

Low At-admission Serum Omentin-1 Levels with High Delta-SOFA Are Early Predictors of the Outcome of Sepsis Patients Admitted to Surgical ICU**Ibrahim EM Mostafa^a, Mahmoud Mohamed Elnady^a, Hamasat A Alnoury^b,
Ahmed Said Elnoury^{a*}**^aDepartment of Anesthesia, ICU & Pain, Faculty of Medicine, Benha University, Benha, Egypt.^bDepartment of Chemical & Clinical Pathology, Faculty of Medicine, Benha University, Benha, Egypt.**Abstract****Background:** Despite the progress in the management of sepsis, the shortcomings of routine investigations necessitated the search for new biomarkers to be used as early predictors for sepsis outcomes.**Objectives:** To define the relations of progress to septic shock (SS) and mortality rate (MR) among sepsis patients with serum omentin-1 levels estimated at admission to the surgical ICU.**Patients and methods:** 160 sepsis patients were evaluated using the quick sepsis-related Organ Failure Assessment (q-SOFA) score and SOFA score at admission (T0-time) and 24 h thereafter (T24) to calculate delta-SOFA (Δ SOFA). The frequency of SS and the 28-d MR were determined. The study outcome is defining the relation of lab parameters estimated at T0-time and Δ SOFA for the incidence of SS and MR.**Results:** SS was diagnosed in 53 patients, and the total MR was 23.125%. The incidence of the development of SS and ICU mortality was positively correlated with Δ SOFA but was negatively correlated with at-admission serum omentin-1 levels. Serum omentin-1 levels showed a negative significant correlation with Δ SOFA ($P=0.008$) and serum levels of C-reactive protein ($P=0.030$), interleukin-6 ($P=0.004$), and tumor necrosis factor- α ($P=0.014$).**Conclusion:** The calculated Δ SOFA at 24 h after ICU admission is preferable to SOFA scoring to determine the change in evaluated parameters through 24 h. Combined high Δ SOFA and at-admission low serum omentin-1 were significantly correlated with the incidence of SS and mortality at the surgical ICU and might be used as early identifiers for patients vulnerable to bad outcomes.**Keywords:** Sepsis; Surgical ICU, mortality; Omentin-1; SOFA;q-SOFA; Inflammatory cytokines.**DOI:** 10.21608/SVUIJM.2024.332012.2002***Correspondence:** aelnoury78@gmail.com**Received:** 18 November,2024.**Revised:** 18 December ,2024.**Accepted:** 21 December,2024.**Published:** 5 January, 2025**Cite this article as:** Ibrahim EM Mostafa, Mahmoud Mohamed Elnady, Hamasat A Alnoury, Ahmed Said Elnoury.(2024). Low At-admission Serum Omentin-1 Levels with High Delta-SOFA Are Early Predictors of the Outcome of Sepsis Patients Admitted to Surgical ICU. *SVU-International Journal of Medical Sciences*. Vol.7, Issue 2, pp: 967-981.

Copyright: © Mostafa et al (2024) Immediate open access to its content on the principle that making research freely available to the public supports a greater global exchange of knowledge. Users have the right to Read, download, copy, distribute, print or share link to the full texts under a [Creative Commons BY-NC-SA 4.0 International License](https://creativecommons.org/licenses/by-nc-sa/4.0/)

Introduction

The progress in the diagnosis and management to improve outcomes of sepsis patients admitted to the ICU is progressing rapidly; however, the results of the race are unfortunately in favor of sepsis (Ning et al., 2023). This may be due to the lack of definite definitions for sepsis because of the reliance on Bone's criteria that led to the over-diagnosis of sepsis, maluses of antimicrobials, development of nosocomial resistant strains, and consumption of resources (Churpek et al., 2015).

Further, the shortcomings of routine investigations, such as the deficient specificity and failures in the early detection of sepsis, together with the delay in getting the result of blood culture, are other factors that hampered the success of control on sepsis outcomes (Gong et al., 2020). Moreover, the applications of new diagnostic technologies, as the detection of gene signatures that could accurately discriminate between blood culture-positive sepsis and aseptic inflammation in patients receiving antibiotics, outperformed multiple sepsis-biomarkers, such as C-reactive protein (CRP), but were comparable to procalcitonin (Denny et al., 2023). Also, microbial cell-free DNA sequencing, despite being promising for the detection of pathogens before blood culture, is limited in its application by a lack of clinical validation (Cao et al., 2023).

Regrettably, sepsis patients' medical status and general health change rapidly, and the delay in receiving adequate therapy and appropriate antimicrobial treatment can increase the risk of mortality by 4-7% per hour (Ning et al., 2023). Thus, early prediction of sepsis severity and its probable outcomes is mandatory and may be the weapon to defend against mortality.

Omentin-1 is a 313-amino-acid hydrophilic polypeptide that is mainly expressed in visceral adipose tissue and exhibits multiple physiological functions (Chen et al., 2020), but most prominently, its insulin-sensitizing, anti-atherosclerotic, and cardiovascular protective effects (Guclu-Geyik et al., 2023). The aim of the present study was to evaluate the relation between serum omentin-1 levels estimated at the time of admission to the surgical ICU (T0-time) and the T0 levels of other inflammatory markers and the oncoming mortality rate of sepsis patients.

Patients and methods

Study Design: Prospective observational non-randomized clinical trial.

Setting: Departments of Anesthesia and Surgical ICU, and Clinical Pathology, Faculty of Medicine, Benha University.

Ethical considerations: The Institutional Ethical Committee at Benha University Hospital approved the study protocol number 2.9.2023.

Inclusion criteria: All cases were admitted to the surgical ICU and signed the written fully informed consent personally or by one of the patients akin were included in the study.

Exclusion criteria: These comprised the presence of manifest diabetes mellitus, metabolic syndrome, chronic renal and liver disorders, failure or a history of neurological deficits, and psychological disorders. Ages out of the range of 18-65 years and pregnancy or its related complications are other exclusion criteria.

