RESEARCH ARTICLE

Elevated D-dimer is Associated with Anemia, Immune Dysregulation, and Hepatic–Renal Dysfunction in Acute Burn Patients

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Abstract

BACKGROUND: Burn injury induced increased risk of venous thromboembolism (VTE) due to hypercoagulability, immobilization, and endothelial injury. Despite this risk, VTE in burn patients often remains clinically undetected. Although D-dimer is widely used as a VTE marker, its utility in burn patients is inconsistent, particularly in the early post-burn period. Therefore, this study was conducted to evaluate the correlation between D-dimer levels and factors related to VTE, including hematologic, coagulation, immunologic, organ function parameters, and burn characteristics.

METHODS: An analytical observational study was conducted involving adult patients with acute burn injuries enrolled in Dr. Soetomo General Hospital from March to June 2025. Demographic, anthropometric, burn characteristic, and existing comorbid were documented from subjects' medical records. Blood samples from subjects were collected immediately via venipuncture. D-dimer was analyzed with Enzyme-Linked Fluorescent Assay (ELFA) method, hematology and coagulation profiles were also assessed using hematology analyzer and automated coagulation system, respectively. Meanwhile, hepatic and renal function were analyzed with chemistry analyzers.

RESULTS: Most burn subjects (18 of 20) demonstrated elevated D-dimer levels. Higher D-dimer levels were associated with increased leukocyte counts and upward trend of RDW-CV and RDW-SD. Further analysis among the subjects with elevated D-dimer level showed significant negative correlations were observed between D-dimer levels and anemia-related parameters, including hemoglobin, erythrocyte count, and hematocrit (all $p<0.05$). Elevated D-dimer was also associated with immune dysregulation, reflected by increased basophil percentages and decreased immunoglobulin (Ig) levels. Additionally, D-dimer levels showed significant positive correlations with aspartate aminotransferase (AST), alanine aminotransferase (ALT), and blood urea nitrogen (BUN), suggesting a link between hypercoagulability and kidney as well as renal dysfunction following burn injury.

CONCLUSION: Leukocyte count, RDW-CV, and RDW-SD are higher in burn patient with elevated D-dimer levels, suggesting that high D-dimer might be correlated with VTE. Elevated D-dimer in burn patients correlates with several VTE risks including anemia, immune dysregulation, and hepatic–renal dysfunction, indicating early coagulation activation and systemic injury following burn injury.

KEYWORDS: burn injury, D-dimer, hypercoagulability, VTE, anemia, immune dysregulation, organ dysregulation

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Introduction

Burn injury is a major global health problem that highly contributing to morbidity and mortality.(1,2) Approximately 180,000 burn-related deaths occur annually, largely due to shock, infection, and multiorgan failure.(3,4) Conditions such as immunosuppression and burn-related anemia are also often happened in burnt patient, increasing the mortality rate even higher.(4,5) Since severe burn often result in prolonged hospitalization and substantial economic burden, it requires immediate medical attention before the condition get worse and complication may happened.(6,7)

Burn patients are at a markedly increased risk of thrombosis due to the simultaneous presence of all three components of Virchow's triad, which includes endothelial injury from thermal trauma and inflammation, venous stasis due to immobilization and mechanical ventilation, and hypercoagulability driven by inflammatory and coagulation cascades that elevate coagulation factors.(8-10) Severe burns initiate a profound systemic inflammatory response that rapidly induces hypercoagulability, accompanied by some hematologic alterations, immune dysregulation, and hepatic and renal dysfunction, collectively predisposing patients to venous thromboembolism (VTE).(3,11,12) VTE represents a preventable yet frequently underrecognized complication, with an incidence ranging from 0.2% to 25%.(13)

Despite the higher risk of VTE occurrence in burn patient, VTE usually remains clinically undetected. In burn patients, elevated D-dimer levels are often correlated with an increased risk of VTE, which are linked to greater burn severity and poorer outcomes.(8,14) D-dimer is known as a sensitive but nonspecific marker that might supports VTE exclusion when used with clinical assessment.(10,15) However, the clinical utility of D-dimer in burn patients remains uncertain, with studies reporting inconsistent associations between D-dimer levels and other burn-related outcomes.(9,16) Notably, data focusing on very early coagulation responses and comprehensive biological markers as determinants of D-dimer levels in burn patient remain limited, particularly in low- and middle-income country settings. Therefore, this study was conducted to evaluate the correlation between D-dimer levels and other variables related to VTE, such as haematology and coagulation parameters, immunology parameters, hepatic and renal functions, as well as the burn characteristics itself.

Methods

Study Design and Subjects Recruitment

This prospective analytical observational study was conducted at the Burn Unit of Dr. Soetomo General Hospital, Surabaya, Indonesia, from March to June 2025. Adult patients (aged >18 years old) with acute burn injuries admitted during the study period were consecutively recruited. Subjects were excluded if they had pregnancy, malignancy, hematologic disorders, and use any medications affecting coagulation. Subjects participating in other clinical studies were also excluded. The sample size calculation performed using a correlation formula (α=0.05, β=0.2, r=0.6) yielded a minimum requirement of 20 subjects. The protocol of this study was approved by The Institutional Health Research Ethics Committee, Dr. Soetomo General Hospital (No. 1243/KEPK/II/2025).

