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RESEARCH ARTICLE

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Comparative study between complete blood picture indices and presepsin as early prognostic markers in septic shock patients

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ABSTRACT

Background: Outcome prediction in septic shock is a prime concern as it may facilitate more aggressive interventions to be made at appropriate time to reduce costs and mortality. We evaluated combining complete blood count (CBC) indices [red cell distribution width (RDW), mean platelet volume (MPV), neutrophil–lymphocyte ratio (NLR)] for septic shock early prognostication in comparison to presepsin.

Methods: Sixty adult intensive care unit (ICU) patients with septic shock according to Sepsis-3 were enrolled. Blood assembling on admission and day 3 to determine presepsin level, and CBC indices which were interpreted as RDW, MPV, and NLR. Patients were sorted into survivors (Group I) and non-survivors (Group II).

Results: Presepsin in non-survivors was higher significantly on admission and day 3 ($p < 0.001$, <0.001, respectively). RDW in non-survivors was higher significantly on admission and day 3 ($p = 0.022$, 0.001, respectively). MPV in non-survivors was higher significantly on admission and day 3 ($p = 0.030$, 0.001, respectively). NLR in non-survivors was higher significantly on admission and day 3 ($p = 0.001$, <0.001, respectively). The calculated AUCs were 0.890 ($p < 0.001$) for presepsin, with 92% sensitivity, 83% specificity, and 88% accuracy, and 0.842 ($p < 0.001$) for CBC indices combination, with 89% sensitivity, 85% specificity, and 86% accuracy. Significant positive correlation was found between presepsin and CBC indices combination ($r = 0.417$, $p = 0.001$).

Conclusion: Combination of RDW, MPV, and NLR could be integrated into septic shock early prognostication tools with sensitivity, specificity, and accuracy similar to presepsin.

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Septic shock; presepsin; red cell distribution width (RDW); mean platelet volume (MPV); neutrophil–lymphocyte ratio (NLR); prognosis

1. Introduction

Despite significant therapeutic advancements, septic shock sustains as a crucial mortality contributor with attributed deaths of 30–60% worldwide [1,2]. Septic shock is extremely complex, characterized by profound circulatory abnormalities, tissue hypoperfusion, and eventually organ failure [3]. Outcome prediction is a prime concern as it may facilitate more aggressive interventions to be made at appropriate time to reduce costs and mortality. As sepsis pathophysiology includes almost all tissues, cell types, organ systems, and many inflammatory mediators; sepsis response involves release of many biomarkers; a fact suggesting that portion of them could contribute in sepsis management. There are near 180 molecules that are proposed as biomarkers of sepsis [4].

Presepsin (soluble cluster of differentiation 14 subtype "sCD14-ST") is a (64 amino acid residues, 13 kDa) soluble truncated N-terminal fragment of CD14 generated by cleavage of sCD14 by plasma proteases induced by bacterial phagocytosis, so its level reflects severity of infection rather than degree of inflammation [5,6]. Presepsin revealed significance in sepsis diagnosis [6,7], course monitoring and predicting outcome [8,9].

Physiological changes in sepsis influence complete blood count (CBC) [10]. Red cell distribution width (RDW), mean platelet volume (MPV), and neutrophil–lymphocyte ratio (NLR) are parameters obtained from routine CBC which is rapid, easily evaluated, radially available that do not incur additional costs [11].

RDW displays erythrocytes' size heterogeneity (anisocytosis). It has been used with mean corpuscular volume (MCV) to distinguish causes of anaemias, following that, its relation with several medical conditions was assessed in literatures [12]. Recently, RDW showed significant value in sepsis diagnosis [13], course monitoring, and predicting outcome [11,14].

MPV illustrates the average platelet size and reflects its function. MPV rising is useful in cardiovascular and cerebrovascular thromboembolic events [15], heart failure [16], infective endocarditis [17], venous thromboembolism [18]. MPV is helpful in sepsis diagnosis [19], course monitoring, and prognosis [11,20].

