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RESEARCH ARTICLE

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Combined estimation of presepsin and gelsolin might improve the diagnostic validity of clinical scoring to predict and stratify sepsis in non-sepsis surgical ICU patient

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ABSTRACT

Objectives: This study evaluates the ability of serum presepsin (PSEP) and gelsolin (GSN) levels estimated in blood samples obtained at the admission of sepsis-free patients to surgical ICU (SICU) as early predictors for getting sepsis and sepsis-related complications.

Patients & Methods: 260 sepsis-free trauma and postoperative patients who were admitted to SICU were clinically evaluated. At-admission blood samples were obtained for total and differential leucocytic counting and ELISA estimation of serum C-reactive protein (CRP), procalcitonin (PCT), PSEP and GSN, and PSEP/GSN ratio was calculated (PGR). Patients were observed for the SICU readmission rate after being ward-discharged for the sepsis rate and mortality rate (MR).

Results: The SICU readmission rate was 7.2%, the sepsis rate was 25.4%, and the sepsis-related MR was 5%. The estimated biomarkers were significantly higher in patients than negative controls but were lower than positive controls except serum levels of GSN that were significantly lower in patients' samples than in negative, but higher than in positive controls. Statistical analyses defined high serum PSEP and lower serum GSN levels with high PGR as significant predictors for all the study outcomes.

Conclusion: Among sepsis-free patients who are admitted to SICU, getting septic complications is not an uncommon event and accounts for 5% of SICU mortalities. Estimated serum levels of PSEP and GSN might be valuable biomarkers for early distinguishing patients vulnerable to developing septic complications and predicting the possibility of non-surviving. The calculated PSEP/GSN ratio might be a collective early indicator for outcomes of patients admitted to SICU.

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KEYWORDS
Surgical ICU; sepsis; presepsin; gelsolin; mortality rate

1. Introduction

Sepsis is the underlying cause of about 6 million deaths worldwide [1]. Sepsis is a severe medical condition and is characterized by varied degrees of immunoparalysis among the affected patients [2]. Host immune dysfunction of patients affected by sepsis occurs when the body's immune system overreacts to an infection, leading to life-threatening organ dysfunction [3].

Sepsis has a deleterious impact on surgical patients who require admission to the surgical ICUs (SICUs) [1] and is a major risk factor for multiple organ failure, shock, and sepsis-induced acute kidney injury which is one of its most frequent complications and portends a heavy burden of mortality and morbidity [4].

Presepsin (PSEP) is the soluble N-terminal fragment of CD14, a receptor for lipopolysaccharide that is expressed on the surface of monocytes and macrophages [5]. PSEP was produced through the cleavage of CD14 by a serine protease associated with phagocytosis by monocytes and neutrophils [6] and by cathepsin D, a lysosomal enzyme that cleaves sCD14 and produces PSEP [7]. PSEP is excessively shed into the systemic circulation upon stimulation by exogenous bacterial antigens and its blood concentration increases within 2-h peaks at 3-h after induction, and remains elevated for up to 4–5 days [8].

Actin filament dynamics plays a pivotal role in cellular processes [9]. Gelsolin (GSN) is actin filament capping protein, which is essential for the modulation of actin filament dynamics by influencing the number of actin filament ends [10]. GSN exists as an extracellular cytoplasmic form containing a "plasma extension" of 24 amino acid sequences and a disulfide bond and this augments its stability in the extracellular environment [11,12]. GSN has a protective role in the body for being an essential component of the extracellular actin scavenger system acting through induction of depolymerization of the circulating actin filaments and may also

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bind to pro-inflammatory mediators and bacterial wall components.

2. Objectives

This study tried to evaluate the utility of at-admission estimated serum levels of PSEP and GSN as early predictors for the development and outcomes of sepsis in surgical patients admitted to SICU and who were free of sepsis.

3. Design

Prospective non-randomized multicenter study.

4. Setting

Anesthesia, Pain & ICU department, Faculty of Medicine, Benha University in conjunction with multiple private ICUs at Benha & Cairo and ESTH, UK.

5. Ethical considerations

The study protocol was approved by the departmental committee before the start of case collection. After completion of case collections, obtaining the results and formulating the outcomes, the approval of the Local Ethical Committee was obtained and the study was registered by number: RC: 24 November 2023.

6. Authors' contributions and blindness

Clinical evaluations of the enrolled patients admitted to SICU were conveyed by Daboor YS and Eid AM who were blinded about the results of the lab investigations. The clinical pathologist was also blinded about the indications for the requested lab investigations. The interpretation of the clinical and lab findings and discussing it was the duty of Shahab HA.

7. Patients

All patients admitted to the SICU and were free of manifestations of sepsis that were evaluated for general condition and criteria of enrolment in the study.

8. Exclusion criteria

Patients who were maintained on immunosuppressive drugs or receiving therapies for autoimmune disorders and patients who had deregulated hepatic and kidney functions, uncompensated cardiac functions, all-cause sepsis, and traumatic brain injury were excluded from the study.

9. Inclusion criteria

Patients admitted to SICU free of sepsis and exclusion criteria were enrolled in the study.