Data Collection of Subjects Characteristics

Subjects' demographic and anthropometric characteristics, as well as history of existing comorbidities were documented from the subjects' medical records. Any procedures following the burn injury and complication that occurred after the injury were also documented. Burn area and burn extent was assessed using the Rule of Nines or Lund–Browder chart, while burn thickness was classified according to Australian and New Zealand Burn Association (ANZBA) criteria (epidermal, superficial-dermal, mid-dermal, deep-dermal, and full-thickness).(17) Subjects were followed until July 2025 to document the subjects' length of stay (LOS) at the hospital, adverse event, and survival status.

Measurement of D-Dimer Level

All blood samples were collected immediately via venipuncture within 0-48 hours post injury from subjects and centrifuged to separate the plasma. As much as 200 µL of the plasma obtained was used for the D-dimer measurement using the VIDAS® D-Dimer Exclusion II™ kit (Catalog No. 30455; BioMérieux SA, Marcy-l'Étoile, France) with automated Enzyme-Linked Fluorescent Assay (ELFA) method. Initially, the plasma was pipetted into the D-Dimer Exclusion II (DEX2) strip, then the DEX2 strips and the associated solid phase receptacle (SPR) were loaded into the VIDAS instrument. The test was performed for 20 minutes, and the D-dimer concentration were reported in ng/mL (FEU).

Measurement of Complete Blood Count and Coagulation Profiles

Hematology and coagulation profiles of the burn subjects were also investigated to see their correlation with VTE. The hematology profiling was performed by collecting the whole blood in an ethylenediaminetetraacetic acid (EDTA) tube and analyzing the complete blood count using an automated hematology analyzer (Sysmex XN-3000, Sysmex Corporation, Kobe, Japan) following the manufacturer instruction.

Meanwhile, plasma samples from the subjects were collected for the coagulation profiles analysis. The plasma is mixed with specific reagents and calcium, and then the coagulation parameters including the partial thromboplastin time (PTT) and the activated partial thromboplastin time (aPTT) were assessed using a fully automated coagulation system (Sysmex CS-2500, Sysmex Corporation) following the manufacturer instruction.

Hepatic and Renal Function

Serum samples from subjects were collected for the analysis of hepatic and renal function associated with burn injury. Hepatic function parameters, including aspartate aminotransferase (AST), alanine aminotransferase (ALT), and albumin, as well as renal function parameters including blood urea nitrogen (BUN) and creatinine, were analyzed using an automated chemistry analyzer (Dimension EXL with LM, Siemens Healthineers, Newark, DE, USA) following the manufacturer instruction.

Statistical Analysis

For categorical variables, distributions were outlined using frequency and percentage, whereas continuous variables were presented as median and the corresponding minimum–maximum interval. Comparisons between groups and correlation analysis were performed with statistical significance set at $p<0.05$. Data analysis was performed using SPSS v. 25.0 (IBM Corporation, Armonk, NY, USA).

Results

Subjects' Baseline and Burn Characteristics

Total of 20 burn subjects were recruited during the study period, with the cohort being predominantly male (75%). The median age of subjects was 36.5 (21.0–58.0) years old. Seven subjects had existing comorbid before the burn injury, which include hypertension, type 2 diabetes mellitus, asthma, and congestive heart disease (Table 1).

In this study, the most common etiology of the burn injury was caused by flame (60%), followed by electrical burns and scalds. Among these 20 subjects, 40% of subjects had burn injuries that reached full-thickness, 15% of subjects had burn injuries that reached deep-dermal, 25% of subjects

Table 1. Subjects' demographic, anthropometric, and burn characteristics (n=20).

Characteristic	Value
Age, median (min-max)	36.5 (21.0–58.0)
Gender, n (%)	
Male	15 (75)
Female	5 (25)
BMI, median (min-max)	24.6 (18.0–33.1)
BMI, n (%)	
<18.5 (underweight)	1 (5)
18.5-24.9 (normal)	10 (50)
25.0-29.9 (overweight)	8 (40)
>30.0 (obese)	1 (5)
History of Comorbid	
Yes, n (%)	7 (35)
Hypertension	3 (15)
Type 2 Diabetes Mellitus	1 (5)
Asthma	1 (5)
Congestive Heart Disease	1 (5)
Others	1 (5)
No, n (%)	13 (65)
Source/Etiology of Burn Injury, n (%)	
Flame	12 (60)
Electrical	3 (15)
Scald	2 (10)
Blast injury	1 (5)
Chemical	1 (5)
Flame-scald	1 (5)
Burn Thickness, n (%)	
Epidermal	0 (0)
Superficial-dermal	4 (20)
Mid-dermal	5 (25)
Deep-dermal	3 (15)
Full-thickness	8 (40)
Surgical Procedure Following Burn Injury, n (%)	
Yes	2 (10)
No	18 (90)
Inhalation Trauma After Burn Injury, n (%)	
Yes	14 (70)
No	6 (30)
Other Complications After Burn Injury, n (%)	
Yes	8 (40)
No	12 (60)
D-dimer Levels (ng/mL), median (min-max)	1076.5 (270-35000)
D-dimer Levels Classification, n (%)	
Normal (<500 ng/mL)	2 (10)
Elevated (≥500 ng/mL)	18 (90)