NLR calculation is dependent on CBC sample. NLR proved significance in various malignancies [21],

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cardiovascular disease [22], pulmonary embolism [23], and cerebrovascular strokes [24]. Also, NLR helps in various aspects of sepsis management [25,26].

Since outcome predictors are needed in intensive care unit (ICU), identifying simpler, cost-effective, and reliable tool becomes necessary. In view of this, we aimed to evaluate the prognostic significance of combining CBC indices (RDW, MPV, NLR) in septic shock in comparison to the already proven strength marker "presepsin".

2. Materials and methods

2.1. Study design and population

The prospective, observational study executed on 60 adult patients with diagnosis of septic shock according to (Sepsis-3) [3], admitted to ICU in Alexandria Armed Forces Hospital. Study approval was guaranteed by the Medical Ethics Committee of Alexandria Faculty of Medicine, Alexandria, Egypt before conducting the study (approval number: 0105031). Informed written consent from the next of kin was taken.

We excluded (1) patients ≤ 18 years; (2) pregnant females; (3) patients with other causes provoking increase in RDW as coronary disease, heart failure, pulmonary hypertension, pulmonary embolism, cardiac arrest, recent stroke, liver disease, peripheral artery disease, acute bleeding, blood transfusion, recent chemotherapy, and hematological disorders; (4) patients with other causes provoking increase in MPV as coronary disease, acute bleeding, blood transfusion, malignancy, and hematological disorders; (5) patients with other causes provoking increase in NLR as immune suppression from the study.

Patients were observed until hospital discharge, and then sorted according to outcome (survival) into survivors (Group I) and non-survivors (Group II).

2.2. Sample size calculation

The calculation was performed by Department of Medical Statistics, Medical Research Institute, Alexandria University, Alexandria, Egypt based on pre-test probability of mortality among critically ill patients with septic shock using R software developed by R Foundation for Statistical Computing (Wirtschaftsuniversität Wien, Vienna, Austria) to achieve 80% power and 95% confidence level (CI). The sample size for our study was 60 patients.

2.3. Data collection

The characteristics of study population including gender, age, comorbidities, infection site were obtained. Calculation of Acute Physiology and Chronic Health Evaluation II (APACHE-II) score on admission and Sequential Organ Failure Assessment (SOFA) score on admission and day 3. Mechanical ventilation requirement, mechanical ventilation span, vasopressor span, need for renal replacement therapy (RRT), ICU span, hospital span, and mortality were recorded.

2.4. Laboratory analysis

Blood assembling on admission and day 3 via venipuncture in EDTA anticoagulated vacutainer. CBC analysis was accomplished by auto hematology analyzer BC-5500 (Mindray Bio-Medical Electronics Co., Ltd., China) and results were interpreted as regard RDW, MPV, and NLR. Presepsin concentration picogram/milliliter (pg/ml) was measured using PATHFAST™ System (Mitsubishi Chemical Medience Corporation, Japan), based on non-competitive chemi-luminescence enzyme immunoassay (CLEIA), the assessment time was 15 min.

2.5. Management

Patients were managed according to Surviving Sepsis Campaign (SSC) recommendations [2].

2.6. Statistical analysis

SPSS v.20.0 (IBM Corp., Armonk, NY, USA) was used to execute statistical analyses. Data were illustrated as mean ± SD, median (interquartile range [IQR]), and percentages (%). Statistical significance ($p < 0.05$) was tested by Student's *t*-test or Mann–Whitney *U* test (continuous variables) and Pearson chi-square (χ^2) or Fisher's exact tests (categorical variables). Prognostic performance of all studied parameters was analyzed by receiver operating characteristic (ROC) areas under the curve (AUCs); optimal prognostic cutoff values were calculated. The agreement of presepsin, RDW, MPV, and NLR to differentiate between outcomes was expressed as sensitivity, specificity, and accuracy. Correlation between CBC indices combination and presepsin was executed by Pearson correlation.