10. Evaluation tools

10.1. Disease severity status was evaluated using the following tools

(1) **Acute Physiology and Chronic Health Evaluation II (APACHE II) Score:** The impact of the indication for ICU admission on patients' physiological status was evaluated using the APACHE II scoring system that included three domains: the Acute Physiology Score, age and chronic health points, and the total APACHE II score was calculated as the sum of the scores of the three domains with the higher total score, the worst is the patient's prognosis [13,14].

(2) **The Sequential Organ Failure Assessment (SOFA) Score:** The SOFA score evaluates the effect of the disease process on body organs using a 0-4 Likert scale for each organ and higher scores correlate with mortality rate [15,16]. SOFA score was determined at 24-h and 72-h after SICU admission to assess the progress of the patient's organ functions that was presented as ΔSOFA, which equals 24-h score minus 72-h score.

10.2. Impact of disease on inflammatory response

This was evaluated on both cellular and serum levels of the primary phase reactant as follows:

(1) Total leucocytic count (TLC) and differential leucocytic count to calculate the neutrophil/lymphocyte ratio (NLR) as the result of dividing neutrophil count by the lymphocytic count.

(2) Serum levels of primary phase reactants include C-reactive protein (CRP) and procalcitonin (PCT).

11. Lab investigations

11.1. Blood sampling

- Blood samples were obtained under complete asepsis at the time of SICU admission from the study-enrolled patients to evaluate the utility of the estimated biomarkers as early predictors.
- For comparative purposes of the estimated serum levels of lab parameters, 75 patients diagnosed to have sepsis were included as positive controls and 25 volunteers of those who attended the blood banks for blood donation and had passed the pre-donation investigations, gave blood samples as negative controls.

– Blood samples were divided into two parts; the 1st part was collected in an EDTA-containing tube for complete blood count (CBC) including differential leucocytic count. The 2nd part was collected in a plain tube, allowed to clot and was centrifuged at 1500 rpm for 10 min to separate serum. Serum was collected in numbered clean and dry Eppendorf tubes and frozen down to −20°C till being assayed.

11.2. Estimation procedure

The studied biomarkers were estimated using the enzyme-linked immunosorbent assay (ELISA) provided by ELISA kits according to the pamphlet guidelines using the quantitative sandwich enzyme immunoassay technique and results of the analysis were read by an ELISA reader (Dynatech. MR 7000) using a 96-well microplate.

11.3. Investigation

The studied biomarkers included the estimation of serum levels of

(a) Human Presepsin (Cat. No. MBS766136, MyBioSource Inc., San Diego, California, USA).
(b) Human Gelsolin, C-reactive protein and Procalcitonin (Abcam Inc., Cambridge, USA; Cal. No. ab270215, ab260058 and ab221828, respectively).

12. Outcomes

(1) The primary outcome is the determination of the incidence of sepsis and sepsis-related mortalities among sepsis-free patients who were admitted to SICU.
(2) The secondary outcome is the utility of PSEP and GSN alone or as their in-between ratio (PGR) as early predictors for the incidence of sepsis and sepsis-related mortalities in comparison with clinical scorings and other biomarkers.

13. Statistical analyses

The IBM® SPSS® Statistics software (Ver. 26, 2019; IBM Corporation; Armonk, USA) was used for analyses of the obtained results. Data were subjected to correlation analyses using Pearson's Correlation analysis and correlated data were verified using the Receiver Operating Characteristic (ROC) curve analysis as judged by the significance of the difference between the area under the curve (AUC) for each variate and the area under the reference line (AUC = 0.5). The significance of the variates determined by the ROC curve analysis was assured by the Univariate Regression analysis and then by the Multivariate Regression analysis to determine the highly significant predictors for the outcome. The significance of the analysis results was evaluated at the cutoff point of P less than 0.05.

14. Results

Trauma represented the highest indication (20.8%) for SICU admission and the remaining 79.2% of the admitted patients had surgical procedures for multiple indications. During the SICU stay, 209 patients (80.4%) were discharged to the ward uneventfully, while 51 patients (19.6%) showed manifestations of sepsis and continued their SICU stay. Among the ward-discharged patients, 15 patients (7.2%) developed sepsis and were readmitted to SICU. Among sepsis-free patients who were admitted to SICU, the total sepsis rate was 25.4% and the sepsis-related mortality rate was 5% (Figure 1). Indications for SICU admission and patients' enrollment demographic and clinical scorings' data, and routine lab findings are shown in Table 1.

Mean serum CRP, PCT and PSEP levels estimated in at-admission patients' samples were significantly higher than in samples of negative controls, while were significantly lower in comparison with levels estimated in samples of positive controls. On the contrary, serum GSN levels were significantly higher in samples of negative controls than in samples of patients and positive controls (Figure 2).

The calculated PGR was significantly higher in samples of positive controls than in samples of patients and negative controls with significantly higher PGR in patients' samples than in samples of negative controls (Table 2, Figure 3).

