Clinical research

Association of von Willebrand factor Ag-to-ADAMTS13 ratio with early sepsis-related mortality

Alaa Efat[1], Sabry Shoeib[1], Ayman Arafa[2], Ashraf Dawod[3], Saleh Saleh[1], Mohamed Abdelhafez[1]

[1]Department of Internal Medicine, Hematology Unit, Faculty of Medicine, Menoufia University, Menoufia, Egypt
[2]Department of Internal Medicine, Hematology Unit, Faculty of Medicine, Zagazig, Egypt
[3]Departement of Biochemistry, Faculty of Medicine, Menoufia University, Menoufia, Egypt

Corresponding author:
Alaa Efat
Department of Internal Medicine Hematology Unit
Faculty of Medicine
Menoufia University
Menoufia, Egypt
E-mail:
alaaefat23@gmail.com
A.hassan14@med.menofia.edu.eg

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Abstract

Introduction: Sepsis is a highly complex syndrome with highly heterogeneous clinical manifestations, which makes it difficult to detect and treat. Von Willebrand factor (vWF) functions differently depending on its multimeric size and adhesive properties, which are regulated by ADAMTS 13. Thus, a decrease in ADAMTS 13 activity results in the persistence of ultralarge vWF and the formation of microvascular thrombi, ischaemia, and organ failure. The aim of the study was to identify the role of von Willebrand factor antigen-to-ADAMTS 13 ratio in predicting early sepsis-related mortality.
Material and methods: This is a cohort of 70 sequentially selected adults with sepsis. The patients were classified into two groups: A (survivors) and B (non-survivors) based upon their survival within 7 days of hospital admission.
Results: VWF Ag, ADAMTS13, and vWF/ADAMTS13 ratio were significant predictors of early hospital mortality. For vWF Ag at a cut-off level of ≥ 3560 ng/l, sensitivity was 76% and specificity was 88.9%. For ADAMTS at a cut-off level of ≤ 210 ng/l, sensitivity was 84% and specificity was reported as 68.9%. For vWF/ADAMTS ratio at a cut off level of ≥ 17, sensitivity was 80% and specificity was 84.4%. There was a statistically highly significant positive correlation between non-survival and levels of vWF and vWF/ADAMTS 13 ratio, and there was a statistically highly significant negative correlation between non-survival and ADAMTS 13 level.
Conclusions: High vWF/Ag and vWF/Ag/ADAMTS13 ratios on day 1 of admission are associated with increased early (7 days) sepsis-related mortality.

Key words: von Willebrand factor, ADAMTS-13, sepsis.

Introduction

Sepsis has been redefined as a life-threatening organ dysfunction caused by dysregulated host response to infection [1].

The incidence of sepsis is 270 cases per 100,000 persons yearly, with an acute mortality rate of 26.0%. A number of factors suggest thatr even this underestimates the magnitude of sepsis [2].

Sepsis cases represent either a new organ dysfunction or worsening of chronic organ dysfunction [3].

Alongside this underestimated incidence globally, the short-term mortality from sepsis is improving. This epidemiology pattern generates approximately 14 million sepsis survivors globally, increasing yearly, with ongoing health care needs [4].

The sepsis response is triggered by an invading pathogen, (bacterial, viral, fungal, etc.), or a pathogen-produced substance, such as endotoxin, called a pathogen-associated molecular pattern. These bind to pattern recognition receptors (PRRs) present on macrophages, and polymorphonuclear and endothelial cells to initiate the release of proinflammatory mediators that cause endothelial cell dysfunction [5].

Von Willebrand factor (vWF) is involved in this process by mediating platelet adhesion and aggregation at sites of vascular injury. It is released from the stimulated endothelium to form hyperactive and ultralarge von Willebrand factor (UL-vWF). vWF functions differently depending on its multimeric size and adhesive properties, which are regulated by a protease, disintegrin and metalloprotease with a thrombospondin type 1 motif, member 13 (ADAMTS 13) [6].

Early diagnosis of sepsis is one of the most important elements of effective treatment, and the availability of accurate sepsis biomarkers to facilitate diagnosis could be of use to enable timely appropriate treatment to be started, thus optimizing a patient's chances of survival [7].

Many co-morbidities, age, and chronic diseases are risk factors both for sepsis and for impaired quality of life; also, poor functional status is a risk factor for becoming critically ill as well as a frequent consequence thereof. Therefore, it is important to distinguish studies that have tried to separate out the potential causal effects of sepsis from those that simply describe morbidity and mortality events [8].