3. Results

During the study, initially 71 patients met inclusion criteria; of them 11 patients were excluded: 7 patients died before day 3, and 4 patients received blood products (Figure 1). The final analyzed 60 patients were sorted according to outcome (survival) into survivors (Group I) and non-survivors (Group II).

Study population characteristics are delineated in Table 1. Non-survivors (56.7%) were older (67.12 ± 6.94 years), more males (67.6%), with more comorbidities. Respiratory tract was the commonest source and elicited higher mortality, followed by urinary tract which elicited lower mortality. Gram-

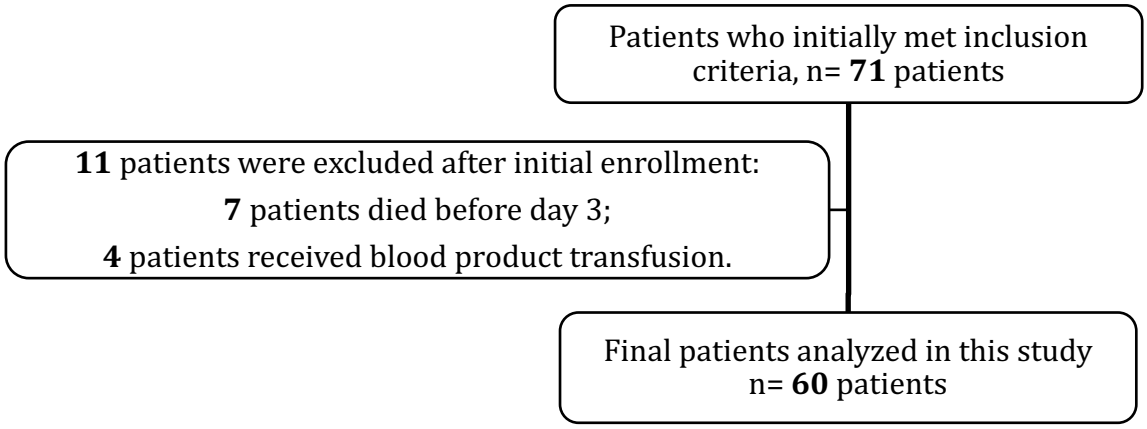

Figure 1. Flow chart of patient enrollment.

Table 1. Study population characteristics.

Characteristic	Total $n = 60$ (100%)	Survivors $n = 26$ (43.3%)	Non-survivors $n = 34$ (56.7%)	p-value
Age, years	53–78 (65.23 ± 7.28)	53–76 (62.77 ± 6.89)	54–78 (67.12 ± 6.94)	0.021*
Males, *n* (%)	37 (61.7%)	14 (53.8%)	23 (67.6%)	0.284
Comorbidities, *n* (%)				
DM	38 (63.3%)	15 (57.7%)	23 (67.6%)	0.428
HTN	34 (56.7%)	14 (53.8%)	20 (58.8%)	0.700
IHD	27 (45.0%)	9 (34.6%)	18 (52.9%)	0.157
CLD	21 (35.0%)	7 (26.9%)	14 (41.2%)	0.251
CVS	25 (41.7%)	8 (30.8%)	17 (50.0%)	0.134
CKD	19 (31.7%)	6 (23.1%)	13 (38.2%)	0.211
No. of comorbidities, *n* (%)				
One comorbidity	5 (8.3%)	5 (19.2%)	0 (0.0%)	0.001*
Two comorbidities	17 (28.3%)	12 (46.2%)	5 (14.7%)	
Three comorbidities	30 (50.0%)	7 (26.9%)	23 (67.6%)	
Four comorbidities	5 (8.3%)	1 (3.8%)	4 (11.8%)	
Five comorbidities	3 (5.0%)	1 (3.8%)	2 (5.9%)	
Infection source, *n* (%)				
Respiratory	28 (46.7%)	8 (30.8%)	20 (58.8%)	0.031*
Urinary tract	16 (26.7%)	12 (46.2%)	4 (11.8%)	0.002*
Intra-abdominal	5 (8.3%)	1 (3.8%)	4 (11.8%)	0.279
Blood stream	7 (11.7%)	2 (7.7%)	5 (14.7%)	0.410
Skin and soft tissue	4 (6.7%)	3 (11.5%)	1 (2.9%)	0.192
Organism(s), *n* (%)				
Gram –ve	37 (61.7%)	12 (46.2%)	25 (73.5%)	0.031*
Gram +ve	23 (38.3%)	14 (53.8%)	9 (26.5%)	
Monomicrobial	41 (68.3%)	22 (84.6%)	19 (55.9%)	0.017*
Polymicrobial	19 (31.7%)	4 (15.4%)	15 (44.1%)	
RRT need, *n* (%)	28 (46.7%)	8 (30.8%)	20 (58.8%)	0.031*
MV need, *n* (%)	56 (93.3%)	22 (84.6%)	34 (100%)	0.018*
MV duration, days	0–11 (6.35 ± 2.79)	0–8 (4.19 ± 2.43)	5–11 (8.00 ± 1.70)	0.001*
Vasopressor duration, days	2–12 (6.93 ± 2.68)	2–7 (4.58 ± 1.42)	5–12 (8.74 ± 1.96)	0.001*
	4–13 (8.75 ± 1.87)	4–10 (7.96 ± 1.63)	6–13 (9.35 ± 1.81)	0.004*
ICU stay, days	6–14 (9.57 ± 1.77)	7–14 (9.85 ± 1.68)	6–13 (9.35 ± 1.81)	0.294
Hospital stay, days	30 (28–33)	28 (23–29)	33 (30–36)	<0.001*
APACHE II				
SOFA	10 (9–11)	9 (8–10)	11 (10–12)	<0.001*
Admission	10 (8–11)	8 (7–9)	11 (10–12)	<0.001*
Day 3				

