We included all patients who developed a hemostatic disorder during their ICU stay, supported by clinical and/or laboratory findings suggestive of a hemorrhagic diathesis. Inclusion was independent of the reason for ICU admission and of any specific underlying condition, in order to capture the full spectrum of coagulopathies encountered in critical care.

2.3 Exclusion criteria:

Records that were incomplete, illegible, or missing key data preventing interpretation of coagulation parameters were excluded. Patients presenting only with abnormalities consistent with hypercoagulability (thrombophilia or isolated venous/arterial thrombosis) were not included.

2.4 Definition of hemostatic disorders:

Hemostatic disorders were defined as an imbalance of the hemostatic system associated with an increased bleeding risk, excluding isolated hypercoagulability. A hemostatic disorder was considered present when at least one of the following abnormalities was identified: thrombocytopenia confirmed on two consecutive platelet counts $<150{,}000/mm^3$ at least 12 hours apart; prothrombin time activity <70%; prolonged activated partial thromboplastin time (aPTT) with a patient-to-control ratio >1.2; hypofibrinogenemia with fibrinogen <2 g/L; elevated D-dimer level >500 µg/L; or coagulation factor deficiency with factor level <50%.

2.5 Data collection:

Data were extracted from medical records using a standardized collection form and included age, sex, medical history, hemodynamic, respiratory, neurological, and infectious status, hemorrhagic manifestations, severity scores, complete blood count, coagulation tests, bone marrow examination when available, liver and kidney function tests, infectious and inflammatory workup, reason for ICU admission, referring department, presumed etiology of the hemostatic disorder, treatments administered, complications, length of ICU stay, and mortality.

2.6 Statistical analysis:

The quantitative variables were expressed as mean ± standard deviation (SD), and qualitative variables as percentages. Descriptive analyses were performed for the overall population, followed by comparative analyses between patients with and without hemostatic disorders. Proportions were compared using the chi-square test, with statistical significance set at $p < 0.05$.

3 Résultats :

3.1 Incidence and distribution by sex and age :

During 2020, a total of 442 patients were admitted to the intensive care unit (ICU) of 20 Août 1953 Hospital. Among them, 80 patients met the inclusion criteria for a haemostatic disorder, corresponding to an overall incidence of 18.1% (80/442).

The mean age was 43.7 ± 20.3 years (range: 6-91 years). The most represented age group was 21-30 years, comprising 21 patients (26.3%). There was a slight male predominance, with 44 patients (55%) being male and 36 patients (45%) being female, yielding a male-to-female ratio of 1.22.

3.2 Reasons for ICU admission and referral departments

The indications for ICU admission were diverse. Haematological disorders and postoperative conditions were the most frequent causes of admission, each accounting for 11 patients (13.8%). Severe head trauma and hepatic encephalopathy were each observed in 7 patients (8.8%). Thrombocytopenia was the primary reason for admission in 6 patients (7.5%), while polytrauma was reported in 5 patients (6.3%). Other admission diagnoses included post-chemotherapy haemorrhagic complications, shock states, diabetic ketoacidosis, pulmonary embolism, and other medical conditions.

Most patients were referred from medical departments, followed by the emergency department and surgical specialties. The haematology department accounted for the largest proportion of referrals, followed by the pulmonology and otolaryngology departments (Figure 1).