Study protocol: Surgical ICU patients had no exclusion criterion and underwent diagnosis of sepsis according to the flowchart for diagnosis of sepsis and septic shock (SS) as proposed by The Third

International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) (Singer et al., 2016), using the following tools applied at T0-time:

1. The Glasgow Coma Scale (GCS) evaluates the eye-opening, verbal, and motor responses for a maximum score of 15 (= Best response) and a minimum score of 3 (= unresponsive client) (Teasdale and Jennett, 1976).
2. The quick Sepsis-related Organ Failure Assessment (q-SOFA) score evaluates the respiratory rate (RR), systolic blood pressure (SBP), and GCS; 1 point to each. Patients had SBP < 100 mmHg, RR > 22/min, and GCS < 13, patients had a q-SOFA score of 3; patients who had q-SOFA of < 2 were re-evaluated 24 h later, and those who had q-SOFA \geq 2 were evaluated for evidence of organ dysfunction using items and scores

of the SOFA score (Estella et al., 2018).

3. SOFA score evaluates 7 items that can be scored from zero to 4, with a SOFA score of 0, indicating no organ dysfunction. Items and scoring of SOFA and subsequent management are shown in (Table.1) (Vincent et al., 1996). Patients who failed to respond to fluid therapy to readjust their blood pressure received vasopressor therapy and were evaluated for organ hypoperfusion as judged by metabolic shift with subsequent hyperlactatemia (> 18 mg/dl), and were diagnosed as septic shock (Jourdiere and Annane, 2020). The combination of hypotension, vasopressor use, and hyperlactatemia could identify patients vulnerable to death with a mortality rate (MR) of 35-55% (Song et al., 2020).

Table 1.Sepsis-related Organ Failure Assessment (SOFA) score (Vincent et al., 1996)

System or organ	Measures	SOFA score				
		0	1	2	3	4
Respiratory	PaO ₂ /FiO ₂ , mmHg	\geq 400	300-399	200-299	100-199 with support	<100 with support
Coagulation	Platelets, 10 ³ / μ L	\geq 150	100-149	50-99	20-49	<20
Liver	Bilirubin, μ mol/L(mg/dl)	< 20 (1.2)	20-32 (1.2-1.9)	33-101 (2.0-5.9)	102-204 (6.0-11.9)	>204 (12.0)
Circulatory	Mean arterial pressure, mmHg	\geq 70	<70	Low-dose dopamine or any dose of dobutamine	Low-medium dose noradrenalin or adrenalin; medium dose dopamine	High dose noradrenalin, adrenalin, or dopamine
CNS	Glasgow coma scale score	15	13-14	10-12	6-9	<6
Renal	Creatinine, μ mol/L (mg/dl)	<110 (1.2)	110-170 (1.2-1.9)	171-299 (2.0-3.4)	300-440 (3.5-4.9)	>440 (5.0)
	Urine output (ml/d)	–	–	–	<500	<200

PaO₂ = partial pressure of oxygen (arterial). FiO₂ = fraction of inspired oxygen.

Lab workup

At T0-time, blood samples were obtained aseptically and divided into multiple tubes according to type of lab analysis:

1. Sterile plain tube for blood culture and sensitivity test for antimicrobials.
2. EDTA-containing tube for determination of hemoglobin concentration (HBC), total leucocytic count (TLC), and platelet count.
3. Sodium fluoride tubes for preserving blood glucose levels till being estimated by the glucose oxidase method (**Tinder, 1969**) and blood lactate level using Beckman Coulter analyzers (**Wasserman et al., 1985**).
4. Perchloric acid (6%) pre-chilled tubes, 1 ml blood to 2.5 ml of perchloric acid for spectrophotometric estimation of blood pyruvate level as described previously (**Chung et al., 2006**).
5. Plain tube to allow blood to clot and then was centrifuged at 1500 × g for 15 min to get the serum that were divided; part for immediate estimation of serum creatinine (SCr) and total bilirubin (TB) and another was frozen until ELISA estimation of serum levels of human:
 - CRP using Abcam ELISA kits (Cat. No. ab260058 Abcam Inc., San Francisco, USA) (**Volkova et al., 2011**). That kit is a colorimetric quantitative test with a detection range of 18.75-1200 pg/mL, but it is sensitive down to 5.36 pg/mL with intra-assay CV 1.4 and inter-assay CV 4.
 - Tumor necrosis factor- α (TNF- α) using Abcam ELISA kits (Cat. No. ab46087 Abcam Inc., San Francisco, USA) (**Coughlan et al., 2001**). That kit is a colorimetric quantitative test with

a detection range of 15.63-1000 pg/mL, but it is sensitive down to 4.32 pg/mL with intra-assay CV 2.5 and inter-assay CV 3.1.

- Interleukin-6 (IL-6) using Abcam ELISA kits; Cat. No. ab187013 Abcam Inc., San Francisco, USA) (**Gaines-Das and Poole 1993**). That kit is a colorimetric quantitative test with a detection range of 7.8-500 pg/mL, but it is sensitive down to 1.6 pg/mL with intra-assay CV 2.1 and inter-assay CV 2.4.
- Omentin-1 using Abcam ELISA kits; Cat. No. ab260058, Abcam Inc., San Francisco, USA). (**Yin et al., 2015**). That kit is a colorimetric quantitative test with a detection range of 0.3-20 ng/mL, but it is sensitive down to 0.21 ng/mL with intra-assay CV 3.8 and inter-assay CV 7.1.

Follow-up design

1. Patients were evaluated using the SOFA score at T0-time and (T24), and Δ SOFA was calculated.
2. The frequency of patients diagnosed as SS.
3. The 28-d patients' outcomes were registered as discharged alive (survivor) or dead (non-survivors), and the mortality rate was determined.

Study outcomes

1. The predictability of T0 levels of lab parameters and Δ SOFA for the progress of sepsis patients to SS and the oncoming mortality.
2. The interrelation between the estimated lab variate.

Statistical analysis

The data normality was assessed using the Kolmogorov-Smirnov normality test and the normal Q-Q plots. The data are presented as mean, standard deviation, numbers, and percentages. The intergroup differences were compared using the unpaired t-test and Chi-square test.

Pearson’s correlation analysis was applied to evaluate correlations between at-admission variables and MR. Statistical analyses were conveyed by the IBM® SPSS® Statistics software (Ver. 27, 2020; IBM Corporation; Armonk, USA). The significance of the analysis was evaluated at the cutoff point of P less than 0.05.

