ORIGINAL PAPER

doi: 10.5455/medarh.2023.77.433-439
MED ARCH. 2023; 77(6): 433-439
RECEIVED: OCT 12, 2023
ACCEPTED: NOV 27, 2023

Serum Thrombomodulin Level Can Predict Mortality in Patients With Sepsis?

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ABSTRACT

Background: Thrombomodulin (TM) is a type-1 trans-membrane glycoprotein on endothelial cells which is known to be involved in various biochemical pathways. TM can be detected in biological fluids such as blood and urine under many forms. Soluble thrombomodulin (sTM), consist of various particles of TM, is the predominant agent which is created by enzymatic or chemical catalysis of the whole protein under divergent conditions. TM plays a vital role in protein C system and is crucial in the pathogenesis of Sepsis. **Objective:** To identify the serum level of soluble thrombomodulin (sTM) in groups of patients: sepsis and septic shock including their survival and fatal in-hospital outcome; and validate the death prediction of serum sTM in patients with sepsis. **Methods:** This prospective observational study was conducted in 63 patients who were diagnosed with sepsis, septic shock according to Sepsis 3 criteria at the ICU Department of Hue Central Hospital, Vietnam, from 3/2022 to 3/2023. **Results:** Twenty participants developed septic shock (31.7%), morality within 28-days was 19 patients (30.2%), 22 patients complicated with acute kidney injury that necessitated renal replacement therapy (34.9%), 30 patients required mechanical ventilation (47.6%), the median length of ICU stay was 8 (3-28) days. Serum level of lactate and creatinine were significantly higher in septic shock group compared with sepsis and survival group ($p<0.05$). The median sTM level in septic shock group and fatal group were 4.68(3.38-6.46) ng/mL and 4.68 (1.69-6.46) ng/mL, respectively. These results were significantly higher than sepsis group [3.62 (1.51-1.94) ng/mL] and survival group [3.73 (1.51-5.9) ng/mL] ($p<0.05$). The death predictive power of DIC score, APACHE II score, creatinine, sTM and SOFA presented with AUC values of 0.723, 0.726, 0.777, 0.803 and 0.807, respectively. There were no significant difference of serum level IL-6 and PCT between survival and fatal group. The median DIC score in fatal group was 7 (3-7), which was significantly higher than survival group 4 (2-7) ($p= 0.001$). **Conclusion:** Sepsis is a common diagnosis among ICU settings which links the critically ill patients to higher complications and mortalities. Serum level of sTM in septic shock and fatal groups were significantly higher than sepsis and survival groups. sTM is a reliable marker and should be used in predict severity and mortality in sepsis patients.

Keywords: Sepsis, septic shock, thrombomodulin.

1. BACKGROUND

Thrombomodulin (TM) is a type-1 trans-membrane glycoprotein on endothelial cells which is known to be involved in various biochemical pathways (1, 2). TM can be detected in biological fluids such as blood and urine under many forms. Soluble thrombomodulin (sTM), consist of various particles of TM, is the predominant agent which is created by enzymatic or chemical catalysis of the whole protein under divergent conditions (3). TM plays a vital role in protein C system and is crucial in the pathogenesis of Sepsis (4).

The combination of TM and thrombin increases the activity of protein C up to 1000 times in comparison with thrombin alone (5,6). Activated protein C exerts anticoagulation antioxidative effects, prevents apoptosis and therefore helps reduce thrombosis and in protecting cells (7). In sepsis, the reduced expression of TM on endothelial cell leads to the compromised activation of protein C, which can facilitate inflammation and thrombosis. Also, TM contributes to the effective immune modulation, particularly in neutrophile adhesion, component activation and formation of cytokine (6). Another factor in pathogenesis of sepsis is the injury of endothelial cell caused by uncontrolled inflammatory reaction