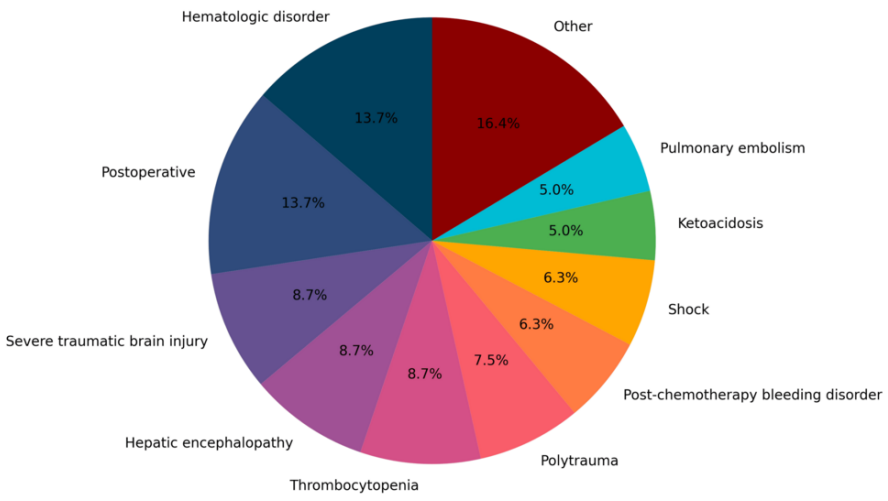

Figure 1: Reason for hospital admission in patients with a hemostasis disorder

3.3 Medical history and clinical presentation at admission

The most common comorbidities were haematological disorders, reported in 20 patients (25%), followed by diabetes mellitus in 14 patients (17.5%) and hypertension in 12 patients (15%). A history of previous surgery was noted in 12 patients (15%).

Neurological manifestations were observed in 30 patients (37.5%), including focal neurological deficits in 1 patient (1.3%). Haemodynamic instability was present in 26 patients (32.5%). Respiratory distress was observed in 31 patients (38.8%), of whom 27 required mechanical ventilation. Fever and hypothermia were recorded in 17 patients (21.3%) and 12 patients (15%), respectively.

The Sequential Organ Failure Assessment (SOFA) score was calculated in 64 patients (80%). The mean SOFA score was 7.1 ± 3.3 (range: 1-19).

Haemorrhagic manifestations were reported in 30 patients (37.5%). Petechial and/or ecchymotic purpura was the most frequent presentation, occurring in 14 patients (17.5%). Major bleeding events, particularly intracranial haemorrhages, occurred in 6 patients (7.5%), including subarachnoid haemorrhage, subdural haematoma, and haemorrhagic stroke. Epistaxis, gingival bleeding, lower gastrointestinal bleeding, and haemoptysis were also observed (Figure 2).