SICU readmission rate was positively correlated with at-admission APACHE II and 24-h SOFA scores, ΔSOFA and at-admission serum levels of PSEP and PCT, and the calculated PGR. Moreover, the SICU readmission rate was negatively correlated with GSN serum levels, while was insignificantly related to other patients' data or clinical and lab variates. ROC curve analysis for these correlated variates excluded ΔSOFA and high serum PCT as predictors for SICU readmission (Figure 4). Univariate regression analysis assured the predictability of high 24-h SOFA score and PGR, but excluded other variates defined by the ROC curve analysis. Furthermore, multivariate regression analysis excluded a high 24-h SOFA score and showed that high PGR at the time of SICU admission is the persistently significant predictor for SICU readmission (Table 3).

The reported In-SICU sepsis rate was positively correlated with the 24-h SOFA scores, at-admission high NLR, and high serum levels of CRP, PESP, PCT, and PGR while showing a negative significant relation with high GSN serum levels. The ROC curve defined high at-admission serum levels of CRP, PSEP and low serum GSN, and high NLR and 24-h SOFA score as the positive

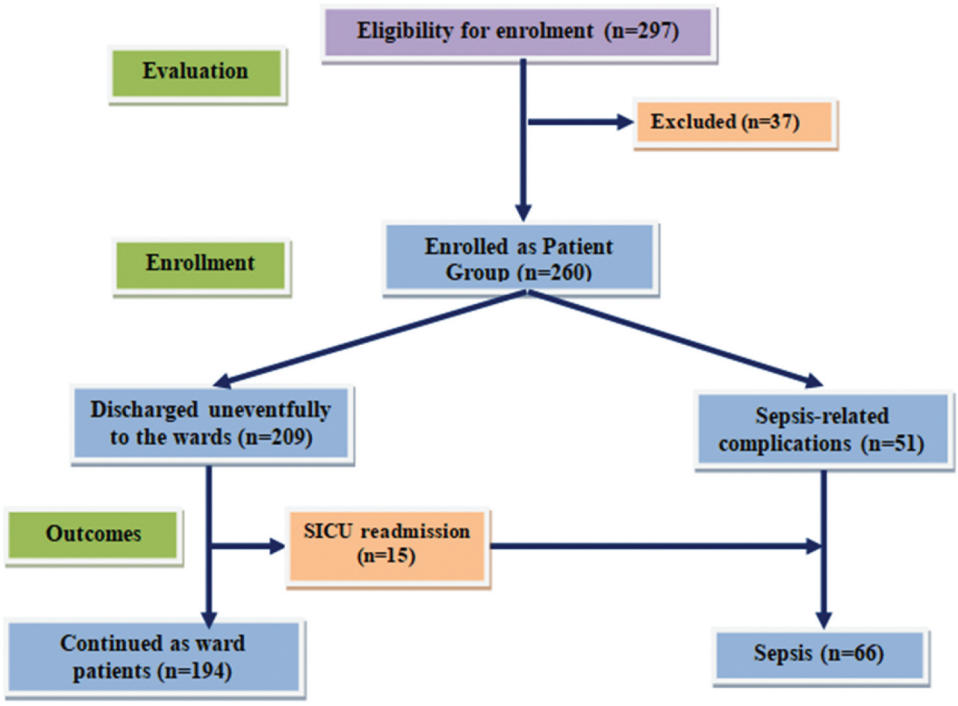

Figure 1. Study flow chart.

Table 1. Indications of SICU admission, patients' enrolment data and outcomes.

Clinical scorings			Number	%
Indications for SICU admission	Trauma		54	20.8
	Postoperative	Coronary artery bypass grafting	36	13.8
		Major Abdominal	37	14.2
		Varied general surgical procedures	35	13.5
		Orthopedic	26	10
		Urological	19	7.3
		Gynecological & Obstetrics	17	6.5
		Neurosurgery	20	7.7
		Chest surgery	16	6.2
		Total	206	79.2
Patients' enrolment data	Gender	Males	160	61.5
		Females	100	38.5
	Data		**Mean (±SD)**	
	Age (years)		53.9 (±7.8)	
	BMI (kg/m^2)		30.6 (±2.3)	
	APACHE II score		15.9 (±5.6)	
	24-h SOFA score		7.05 (±2.8)	
Routine lab findings	Random blood glucose (mg/dl)		123.9 (±15.9)	
	Hemoglobin conc. (%)		9.86 (±0.87)	
	Total leucocytic count (10^3/ml)		11.59 (±1.64)	
	Neutrophil/lymphocyte ratio (NLR)		3.84 (±0.5)	
	Serum total bilirubin (mg/ml)		1.09 (±0.06)	
	Serum direct bilirubin (mg/ml		0.28 (±0.09)	
	Serum creatinine (mg/ml)		0.55 (±0.17)	
Outcome			**Number**	**%**
Sepsis rate			51	19.6
Sepsis-related SICU re-admission rate			15	7.2
Total sepsis rate			66	25.4
Sepsis-related mortality rate			13	5

predictors for In-SICU sepsis rate (Figure 5). Univariate analysis defined high serum levels of PSEP and PCT, and high PGR as the early positive predictors for the possibility for the development of In-SICU septic complications. Multivariate analysis assured the persistently positive predictive value of PGR for oncoming In-SICU septic complications (Table 4).