Elevated sTM level in blood is associated with the severity of sepsis (8,9). sTM is useful in the diagnosis, prognosis, and mortality in sepsis patient (10,11). Positive correlation between sTM level and severity of sepsis including adults and children have been shown in many clinical studies (11,12). In addition, sTM level was found to be higher in sepsis-related deaths than non-infectious ones (12). Study of Zhang et al pointed out that high level of sTM in sepsis patients is an independent predictor of worsen outcome in 60 days. sTM is considered a sensitive biomarker in early anticipation of septic shock and DIC caused by sepsis, with AUC value of 0.765 (0.687-0.842) and 0.864 (0.794-0.935), respectively (9).

sTM concentration can be used to track disseminated intravascular coagulation (DIC) and multiple organ dysfunction syndrome (MODS) as well as sepsis severity and the needs of renal replacement therapy (13,14). Additionally, sTM level strongly associated with the severity of organ dysfunction and therefore is a reliable biomarker in early recognition of sepsis patient, especially one with septic shock (15). Therefore, we conducted this study in order to (1)

2. OBJECTIVE

The aim of this article was to evaluate serum level of soluble thrombomodulin in patients with sepsis and septic shock, and, also, to validate mortality prediction of sTM in sepsis patients.

3. MATERIAL AND METHODS

Participants and research design

Our research was a prospective observational study in patients hospitalized in ICU department of Hue Central Hospital, Vietnam from 3/2022 to 3/2023. The inclusion criteria were the diagnosis of sepsis and septic shock according to The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) (16). DIC and SIC diagnosis were shown in Table 1.

Sepsis patients were categorized into groups: sepsis, septic shock, survival and fatal group. We excluded patients who were (1) under 18 years old; (2) pregnant or lactating; (3) previously diagnosed with end renal stage disease; (4) currently on anticoagulation therapy; (5) organ transplantation; (6) autoimmune disease; (7) hematological disease; (8) hematological disease; (9) malignancy; (10) severe cirrhosis (Child-pugh C); (11) currently infected with HIV, COVID-19 and (12) short stays in ICU (< 24 hours)

Data collection

Glasgow comma scale, SOFA score, APACHE II score, DIC score and SIC score were assessed at time of admission. Complications including mechanical ventilation, renal replacement and 28 day-mortality as well as length of stay in ICU were recorded. Laboratory tests such as prothrombin time, platelets, D-Dimer, fibrinogen, ALT, AST, total bilirubin, serum albumin, IL-6, procalcitonin, serum lactate, arterial blood gas, serum creatinine, and serum thrombomodulin were initially taken at time of hospitalization. With regard to thrombomodulin test, blood sample were obtained through Serum Clot Activator Tubes (URI), after clot has been formed, the blood was centrifuged for 10 minutes at 2000 x g. The samples were then stored at -200C or lower until assayed by enzyme-linked immunosorbent assay (ELISA) technique (repeated freezing and thawing samples were not allowed). Laboratory results were analyzed at Biochemistry Department and Hematology and Blood transfusion Center of Hue Central Hospital, Vietnam. Age, sex, weight, vital signs, comorbidities, and sepsis etiologies were recorded at time of admission.

Statistical analysis

We processed the data using SPSS 22.0 statistical software. The study presented the results using descriptive statistics to summarize the data. Categorical data were presented as numbers and percentages, while continuous data were presented as mean and standard deviation (SD) if normally distributed, and median, minimum, and maximum if non-normally distributed. The normality of the continuous data was assessed using the Shapiro-Wilk test. The differences between categorical variables were evaluated using either the Chi-square test or Fisher's Exact test, and the differences between continuous data were determined using either a t-test or Mann-Whitney test based on their distribution. The receiver operating characteristic (ROC) analysis was conducted to determine cut-off points for predicting death in patients, and the DeLong test was used to compare the areas under the ROC curves. The results were considered statistically significant if the p-value was less than 0.05.

4. RESULTS

The study group was consisted of individuals with an average age of 59.76 ± 17.60 years, and no remarkable differences in age were observed between the sepsis and septic shock groups. Type 2 diabetes, hypertension, and COPD were the most frequently occurring comorbidities among the study group. Furthermore, the respiratory, digestive, and urinary systems were identified as the main infectious etiology (Table 2).