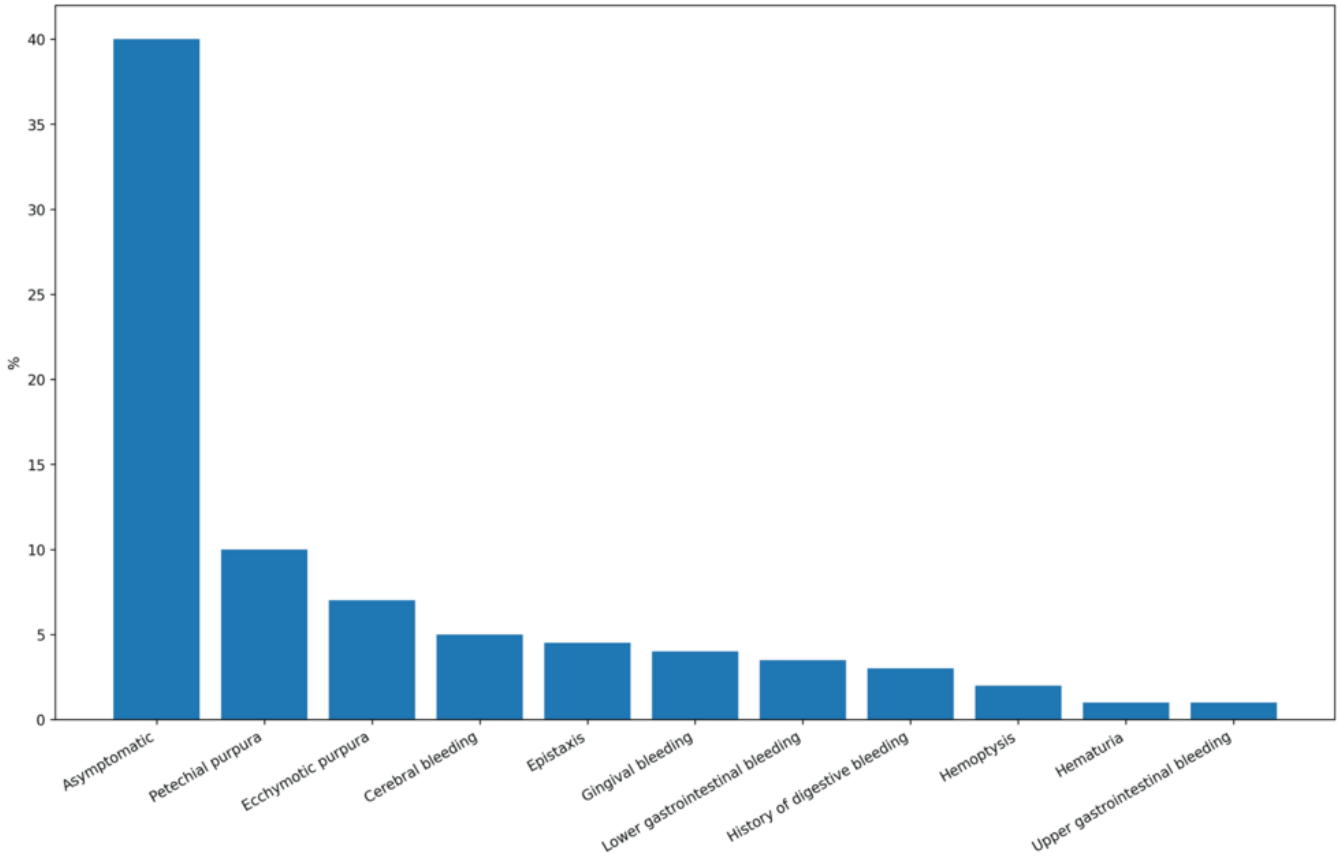

Figure 2: Distribution of symptoms related to hemostasis disorders

3.4 Haemostatic abnormalities at admission and during ICU stay

All patients underwent regular monitoring of haemostatic parameters. At admission, thrombocytopenia was present in 48 patients (60%), prothrombin time (PT) activity below 70% was observed in 59 patients (73.8%), and activated

partial thromboplastin time (aPTT) prolongation was recorded in 51 patients (63.8%). A combination of thrombocytopenia, reduced PT activity, and prolonged aPTT was observed in 22 patients (27.5%) (Table 1).

The mean platelet count was 67,000 ± 43,000/mm^3. Platelet counts between 20,000 and 50,000/mm^3 were observed in 11 patients (13.8%), whereas severe thrombocytopenia (<20,000/mm^3) was present in 9 patients (11.3%).

The mean PT activity at admission was 46.3 ± 8.0% (range: 6-60%). Three patients had uncoagulable coagulation tests at admission. Normal PT activity was observed in 21 patients (26.3%), and remained normal throughout the ICU stay in 10 patients (12.5%) (Figure 3).