Data are expressed as minimum–maximum (mean ± SD), number (%), and median (interquartile range [IQR).
DM: diabetes mellitus; HTN: hypertension; IHD: ischemic heart disease; CLD: chronic lung disease; CVS: cerebrovascular stroke; CKD: chronic kidney disease; UTI: urinary tract infection; Gm: Gram; RRT: renal replacement therapy; MV: mechanical ventilation; APACHE II: acute physiology and chronic health evaluation; SOFA: sequential organ failure assessment.
*p value is significant if ≤0.05.

negative bacteria, polymicrobial infections elicited higher mortality. RRT need, mechanical ventilation need, mechanical ventilation span, and vasopressor span were all higher significantly in non-survivors. ICU span was longer significantly in non-survivors, whereas hospital span was non-significantly longer in survivors. APACHE-II in non-survivors was higher significantly. Also, SOFA in non-survivors was higher significantly on admission and day 3.

The relations between the studied biomarkers and outcome are delineated in Table 2 and Figure 2. Presepsin in non-survivors was higher significantly on

Table 2. Relation between the studied markers and outcome.

	Survivors $n = 26$ (43.3%)	Non-survivors $n = 34$ (56.7%)	p-value
Presepsin			
Admission	950–3750 (1828.50 ± 726.63)	1503–6355 (3303.35 ± 1125.52)	<0.001*
Day 3	736–2964 (1363.46 ± 633.77)	1235–8194 (4153.88 ± 1492.53)	<0.001*
RDW			
Admission	14.65–20.82 (17.94 ± 2.11)	15.92–23.26 (19.30 ± 2.28)	0.022*
Day 3	12.75–19.35 (16.50 ± 2.12)	17.34–24.77 (20.78 ± 2.36)	0.001*
MPV			
Admission	10.04–11.88 (10.68 ± 0.60)	10.10–12.82 (11.42 ± 0.89)	0.030*
Day 3	9.75–12.17 (10.94 ± 0.65)	10.13–13.11 (11.75 ± 0.92)	0.001*
NLR			
Admission	9.50–22.60 (14.87 ± 3.51)	10.10–31.60 (18.36 ± 4.13)	0.001*
Day 3	9.10–25.10 (12.14 ± 3.71)	9.50–30.10 (16.89 ± 4.77)	<0.001*

Data are expressed as minimum–maximum (mean ± SD).
Presepsin is measured by picogram/milliliter (pg/ml); RDW: red cell distribution width is expressed as percentage (%); MPV: mean platelet volume is measured by femtolitre (fL); NLR: neutrophil–lymphocyte ratio.
*p value is significant if ≤0.05.