Clinical features at admission and 28-day follow-up are showed in Table 3. There were statistically significant

		ISTH overt DIC	SIC
Item	Score	Range	Range
Platelet count (K/μL)	2	< 50	< 100
	1	≥ 50, < 100	≥ 100, < 150
FDP/D dimer	3	Strong increase	-
	2	Moderate increase	-
Prothrombin time (PT ratio)	2	≥ 6s	(> 1.4)
	1	≥ 3s, < 6s	(> 1.2, ≤ 1.4)
Fibrinogen (g/mL)	1	< 100	-
SOFA score	2	-	≥ 2
	1	-	1
Total score for DIC or SIC		≥ 5	≥ 4

Table 1. ISTH overt DIC and sepsis-induced coagulopathy scoring systems (33). Abbreviations: ISTH, International Society on Thrombosis and Haemostasis; DIC, disseminated intravascular coagulation; SIC, sepsis induced coagulopathy; SOFA, sequential organ failure assessment; SOFA score is the sum of 4 items (respiratory SOFA, cardiovascular SOFA, hepatic SOFA, renal SOFA).

Characteristic	Total (n =63)	Sepsis group (n = 43)	Septic shock group (n = 20)	p-value*
Age (years)	59.76 ± 17.60	57.98 ± 18.65	61.15 ± 9.95	0.241
Weight (kg)	63.38 ± 12.01	64.42 ± 12.83	64.06 ± 13.29	0.318
Height (cm)	162.93 ± 7.79	163.81 ± 8.35	161.05 ± 6.19	0.192
BMI (kg/m2)	23.55 ± 3.57	23.87 ± 3.81	23.48 ± 2.86	0.688
Gender n (male/female)	63 (40/23)	43 (27/16)	20 (13/7)	0.665
Comorbidity n (%)				
Type 2 diabetes	19 (32.2%)	14 (32.6%)	5 (25%)	
Hypertension	20 (31.7%)	19 (44.2%)	1 (5%)	
COPD	10 (15.9%)	6 (14%)	4 (20%)	N/A
Chronic kidney disease	5 (7.9%)	3 (7.0%)	2 (10%)	
Chronic liver disease	4 (6.3%)	0 (0%)	4 (20%)	
Chronic heart failure	5 (7.9%)	1 (2.3%)	4 (20%)	
Infectious etiology				
Respiratory system	20 (31.7%)	12 (27.9%)	8 (40.0%)	
Digestive system	18 (28.6%)	12 (27.9%)	6 (30.0%)	
Urinary system	12 (19.0%)	8 (18.6%)	4 (20.0)	N/A
Skin and soft tissue	6 (9.5%)	5 (11.6%)	1 (5.0%)	
Nervous system	3 (4.8%)	3 (7.0%)	0 (0.0%)	
Others	4 (6.3%)	3 (7.0%)	1 (5.0%)	

Table 2. General features. Abbreviations: BMI for body mass index; COPD for chronic obstructive pulmonary disease; CKD for chronic kidney disease *N/A: non applicable; continuous data presented using the mean ± standard deviation and categorical data (n,%); p-value*: t-test.

differences between the two groups (sepsis and septic shock) in terms of SBP, DBP, MAP, CVP, and SpO2 (with a p-value < 0.05). Additionally, the Glasgow score, SOFA, APACHE II on admission, rate of mechanical ventilation, rate of renal replacement therapy, and mortality rate within 28-days also showed statistically significant differences between the two groups.

With regard to this study (Table 4), the difference in serum level of PCT, total bilirubin, and PLT between two groups (sepsis and septic shock group) were not statistically significant, with p-value > 0.05. However, the serum levels of IL-6, lactate, creatinine and sTM in the sepsis group were statistically significantly higher than in the septic shock group, with p-value < 0.05.