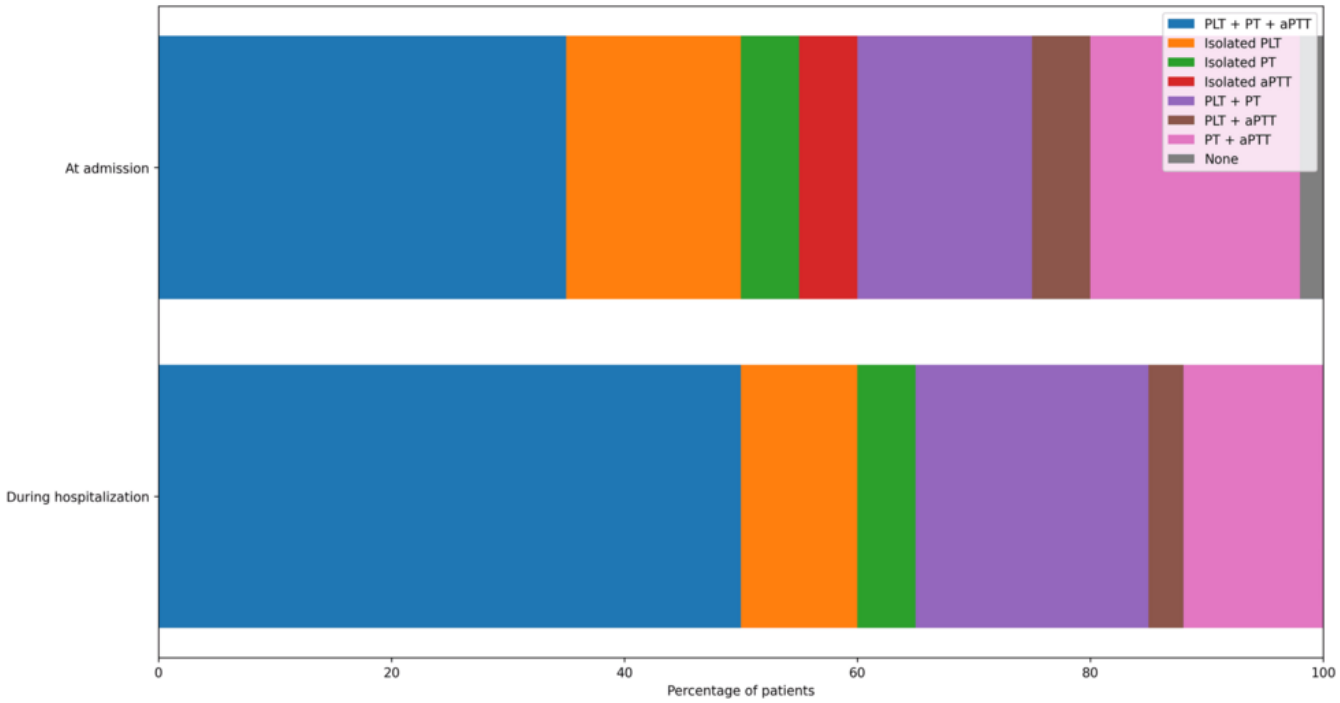

Figure 3: Patterns of hemostasis abnormalities at admission and during hospitalization

International normalized ratio (INR) was available for 8 patients (10%), with a mean value of 4.5 ± 4.0 (range: 1.3-11).

Fibrinogen levels were available for 76 patients (95%). The mean fibrinogen concentration at admission was 3.9 ± 2.2 g/L (range: 0.5-9.3 g/L). Among these patients, fibrinogen levels were below 1 g/L in 5 patients (6.6%), between 1 and 2 g/L in 13 patients (17.1%), within the normal range (2-4 g/L) in 40 patients (52.6%), and above 5 g/L in 18 patients (23.7%).

Specific coagulation factor assays were performed in selected patients with concurrent PT and aPTT abnormalities, suspected disseminated intravascular coagulation (DIC), hepatocellular failure, or vitamin K deficiency. These investigations demonstrated variable reductions in coagulation factors II, V, and X according to the underlying clinical condition.

3.5 Associated laboratory abnormalities

Anaemia was present in 47 patients (58.8%), with a mean haemoglobin level of 9.8 ± 3.3 g/dL. Leukocytosis was observed in 50 patients (62.5%), whereas hypocalcaemia was recorded in 29 patients (36.3%).

D-dimer levels were measured in 9 patients (11.3%), of whom 8 (88.9%) had elevated values (>500 µg/L).

Acute kidney injury was diagnosed in 34 patients (42.5%), while hepatocellular dysfunction was observed in 22 patients (27.5%). Bone marrow aspiration was performed in 15 patients (18.8%) and confirmed several underlying haematological disorders.