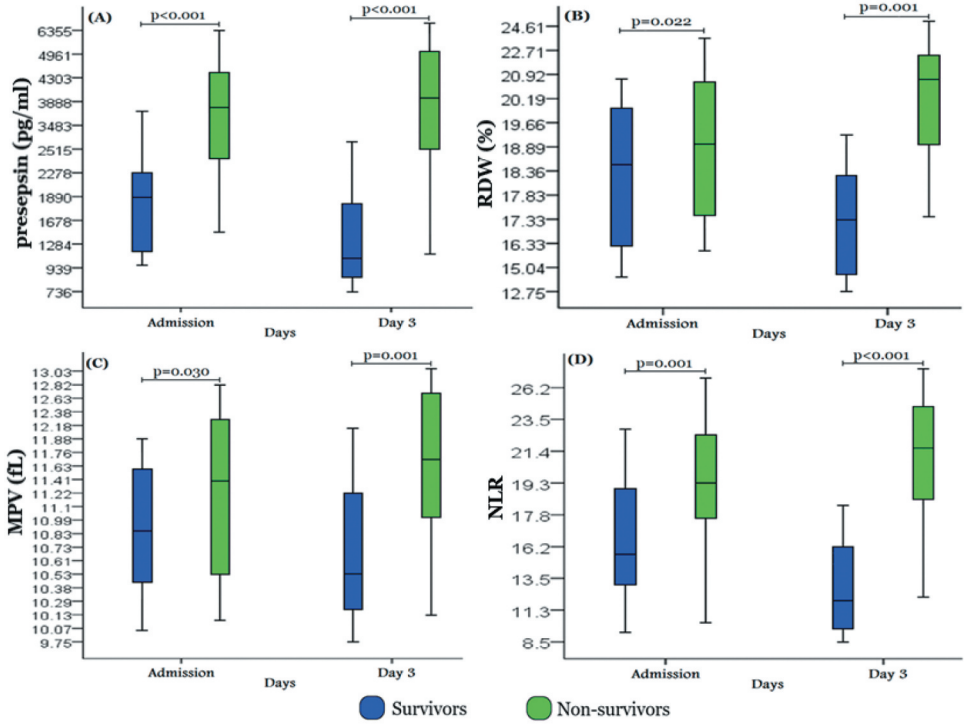

Figure 2. The relation between the studied markers and outcome: (a) presepsin, (b) RDW, (c) MPV, (d) NLR. Significant p-values are indicated on graph at $p < 0.05$. Presepsin is measured by picogram/milliliter (pg/ml); RDW: red cell distribution width is expressed as percentage (%); MPV: mean platelet volume is measured by femtolitre (fL); NLR: neutrophil–lymphocyte ratio is expressed as ratio.

admission (3303.35 ± 1125.52 vs. 1828.50 ± 726.63 pg/ml; $p < 0.001$), day 3 (4153.88 ± 1492.53 vs. 1363.46 ± 633.77 pg/ml; $p < 0.001$). Moreover, survivors' admission value was higher than day 3, whereas non-survivors' day 3 value was higher than admission. RDW in non-survivors was higher significantly on admission (19.30 ± 2.28 vs. 17.94 ± 2.11%; $p = 0.022$), day 3 (20.78 ± 2.36 vs. 16.50 ± 2.12%; $p = 0.001$). Moreover, survivors' admission value was higher than day 3, whereas non-survivors' day 3 value was higher than admission. MPV in non-survivors was higher significantly on admission (11.42 ± 0.89 vs. 10.68 ± 0.60 fL; $p = 0.030$), day 3 (11.75 ± 0.92 vs. 10.94 ± 0.65 fL; $p = 0.001$). Moreover, MPV in non-survivors and survivors was higher on day 3 than admission. NLR in non-survivors was higher significantly on admission (18.36 ± 4.13 vs. 14.87 ± 3.51; $p = 0.001$), day 3 (16.89 ± 4.77 vs. 12.14 ± 3.71; $p < 0.001$). Moreover, NLR in non-survivors and survivors was lower on day 3 than admission.