Characteristic	Total (n =63)	Sepsis (n = 43)	Septic shock (n = 20)	p-value
SBP (mmHg)	114.73 ± 25.89	128.95 ± 18.06	84.15 ± 4.86	<0.001b
DBP (mmHg)	66.71 ± 15.37	74.51 ±12.11	49.95 ±3.59	<0.001b
MAP	82.72 ± 18.10	92.66 ± 12.71	61.35 ± 2.79	<0.001b
SpO2	96.32 ±5.07	99.35 ± 0.65	89.80 ± 4.19	<0.001b
CVP	9.79 ± 4.74	12.01 ±3.49	5.05 ± 3.41	0.001b
Glasgow	15 (10-15)	15 (12-15)	12 (10-13)	< 0.001a
APACHE II on ICU admission	16 (5-34)	14 (5-33)	28.5 (12-34)	0.002a
SOFA on admisson	6 (2-14)	5 (2-13)	10 (3-4)	< 0.001a
RRT	22 (34.9%)	10 (23.3%)	12 (60%)	0.004b
Mechanical ventilation	30 (47.6%)	11 (25.6%)	19 (95.0%)	< 0,001b
ICU lenghth of stay	8 (3-28)	9 (5-28)	5 (3-14)	< 0,001a
Morality within 28-days	19 (30.2%)	3 (7%)	16 (80%)	<0,001c

Table 3. Clinical features at admission and 28-day follow-up. Abbreviations: RRT for Renal replacement therapy; SOFA for Sequential organ failure assessment; APACHE II for Acute physiology and chronic health evaluation II; CVP for Central vennous pressure. p-value : a) Mann-Whitney test; b) Chi-square test; c) Fisher exact test.

The study was discovered that several factors including age, white blood cells, platelets, albumin, PCT, and IL-6 did not show any significant statistical difference (p-value > 0.05) between the two groups of survival and mortality. To the contrary, the serum levels of creatinine, lactate, sTM and SOFA score, APACHE II score, DIC score were found to be higher in the mortality group than in the surviving one, with a p-value < 0.05 (Table 5).

Our research findings indicate that the serum level of sTM and SOFA score are good predictors of mortality in patients with sepsis, with AUC values of 0.803 and 0.807, respectively. Other remain factors have AUCs ranging from 0.723 to 0.777 (Figure 1).

5. DISCUSSION

In our study, the mean age of all participants, in sepsis group and septic shock group were 59.76 ± 17.60, 57.98 ± 18.65 and 61.15 ± 9.95, respectively. There was no significant difference between two groups. 63.5% of patients were male and 36.5% were female. The concomitant diseases were diabetes (32.2%), hypertension (31.7%), COPD (15.9%), chronic kidney disease (7.9%), chronic liver disease (6.3%), chronic heart failure (7.9%). Infectious etiologies were identified from respiratory tracts (31.7%), gastrointestinal tract (28.6%), urinary tract (19%), skin and soft tissue (9.5%), nervous system (4.8%) and other source (6.3%).

According to a study of Liu et al in 2021, the present of comorbidities were 37.9% for diabetes, 54.5% for hypertension, 25.8% for cardiovascular disease, 36.4% for chronic kidney disease, 13.6% for chronic lung disease. Sepsis etiologies were documented from respiratory tract (69.7%), urinary tract (34.8%), intra-abdominal infection (18.2%), soft tissue (4.5%) (17). One study of Chen et al in 680324 patients showed that the most common etiology of sepsis was the infection of lower respiratory tract (54%), following by the urinary tract (33.9%), intra-abdominal origin (5.8%), skin and soft tissues infection (5%), whole body fungal infection (2.4%), musculoskeletal infection (1.5%) and biliary tract (1.1%) (18).

The rate of mechanical ventilation according to our study was 47.6%, This rate was significantly higher in septic shock group than in sepsis group (p<0,001). Gameiro et al pointed out in their study that the mechanical ventilation rate in severe sepsis and septic shock were 71.1% (19). Study of Inkinen et al showed that the mechanical ventilation among sepsis patients in ICU settings was 65.3%, there was a significant difference between mechanical ventilation in survival and non-survival group with p-value < 0.001 (20). The mean of ICU stay in our study was 8 days, the septic shock group had a shorter hospital stay than the sepsis group. Inkinen et al pointed out in his study that the mean of ICU stay was 4 days (20). The study of Zhang et al found that the mean ICU stays in septic group, in shock and non-shock group were 14, 12 and 15 days, respectively, these differences was statistically insignificant (9).