3.6 Aetiologies of haemostatic disorders

The causes of haemostatic disorders were diverse. Sepsis was the leading aetiology, identified in 37 patients (46.3%), followed by malignant haematological disorders in 16 patients (20%), traumatic coagulopathy in 9 patients (11.3%), and dilutional coagulopathy in 5 patients (6.3%). Disseminated intravascular coagulation (DIC), which could coexist with other underlying conditions, was identified in 21 patients (26.3%).

Sepsis was most commonly of pulmonary origin. Nosocomial infections occurred in 22 of the 37 septic patients (59.5%). The most frequently isolated microorganisms were Pseudomonas aeruginosa, Klebsiella pneumoniae, Escherichia coli, coagulase-negative staphylococci, Acinetobacter baumannii, Mycobacterium tuberculosis, Candida species, and SARS-CoV-2.

3.7 Duration of haemostatic disorders

The mean duration of haemostatic disorders was 6.6 ± 1 days. In approximately one-third of patients, these abnormalities lasted less than 48 hours, whereas they persisted for more than 10 days in 20 patients (25%).

3.8 Therapeutic management

Treatment was mainly supportive and relied largely on blood product transfusion. Overall, 57 patients (71.3%) received at least one blood product.

Red blood cell concentrates were administered to 46 patients (57.5%), with a mean of 1.7 ± 2.3 units per patient (range: 1-12 units). The mean haemoglobin threshold for transfusion was 7 g/dL, which was increased to 9 g/dL in patients with severe head trauma.

Platelet concentrates were transfused in 30 patients (37.5%), with a mean of 3.3 ± 6 units, while fresh frozen plasma was administered to 20 patients (25%), with a mean of 2.1 ± 5.2 units.

All patients received fluid resuscitation. Vasopressor support was required in 50 patients (62.5%), predominantly norepinephrine, whereas epinephrine was administered in 14 patients (17.5%). Empirical antibiotic therapy was initiated in 72 patients (90%) and subsequently adapted according to microbiological findings.

Vitamin K was administered to 29 patients (36.3%), tranexamic acid to 4 patients (5%), and proton pump inhibitors to all patients.

3.9 Outcomes, complications, mortality, and length of stay

A favourable clinical outcome was observed in 37 patients (46.3%), whereas 43 patients (53.8%) died during their ICU stay.

Mortality was significantly higher in patients with haemostatic disorders than in those without haemostatic disorders (53.8% vs. 16.6%; $p < 0.00001$; OR = 3.83) (Figure 4).