3.1. The prognostic performance of all studied parameters

ROC AUCs of the studied biomarkers were calculated (Table 3, Figure 3). The AUC for presepsin was 0.890 ($p < 0.001$) with 2100 pg/ml as the best prognostic cutoff value, at that level sensitivity was 92%, specificity was 83%, and accuracy was 88%. The AUC for RDW was 0.743 ($p = 0.001$) with 17.92% as the best prognostic cutoff

Table 3. Prognostic performance of studied parameters in predicting outcome.

	AUC	*p*-value	Cutoff	Sensitivity	Specificity	Accuracy
Presepsin	0.890	<0.001*	2100	92%	83%	88%
RDW	0.743	0.001*	17.92	76%	77%	74%
MPV	0.659	0.036*	11	65%	67%	64%
NLR	0.758	0.001*	17	75%	79%	76%

RDW: red cell distribution width; MPV: mean platelet volume; NLR: neutrophil–lymphocyte ratio; AUC: area under the curve.
*p value is significant if ≤0.05.

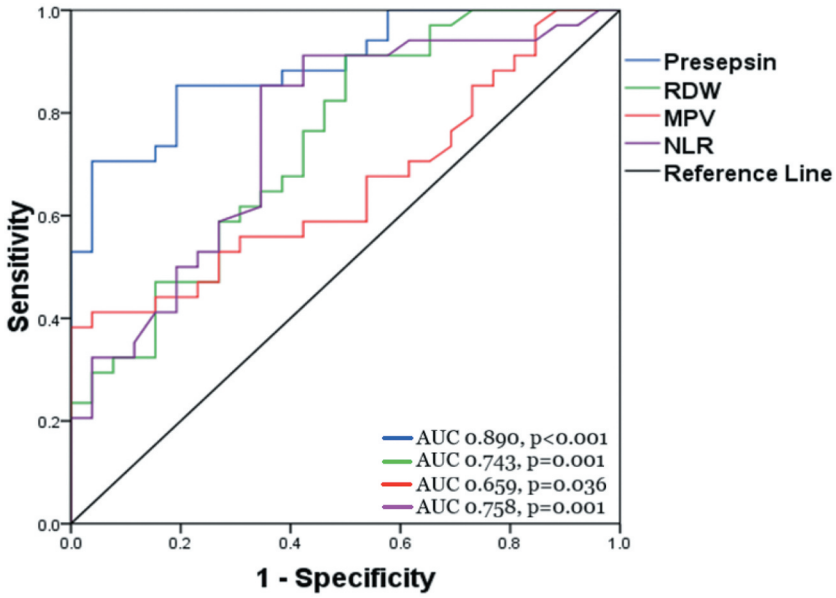

Figure 3. Prognostic performance of presepsin and CBC indices in predicting outcome. Significant *p*-values are indicated on graph at $p < 0.05$.

Table 4. Prognostic performance of CBC indices combination in comparison with presepsin in predicting outcome.

	AUC	*p*-value	Sensitivity	Specificity	Accuracy
Presepsin	0.890	<0.001*	92%	83%	88%
Combination of RDW + MPV + NLR	0.842	<0.001*	89%	85%	86%

RDW: red cell distribution width; MPV: mean platelet volume; NLR: neutrophil–lymphocyte ratio; AUC: area under the curve.
*p value is significant if ≤0.05.

value, at that level sensitivity was 76%, specificity was 77%, and accuracy was 74%. The AUC for MPV was 0.659 ($p = 0.036$) with 11 fL as the best prognostic cutoff value, at that level sensitivity was 65%, specificity was 67%, and accuracy was 64%. The AUC for NLR was 0.758 ($p = 0.001$) with 17 as the best prognostic cutoff value, at that level, sensitivity was 75%, specificity was 79%, and accuracy was 76%. RDW, MPV, and NLR were combined to predict the outcome. The ROC curve yielded an AUC of 0.842 ($p < 0.001$), sensitivity was 89%, specificity was 85%, and accuracy was 86% (Table 4, Figure 4). There was significant positive correlation between presepsin and CBC indices combination ($r = 0.417$, $p = 0.001$) (Table 5).