The reported MR was positively correlated with old age, high APACHE II and SOFA scores, ΔSOFA, NLR, and serum levels of CRP, PSEP, PCT and PGR while showing a negative relation to serum GSN. Moreover, MR showed a positive significant correlation with the incidence of SICU readmission and with the development of In-SICU sepsis. The ROC curve analysis defined high at SICU admission APACHE II and SOFA scores, and high serum PSEP and PGR as early positive significant predictors, while high serum GSN was a significant predictor for the possibility of death secondary to

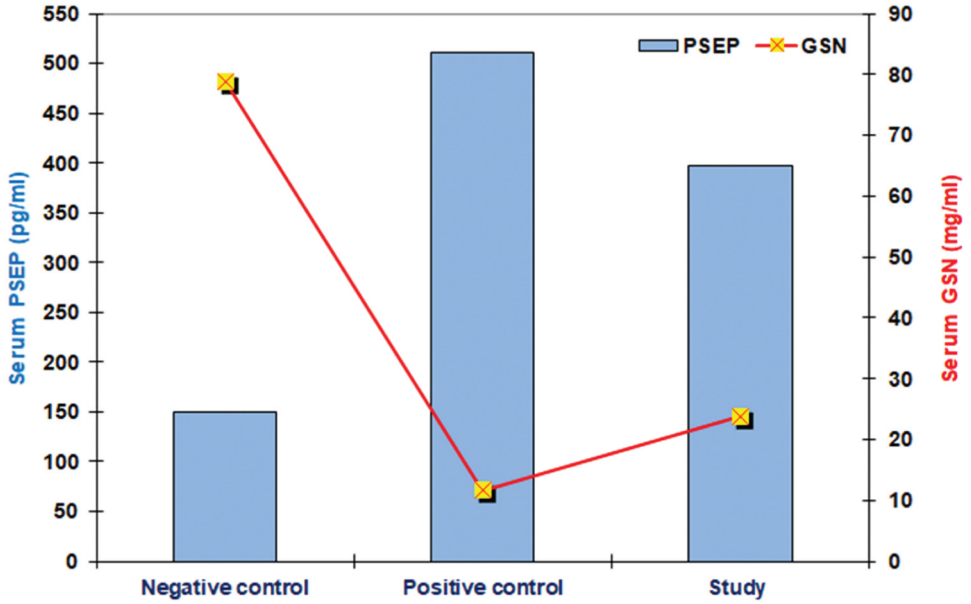

Figure 2. Serum levels of PSEP & GSN estimated at-admission of patients to SICU compared positive and negative controls.

Table 2. Mean serum levels of the parameters estimated in at-admission samples of the enrolled patients compared to levels estimated in negative and positive controls.

Parameter Group		Negative control	Positive control	Study
Serum CRP (mg/L)	Mean (±SD)	0.544±0.21	137±31.5	115.8±38.2
	p value vs. negative control		<0.001	<0.001
	p value vs. positive control			0.0002
Serum PCT (µg/L)	Mean (±SD)	0.048±0.031	6.35±3.81	2.66±2.59
	p value vs. negative control		<0.001	<0.001
	p value vs. positive control			<0.001
Serum PSEP (pg/ml)	Mean (±SD)	149.8 (±52.4)	511±221.8	397±147.4
	p value vs. negative control		<0.001	<0.001
	p value vs. positive control			<0.001
Serum GSN (mg/ml)	Mean (±SD)	78.9±8.5	11.7±4.2	23.9±12.4
	p value vs. negative control		<0.001	<0.001
	p value vs. positive control			<0.001
PGR	Mean (±SD)	1.93±0.73	50.49±29	22.29±16
	p value vs. negative control		<0.001	<0.001
	p value vs. positive control			<0.001