Results	Total (n =63)	Sepsis (n = 43)	Septic shock (n = 20)	p-value
WBC (K/µL)	15.52 ± 8.94	14.67 ± 7.76	17.32 ± 11.06	0.277b
RBC (M/µL)	3.67 ± 0.80	3.66 ± 0.72	3.71 ± 0.97	0.822b
Hb (g/dL)	10.52 ± 2.30	10.47 ± 2.05	10.62 ± 2.80	0.821b
Hct (%)	32.38 ± 6.75	32.10 ± 5.99	32.97 ± 8.29	0.640b
PLT (K/µL)	136 (7-439)	163(9-439)	111.50 (7-405)	0.082a
ALT (U/L)	61.01 (5.63-3443)	51.3 (5.63-500)	99(10.36-3443)	0.034a
AST (U/L)	70.24 (11.61-5970)	52.20 (11.61-540)	190.95 (12.67-5970)	0.024a
Total bilirubin (µmol/L)	21(4.3-526.7)	18(4.3-526.7)	26.95 (6.2-417.7)	0.504a
Albumin (g/L)	27.14 ± 4.70	27.30 ± 4.40	26.95 ± 5.08	0.293b
Lactat (mmol/L)	2.8(7-14.5)	2.3(0.7-11.9)	3.3(1.1-14.5)	0.039a
Creatinin (µmol/L)	109(41-325.5)	96(41-320)	191.41(101-325.5)	0.001a
PCT (ng/mL)	14.82(0.12-100)	14.82(0.13- 100)	20.06(1.5-100)	<0.358a
IL-6 (pg/mL)	296.3(3.53-5000)	176.2(3.53-5000)	1310(57.38-5000)	0.012a
sTM (ng/mL)	4.07(1.51-6.46)	3.62(1.51-5.94)	4.68(3.38-6.46)	<0.001a

Table 4. Laboratory results at admission. Abbreviations: sTM for soluble thrombomodulin; PCT for procalcitonin; IL-6 for interleukin-6; AST for Aspartate aminotransferase; ALT for alanine aminotransferase; p-value: a) Mann Whitney test; b) t-test.

Characteristics	Total (n = 63)	Survival group (n=44)	Non-survival group (n=19)	p-value
Age	59.76 ± 17.60	59.34 ±18.45	60.74 ± 15.91	0.775b
WBC	15.52 ± 8.94	14.61 ± 7.88	17.60 ±10.96	0.226b
PLT	157.84 ± 101.18	164.34 ± 101.50	142.79 ± 101.53	0.442b
Creatinin (µmol/l)	135.51 ± 75.07	113.22 ± 60.16	187.13 ± 82.07	<0.001b
Albumin	27.17 ± 4.75	26.74 ± 4.70	28.17 ± 4.84	0.274b
PCT	14.82(0.14-100)	16.62(0.14-100)	8.07(0.56-100)	0.916a
Lactat	2.8(0.7-14.5)	2.45(0.7-11.9)	3.0(1.1-14.5)	0.043a
IL-6	296.3(3.53-5000)	227.15(3.53-5000)	837.4(8.2-5000)	0.108a
sTM	4.07(1.51-6.46)	3.73(1.51-5.90)	4.68(1.69-6.46)	<0,001a
SIC score on admisson	3(2-6)	3(2-6)	3(2-6)	0.872a
DIC score on admisson	4(2-7)	4(2-7)	7(3-7)	0.001a
SOFA on admisson	6(2-14)	5(2-10)	10(3-14)	<0,001a
APACHE II on admisson	16(5-34)	14.5(6-33)	30(5-34)	0.003a

Table 5. Characteristics of survival and fatal group. Abbreviations: sTM for soluble thrombomodulin; PCT for procalcitonin; SOFA for Sequential organ failure assessment; APACHE II for Acute physiology and chronic health evaluation II; DIC for disseminated intravascular coagulation; SIC for sepsis induced coagulopathy; p-value: a) Mann Whitney test; b) t-test