5. Discussion

Mortality prediction is an emerging tool in medicine especially in ICU as it helps in identifying at-risk patients at earlier stages to give special attention and tailor therapy for better outcome. Different methods are evaluated to predict outcome. However, none of them is a gold standard due to the complexity, non-availability and costliness of certain tests. Hence, identifying a simpler, cost-effective, and reliable tool becomes necessary.

The current study demonstrated that presepsin showed significant association with mortality on admission and day 3. In agreement, Masson et al. [27] reported that presepsin in decedents was higher significantly on first, second, and seventh days. Also, Carpio et al. [28] found that presepsin in non-survivors was higher significantly on admission and day 3. In addition, Behnes et al. [8] reported that presepsin was useful for prognosis on admission and third day. In survivors, presepsin level was higher on admission than day 3, whereas in non-survivors, it was higher on day 3 than admission. In agreement, Carpio et al. [28] reported that median presepsin level in survivors was higher on admission than after 72 h, whereas in non-survivors, it was higher after 72 h than admission.

During sepsis, various pathophysiological mechanisms affect RDW, such as oxidative stress, proinflammatory cytokines, systemic inflammatory response, and renal dysfunction [29]. RDW showed significant association with mortality on admission and day 3. In

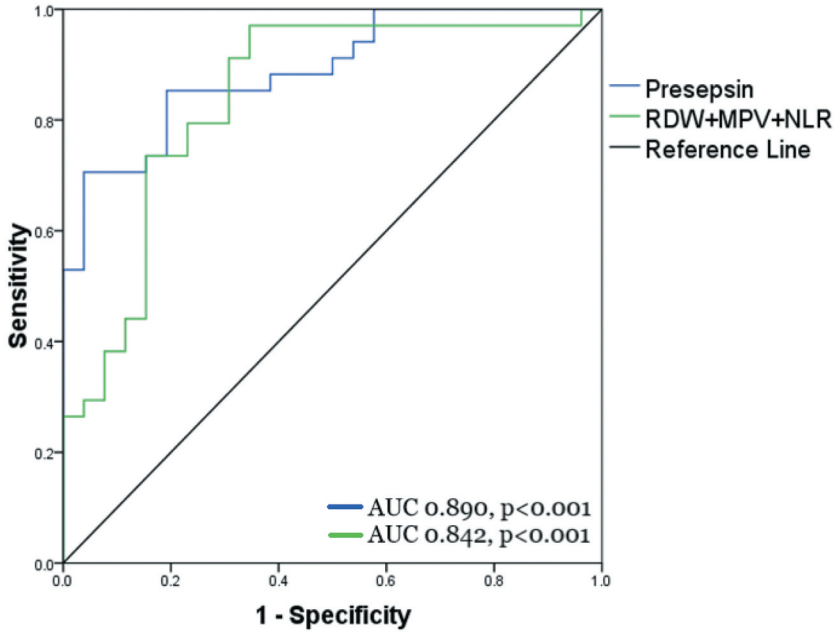

Figure 4. Prognostic performance of CBC indices combination and presepsin in predicting outcome. Significant *p*-values are indicated on graph at $p < 0.05$.

Table 5. Correlation between presepsin and CBC indices combination.