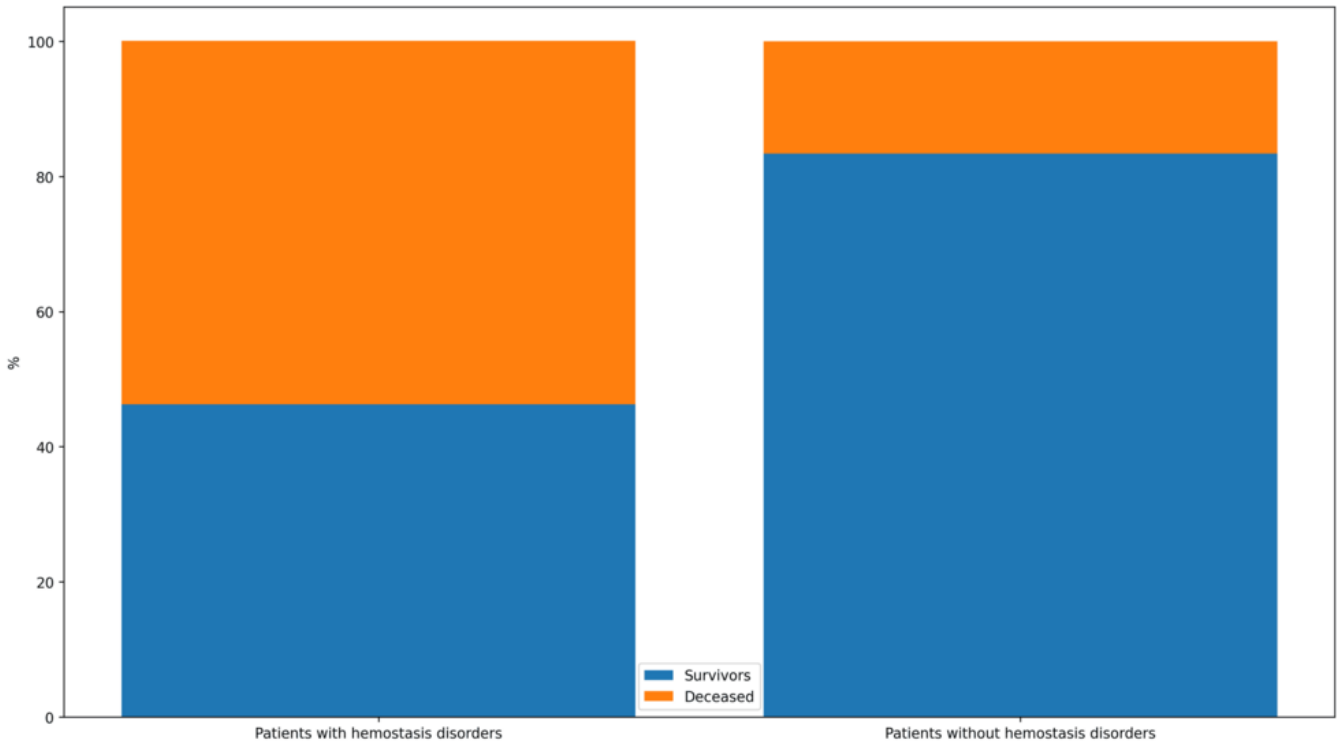

Figure 4: Mortality according to the presence of hemostasis disorders

Septic shock was the leading cause of death, accounting for 18 of 43 deaths (41.9%), followed by multiple organ failure (13/43, 30.2%), acute kidney injury (5/43, 11.6%), cerebral herniation (4/43, 9.3%), and cardiogenic shock (3/43, 7.0%).

The mean ICU length of stay was 9.5 ± 6 days.

Table 1: Distribution of hemostasis abnormalities by laboratory parameters (Platets(PLT), prothrombin time (PT), activated partial thromboplastin time(aPTT)) at admission and during hospitalization

Trouble	At admission – Number of patients (n)	At admission- %	During the hospital stay – Number of patients(n)	During the hospital stay - %
PLT PT aPTT	22	27,5 %	34	42,5 %
Isolated PLT	10	12,5 %	8	10,0 %
Isolated PT	3	3,8 %	3	3,8 %
Isoleted aPTT	3	3,8 %	0	0,0 %
PLT PT	12	15,0 %	18	22,5 %
PLT aPTT	4	5,0 %	2	2,5 %
PT aPTT	22	27,5 %	15	18,8 %

4 Discussion :

4.1 Physiopathology

Under normal conditions, hemostasis depends on a finely regulated balance between primary hemostasis, the coagulation cascade, and fibrinolysis. This balance involves a close interaction between the endothelium, platelets, coagulation factors, natural anticoagulants, and the fibrinolytic system [4,5]. In critically ill patients, however, this equilibrium is often disturbed. The severity of the underlying disease, particularly sepsis, organ dysfunction, hematologic disorders, or trauma, can profoundly alter coagulation mechanisms. In addition, some therapeutic interventions used in the ICU may further contribute to these disturbances. As a consequence, ICU patients may be exposed simultaneously to bleeding complications and thrombotic events, making hemostatic abnormalities a particularly relevant indicator of disease severity [5,6,8,9].

4.2 Incidence

In our series, hemostatic disorders were found in 18% of ICU patients. This figure is in line with previously published data, although the incidence reported in the literature varies widely depending on the study population, diagnostic criteria, and timing of assessment [8,10].