The present study was designed to identify the association of the vWF Ag-to-ADAMTS13 ratio with early sepsis-related mortality.

Material and methods

This single-centre prospective cohort study was carried out at the intensive care unit (ICU) of Menoufia University Hospitals from December 2019 to November 2020. A cohort of sequentially selected 70 adults with sepsis were included. Sepsis was diagnosed according to sepsis 3 criteria.

Patients

Pregnant females, patients < 18 years old, patients with chronic liver disease (CLD), patients with chronic kidney disease (CKD), patients with chronic cardiopulmonary disease, patients with autoimmune diseases or blood disorders, and patients with recent (antecedent 2 weeks) anticoagulant, antiplatelet, or anti-inflammatory therapy were excluded.

Seventy adult patients diagnosed as having sepsis were then classified into 2 groups (A and B) based on their survival within 7 days of hospital admission: Group (A) – survivors; Group (B) – non-survivors.

Ethical considerations

The study protocol was submitted for approval by the Institutional Research Board (IRB) of the Faculty of Medicine, Menofia University. Informed consent was obtained from the hospital authorities. Informed verbal consent was obtained from each participant in the study. Confidentiality and personal privacy was respected in all levels of the study. Collected data are not to be used for any other purpose.

Methods

At presentation (day 1 of ICU admission) all patients were subjected to routine initial work up:

1. Comprehensive history taking, included age, sex, family history, and any other medical or surgical history.
2. Clinical evaluation: included general complete examination and estimation of quick Sequential Organ Failure Assessment (qSOFA) score of 3 points, which comprises altered mentation (Glasgow Coma Scale – GCS < 15), systolic blood pressure (≤ 100 mm Hg), and respiratory rate (≥ 22 breaths/min) was used primarily to select patients.
3. SOFA scoring then was done for all enrolled patients.
4. Routine investigation including the following: routine laboratory tests including complete blood count (CBC), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), serum creatinine, random plasma glucose, liver enzymes, blood culture, and urine analysis.
5. Plasma level estimation of vWF Ag and ADAMTS 13.

Statistical analysis

Data input and analysis was done using the software Statistical Package for the Social Sciences (SPSS) version 24. All results were expressed as mean ± standard deviation. Mean values of the different groups were compared using one-way analysis of variance. Least significant difference (LSD) post hoc analysis was used to identify significantly different mean values. $P < 0.01$ was accepted to denote a highly significant difference.

Results

The mean age of included patients was 60.98 ±7.47 years, 60% of them were male, and 40% female. Pulmonary primary site of infection was found in 44% of patients, while 2.9% of them had gastrointestinal (GIT) infection. Diabetes was re-

ported in 48.6% of patients, while 18.6% of them had cerebrovascular disease. 41.4% of patients needed mechanical ventilation. Mean heart rate, respiratory rate, and temperature were 57 ±9.10 bpm, 22.82 ±2.57 bpm, and 38.49° ±0.69°, respectively. Mean SOFA score was 7.93 ±3.06. Other laboratory results (mean values) were as follows: activated partial thromboplastin time (aPTT) 35.87 ±6.70 s, CRP 65.19 ±17.16 mg/l, ESR 75.74 ±14.98 ml/s, creatinine 1.86 ±0.43 mg/dl, aspartate aminotranspherase (AST) 69.74 ±16.81 U/ml, alanine aminotranspherase (ALT) 73.90 ±16.57 U/l, white blood cells count (WBC) 19.42 ±4.40 × 1000/mm^3, platelet 108.56 ±34.61, hemoglobin (Hb) 10.74 ±0.46 gm/dl, and total bilirubin 1.95 ±0.69 mg/dl. Mean biomarker values were as follows: vWF Ag 3231.7 ±689.5 ng/l, ADAMTS 13 213.1 ±65.6 ng/l, and vWF/ADAMTS13 ratio 18.6 ±13.9 ng/l (Table I).

In the studied patients, non-survival was highly significantly associated with lung infection ($p < 0.01$). Regarding clinical data, non-survival was highly significantly associated with higher respiratory rate and frequency of using ventilator than among the survivors group ($p < 0.01$). SOFA score was significantly higher in non-survivor cases than among survivors ($p < 0.01$). Other laboratory investigations such as APTT, CRP, and WBC are highly significantly higher in non-survivor cases than among survivors ($p < 0.01$). On the other hand, platelet counts were significantly lower in non-survivor cases than among survivors ($p < 0.01$). The vWF Ag and vWF/ADAMTS13 ratio were significantly higher in non-survivor cases than survivors ($p < 0.01$). ADAMTS 13 was highly significantly lower in non-survivor cases than among survivors ($p < 0.01$) (Table II).