The preliminary evaluation included 173 patients; 13 were excluded because 5 patients had manifest diabetes, 3 patients had chronic kidney disease, and one of them was maintained on regular hemodialysis; 3 patients were older than 65 years, and two women had post-caesarean section preeclampsia (Fig. 1).

Results

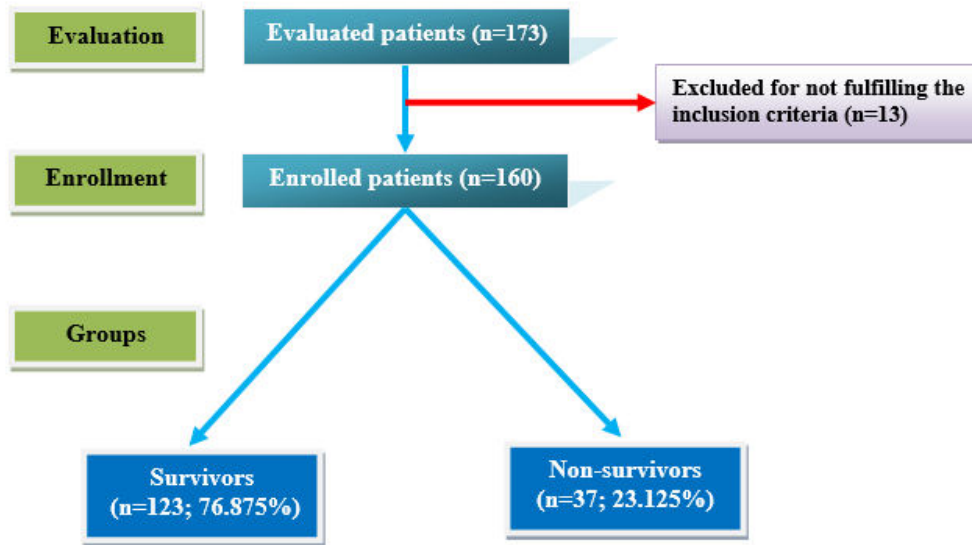


Fig.1. Study Flow Chart

Fifty-three patients (33.125%) had the diagnostic criteria for SS, while the remaining 107 patients had manifestations of sepsis with varying severity. Unfortunately, 37 patients died during ICU stay; 21 patients had SS, and 16 had sepsis for a total mortality of 23.125%. The MR among

SS patients was significantly higher than among sepsis patients (58.5% vs. 5.6%). Non-survivors were significantly (P=0.0135) older and obese (P=0.0177) with non-significant difference as regards gender and obesity distribution (Table.2).

Table 2. At-admission patients' data

Data		Survivors (N=123)	Non-survivors (N=37)	P-value
Diagnosis†	SS	22 (17.9%)	31 (83.8%)	<0.001
	Sepsis	101 (82.1%)	6 (16.2%)	
Age (years)*		53.1±4.5	55.2±4.9	0.015
Gender†	Male	64 (52%)	21 (56.8%)	0.614
	Female	59 (48%)	16 (43.2%)	
BMI (kg/m ²)		30.25±2.37	31.32±2.41	0.0177
Obesity grade†	Overweight	66 (53.7%)	25 (67.6%)	0.134
	Obesity	57 (46.3%)	12 (32.4%)	

*Unpaired t-test; †Chi-square test; SS: Septic shock; BMI: Body mass index

The frequency of patients showed q-SOFA of ≥ 2 was 13.125%, and 24.375%; at T0 and T24. The frequency of patients had q-SOFA scores ≥ 2 , and the mean score was significantly higher in non-survivors, but Δ q-SOFA showed insignificant differences. On the contrary, T0 and T24 SOFA scores were significantly

higher in non-survivors, and Δ SOFA showed a significant difference between both groups (Table.3, Fig. 2). Further, the mean value of Δ SOFA of SS patients (5.2 ± 1.7) was significantly ($P = 0.0025$) higher than that of sepsis patients (4.4 ± 1.5) as shown in (Fig. 2).

Table 3. q-SOFA and SOFA scores of the enrolled patients determined at T0 and T24

Data		Survivors (N=123)	Non-survivors (N=37)	P-value	
q-SOFA score	Frequency†	T0-time	10 (8.13%)	11 (29.73%)	0.0006
		T24	22 (17.89%)	17 (45.95%)	0.0005
	Mean (\pm SD)*	T0-time	0.51 ± 0.67	0.92 ± 0.95	0.0037
		T24	0.75 ± 0.79	1.32 ± 1.13	0.0007
	Δ q-SOFA	0.24 ± 0.45	0.41 ± 0.64	0.0715	
SOFA score	T0-time*		5.35 ± 2	6.8 ± 3.5	0.0017
	T24*		9.76 ± 2.54	12 ± 3.9	0.0001
	Δ SOFA*		4.41 ± 1.68	5.1 ± 1.9	0.035

*Unpaired t-test; †Chi-square test; q-SOFA: quick sepsis-related Organ Failure Assessment; SOFA: Sepsis-related Organ Failure Assessment; Δ SOFA: the change in SOFA score between T0 and T24