had burn injuries that reached mid-dermal, and 20% of subjects reached superficial-dermal (Table 1). To illustrate the burn characteristics assessed in this study, macroscopic examples of acute burn injuries are provided, focusing on the representative areas evaluated for burn depth (Figure 1). After the burn injury, two subjects had to undergo surgical procedures for debridement and escharotomy. Fourteen subjects suffered from inhalation trauma, while eight subjects also suffered from other complications such as hypoalbuminemia, metabolic acidosis, or elevated liver enzymes.

Subjects' Characteristics Based on D-dimer Classification

The median D-dimer level was 1076.5 (270.0-35000.0) ng/mL. Based on the D-dimer standard cut-off, the subjects were then further classified into subjects with normal D-dimer (<500 ng/mL) and elevated D-dimer (≥500 ng/mL) levels.(18) Only two subjects among 20 recruited subjects had normal D-dimer level, while the other 18 subjects had elevated D-dimer level (Table 1). Therefore, comparisons between the normal D-dimer subjects and elevated D-dimer subjects were further analyzed. Based on the D-dimer cut-off, there was a significant difference of D-dimer level on Normal D-dimer group and Elevated D-dimer group (p=0.023) (Table 2).

Though not statistically different, the percentage of the burn area was higher in the Elevated D-dimer group compared to the Normal D-dimer group. The RDW-CV and RDW-SD were also showing tendency to be higher in the Elevated D-dimer group than the Normal D-dimer group. A significant higher leucocyte count was found in the Elevated D-dimer group compared to the Normal D-dimer group, with p=0.023 (Table 2). Since these parameters likely represent a heightened inflammatory and hypercoagulable state associated with VTE, further analysis focusing on the subjects with elevated D-dimer level was performed.

Higher D-dimer was Correlated with Burn-related Anemia in Elevated D-dimer Group

Using the cut-off of ≥500 ng/mL, 18 subjects with the elevated D-dimer was then further classified into four category: 500–<1000 ng/mL group, 1000–<5000 ng/mL group, 5000–<10000 ng/mL group, and ≥10000 ng/mL group.(19) Based on this classification, several hematology parameters related to anemia, namely hemoglobin (r=-0.527, p=0.025), erythrocyte count (r=-0.552, p=0.018) and hematocrit (r=-0.511, p=0.030), were found to be significantly correlated with D-dimer levels. Consistent with the negative correlation coefficients, the hemoglobin, erythrocyte, and hematocrit levels demonstrated a downward trend as D-dimer levels increased (Table 3, Figure 2). These findings suggested that elevated D-dimer levels might be associated with burn-related anemia in burn subjects.

Higher D-dimer was Correlated with State of Immune Dysregulation Following Burn Injury in Elevated D-dimer Group

When the D-dimer level classified as mentioned above, some immune-related parameters also demonstrated distinct trends across the groups. Basophil percentage showed an overall upward tendency along with the increasing D-dimer levels and also shown to have significant positive correlation (r=0.688, p=0.002) (Table 3, Figure 3). In contrast, immunoglobulin (Ig) percentage and absolute Ig displayed a gradual decreasing trend along with the increase of D-dimer level, which also supported by the negative correlation coefficient in both parameters (r=-0.472, p=0.048 and r=-0.497, p=0.036, respectively). The upward trend of basophil counts and downward trend in Ig levels observed in this study might suggest a state of immune dysregulation following burn injury as reflected by elevated D-dimer level.

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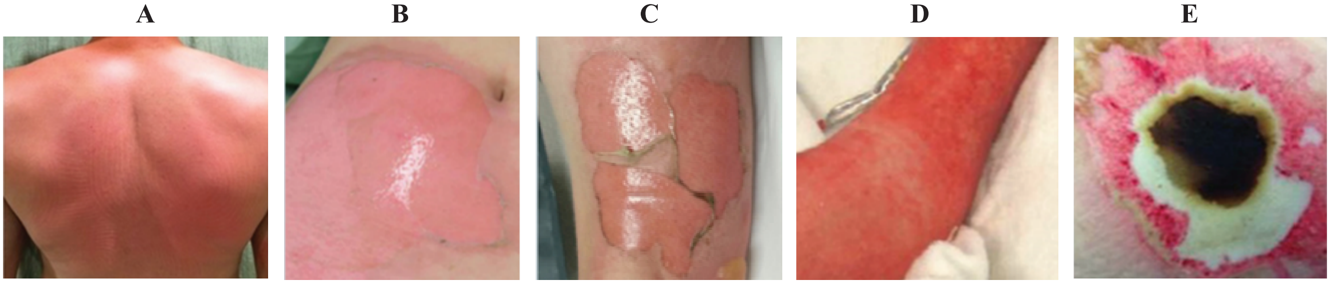