The rate of acute kidney injury in sepsis patient was reported as 54% in one multi-center study including 24 European countries (21). In our research, 34.9% of patient required renal replacement therapy (RRT). The RRT rate was significantly higher in septic shock group than sepsis group (p=0.004). With regard to one study of Bae et al, the requirement of RRT among documented bacteremia, shock patient was 15.3%, RRT rate was lower in survival group compared with non-survival group (p<0.01) (22). Wu et al found in their research that 60.7% of their sepsis patients required RRT because of uremia, other causes were fluid overload (60.7%), electrolyte disturbance (39.9%), metabolic acidosis (51.8%), anuria (68.8%) and uremic encephalopathy (7%) (23).

In our study, the value of white blood cells (WBC) and platelet (PLT) were identical between sepsis group and septic shock group, as well as between survival and non-survival group. Katayama found in his study that the mean value of WBC and PLT were 9.9 x 109/L and 144 x 109/L, respectively. With regard to research of Liu et al, mean value of PLT in sepsis and septic shock patients was 169.7 x 109/L, there were no difference between survival and fatal group (17,24). For decades, total blood count has played an important role in diagnosis of septic shock, this parameter is practical because it is obtained in every hospitalized patient, however, WBC is less useful in this clinical scenario. Currently, the use of neutrophil-to-lymphocyte ratio (NLR) in prognosis of sepsis has been validated in numerous studies. Sepsis activates the apoptosis of lymphocyte, therefore, septic

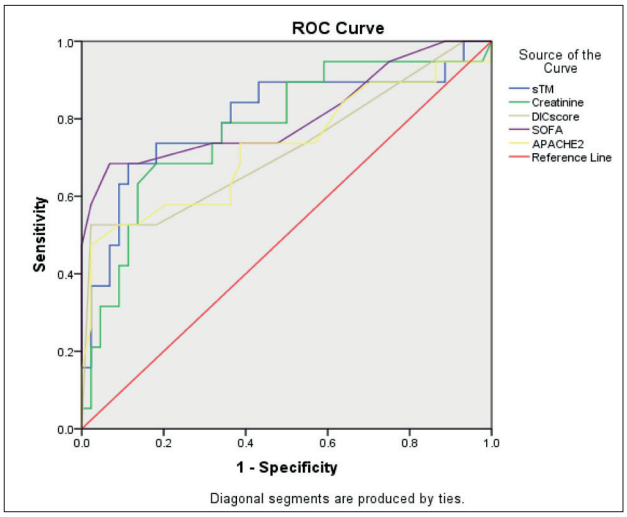

Figure 1. Receiver operating characteristic (ROC) curve of sTM, creatinine, DIC, SOFA, and APACHE 2 in mortality prediction

shock can profoundly rise the NLR value, this elevation is more serious than other physiology stress (25).

In our study, the difference of albumin, PCT and IL-6 level between survival and non-survival group were statistically insignificant. Nadeem et al studied about sepsis patients with documented bacteremia and found no significant difference between survived and fatal group (26). According to a study of Inkinen et al, among sepsis patients, IL-6 level was not significantly different between survival and non-survival group (20). One study of Liu et al showed that there was no significant difference between survival and non-survival group considering the level of PCT, however the level of IL-6 was significantly different between two group ($p<0.05$) (17). Another study found that the level of IL-6 during first day of hospitalization was significantly different between survial and non-survival group (27). In our study, serum creatinine and lactate level were found to be significantly different between sepsis and septic shock group as well as between survival and non-survival group. Wu et al found in their research the same conclusion with significant difference of creatinine and lactate level among (1) sepsis and septic shock patients (2) between survival and non-survival group (23). Regarding to the study of Liu et al, serum level of lactate was statistically different between survival and fatal group, the level of creatinine was however identical between the two groups. One study conducted in 367 sepsis and septic shock patients illustrated that there was a significant difference of serum lactate level between survival and non-survival group ($p<0.05$) (27).