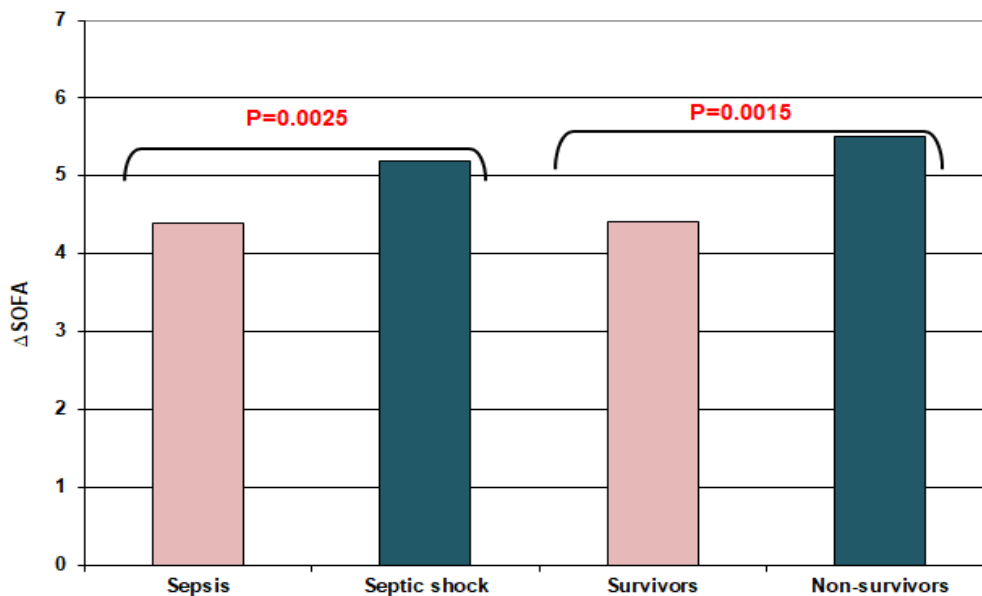


Fig. (2): Δ SOFA of the studied patients categorized according to sepsis severity and survival

The estimated HBC was insignificantly lower in SS patients ($P = 0.517$) and in non-survivors ($P = 0.0013$) than in sepsis patients and survivors, respectively. Platelet count was insignificantly lower in SS patients but was significantly ($P =$

0.0012) lower in non-survivors. Other estimated routine lab parameters were significantly higher in SS patients and in non-survivors in comparison to sepsis and survivors, respectively (Table.4).

Table 4. Routine lab parameters estimated in T0 samples of the studied patients

Group Lab parameters	Sepsis severity			Survival		
	Sepsis (N=107)	SS (N=53)	P- value	Survivors (N=123)	Non- survivors (N=37)	P- value
HBC (%)	10.1±0.5	9.9±0.6	0.517	10.1±0.5	9.8±0.6	0.0027
TLC (10 ³ /ml)	9.2±2.2	10.5±1.9	0.0003	9.37±2.2	10.83±2	0.0004
Plat. C (10 ³ /ml)	227.2±63.9	214.3±56.7	0.215	227.8±59.8	188±46.5	0.0003
RBG (mg/dl)	104±15.3	110±13.9	0.018	103.9±14.4	112.9±15.4	0.0012
LPR	6.9±6.1	9.1±10.5	0.096	6.62±6.5	11±11	0.003
TB (mg/ml)	0.89±0.15	0.98±0.2	0.0017	0.9±0.14	0.99±0.24	0.004
SCR (mg/ml)	0.56±0.16	0.58±0.17	0.467	0.55±0.15	0.61±0.2	0.043

*Unpaired t-test; SS: Septic shock; HBC: Hemoglobin concentration; TLC: Total leucocytic count; Plat. C: Platelet count; RBG: Random blood glucose; LPR: Lactate/pyruvate ratio; TB: Total bilirubin; SCR: Serum creatinine

Serum levels of inflammatory cytokines were significantly higher, while serum omentin-1 levels were significantly lower in T0 samples of SS

patients and non-survivors than in samples of sepsis patients and survivors (Table.5, Fig.3).

Table 5. Inflammatory cytokines and omentin-1 estimated in T0 samples of studied patients

Group Lab parameters	Sepsis severity			Survival		
	Sepsis (n=107)	SS (n=53)	P- value	Survivors (n=123)	Non- survivors (n=37)	P- value
CRP (mg/dl)	80.1±32	85±29.5	0.351	77.6±30.6	98.4±25.4	0.0002
IL-6 (ng/ml)	52.1±18.8	58.2±15.5	0.043	51.8±21.2	61±17.8	0.0175
TNF- α (ng/ml)	13.1±4.7	15.4±5.3	0.0058	13±4.3	16.6±5.7	0.0001
Omentin-1 (ng/ml)	600.5±141.2	534.8±140.4	0.006	597±144	518±127.2	0.003

*Unpaired t-test; SS: Septic shock; CRP: C-reactive protein; IL-Interleukin; TNF- α : Tumor necrosis factor- α

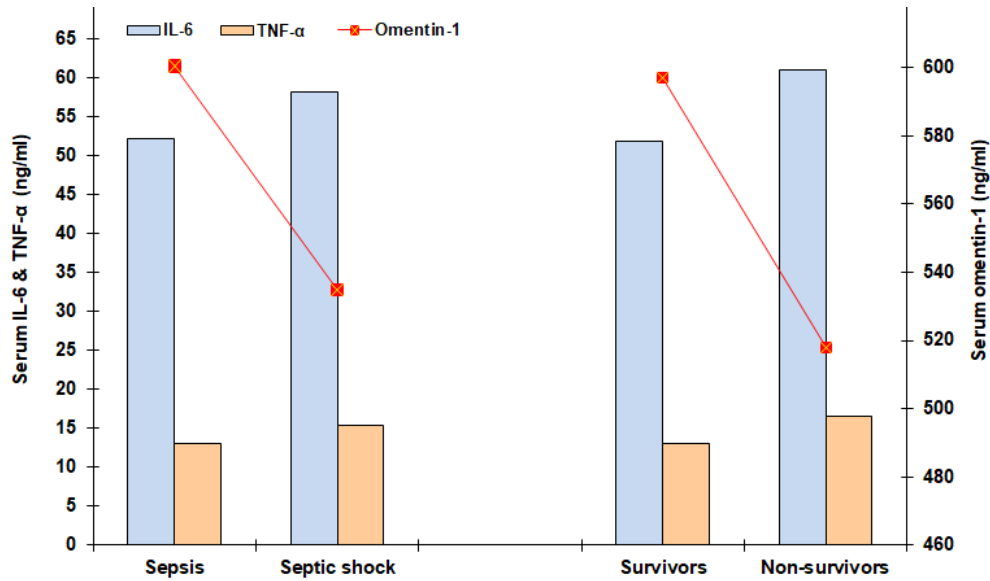


Fig. (3): Mean serum levels of IL-6, TNF-α and omentin-1 estimated in T0 samples of patients categorized according sepsis severity and survival

The incidence of progress of sepsis to SS was significantly correlated with Δ SOFA, and serum levels of TNF α , and omentin-1 with positive correlation with Δ SOFA and TNF α while with omentin-1 it was negative. Mortality rate showed a positive significant correlation with Δ SOFA, serum levels of IL-6, TNF α ,

and CRP, while showed a negative significant correlation with serum levels of omentin-1. On the contrary, serum omentin-1 levels showed a negative significant correlation with Δ SOFA and with serum levels of CRP, IL-6, and TNF α levels (Table. 6, Fig. 4a-c).