Figure 1. Macroscopic visualization of acute burn tissue showing typical characteristics evaluated according to ANZBA criteria. A: Epidermal burn; B: Superficial-dermal burn; C: Mid-dermal burn; D: Deep-dermal burn; E: Deep-dermal.

Table 2. Comparison of VTE-related variables between subjects with normal and elevated D-dimer levels.

Parameter	Median (min-max)		*p*-value
	Normal D-dimer (n=2)	Elevated D-dimer (n=18)	
D-dimer (ng/mL)	270.0 (270.0–270.0)	1127.0 (539.0–35300.0)	0.023*
Burn Area (%)	24.7 (22.5–27.0)	32.7 (3.0–93.5)	0.450
Hemoglobin (g/dL)	13.6 (12.1–15.1)	16.1 (11.8–21.8)	0.207
Erythrocyte (10^6/μL)	5.1 (4.1–6.1)	5.6 (3.9–3.4)	0.614
Hematocrit (%)	40.6 (36.6–44.6)	46.3 (34.0–67.0)	0.208
Leucocyte (10^3/μL)	9.0 (8.4–9.7)	18.3 (10.6–43.6)	0.023*
Platelet (10^3/μL)	326.5 (287.0–366.0)	293.5 (16.8–1174.0)	0.705
Basophil (%)	0.6 (0.6–0.6)	0.3 (0.1–83.6)	0.051
Eosinophil (%)	2.1 (2.0–2.3)	0.1 (0.0–28.1)	0.085
Neutrophil (%)	53.5 (43.7–63.4)	84.6 (24.0–94.0)	0.131
Lympocyte (%)	36.6 (27.8—45.4)	7.6 (1.9–104.0)	0.059
Monocyte (%)	7.1 (6.2–8.0)	6.0 (1.1–41.4)	0.488
Ig (%)	0.4 (0.2–0.7)	0.6 (0.3–2.9)	0.281
Ig Absolute (10^3/μL)	0.0 (0.0–0.0)	0.1 (0.0–1.0)	0.163
MCV (fL)	81.8 (73.2–9.4)	83.4 (74.8–91.5)	0.801
MCH (pg)	27.3 (24.8–29.9)	28.1 (24.9–31.3)	0.752
MCHC (g/dL)	33.5 (33.1–33.9)	33.5 (31.2–36.4)	0.950
RDW-CV (%)	12.7 (12.5–13.0)	13.1 (11.7–41.1)	0.527
RDW-SD (fL)	37.4 (31.8–43.1)	39.8 (33.8–45.5)	0.900
NRBC Absolute (10^3/μL)	0.0 (0.0–0.0)	0.0 (0.0–0.2)	0.542
PDW (fL)	9.8 (9.3–10.4)	10.3 (8.1–13.2)	0.488
MPV (fL)	9.1 (9.0–9.3)	9.5 (8.5–10.8)	0.313
P-LCR (%)	17.9 (15.5–20.3)	21.3 (12.9–31.7)	0.208
PPT (sec)	13.5 (13.2–13.8)	13.1 (9.8–24.6)	0.528
aPPT (sec)	25.7 (24.8–26.7)	26.5 (23.3–46.9)	0.488
AST (U/L)	30.0 (28.0–32.0)	49.5 (19.0–280.0)	0.207
ALT (U/L)	41.5 (30.0–53.0)	33.0 (18.0–208.0)	0.488
Albumin (g/dL)	3.9 (3.9–3.9)	3.3 (1.4–4.4)	0.207
BUN (mg/dL)	12.5 (10.0–15.0)	11.0 (6.0–22.0)	0.657
Creatinine (mg/dL)	1.3 (1.2–1.3)	0.9 (0.5–1.9)	0.165
Length of Stay (days)	15.5 (12.0–19.0)	22.5 (3.0–67.0)	0.449

*Significant if $p<0.05$, analyzed with Mann-Whitney U test.

Higher D-Dimer was Correlated with Hepatic and Renal Dysfunction Following Burn Injury in Elevated D-dimer Group

Based on the correlation analysis, hepatic function parameters including AST and ALT showed very significant positive correlation (r=0.725, p=0.001 and r=0.711 and p=0.001, respectively) with the D-dimer levels classification as previously mentioned. There were also downward tendency in AST and ALT levels from the group with lower D-dimer level to higher D-dimer level (Table 3, Figure 4). These elevated AST and ALT levels along with elevated D-dimer level might suggest hepatic dysfunction following burn injury.