4.3 Demographic characteristics and comorbidities

The mean age of our patients was 43.7 years, reflecting a relatively young population. This finding is similar to that reported in previous studies conducted in critically ill patients with coagulation abnormalities. Men were slightly more represented than women, accounting for 55% of cases, which is consistent with findings reported in previous studies.

Comorbidities likely played an important role in both the occurrence and severity of coagulation disorders. Renal dysfunction, for example, is known to impair platelet function and increase bleeding risk, while liver failure affects the synthesis of several coagulation factors and may lead to a more global hemostatic imbalance [11,12,13,14]. In our cohort, hematologic malignancies were the most frequent comorbidity, followed by diabetes and hypertension. This distribution probably reflects the referral pattern of our ICU, but it may also help explain the relatively high frequency of coagulopathy and hemorrhagic manifestations observed in our patients.

4.4 Clinical presentation

From a clinical point of view, altered consciousness was observed in more than one-third of patients. This is consistent with previous reports, which described a relationship between neurological impairment, sepsis, and coagulation abnormalities [15,16,17]. Hemodynamic instability was also common and affected around one-third of patients, which is comparable to the findings reported by Chiolero [18].

Respiratory distress was present in nearly 40% of cases, and mechanical ventilation was frequently required. Altogether, these findings suggest that coagulation disorders in the ICU rarely occur in isolation and are more often part of a broader picture of multiple organ dysfunction [18].

The mean SOFA score was 7.1 ± 3.3, reflecting the severity of illness in our population and being consistent with values reported in patients with severe sepsis or disseminated intravascular coagulation [19].

Hemorrhagic manifestations were observed in 30 patients (37.5%), mainly as purpura and deep intracranial bleeding. Similar findings have been reported in previous studies [10,20], especially in patients with severe thrombocytopenia related to hematologic disease.

4.5 Biological profile and associated abnormalities

Among the biological abnormalities, thrombocytopenia was the most frequent finding. This is in keeping with the literature, where it is consistently described as one of the most common hemostatic abnormalities in critically ill

patients. In our study, it was present in 60% of patients with coagulopathy, a rate close to that reported in previous studies [4,10,20].

Abnormal standard coagulation tests were also common, with reduced prothrombin time activity and prolonged activated partial thromboplastin time in a large proportion of patients. These findings suggest that several components of the coagulation cascade may be altered simultaneously, involving the extrinsic, intrinsic, and common pathways [11]. Previous studies have also shown that these abnormalities are associated with increased mortality in ICU patients, which gives them clear prognostic value.

Anemia was present in 47 patients (58.8%). This is consistent with published data and may further aggravate bleeding risk, particularly when thrombocytopenia is also present.

Renal impairment and hepatocellular dysfunction were also common, again supporting the strong relationship between organ failure and disordered hemostasis [15].

4.6 Etiologies and the role of sepsis

The causes of coagulopathy in our study were multiple, but sepsis and hematologic malignancies clearly predominated. This is in line with most published series, where severe infection, disseminated intravascular coagulation, hematologic disorders, and liver or kidney dysfunction are among the main contributing factors [5,20].

Other causes identified in our cohort, such as traumatic coagulopathy, dilutional coagulopathy, and treatment-related causes including anticoagulants, antiplatelet agents, or chemotherapy, further highlight the multifactorial nature of hemostatic disorders in critically ill patients.

The high frequency of sepsis and nosocomial infections, especially those related to multidrug-resistant organisms, strongly suggests that infection played a central role in the development of coagulation abnormalities in our ICU. Through excessive activation of coagulation pathways and simultaneous inhibition of fibrinolysis, sepsis creates a prothrombotic but unstable hemostatic state that can rapidly evolve toward overt coagulopathy [5,6].

4.7 Therapeutic management

Overall, the therapeutic approach in our study was broadly consistent with current recommendations, including fluid resuscitation, norepinephrine for persistent hypotension, and empiric antimicrobial therapy in suspected sepsis [1].