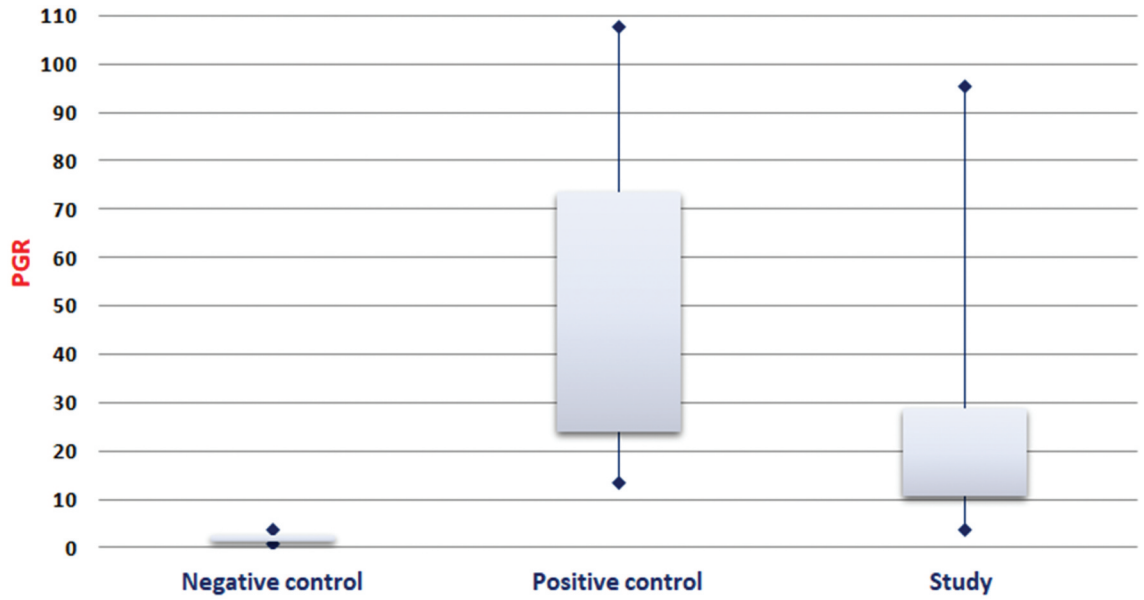

Figure 3. The calculated PGR in the studied samples.

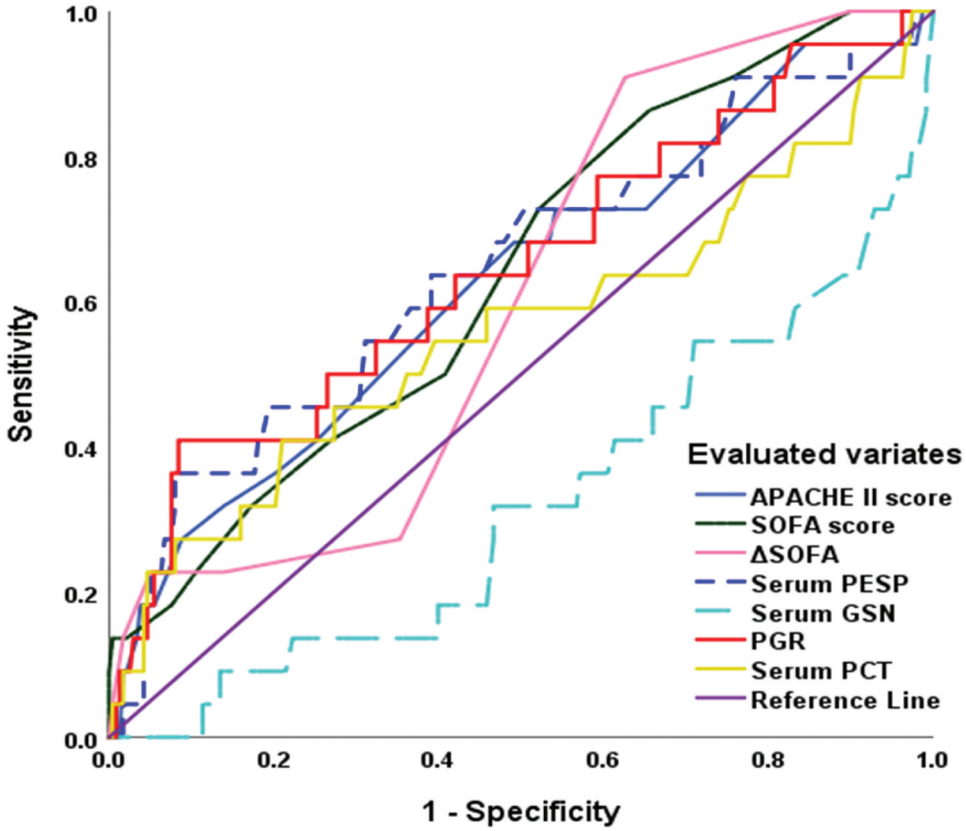

Figure 4. ROC curve analysis of the variates correlated with the SICU readmission rate.

Table 3. Statistical analyses for the clinical and lab data as predictors for SICU readmission.

Analyses	Correlations		Receiver Operating Characteristic (ROC) curve				Univariate Regression		Multivariate Regression	
Independent variates	r	P	AUC	Std.	P	95% CI	β	P	β	P
APACHE II	0.135	0.030	0.629	0.066	0.048	0.497–0.755	0.069	0.305	Excluded	
SOFA	0.166	0.007	0.637	0.059	0.033	0.522–0.752	0.136	0.029		
ΔSOFA	0.145	0.020	0.604	0.055	0.107	0.496–0.712	0.093	0.158		
PSEP	0.156	0.012	0.645	0.067	0.025	0.514–0.776	0.076	0.290		
GSN	−0.147	0.017	0.322	0.063	0.006	0.198–0.445	−0.057	0.466		
PGR	0.181	0.003	0.646	0.067	0.024	0.515–0.777	0.154	0.013	0.181	0.003
PCT	0.145	0.019	0.561	0.075	0.346	0.413–0.708	0.103	0.111	Excluded	

sepsis. Also, the ROC curve analysis defined the development of In-SICU sepsis as a positive significant predictor for sepsis-related mortalities (Figure 6). Univariate regression also defined high PGR as an early predictor for sepsis-related mortality and this was assured by the multivariate regression. The development of sepsis during SICU stay was defined by univariate regression as a positive predictor for sepsis-related mortality, while multivariate regression excluded this possibility (Table 5).