SOFA score ≥ 8 had sensitivity 96% and specificity100%. APTT ≥ 38 s had sensitivity 64% and specificity 95.6%. CRP at a cut-off level of > 65 had sensitivity 80% and specificity 80%. WBCs ≥ 19000.4 cells/µl reported sensitivity 80% and specificity 97.8%. Platelets ≤ 105000 cells/µl reported sensitivity 100% and specificity 95.6%. vWF Ag at a cut-off level of ≥ 3560 ng/l had sensitivity 76% and specificity 88.9%. ADAMTS at a cut-off level of ≤ 210 ng/l had sensitivity 84% and specificity 68.9%. VWF/ADAMTS at a cut-off level of ratio ≥ 17 had sensitivity 80 % and specificity 84.4 % (Table III).

There was a statistically highly significantly positive correlation between SOFA score and each of vWF Ag, vWF/ADAMTS13 ratio, respiratory rate, and laboratory investigations (APTT, CRP, WBC) ($p \leq 0.01$). On the other hand, there was a statistically highly significant negative correlation between SOFA score and both ADAMTS 13 platelet level ($p \leq 0.01$) (Table IV).

There was a highly significant positive correlation between vWF Ag and vWF/ADAMTS 13 ratio and respiratory rate, APTT, CRP, and WBC. Also, there was a significant positive correlation between biomarker ADAMTS 13 and platelet level ($p < 0.001$). There was a significant negative correlation

Table I. Baseline characteristics of the studied patients ($n = 70$)

Variables	Studied patients ($n = 70$)
Age [years] mean ± SD	60.98 ±7.47 (38–73)
Sex, *n* (%):	
Male	42 (60)
Female	28 (40)
Site of infection, *n* (%):	
Lung	31 (44.3)
Abdominal cavity	19 (27.2)
Urinary	4 (5.7)
GIT	2 (2.9)
Skin and soft tissue	6 (8.6)
Hepatobiliary	8 (11.4)
History of previous diseases, *n* (%):	
HTN	40 (57.1)
DM	34 (48.6)
Clinical data, mean ± SD:	
Heart rate [beat/min]	106.57 ±9.10
Respiratory rate [breath/min]	22.82 ±2.57
Temperature [°C]	38.49 ±0.69
Ventilator, *n* (%)	29 (41.4)
MABP [mm Hg]	79.10 ±5.51
Altered mental status, *n* (%)	31 (44.3)
SOFA score, mean ± SD (range)	7.93 ±3.06 (1–14)
Laboratory investigation, mean ± SD:	
WBC [10^3/ mm^3]	19.42 ±4.40
Platelets [10^3/mm^3]	108.56 ±34.61
Hb [g/dl]	10.74 ±0.46
Creatinine[mg/dl]	1.86 ±0.43
AST [U/ml]	69.74 ±16.81
ALT [U/ml]	73.90 ±16.57
Total bilirubin [mg/dl]	1.95 ±0.69
aPTT [s]	35.87 ±6.70
CRP [mg/l]	65.19 ±17.16
ESR [ml/min]	75.74 ±14.98
vWF Ag [ng/l]	3231.7 ±689.5
ADAMTS 13 [ng/l]	213.1 ±65.6
VWF/ADAMTS 13 ratio	18.6 ±13.9

MABP – mean arterial blood pressure, SOFA – sequential organ failure assessment, aPTT – activated partial thromboplastin time, CRP – C-reactive protein, vWF – von Willebrand factor, ADAMTS-13 – a disintegrin-like and metalloprotease with thrombospondin type 1 motif.

Table II. Comparison between survivors and non-survivors regarding baseline characteristics of the studied patients (n = 70)