Similar with hepatic function parameter, the renal function parameter, BUN also showed an increasing trend along with increasing D-dimer level, with the lowest BUN level in 500–<1000 ng/mL D-dimer group and the highest level in ≥10000 ng/mL D-dimer group. This increase was also aligned with the significant positive correlation (r=0.473, p=0.047) based on the correlation analysis (Table 3, Figure 4), thus showing that elevated D-dimer might be also related to renal dysfunction in subjects with burn injury.

Table 3. Comparison of VTE-related variables in subjects with elevated D-dimer levels based on the D-dimer level classification.

Parameter	Median (min-max)				Correlation with D-dimer Classification	
	D-dimer 500-999.9 ng/mL (n=6)	D-dimer 1000-4999.9 ng/mL (n=10)	D-dimer 5000-9909.9 ng/mL (n=1)	D-dimer ≥10000 ng/mL (n=1)	Coefficient r	*p*-value
D-dimer (ng/mL)	763.0 (539.0–943.0)	1223.5 (1062.0–4459.0)	7310.0 (7310.0–7310.0)	35300(35300.0–35300.0)	0.778	0.000*
Burn Area (%)	37.0 (3.0–73.0)	34.5 (7.5–93.5)	20.0 (20.0–20.0)	9.0 (9.0–9.0)	-0.304	0.219
Hemoglobin (g/dL)	19.5 (12.8–20.9)	15.7 (11.8–21.8)	13.5 (13.5–13.5)	12.5 (12.5–12.5)	-0.527	0.025*
Erythrocyte (10^6/µL)	6.9 (4.9–8.4)	5.5 (3.9–0.9)	5.4 (3.9–7.0)	4.4 (4.4–4.4)	-0.552	0.018*
Hematocrit (%)	57.3 (39.6–67.0)	45.5 (34.0–64.5)	42.2 (42.2–42.2)	37.2 (37.2–37.2)	-0.511	0.030*
Leucocyte (10^3/µL)	28.6 (15.3–43.6)	16.7 (10.6–27.1)	14.1 (14.1–14.1)	14.6 (14.6–14.6)	-0.572	0.013*
Platelet (10^3/µL)	338.5 (259.0–1174.0)	281.0 (16.8–430.0)	198.0 (198.0–198.0)	274.0 (274.0–274.0)	-0.336	0.172
Basophil (%)	0.2 (0.2–0.6)	0.3 (0.1–0.4)	0.4 (0.4–0.4)	83.6 (83.6–83.6)	0.688	0.002*
Eosinophil (%)	0.0 (0.0–2.0)	0.1 (0.0–6.6)	0.1 (0.1–0.1)	28.1 (28.1–28.1)	0.681	0.002*
Neutrophil (%)	91.4 (79.5–94.0)	83.5 (24.0–86.4)	87.0 (87.0–87.0)	33.6 (33.6–33.6)	-0.542	0.020*
Lympocyte (%)	4.1 (3.2–11.3)	8.7 (1.9–31.5)	7.5 (7.5–7.5)	13.6 (13.6–13.6)	0.142	0.574
Monocyte (%)	4.1 (1.7–7.0)	6.9 (1.1–9.3)	5.0 (5.0–5.0)	41.4 (41.4–41.4)	0.731	0.001*
Ig (%)	1.0 (0.3–2.9)	0.5 (0.3–1.1)	0.4 (0.4–0.4)	0.3 (0.3–0.3)	-0.472	0.048*
Ig Absolute (10^3/µL)	0.2 (0.0–1.0)	0.1 (0.0–0.3)	0.1 (0.1–0.1)	0.0 (0.0–0.0)	-0.497	0.036*
MCV (fL)	81.7 (74.8–83.2)	86.0 (80.8–91.5)	78.0 (78.0–78.0)	83.6 (83.6–83.6)	0.216	0.389
MCH (pg)	26.5 (24.9–29.8)	28.9 (28.0–31.3)	25.0 (25.0–25.0)	28.1 (28.1–28.1)	0.146	0.563
MCHC (g/dL)	33.0 (31.2–35.9)	33.9 (32.5–36.4)	32.0 (32.0–32.0)	33.6 (33.6–33.6)	-0.027	0.915
RDW-CV (%)	15.7 (12.8–41.1)	12.5 (11.7–13.7)	14.3 (14.3–14.3)	13.6 (13.6–13.6)	-0.331	0.179
RDW-SD (fL)	39.5 (35.8–41.8)	39.4 (33.8–45.5)	39.8 (39.8–39.8)	41.4 (41.4–41.4)	0.161	0.523
NRBC Absolute (10^3/µL)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	-0.098	0.700
PDW (fL)	10.5 (9.3–13.2)	10.6 (8.8–13.0)	9.9 (9.9–9.9)	8.1 (8.1–8.1)	-0.397	0.103
MPV (fL)	9.5 (9.0–10.8)	9.7 (8.9–10.7)	9.3 (9.3–9.3)	8.5 (8.5–8.5)	-0.364	0.137
P-LCR (%)	21.7 (16.6–31.7)	22.1 (16.1–28.9)	20.7 (20.7–20.7)	12.9 (12.9–12.9)	-0.375	0.125
PPT (sec)	12.7 (9.8–18.0)	13.2 (10.7–24.6)	11.5 (11.5–11.5)	15.1 (15.1–15.1)	0.037	0.883
aPPT (sec)	28.9 (23.3–46.9)	26.5 (24.3–39.0)	25.9 (25.9–25.9)	28.7 (28.7–28.7)	-0.172	0.495
AST (U/L)	44.5 (28.0–95.0)	52.5 (19.0–83.0)	154.0 (154.0–154.0)	280.0 (280.0–280.0)	0.725	0.001*
ALT (U/L)	38.0 (23.0–53.0)	40.5 (18.0–43.0)	99.0 (99.0–99.0)	208.0 (208.0–208.0)	0.711	0.001*
Albumin (g/dL)	3.2 (2.5–4.4)	3.4 (1.4–4.1)	4.4 (4.4–4.4)	3.6 (3.6–3.6)	0.213	0.396
BUN (mg/dL)	8.5 (6.0–16.0)	11.0 (7.0–22.0)	13.0 (13.0–13.0)	21.0 (21.0–21.0)	0.473	0.047*
Creatinine (mg/dL)	0.9 (0.5–1.9)	0.8 (0.5–1.4)	0.9 (0.9–0.9)	0.9 (0.9–0.9)	-0.127	0.617
Length of Stay (days)	28.5 (8.0–67.0)	24.0 (3.0–65.0)	11.0 (11.0–11.0)	21.0 (21.0–21.0)	-0.208	0.408