Table 6: Pearsons’ correlations of the studied variables

Variables	SS		Mortality		Omentin-1	
	“r”	P-value	“r”	P-value	“r”	P-value
Δ SOFA	0.237	0.003	0.302	<0.001	-0.210	0.008
Omentin-1	-0.372	<0.001	-0.346	<0.001	-	-
CRP	0.121	0.132	0.209	0.008	-0.172	0.030
IL-6	0.160	0.097	0.280	<0.001	-0.227	0.004
TNF- α	0.213	0.005	0.309	<0.001	-0.194	0.014

SS: Septic shock; Δ SOFA: the change in SOFA score between T0 and T24; CRP: C-reactive protein; IL-Interleukin; TNF- α : Tumor necrosis factor- α

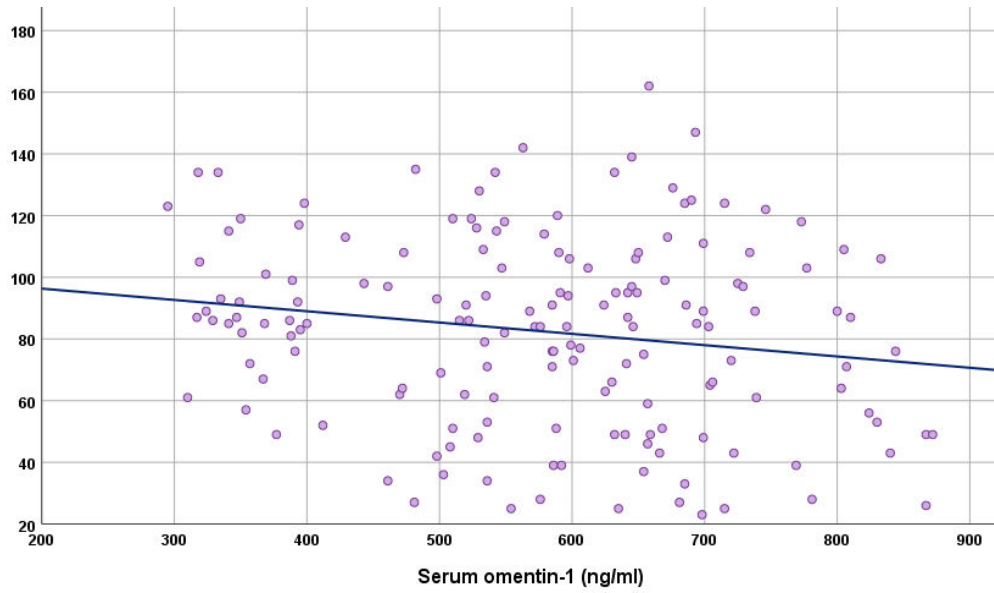


Fig. (4a): Correlation between serum levels of omentin-1 and CRP in the T0 samples of the studied patients, irrespective of their outcomes

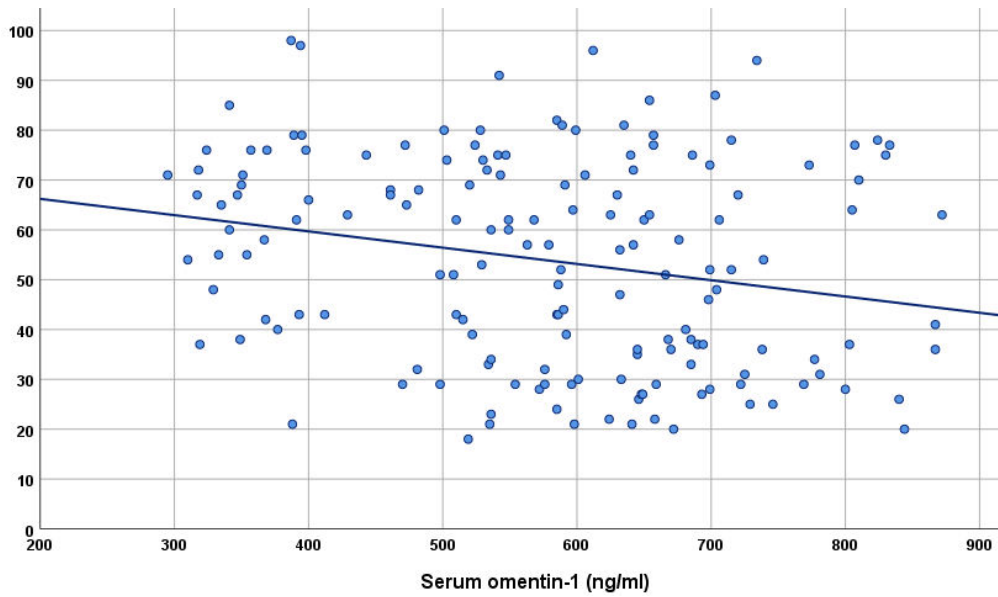


Fig. (4b): Correlation between serum levels of omentin-1 and IL-6 in the T0 samples of the studied patients, irrespective of their outcomes