15. Discussion

Serum levels of PSEP and primary phase reactants; PCT and CRP were significantly higher in patients admitted to SICU after major surgical procedures or trauma-necessitated admission in comparison with negative controls. Moreover, there was a positive significant relation between the In-SICU sepsis rate and at-admission high NLR, and serum CRP, PSEP, and PCT levels. Further, ROC curve and regression analyses assured the high predictability of high at-admission serum levels of CRP, and PSEP for the possibility of committing sepsis during SICU stay.

These results illustrate the exacerbated inflammatory response to severe surgical and trauma-induced tissue injury and the possibility of using these biomarkers especially PSEP for early prediction of oncoming septic complications. In line with these findings, multiple recent studies detected significantly higher perioperative serum PSEP levels in patients admitted to SICU and developed infectious complications after esophagectomy [17], liver transplantation [18], cardiac surgery [19], and gastrectomy [20], and these studies concluded that PSEP is a valuable early indicator for PO infectious complication's detection than leukocyte count, CRP and PCT.

In support of the efficacy of high perioperative serum PSEP as an early indicator for patients

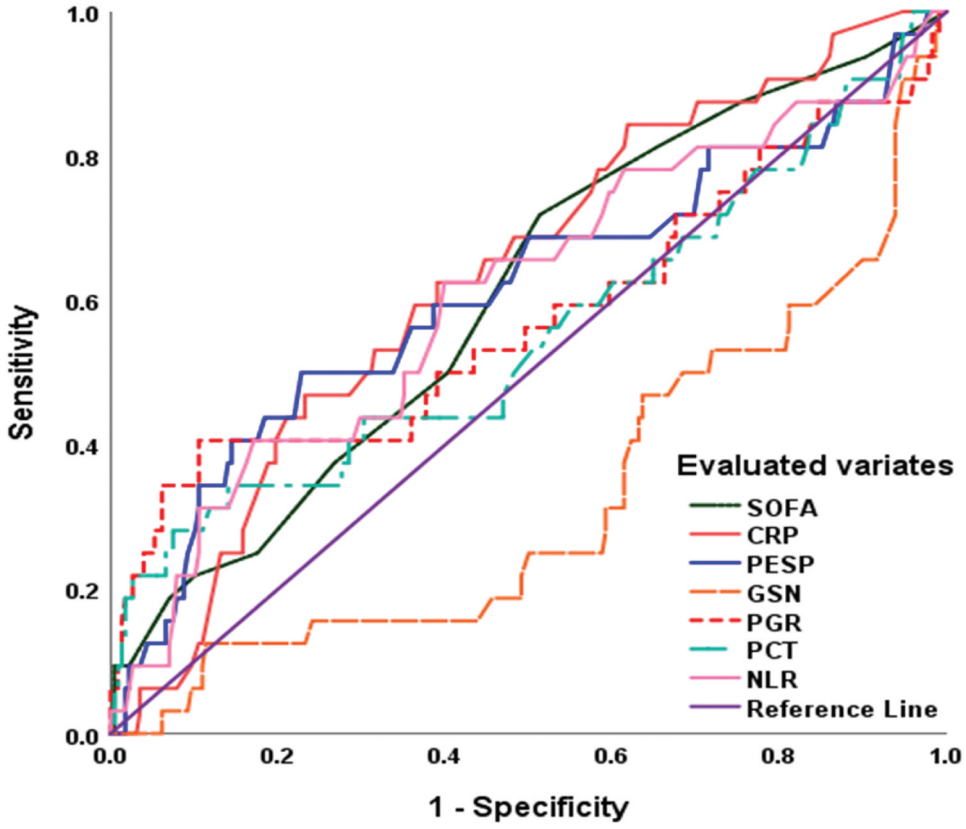

Figure 5. ROC curve analysis of the variates correlated with the In-SICU sepsis rate.

Table 4. Statistical analyses for the clinical and lab data as predictors for In-SICU sepsis rate.

Analyses	Correlations		Receiver Operating Characteristic (ROC) curve				Univariate Regression		Multivariate Regression	
Independent variates	r	P	AUC	Std.	P	95% CI	β	P	β	P
Age	0.051	0.410			Excluded			Excluded		Excluded
Male	0.080	0.201								
BMI	0.053	0.095								
APACHE	0.101	0.103								
SOFA	0.144	0.020	0.608	0.053	0.047	0.505–0.712	0.100	0.104		
ΔSOFA	0.043	0.487			Excluded			Excluded		
NLR	0.136	0.029	0.608	0.057	0.047	0.496–0.721	0.110	0.076		
CRP	0.141	0.023	0.612	0.060	0.041	0.494–0.730	0.075	0.292		
PSEP	0.157	0.011	0.635	0.050	0.013	0.537–0.733	0.140	0.029		
GSN	−0.167	0.007	0.327	0.053	0.002	0.222–0.432	−0.019	0.802		
PGR	0.227	<0.001	0.577	0.065	0.160	0.450–0.703	0.170	0.008	0.227	<0.001
PCT	0.201	0.001	0.554	0.062	0.322	0.432–0.676	0.121	0.045	Excluded	