*Significant if $p<0.05$. Correlation analysis performed with Pearson correlation test.

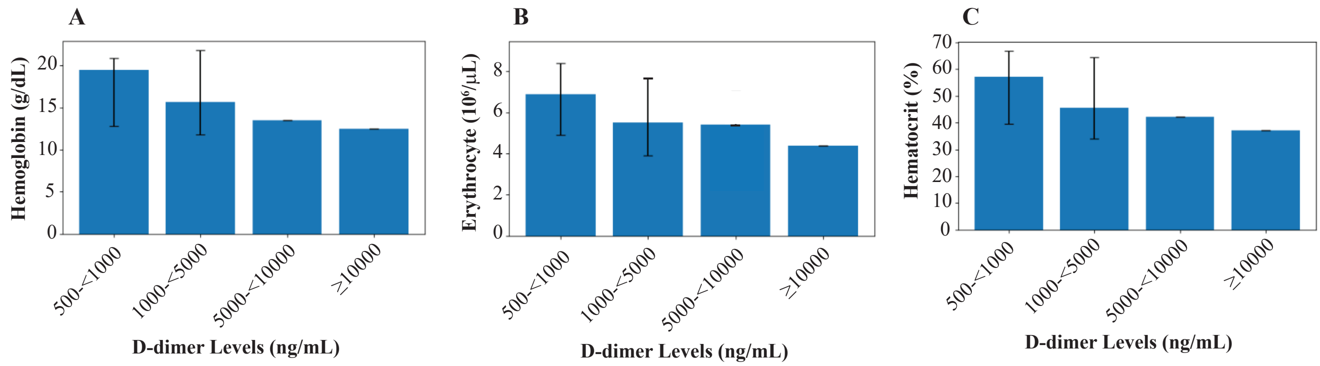

Figure 2. The downward tendency of anemia-related parameter in elevated D-dimer subjects. A: Hemoglobin. B: Erythrocyte count. C: Hematocrit.

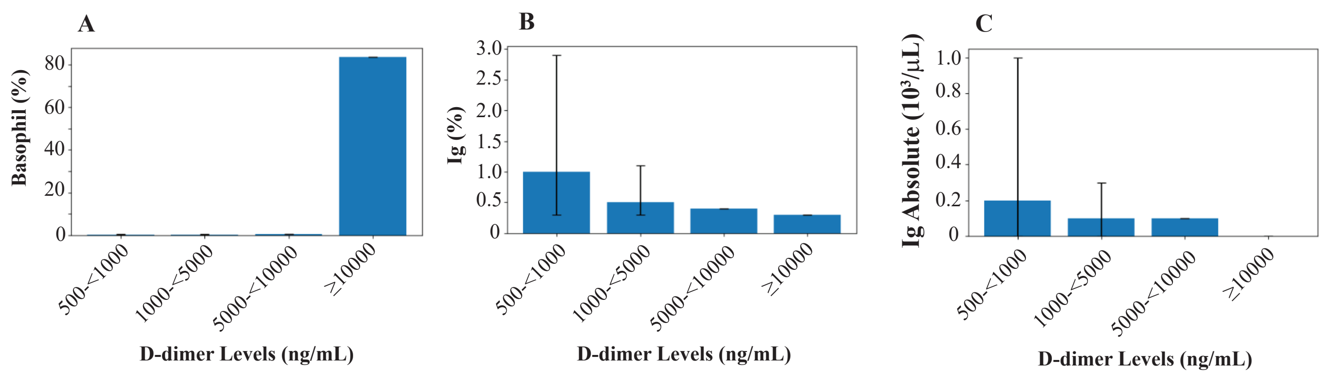

Figure 3. The upward tendency of basophil count and downward tendency of Ig levels in elevated D-dimer subjects. A: Basophils count. B: Ig percentage. C: Ig absolute.