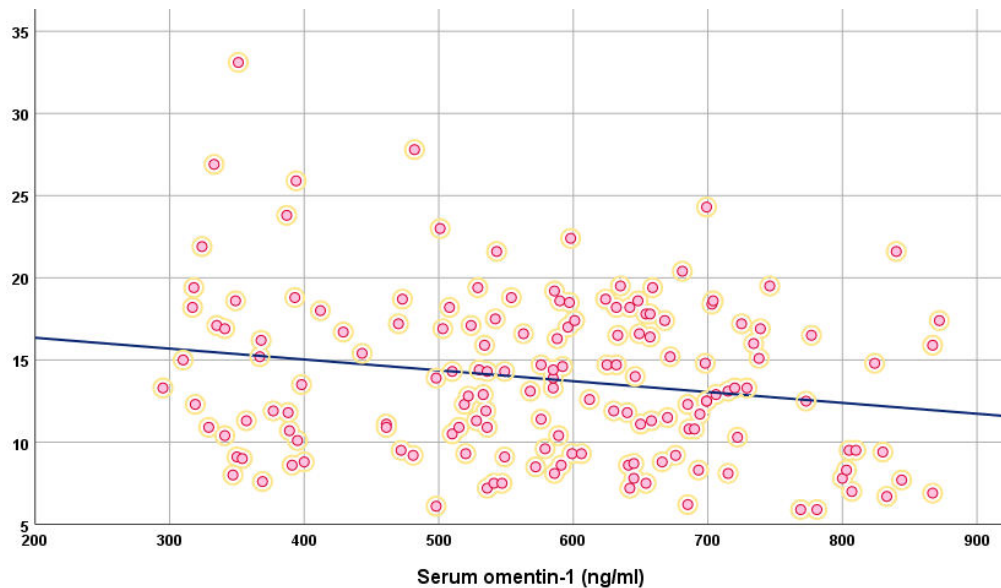


Fig. (4c): Correlation between serum levels of omentin-1 and TNF- α in the T0 samples of the studied patients, irrespective of their outcomes

Discussion

The Δ SOFA, which represents the change in evaluation parameters over 24 hours was significantly higher in SS than in sepsis patients and non-survivors than in survivors. Considering the components of SOFA, high serum creatinine and total bilirubin with low platelet count and tissue hypoperfusion as manifested by low MAP that requires vasopressors to respond and high lactate with low pyruvate levels that point to multiple organ failure, which is the hallmark of SS, thus deteriorated organ function as manifested by high Δ SOFA could be considered as the best clinical-laboratory predictor for mortality, not the high SOFA alone or the development of clinical manifestations of SS. Furthermore, statistical analyses detected a positive significant relation between the possibility of progress of sepsis to SS and the oncoming ICU mortality and Δ SOFA with the ability of high Δ SOFA to be an early significant predictor for oncoming ICU mortality.

Similarly, **Liu et al. (2022)** detected significant differences in age, SOFA and q-SOFA scores, and Δ SOFA

score between survival and death groups and showed that the AUC curve for sepsis was higher if assessed by a combination of Δ SOFA, SOFA, and q-SOFA scores than by SOFA and q-SOFA scores, so they concluded that SOFA, q-SOFA and Δ SOFA are risk factors for the sepsis severity and for prognosis of sepsis patients and adding Δ SOFA for evaluation parameters improved the assessment of both the condition and its prognosis. Furthermore, **Martocchia et al. (2023)** found sepsis patients presented higher comorbidity with increased creatinine; high CRP and high Δ SOFA are liable to catastrophic outcomes.

The estimated routine lab parameter showed significant differences between patients categorized according to sepsis severity and survival outcomes. Similarly, **Wang et al. (2023)** retrospectively detected high MR among ICU patients with a high ratio of blood urea nitrogen (BUN) and albumin and **Liu et al. (2023)**, reported that age, continuous renal replacement therapy, highest serum creatinine, BUN, lowest platelet count, and highest TLC are significant predictors

for ICU mortality. In another retrospective study, **Ruan et al. (2023)** assured that age older than 60, high BUN and lactate with low platelet counts are independent risk factors for 1-year mortality secondary to acute respiratory failure. Prospectively, **Zhou et al. (2022)** found thrombocytopenia developed within the 1st 7 day of ICU admission has a relatively clinical predictive value for bad sepsis patients' prognosis.

The present study detected significant T0 serum CRP, IL-6, and TNF- α in SS and non-survivors and high serum TNF- α and IL-6 were defined as significant predictors for sepsis progress to SS and oncoming ICU mortality. These findings supported that previous report by **Ikeda et al. (2019)**, who found serum IL-6 levels in sepsis patients are correlated to levels of endotoxin activity, which are highly correlated with disease severity and patient survival. Also, **Li and Wang (2023)** reported significantly higher serum IL-6 levels in samples obtained on the 1st day of ICU admission in sepsis than in non-sepsis ICU patients, in SS than in sepsis patients, and in death than in the survival group and concluded that IL-6 has good value as a biomarker for the diagnosis of sepsis. Furthermore, multiple recent experimental and animal studies approved the relation between high expression and serum levels of TNF- α and sepsis severity and outcomes (**Dutta and Bishayi, 2023; Okan et al., 2023; Kong et al., 2023**).

Regarding estimated serum levels of omentin-1, SS patients and non-survivors had significantly lower omentin-1 levels in at-admission samples in comparison to sepsis patients and survivors, respectively. Similarly, **Gültekin et al. (2021)** detected lower omentin-1 levels in dead than alive patients and in non-

sepsis than in sepsis and SS patients. Recently, **Karampela et al. (2023)** detected higher omentin-1 at sepsis onset and decreased progressively with significant correlation with the severity scores, TLC, coagulation biomarkers, and CRP, and with the 28-day mortality of sepsis, and concluded that omentin-1 may be a promising biomarker of sepsis severity and prognosis.

The detected negative significant correlation between serum levels of omentin-1 and inflammatory cytokines was previously detected in several disease states other than sepsis, wherein **Yang and Gao (2020)** and **Zhang et al. (2020)** reported lower serum omentin-1 levels in atherosclerotic acute cerebral infarction and acute intracerebral hemorrhage patients, respectively, and both studies detected negative relation between serum omentin-1 levels and disease severity and a positive relation to the functional outcomes. Also, **He et al. (2020)** detected lower omentin-1 levels in patients with benign prostatic hyperplasia than in controls and found these low levels were in line with increased IL-8 and IL-18 expression levels. Also, **Franik et al. (2020)** found PCOS women had lower omentin-1 levels than non-PCOS women with an inverse relation to estimated TNF- α levels. Thereafter, **Kukla et al. (2021)** in a series of COVID-19 patients, detected lower serum levels of adipokines that were not related to disease severity. Furthermore, **Peña-Cano et al. (2022)** detected lower circulating omentin-1 levels, while levels of pro-inflammatory markers were higher in pregnant women who developed gestational diabetes mellitus than in normal pregnant women.