We found a significant difference considering the level of sTM, serum creatinine, DIC score, SOFA score and APACHE II score between survival and non-survival group. The DIC score, APACHE II score, serum creatinine, sTM and SOFA score were shown to be potential tools in predicting of mortality with the AUC value ranged from 0.723 to 0.807. Ding et al found in their study of sepsis patients that SIC and DIC score were higher in fatal group in comparison to survival group ($p<0.001$), APACHE II score, DIC score, SIC score presented as independent risk factors for sepsis mortality in ICU. There SIC score showed no advantage in diagnosing sepsis-associated coagulopathy or DIC (28). One study showed that SIC prevalence among sepsis patients was approximately 60%, which was two-fold higher than overt DIC, almost all sepsis patients complicated by DIC were previously diagnosed with SIC, the mortality rate of SIC was reported to be 30% or higher, therefore, the presence of SIC is considered an indication for anticoagulant therapy among sepsis patients (29). SOFA score and APACHE II score are frequently used for the prediction of mortality among critically ill patients in ICU. In our study we revealed that in predicting mortality, SOFA and APACHE II score performed well, particularly SOFA score. Studies of Zhou et al, Wu et al showed that SOFA and APACHE II score were significantly lower among sepsis patient compared with septic shock group (15,23). Liu et al observed in their study of sepsis patient that in predicting 28-days mortality, the value of AUC of SOFA and APACHE II score were 0.732 and 0.850, respectively (17). Another study demonstrated that among sepsis patients in ICU, APACHE II score was not statistically different in survival group compared with non-survival group, however there were a significant difference between AKI and non-AKI group (30).

Inkinen et al showed in their study that the serum level of sTM in fatal sepsis patients was higher than the survival group. The level of serum sTM can be used in monitoring DIC and MODS in sepsis patient (13). The concentration of sTM in serum was found to be significantly higher in septic shock patients in comparison to sepsis group, as well as fatal compared with survival group. Elevated sTM level was discovered in sepsis children at various severity (12). Study of Khattab et al observed the high level of serum sTM among pediatric patients with SIRS, sepsis, severe sepsis in comparison to heathy group ($p<0.001$). Moreover, sTM serum was significantly higher in fatal patients than in survival ones ($p=0.005$), its value of AUC in predicting sepsis and mortality were 0.915 and 0.711, respectively. sTM is currently a promising tool for sepsis children, measuring the level of sTM can aid in early diagnosis of sepsis among critically ill pediatric patients (31). The concentration of serum sTM was associated with the severity of organs dysfunction considering sepsis patients, which proved its utility in early diagnosis of sepsis, especially septic shock (15,32). sTM was found to be a sensitive biomarker in predicting septic shock and sepsis-induced DIC with the value of AUC of 0.765 (0.687-0.842) and 0.864 (0.794-0.935), respectively.

6. CONCLUSION

Sepsis is common among critically ill patients in ICU settings, the present of sepsis burdens the patient with complications and remarkably rises mortality. Thrombomodulin is useful in early diagnosis and prognosis of sepsis patient, particularly septic shock and death. It can also be used to monitor disseminated intravascular coagulation (DIC), and multiple organs dysfunction (MODs) as well as disease's severity and the needs of re-

nal replacement therapy. In our study, the level of serum sTM in septic shock group and fatal groups was significantly higher than sepsis group and survival group. The indication for mechanical ventilation and renal replacement therapy was significantly higher in septic shock group in comparison with sepsis group. The presence of DIC in fatal group was significantly higher than survival group. Serum concentration of sTM and SOFA score are powerful tool to predict mortality in sepsis patients.

- **Declaration of patient consent**: The authors certify that they have obtained all appropriate patient consent forms. haring Statement: The datasets generated and/or analysed during the current study are not publicly available due to privacy concerns but are available from the corresponding author on reasonable request.
- **Author contributions**: All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.
- **Conflict of interest**: The authors declare no conflict of interests.
- **Financial support and sponsorshipunding**: The study received no fundings.

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