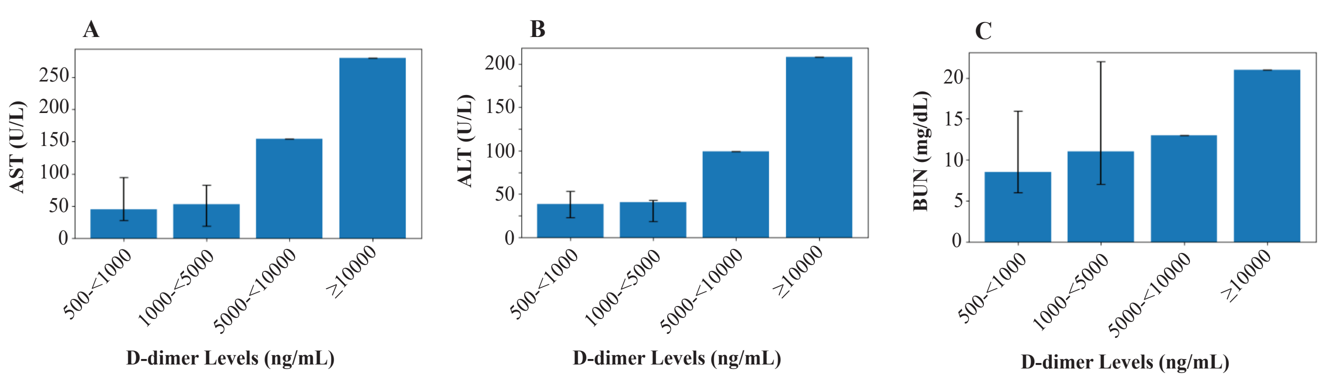

Figure 4. The upward tendency of hepatic and renal function parameters in elevated D-dimer subjects. A: AST. B: ALT. C: BUN.

Discussion

The result of this study demonstrates that elevated D-dimer levels were highly prevalent among burn subjects (18 out of 20 subjects) and were associated with several markers of hematological alterations, immune imbalance, and organ dysfunction which are often associated with VTE. The majority of subjects exhibited D-dimer levels above the standard cut-off (Table 1), reflecting early activation of coagulation and fibrinolytic pathways triggered by tissue injury and systemic inflammation during the acute phase of burn injury, particularly within the first 48 hours post-burn.(10,14,20) However, early burn-induced coagulopathy is heterogeneous, and D-dimer elevation might be influenced by multiple variables, either burn-related or non-burn related.(15) For the burn-related variables, in this study, the source of the burn was showing significant correlation with D-dimer levels, where D-dimer levels were higher in non-flame burns than in flame burns. The higher D-dimer levels observed in non-flame burns may reflect deeper tissue destruction and more extensive endothelial and microvascular injury, particularly in electrical and blast-related mechanisms, which are known to induce pronounced coagulation activation disproportionate to the apparent cutaneous injury.(21,22)

As for the non-burn-related variables that might influence D-dimer level in burn subjects, several variables in this study markedly show significant results. The significantly higher leukocyte counts were observed in the elevated D-dimer group compared to the normal D-dimer group (Table 2), further reinforce the link between hypercoagulability and systemic inflammatory response. In parallel, increased RDW indices (RDW-CV and RDW-SD) in the elevated D-dimer group (Table 2) might suggest the anisocytosis driven by inflammation, oxidative stress, and impaired erythropoiesis, which are known to predict adverse outcomes in severe burns and other critical illnesses.(23,24) Together, these findings are consistent with the established interaction between inflammation and coagulation in burn pathophysiology, where endothelial injury and altered red cell morphology contribute to a prothrombotic state and is associated with VTE.(23-25)