vulnerable to sepsis and sepsis-related complications, Kim et al. [21] and Shimoyama et al. [22] found plasma PSEP level might be used as a valuable biomarker for the prediction of sepsis AKI in patients admitted to emergency department [21] and for the progression of septic subclinical to septic AKI in patients admitted to ICU [22]. Additionally, Jeong & Kim [23] found PSEP diagnostic accuracy for sepsis or septic shock acute PO period override that of procalcitonin especially for prediction on day of admission and next day and concluded that monitor newly developed sepsis with PSEP especially after surgical interference to eliminate intra-abdominal infection. Also, Paraskevas et al. [24] suggested using PSEP as a promising biomarker for triage and early diagnosis of sepsis and You et al. [25] demonstrated superior sensitivity and specificity of PSEP over CRP and PCT for detecting PO infectious complications across various surgical procedures. Additionally, Puspaningtyas et al. [26] detected progressive increases of serum PSEP in patients who developed PO infection than in non-infected patients and concluded that serial estimations of PSEP after surgery are helpful diagnostic markers to detect PO infectious complications.

Furthermore, correlation analyses detected a positive relation between serum PSEP and sepsis-related mortality rate and the ROC curve analysis defined PSEP level as a positive predictor for oncoming mortalities. Following these results, Lee et al. [27] detected the effectiveness of PSEP in differentiating sepsis from non-infectious organ failure and concluded that it might be used as an independent risk factor for

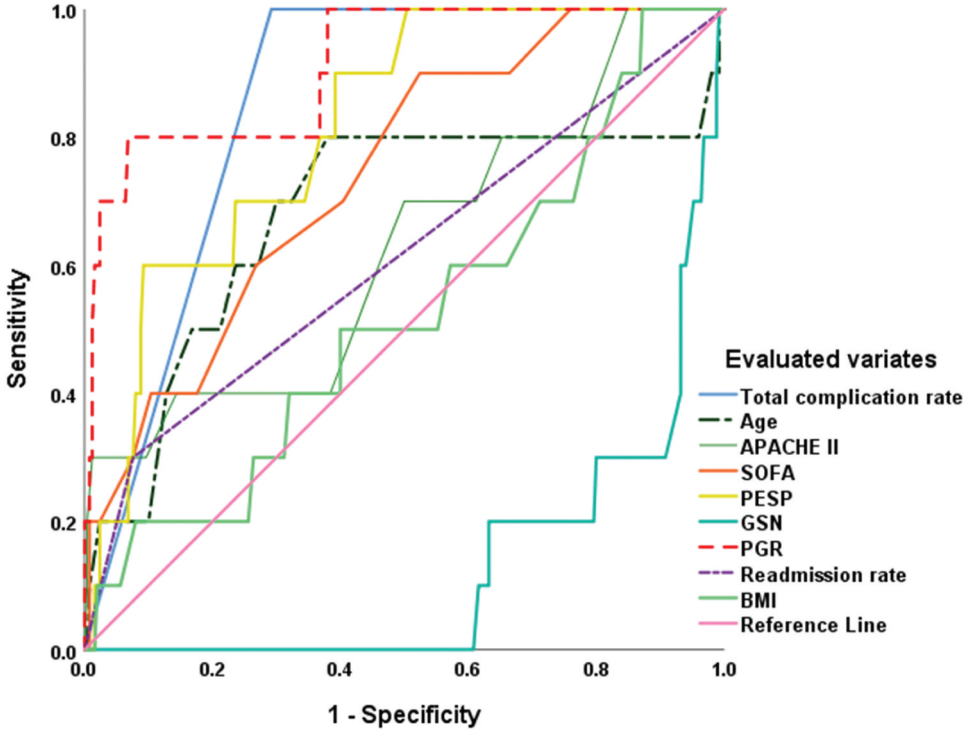

Figure 6. ROC curve analysis of the variates correlated with the In-SICU sepsis-related mortality.

Table 5. Statistical analyses for the clinical and lab data as predictors for SICU sepsis-related mortality.

Analyses	Correlations		Receiver Operating Characteristic (ROC) curve				Univariate Regression		Multivariate Regression	
Independent variates	r	P	AUC	Std.	P	95% CI	β	P	β	P
Age	0.148	0.017	Excluded				Excluded		Excluded	
Male	0.006	0.919								
BMI	0.074	0.232								
APACHE	0.144	0.020	0.659	0.098	0.039	0.436–0.822				
SOFA	0.185	0.003	0.742	0.073	0.009	0.599–0.885	0.073	0.176		
ΔSOFA	0.149	0.016	Excluded				Excluded			
NLR	0.176	0.004								
CRP	0.168	0.007								
PSEP	0.230	<0.001	0.816	0.054	0.001	0.710–0.923	−0.075	0.292		
GSN	−0.201	0.001	0.128	0.045	<0.001	0.040–0.216	−0.019	0.802		
PGR	0.488	<0.001	0.912	0.046	<0.001	0.821–1.00	0.556	<0.001	0.227	<0.001
PCT	0.155	0.012	Excluded				Excluded		Excluded	
Readmission	0.161	0.009								
In-SICU sepsis	0.534	<0.001	0.854	0.032	<0.001	0.791–0.917	0.187	0.001	0.172	0.187