Variables	Survivor (n = 45)	Non survivor (n = 25)	P-value
Age [years] mean ± SD	59.64 ±7.92	63.40 ±5.99	0.043
Sex, n (%):			
Male	26 (57.8)	16 (64)	0.1228
Female	19 (42.2)	9 (36)	0.0588
Site of infection, n (%):			
Lung	15 (33.3)	16 (64)	0.0039*
Abdominal cavity	11 (15.7)	8 (11.4)	0.6195
Urinary	4 (8.9)	0	0.1275
GIT	2 (4.4)	0	0.2883
Skin & soft tissue	5 (11.1)	1(4)	0.3120
Hepatobiliary	8 (17.8)	0	0.4260
History of previous diseases, n (%):			
HTN	25 (55.5)	20 (80)	0.0232
DM	20 (44.4)	14 (56)	0.3574
Clinical data, mean ± SD or n (%):			
Heart rate [beats/min]	102.1 ±8.4	114.6 ±6.6	0.031
Respiratory rate [breaths/min]	21.5 ±1.7	25.3 ±1.9	< 0.001*
Temperature [°C]	38.3 ±0.9	38.9 ±0.5	0.031
Ventilator	12 (26.7)	17 (68)	0.0008*
MABP [mm Hg]	79.3 ±5.9	79.2 ±4.1	0.904
Altered mental status	15 (33.3)	16 (64)	0.0039*
SOFA score, mean ± SD	6.1 ±1.1	11.2 ±2.6	< 0.001*
Laboratory investigation, mean ± SD:			
WBC [10^3/mm^3]	17.01 ±2.1	23.8 ±4.1	< 0.001*
Platelets [10^3/mm^3]	127.4 ±25.9	74.6 ±18.3	< 0.001*
Hb [g/dl]	10.6 ±0.4	10.4 ±0.4	0.041
Creatinine [mg/dl]	1.5 ±0.8	1.9 ±0.6	0.0327
AST [U/ml]	76.2 ±10.8	83.4 ±17.3	0.0355
ALT [U/ml]	75.8 ±11.5	86.7 ±16.7	0.0411
Total bilirubin [mg/dl]	1.5 ±0.3	2.2 ±0.6	0.021
aPTT [s]	32.5 ±3.9	42 ±6.4	< 0.001*
CRP [mg/l]	57.8 ±12.4	78.5 ±16.6	< 0.001*
ESR [ml/min]	68.8 ±13.9	75.2 ±5.9	0.0320
Serum biomarkers, mean ± SD:			
vWF Ag [ng/l]	2873.9 ±471.4	3875.6 ±536.5	< 0.001*
ADAMTS 13 [ng/l]	243.9 ±51.3	157.7 ±50.4	< 0.001*
vWF/ADAMTS 13 ratio	12.6 ±4.6	29.3 ±18.1	< 0.001*

*MABP – mean arterial blood pressure, SOFA – sequential organ failure assessment, aPTT – activated partial thromboplastin time, CRP – C-reactive protein, vWF – von Willebrand factor, ADAMTS-13 – a disintegrin-like and metalloprotease with thrombospondin type 1 motif. *Statistically significant.*

between biomarkers vWF Ag and vWF/ADAMTS 13 ratio and platelet level ($p < 0.001$). Also, there was a statistically highly significant negative correlation between ADAMTS 13 and respiratory rate, APTT, CRP, and WBC ($p < 0.001$) (Table V).

There was a statistically highly significant positive correlation between non-survival and use of a ventilator, levels of vWF, vWF/ADAMTS 13 ratio, SOFA score, and laboratory results of CRP and WBC (r +ve, $p \leq 0.01$). On the other hand, there was a statistically highly significant negative correlation between non-survival and ADAMTS 13 and platelet level (r -ve, $p \leq 0.01$). The odds ratio represents the ratio of incidence of the variable between non-survivor cases and survivor cases (Table VI).

Table III. Predictive value of variables affecting mortality by 7th day by receiver operating characteristic curve (ROC)

Variables	AUC	Cut off	Sens%	Spec%	PPV	NPV	ACC	*P*-value
SOFA score	0.960	> 8	96	100	77.8	90.7	96	< 0.0001*
WBC [thousand/mm^3]	0.947	> 19.4	80	97.8	68	82.8	94.7	< 0.0001*
Platelet [thousand/mm^3]	0.972	≤ 105	100	95.6	74.1	88.4	97.2	< 0.0001*
aPTT [s]	0.884	> 38	64	95.6	88.9	82.7	88.4	< 0.0001*
CRP [mg/l]	0.837	> 65	80	80	84.3	86.2	83.7	< 0.0001*
VWF Ag [ng/l]	0.847	> 3560	76	88.9	79.2	87	84.7	< 0.0001*
ADAMTS 13 [ng/l]	0.779	≤ 210	84	68.9	60	88.6	77.9	< 0.0001*
VWF/ADAMTS 13 ratio	0.826	> 17	80	84.4	74.1	88.4	82.6	< 0.0001*