To further analysed various variable that might be related to non-burn related variables that might influence D-dimer, further analysis focusing on the 18 subjects with elevated D-dimer level was performed. Based on correlation analyses it was assumed that elevated D-dimer level might be related to anemia, immune dysregulation, and systemic organ dysfunction following acute burn injury, supporting the finding of previous studies.(16,26,27) Among the elevated D-dimer subjects, in this study, increasing D-dimer levels were significantly correlated with declining hemoglobin, erythrocyte count, and hematocrit level, demonstrating a clear downward trend in anemia-related parameters, suggesting that heightened fibrinolytic activity may parallel the severity of burn-related anemia. These observed negative associations suggest a shared pathophysiological response to burn injury rather than an isolated hematologic abnormality.(9,27) Burn-related anemia, resulting from blood loss, hemodilution, hemolysis, and inflammation-mediated suppression of erythropoiesis, may contribute to tissue hypoxia and endothelial activation.(28) Hypoxia-induced procoagulant signaling and hemolysis-associated nitric oxide depletion can enhance thrombin generation and fibrin turnover, thereby increasing circulating D-dimer levels. These findings support the concept that anemia in burn patients reflects systemic injury severity and inflammatory-coagulatory crosstalk, which may predispose patients to VTE.(9,29)

In addition to hematologic changes, D-dimer levels were significantly associated with markers suggestive of immune dysregulation. A strong positive correlation was observed between D-dimer and basophil percentage, with an upward trend across increasing D-dimer strata. Conversely, Ig percentage and absolute Ig levels demonstrated significant negative correlations and a progressive decline as D-dimer levels increased. The tendency of elevated basophil counts and trend in the reduction of Ig observed suggests a state of immune dysregulation following acute burn injury.(30,31) While basophils contribute to inflammatory signaling through the release of histamine and Th2-associated cytokines, impaired humoral immunity may limit effective immune regulation, resulting in persistent endothelial activation. This sustained inflammatory–endothelial interaction can promote ongoing coagulation cascade activation and fibrin turnover, as reflected by elevated D-dimer levels.(32) Although neither basophilia nor hypogammaglobulinemia independently predicts VTE, their coexistence may indicate a prolonged prothrombotic milieu in burn patients.

Furthermore, higher D-dimer levels were strongly correlated with elevations in hepatic transaminases and BUN, indicating an association with hepatic and renal dysfunction. The significant positive correlations between D-dimer and AST, ALT, and BUN suggest that coagulation activation may parallel the extent of organ injury. In severe burns, systemic inflammation, hypoperfusion, and microvascular thrombosis contribute to multiorgan dysfunction.(33) Burn-related hepatic injury may disrupt the balance between procoagulant and anticoagulant pathways, favouring thrombin generation and increased fibrin turnover.(34,35) While renal dysfunction may reduce the clearance of fibrin degradation products and perpetuate inflammatory signaling. This concurrent renal dysfunction, reflected by elevated BUN, may further perpetuate endothelial activation and impair the clearance of proinflammatory and procoagulant mediators.(36) Together, these alterations might indicate a sustained prothrombotic milieu associated with multiorgan stress, which may increase susceptibility to VTE rather than directly indicating overt thrombosis post burn injury.

These findings suggest D-dimer elevation reflects systemic inflammatory and coagulation responses involving hematologic, immunologic, and organ function derangements in acute burn injury. Elevation of D-dimer levels beyond normal thresholds supports the presence of early activation of the coagulation and fibrinolytic systems in burn patients (10), underscoring its potential role as a biomarker of systemic pathophysiological response following thermal injury. The current correlation analysis results showed that elevated D-dimer level is associated with various variables related to VTE, however the association with these variables is mainly as a marker of underlying systemic injury rather than a direct cause. Therefore, although this study demonstrates some significant associations of D-dimer levels with burn-related and non-burn-related variables that might be linked to VTE, these findings do not allow confirmation of D-dimer as a definitive biomarker of burn severity. The cross-sectional design, small sample size, single time-point measurement, and limited control of potential confounders restrict the causal interpretation. Given these limitations in establishing causality, future prospective longitudinal studies with larger cohorts, serial measurements, comprehensive coagulation assessment, and careful adjustment for clinical confounders are warranted to clarify the temporal relationship and prognostic relevance of D-dimer in burn injury and its association with clinical outcomes.

Conclusion

The results of this study show that leukocyte count, RDW-CV, and RDW-SD are higher in burn patients with elevated D-dimer levels, suggesting that high D-dimer might be correlated with VTE. Among the elevated D-dimer patients, decreasing hemoglobin, erythrocyte count, and hematocrit levels are correlated with the increase of D-dimer level, indicating its association with burn-related anemia. In addition, progressive increases in basophil counts, decreases in Ig levels and elevations in AST, ALT, and BUN, were observed in parallel with rising D-dimer levels, suggesting that higher D-dimer levels may be associated with immune and systemic organ dysfunction following acute burn injury.

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Authors Contribution

AP, IDS, IH, NHS, and FS were involved in conceptualizing and planning the research. AP performed the subjects recruitment and conducted data acquisition/collection. AP and NMD calculated the experimental data, performed statistical analyses, and designed the tables and figures. AP, NMD, and FS interpreted the results and drafted the initial manuscript. IDS, IH, and NHS gave critical revision and supervised the study. All authors contributed to the final critical revision of the manuscript.

Conflict of Interest

The authors declare no conflicts of interest or competing interests related to the content of this manuscript.

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