The reported lower serum levels of omentin-1 in deteriorated patients and non-survivors could be

attributed to the finding of the earlier studies that detected decreased gene expression and plasma levels of omentin-1 in adipose tissue in obese individuals and type-2 diabetics than in lean and normoglycemic subjects (Batista et al., 2007; Pan et al., 2010). In support of this assumption, the current study detected a higher BMI of non-survivors than survivors.

Another explanation for the detected lower serum omentin-1 levels which are inversely related to serum levels of inflammatory cytokines, is the possibility of consumption of omentin-1 during the start of the sepsis process up to the diminution of its serum levels with fulminant sepsis that was manifested as septic shock. In line with this assumption, McMahan et al. (2020) found omentin-1 blocks the pro-inflammatory actions of TNF- α , down-regulates the expression of adhesion molecules and as a ligand to bacterial-specific carbohydrate residues plays a part in microbial surveillance and recognition by macrophages (McMahan et al., 2020). Thereafter, Kobayashi et al. (2022) documented that omentin-1 is an anti-inflammatory adipokine that acts through inhibition of the nuclear factor κ B signaling pathway and suppression of the inflammatory response via activation of AMP-activated protein kinase. As another support of this assumption, the recently detected lower serum omentin-1 levels in various disease conditions associated with inflammation (Yang and Gao 2020; Kukla et al., 2021).

Limitations: The impact of the kinetics of the estimated cytokines levels on outcome is a limitation of the study.

Recommendation: Future studies are mandatory to determine cutoff points for the estimated cytokines and to evaluate their

diagnostic performance for sepsis outcomes.

Conclusion

Estimation of serum cytokine levels in sepsis patients at surgical ICU admission may help to distinguish patients vulnerable to deterioration or death and enforce the diagnostic performance of clinical evaluations and scoring. The calculated Δ SOFA at 24 h after ICU admission is preferable to just SOFA scoring to determine the change in evaluated parameters through 24 h. Combined high Δ SOFA and at-admission low serum omentin-1 might be used as early identifiers for patients vulnerable to bad outcomes.

References

- Batista CM, Yang RZ, Lee MJ, Glynn NM, Yu DZ. (2007) Omentin plasma levels and gene expression are decreased in obesity. *Diabetes*, 56:1655–1661
- Cao Y, Jiang T, Lin Y, Fang X, Ding P, Song H, et al. (2023) Time-series prediction and detection of potential pathogens in bloodstream infection using mcfDNA sequencing. *Frontiers in Cellular and Infection Microbiology*, 13:1144625.
- Chen L, Li J, Yang G. (2020) A comparative review of intelectins. *Scandinavian Journal of Immunology*, 92(1): e12882.
- Chung CK, Wang TJ, Yeung CY. (2006) Interference and blood sample preparation for pyruvate enzymatic assay. *Clinical Biochemistry*, 39:74-7.
- Churpek MM, Zdravetz FJ, Winslow C, Howell MD, Edelson DP. (2015) Incidence and prognostic value of the systemic inflammatory response syndrome and organ dysfunctions in ward patients. *American Journal of Respiratory and Critical Care Medicine*, 192(8):958–964.

- **Coughlan MT, Oliva K, Georgiou HM, Permezel JMH, Rice GE. (2001)** Glucose-induced release of tumor necrosis factor-alpha from human placental and adipose tissues in gestational diabetes mellitus. *Diabetic Medicine*, 18:921-7.
- **Denny K, Lea R, Lindell-Innes R, Haupt L, Heffernan A, Harvey N, et al. (2023)** Diagnosing sepsis in the ICU: Comparison of a gene expression signature to pre-existing biomarkers. *Journal of Critical Care*, 76:154286.
- **Dutta P, Bishayi B. (2023)** IL-10 in combination with IL-12 and TNF- α attenuates CXCL8/CXCR1 axis in peritoneal macrophages of mice infected with *Staphylococcus aureus* through the TNFR1-IL-1R-NF- κ B pathway. *International Immunopharmacology*, 120:110297.
- **Estella A, Rio JG, Álvarez-Manzanares J, Julián-Jiménez A, Del Castillo JG. (2018)** Prognostic accuracy of qsofa according to the site of infection in older patient attended in Emergency Department. *European Journal of Internal Medicine*, 50: e13-e15.
- **Franik G, Sadlocha M, Madej P, Owczarek A, Skrzypulec-Plinta V, Plinta R, et al. (2020)** Circulating omentin-1 levels and inflammation in polycystic ovary syndrome. *Ginekologia Polska*, 91(6):308-312.
- **Gaines-Das RE, Poole S. (1993)** The international standard for interleukin-6—evaluation in an international collaborative study. *Journal of Immunological Methods*, 160: 147-53.
- **Gong F, Ji R, Wang Y, Yang Z, Chen Y, Mao E, et al. (2020)** Identification of Potential Biomarkers and Immune Features of Sepsis Using Bioinformatics Analysis. *Mediators of Inflammation*, 2020:3432587.
- **Guclu-Geyik F, Koseoglu P, Guven G, Can G, Kaya A, Coban N, et al. (2023)** Association of Intelectin 1 Gene rs2274907 A > T Polymorphism with Obesity, Type 2 Diabetes, Serum Intelectin-1 Levels and Lipid Profiles in Turkish Adults. *Biochemical Genetics*, 61(6):2276-2292.
- **Gültekin Y, Biri I, Gojayeve A, Işıkhan S, Akçin O, Kılıç Y. (2021)** Can omentin-1 be a prognostic marker in surgical intensive care patients? *Turkish Journal of Medical Sciences*, 51(5):2485-2493.
- **Ikeda T, Kamohara H, Suda S, Nagura T, Tomino M, Sugi M, et al. (2019)** Comparative Evaluation of Endotoxin Activity Level and Various Biomarkers for Infection and Outcome of ICU-Admitted Patients. *Biomedicine*, 7(3):47.
- **Jourdier S, Annane D. (2020)** From sepsis to septic shock. *Revue de l'Infirmiere*, 69(260-261):16-18.
- **Karampela I, Vallianou N, Tsilingiris D, Christodoulatos G, Antonakos G, Marinou I, et al. (2023)** Diagnostic and Prognostic Value of Serum Omentin-1 in Sepsis: A Prospective Study in Critically Ill Patients. *Medicina (Kaunas)*, 59(5):833.
- **Kobayashi H, Uchimura K, Ishii T, Takahashi K, Mori K, Tsuchiya K, et al. (2022)** Intelectin1 ameliorates macrophage activation via inhibiting the nuclear factor kappa B pathway. *Endocrine Journal*, 69(5):539-546.
- **Kong C, Zhu Y, Xie X, Wu J, Qian M. (2023)** Six potential biomarkers in septic shock: a deep bioinformatics and prospective observational study. *Frontiers In Immunology*, 14:1184700.