**Statistically significant.*

Table IV. Correlation coefficient between SOFA score and other variables (n = 70)

Variable	SOFA score	
	Correlation coefficient (r^{sp})	*P*-value
Reparatory rate [breaths/min]	0.570	< 0.0001*
WBC [× 10^3/mm^3]	0.788	< 0.0001*
Platelet [× 10^3/mm^3]	–0.709	< 0.0001*
aPTT [s]	0.848	< 0.0001*
CRP [mg/l]	0.662	< 0.0001*
vWF Ag [ng/l]	0.784	< 0.0001*
ADAMTS 13 [ng/l]	–0.732	< 0.0001*
vWF/ADAMTS 13	0.699	< 0.0001*

**Statistically significant.*

Table V. Correlation coefficients between vWFAg, ADAMTS 13, and vWFAg/ADAMTS 13 ratio and other variables (n = 70)

Variable		vWF Ag	ADAMTS 13	vWF/ADAMTS 13
Respiratory rate [cycle/min]	r^{sp}	0.418	–0.343	0.265
	P-value	0.0004*	0.0035*	0.0293
WBC [× 10^3/mm^3]	r^{sp}	0.760	–0.755	0.742
	P-value	< 0.0001*	< 0.0001*	< 0.0001*
Platelet [× 10^3/mm^3]	r^{sp}	–0.736	0.677	–0.613
	P-value	< 0.0001*	< 0.0001**	< 0.0001*
aPTT [s]	r^{sp}	0.589	–0.548	0.507
	P-value	< 0.0001*	< 0.0001*	< 0.0001*
CRP [mg/l]	r^{sp}	0.738	-0.712	0.669
	P-value	< 0.0001*	< 0.0001*	< 0.0001*

**Statistically significant.*

Table VI. Logistic regression for risk of 7 days in sepsis-related mortality

Variables	Odds ratio	Coefficient (r)	95% CI	*P*-value
SOFA score	3.22	1.16967	1.8700–5.5478	< 0.0001*
Ventilator	5.84	1.76537	2.0065–17.0194	0.0012*
WBC [× 10^3/mm^3]	2.32	0.84217	1.4850–3.6289	0.0002*
Platelet [× 10^3/mm^3]	0.90	–0.10027	0.8636–0.9475	< 0.0001*
CRP [mg/l]	1.09	0.093569	1.0498–1.1485	< 0.0001*
vWF Ag [ng/l]	1.002	0.00230	1.0012–1.0034	< 0.0001*
ADAMTS 13 [ng/l]	0.98	–0.016856	0.9733–0.9934	0.0012*
vWF/ADAMTS 13	1.07	0.068348	1.0098– 1.1354	0.0045*

**Statistically significant.*

Discussion

The main aim of this study is to detect the possible association between the baseline of the vWF Ag-to-ADAMTS 13 ratio and early (7 days) sepsis-related mortality in addition to detection of correlation between the baseline of the vWF Ag-to-ADAMTS 13 ratio and other clinico-laboratory variables in non-survivors in a cohort of Egyptian adults with sepsis.

Within the studied patients, non-survival was highly significantly associated with lung infection ($p < 0.01$). Regarding clinical data, non-survival was highly significantly associated with higher RR and frequency of using a ventilator than among survivors ($p < 0.01$). VWF Ag and vWF/ADAMTS 13 ratio were significantly higher in non-survivor cases than in survivors ($p < 0.01$). ADAMTS 13 was highly significantly lower in non-survivor cases than survivors ($p < 0.01$). Other laboratory investigations such as CRP and WBC were significantly higher in non-survivor cases than among survivors ($p < 0.01$). On the other hand, the platelet count was highly significantly lower in non-survivor cases than among survivors ($p < 0.01$).

A physiological immune response eradicates pathogens by a complex process with generation of proinflammatory and anti-inflammatory cytokines. Inappropriate regulation of these normal reactions in sepsis can become generalized and deleterious [9].

Multiple organ dysfunction syndrome (MODS) and refractory shock are the main causes of death [10]. Impaired neutrophil migration to the infectious focus combined with an inappropriate sequestration of these cells in secondary organs, together with endothelial dysfunction, may exaggerate that [11].

Our results agreed with results obtained with Caraballo *et al.* [10], who reported a significantly higher percentage of mechanical ventilation in non-survivors than survivors, and this may indicate an increase in sepsis severity.