30-day mortality among patients with sepsis and septic shock. Also, Xiao et al. [28] documented that in patients with sepsis, PSEP might be used as a guide to shorten the duration of antibiotic therapy, length of hospital stay with reduction of hospitalization costs without risking worse outcomes of death, recurrent infection, and aggravation of organ failure and Wang et al. [29] assured that PSEP may be a valuable early predictor and overrides PCT and SOFA score as regards the accuracy of prediction of secondary sepsis and mortality in ICU patients. Moreover, Baik et al. [30] detected significantly higher serum PSEP in non-survivors than in survivors among patients admitted to ICU and concluded that PSEP could serve as an effective biomarker for prediction of sepsis-induced mortality and evaluation of treatment effectiveness.

The estimated serum levels of GSN were significantly lower in the studied trauma and PO patients in comparison with levels estimated in samples of volunteers, which were significantly higher than in samples of septic patients. Moreover, serum GSN showed a negative relation to the sepsis rate and sepsis-related mortality rate. These results go in hand with Holm et al. [31] who detected decreased serum GSN in critically ill patients with respiratory failure requiring mechanical ventilation. Also, Dinsdale et al. [32] detected significantly reduced levels of GSN in blood samples of burnt patients than in control samples and found administration of blood products restored levels of GSN.

These detected lower GSN levels indicated either consumption of GSN or suppression of its release or

expression with infection in a manner inversely related to infection severity. In support of the suggestion of GSN consumption, a recent study using murine sepsis models found that splenocyte death leads to the release of actin, the DNase I inhibitor, that interferes with cell-free DNA-induced (cfDNA) clearance leading to poor survival outcomes of the infected animal; however, this actin-mediated inhibition was compensated by upregulation of DNase I or GSN acting as actin scavenger leading to its consumption with subsequent defective clearance of cfDNA with progress of infection and resulting in poorer outcomes [33]. In line with the supposition of suppressed GSN expression, using a murine model of pseudomonas aeruginosa sepsis found injection of recombinant plasma gelsolin can modulate the inflammatory response and augment the host antibacterial activity [34].

The results and conclusion of this murine sepsis model are in agreement with the detected by statistical analyses that low serum GSN might be an early predictor for sepsis-related mortalities of patients admitted to SICU. Furthermore, in line with the ability of pre-treatment low GSN for prediction of survival outcomes of ICU patients, Holm et al. [31] found low GSN at time of admission to SICU predicted chance of being "alive and out of ICU at day 14" for surgical patients admitted to SICU and required ventilation for respiratory failure. Also, Dinsdale et al. [32] detected actin in blood samples of burnt patients, but not in control samples with significantly reduced levels of GSN and found administration of blood products restored levels of GSN with increased DNase activity and reduction of the risk of cfDNA host tissue damage and thrombosis.

Considering the contradictory effect of sepsis on serum levels of PSEP and GSN, combining both biomarkers as an in-between relation that was presented as the PSEP/GSN ratio (PGR) that might manifest the impact of infection on both biomarkers. The calculated PGR in the at-admission samples of admitted to patients SICU was significantly higher than that of the negative controls but was significantly lower in comparison with the PGR of the infected patients and the positive controls. Further, the calculated PGR was a significant predictor for readmission of patients who were ward-discharged from SICU, patients who were going to develop sepsis during SICU stay and non-survival outcomes during SICU stay. Unfortunately, review of published literature resulted in one previous work evaluated the value of the PGR for outcomes of ICU non-septic and septic patients and detected significantly higher PGR in samples of patients admitted to ICU in comparison with controls and in patients had sepsis-related AKI than in septic non-AKI, patients had septic shock than in un-shocked septic patients, in septic patients requiring mechanical ventilation than those who did not require MV and in non-survivors than in survivors [35].

16. Conclusion

Among sepsis-free patients who are admitted to SICU, getting septic complications is not an uncommon event and accounts for about 5% of SICU mortalities. Estimated serum levels of PSEP and GSN might be valuable biomarkers for early distinguishing patients vulnerable to developing septic complications and predicting the possibility of non-surviving. The calculated PSEP/GSN ratio might be a collective early indicator for outcomes of patients admitted to SICU.

17. Limitations

The cost-effectiveness of estimation of serum levels of PSEP and GSN, concerning the determination of NLR and serum CRP as primary phase reactants with minimal cost and concerning duration of SICU stays with its inherent costs and patients' outcomes have to be determined. The shortage of articles for comparison of the validity of the PSEP/GSN ratio is another limitation.

18. Recommendations

Further multicenter studies are mandatory to establish the obtained results with special regard to the PSEP/GSN ratio. Also, evaluation of the prognostic value of the preoperative estimation of these parameters to guard agonistic getting infective complications for cases not requiring SICU admission.

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Availability of data and material

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