- **Kukla M, Menzyk T, Dembiński M, Winiarski M, Garlicki A, Bociąga-Jasik M, et al. (2021)** Anti-inflammatory adipokines: chemerin, vaspin, omentin concentrations and SARS-CoV-2 outcomes. *Scientific Reports*, 11(1):21514.
- **Li X, Wang J. (2023)** Diagnostic and prognostic value of neutrophil CD64, IL-6, and PCT in ICU patients with sepsis. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue*, 35(5):463-468.
- **Liu C, Suo S, Luo L, Chen X, Ling C, Ca S. (2022)** SOFA Score in relation to Sepsis: Clinical Implications in Diagnosis, Treatment, and Prognostic Assessment. *Computational and Mathematical Methods in Medicine*, 2022:7870434.
- **Liu X, Zhao Y, Qin Y, Ma Q, Wang Y, Weng Z, et al. (2023)** Correlation between blood pressure indexes and prognosis in sepsis patients: a cohort study based on MIMIC-III database. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue*, 35(6):578-585.
- **Martocchia A, Piccoli C, Notarangelo M, Bentivegna E, Sergi D, et al. (2023)** A bedside ultrasound protocol to the measurement of the systemic vascular resistances: Preliminary results in the patients with sepsis. *Clinical Hemorheology and Microcirculation*, 83(2):163-169.
- **McMahon C, Isabella C, Windsor I, Kosma P, Raines R, Kiessling L. (2020)** Stereoelectronic Effects Impact Glycan Recognition. *Journal of the American Chemical Society*, 142(5):2386-2395.
- **Ning J, Sun K, Wang X, Fan X, Jia K, Cui J, et al. (2023)** Use of machine learning-based integration to develop a monocyte differentiation-related signature for improving prognosis in patients with sepsis. *Molecular Medicine*, 29(1):37.
- **Okan A, Doğanyığıt Z, Yılmaz S, Uçar S, Söylemez E, Attar R. (2023)** Evaluation of the protective role of resveratrol against sepsis caused by LPS via TLR4/NF- κ B/TNF- α signaling pathways: Experimental study. *Cell Biochemistry & Function*, 41(4):423-433.
- **Pan HY, Guo L, Li Q. (2010)** Changes of serum omentin-1 levels in normal subjects and in patients with impaired glucose regulation and with newly diagnosed and untreated type 2 diabetes. *Diabetes Research and Clinical Practice*, 88:29–33.
- **Peña-Cano MI, Valencia-Ortega J, Morales-Ávila E, Díaz-Velázquez M, Gómez-Díaz R, Saucedo R. (2022)** Omentin-1 and its relationship with inflammatory factors in maternal plasma and visceral adipose tissue of women with gestational diabetes mellitus. *Journal of Endocrinological Investigation*, 45(2):453-462.
- **Ruan Z, Li D, Chen X, Qiu Z. (2023)** Association of serum total bilirubin and potential predictors with mortality in acute respiratory failure: A retrospective cohort study. *Heart Lung*, 57:12-18.
- **Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. (2016)** The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*, 315(8):801-10.
- **Song J, Lee J, Park H, Suh G, Jeon K. (2020)** Incidence of Hypotension after Discontinuation of Norepinephrine or Arginine Vasopressin in Patients with Septic Shock: a Systematic Review and

- Meta-Analysis. *Journal of Korean Medical Science*, 35(1):e8.
- **Teasdale G, Jennett B. (1976)** Assessment and prognosis of coma after head injury. *Acta Neurochirurgica*, 34:45-55.
 - **Tinder P. (1969)** Determination of blood glucose. *Annals of Clinical Biochemistry*, 6:24.
 - **Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, et al. (1996)** The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive Care Medicine*, 22:707-10.
 - **Volkova E, Willis JA, Wells JE, Robinson BA, Dachs GU, Currie MJ. (2011)** Association of angiotensin-2, C-reactive protein and markers of obesity and insulin resistance with survival outcome in colorectal cancer. *British Journal of Cancer*, 104(1):51-9.
 - **Wang Y, Gao S, Hong L, Hou T, Liu H, Li M, et al. (2023)** Prognostic impact of blood urea nitrogen to albumin ratio on patients with sepsis: a retrospective cohort study. *Scientific Reports*, 13(1):10013.
 - **Wasserman K, Beaver WL, Davies JA. (1985)** Lactate, pyruvate and lactate-to-pyruvate ratio during exercise and recovery. *Journal of Applied Physiology*, 59(3):935-40.
 - **Yang J, Gao Y. (2020)** Clinical relevance of serum omentin-1 levels as a biomarker of prognosis in patients with acute cerebral infarction. *Brain and Behavior*, 10(7):e01678.
 - **Yin J, Hou P, Wu Z, Nie Y. (2015)** Decreased Levels of Serum Omentin-1 in Patients with Inflammatory Bowel Disease. *Medical Science Monitor*, 21:118–22.
 - **Zhang G, Ye Z, Guan H, Guo M, Zhou X, Xu Y. (2020)** Impact of serum omentin-1 concentrations on functional outcome among acute intracerebral hemorrhage patients. *Clinica Chimica Acta*, 503:169-174.
 - **Zhou H, Li Z, Liang H, Yan Z. (2022)** Thrombocytopenia and platelet count recovery in patients with sepsis-3: a retrospective observational study. *Platelets*, 33(4):612-620.