VWF:Ag remained independently associated with in-hospital mortality after adjustment for inflammatory biomarkers, which supports the hypothesis of additional causes of vWF secretion by endothelial cells (ECs). Indeed, endothelium is emerging as a key target organ of SARS infection [12].

South *et al.* [13] concluded that an imbalance in the vWF/ADAMTS 13 axis causing increased vWF reactivity may contribute to the formation of platelet-rich thrombi in the pulmonary vasculature through immune and inflammatory responses.

It is possible that increased levels of vWF can bind and clear ADAMTS 13 from circulation due to differences in their circulating half-lives [14]. Consistent with this hypothesis, caecal ligation and puncture (CLP)-induced sepsis resulted in an increase in vWF secretion and a decrease in ADAMTS 13 [15].

There are potential consequences of reduced ADAMTS 13 activity and elevated vWF levels. ADAMTS 13 and vWF levels did not normalize in survivors at discharge. The prolonged imbalance in vWF and ADAMTS 13 may contribute to the microvascular thrombosis, ischaemic stroke, and organ damage observed in some patients who survive sepsis [16].

In the current study, white blood cell count and CRP were high; these results agreed with results obtained with Caraballo *et al.* [10], in which it was observed that WBCs and CRP increased in patients with sepsis. It is also in agreement with Shoeib *et al.*, 2020 [17].

Another study [18] demonstrated that aPTT has a sensitivity of 22–55% at admission and 48–74% during intensive care unit (ICU) stay for predicting the diagnosis of sepsis among patients admitted to the surgical ICU, whereas the specificity varied between 92% and 98% at admission and between 81% and 94% during ICU stay. Also, Katoch *et al.* showed that aPTT has very good specificity of 100% and reasonable sensitivity of 55.56% for maternal sepsis at a cut-off value of 38.65 s [19].

Benediktsson *et al.* [20] studied the relationship between international normalized ratio (INR) and APTT and hospital mortality among 647 patients with sepsis, and suggested that raised INR and aPTT prolongation were both related to increased mortality. Also, in another study [21], prolonged aPTT was a strong predictor of mortality in a prospective cohort of 39 patients with septic shock upon ICU admission, which was different from our results. This may be due to inadequate samples with low aPTT.

Sepsis also increases fibrinolysis inhibitors like plasminogen activator inhibitor-1 (PAI-1) and triggers hypofibrinolysis. Overall, all hazardous coagulation factors may result in a change in aPTT and INR. They could also lead to endothelial microparticle diffusion and at least partially stimulate mortal conditions like disseminated intravascular coagulation (DIC), microcirculatory deterioration, and multifarious organ failure [22].

CRP, as we know, is the most used practically marker for sepsis. Orati *et al.* [23] reported that patients with abdominal sepsis had significantly higher serum CRP levels and positive correlation between CRP level and severity of sepsis.

Peetermans *et al.* [24] observed that a decrease in platelet count in parallel with end-organ microthrombosis is consistent with the human phenotype of sepsis-associated thrombocytopaenia and disseminated intravascular coagulation.

In the present study, the SOFA score was significantly higher in non-survivor cases than in survivors ($p < 0.01$).

Freund *et al.* [25] performed an international prospective cohort study and compared the old

and new sepsis criteria, and they found that the accuracy of the SOFA criteria was higher than both the systemic inflammatory response syndrome (SIRS) criteria- and the severe sepsis criteria-based tests in predicting in-hospital mortality.

Toker *et al.* [26] concluded that the SOFA score had a high sensitivity and negative prediction in the diagnosis of sepsis in the emergency department; on the other hand, it was a good predictor of in-hospital sepsis-related mortality estimations.

Gaini *et al.* [27] found SOFA to be a better prognostic tool for predicting mortality and organ failure than quick SOFA and SIRS among sepsis patients admitted to the ICU. Other studies in other settings, including the emergency department [26], and a multicentre study from low- and middle-income countries (LMICs) [28], also found SOFA to be the best scoring system for predicting mortality. Similar findings were also observed in 2 more systematic reviews and meta-analyses [29].

In conclusion, high levels of vWF/Ag and vWF/Ag/ADAMTS 13 ratio on day 1 of admission are associated with increased early (7 days) sepsis-related hospital mortality. On the other hand, low ADAMTS 13 levels on day 1 of admission are associated with early (7 days) sepsis-related hospital mortality. Thus, vWF/Ag, ADAMTS 13 and vWF/Ag/ADAMTS13 ratios may be useful biomarkers for predicting the prognosis in patients with sepsis.

Conflict of interest

The authors declare no conflict of interest.

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