Vitamin K was administered in more than one-third of patients, reflecting the frequency of coagulopathy related to deficiency states, cholestasis, or vitamin K antagonist therapy. Tranexamic acid was used selectively in hemorrhagic shock, in line with evidence supporting benefit when administered early.

Transfusion of packed red blood cells, fresh frozen plasma, and platelets followed commonly accepted thresholds (hemoglobin, PT activity, and platelet count, with higher thresholds in traumatic brain injury) [1]. Indications for platelet concentrates and plasma were consistent with recommendations in central thrombocytopenia, severe bleeding, or multiple coagulation factor deficiencies [1].

Observed transfusion rates were comparable to those reported in the literature [10,11], although some studies describe more frequent use of massive transfusion strategies [18,20].

4.8 Prognosis and impact on mortality

Clinical course was characterized by a mean ICU stay of 9.5 ± 6 days and a mortality rate of 53.8%, a rate comparable to that reported in some published series [19].

Mortality was significantly higher among patients with hemostatic disorders than among those without hemostatic disorders (53.8% vs. 16.6%; OR = 3.83; $p < 0.00001$), highlighting the prognostic impact of coagulation abnormalities in critically ill patients.

The strong association between coagulopathy and death is consistent with published data identifying thrombocytopenia, disseminated intravascular coagulation, and abnormal coagulation tests as adverse prognostic factors, often independent, in critically ill patients [6,19]. Therefore, hemostatic abnormalities should not be viewed as isolated laboratory findings but rather as severity markers requiring close monitoring and targeted management.

4.9 Limitations

This study has some limitations that should be acknowledged. First, its retrospective and single-center design may reduce the generalizability of the findings to other ICUs, especially since a relatively large number of our patients had hematologic malignancies, which may not reflect the case mix of every center. In addition, advanced investigations of hemostasis, such as systematic coagulation factor measurements or global assays such as thromboelastography, were not available for all patients. As a result, some coagulation abnormalities may not have been fully characterized. Another limitation is the absence of follow-up after ICU discharge, which prevented the evaluation of medium- and long-term outcomes. Nevertheless, the number of patients included, the richness of the collected clinical and laboratory data, and the consistency of our results with previously published studies strengthen the overall value of our findings.

5 Conclusion :

Hemostatic disorders are common among critically ill patients in the intensive care unit; in our cohort, they were observed in nearly one in five cases. They generally appear shortly after admission to the intensive care unit and most often occur in the context of organ dysfunction, particularly in cases of sepsis or malignant hematological disease. The most common abnormalities were thrombocytopenia and coagulation disorders. These disorders were associated with considerable morbidity and a significantly higher mortality rate, making them an important marker of severity in the ICU. For this reason, rapid identification of the cause and personalized management based on treating the underlying condition, correcting contributing factors, and implementing an appropriate transfusion strategy remain essential for improving patient outcomes.

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.
Concept and design: Sara Haddady, Kenza Damaan, Mohammed amine El abidi, Sabah Benhamza, Mohamed Lazraq, Youssef Miloudi, Abdelhak Bensaid.

Acquisition, analysis, or interpretation of data: Sara Haddady, Kenza Damaan, Mohammed amine El abidi, Sabah Benhamza, Mohamed Lazraq, Youssef Miloudi, Abdelhak Bensaid

Drafting of the manuscript: Sara Haddady, Kenza Damaan, Mohammed amine El abidi, Sabah Benhamza, Mohamed Lazraq, Youssef Miloudi, Abdelhak Bensaid

Critical review of the manuscript for important intellectual content: Sara Haddady, Kenza Damaan, Mohammed amine El abidi, Sabah Benhamza, Mohamed Lazraq, Youssef Miloudi, Abdelhak Bensaid

Supervision: Kenza Damaan, Abdelhak Bensaid

Disclosures

Human subjects: All authors have confirmed that this study did not involve human participants or tissue.

Animal subjects: All authors have confirmed that this study did not involve animal subjects or tissue.

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following:
Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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