		CBC indices combination
Presepsin	*r*	0.417**
	p	0.001

**Correlation is significant at the 0.01 level (two-tailed).
r: correlation coefficient; *p*: probability.

agreement, Punekar et al. [29] reported that baseline RDW and 72 h later were linked to sepsis outcome. Lorente et al. [30] found higher RDW in non-survivors on first day and 72 h later. Sadaka et al. [31] reported that septic shock survivors showed significant lower RDW on admission and day 3. In survivors, RDW was higher on admission than day 3, while it was higher on day 3 than admission in non-survivors. In agreement, Ju et al. [14] reported that survivors had higher RDW on day 1 than day 4, whereas non-survivors had higher RDW on day 4 than day 1.

MPV increases as a bone marrow compensatory mechanism to sepsis-induced thrombocytopenia explained by impairment of central platelets production, overconsumption and/or destruction peripherally due to interaction of platelets with pathogens, endothelial cells, and immune mediators [32]. MPV showed significant association with mortality on admission and day 3. In agreement, Kim et al. [20] reported that non-survivors exhibited significant higher baseline and day 3 MPV values. Also, İşgüder et al. [33] showed that non-survivors had significant high MPV on admission and 72 h later. MPV in both groups was higher on day 3 than admission; this result is in concordance with study done by Kim et al. in which MPV was higher at 72 h than baseline in both non-survivors and survivors [20].

During sepsis, stimulation of neutrophil production, neutrophil demigration, and neutrophil apoptosis delay result in lengthening of neutrophil function. Conversely, increased catecholamine and cortisol levels, migration and increased sepsis-induced apoptosis of lymphocytes result in lymphocytopenia, thus within hours of infection, neutrophils increase by near 300% and lymphocytes decrease by near 85% [25,26]. NLR showed significant association with mortality on admission and day 3. In agreement, Okashah et al. [34] reported that non-survivors exhibited significant higher baseline NLR and 72 h later. Also, Meng et al. [35] reported that NLR on the first and third days in the death group were higher. NLR in both groups was lower on day 3 than admission, this result is in concordance with study done by Okashah et al. [34] in which NLR was lower after 72 h than on admission in both non-survivors and survivors.

The calculated AUC for presepsin showed good prognostic performance 0.890 with 2100 pg/ml as cut-off value. In agreement, Carpio et al. [28] found that calculated AUC of presepsin for prediction of 30-day death was 0.743, with 825 ng/L as cutoff value. Also, Masson et al. [27] reported that the AUC for ICU survival was 0.69, with 1631 pg/ml as cutoff value. Moreover, Spanuth et al. [36] reported that the ROC curve of presepsin showed a good prognostic accuracy AUC = 0.878 with cutoff value off 1662 pg/ml.

The calculated AUC for RDW was 0.743 with 17.92% as cutoff. In agreement, Lorente et al. [30] reported that the AUC of RDW was 0.62 with proposed cutoff of 15.5%. Also, Jo et al. [37] investigated RDW role for prognostication of septic shock and severe sepsis, they reported an AUC of 0.678. Sadaka et al. [31] studied the association between RDW and mortality in septic

shock, the calculated AUC was 0.740. Kim et al. [38] reported an AUC of 0.733 and for each 1% increase in RDW, the 30-day mortality risk increased by 10–15%.

The yielded AUC for MPV was 0.659 with 11 fL as cutoff. In agreement, Kim et al. [20] reported that the AUC of MPV for 28-day all-cause mortality was 0.653. Zhang et al. studied platelet volume indices and mortality in unselected ICU patients, their results reported that the AUC for MPV 0.65 with cutoff of 11.5 fL [39].

The yielded AUC for NLR was 0.758 with 17 as cutoff. In agreement, Liu et al. [26] assessed NLR prognostic significance in sepsis, their results showed an AUC of 0.695 ± 0.036, and NLR ≥23.8 reported as cutoff value. Akilli et al. [25] studied the prognostic importance of NLR in critically ill; they reported an AUC of 0.61 with 11.9 as cutoff value. Mandal et al. [40] reported that the AUC of NLR for predicting in-hospital mortality was 0.8007, and NLR >10 proposed as optimal cutoff.

Combination of the CBC indices showed a good discriminative power for mortality prediction, AUC = 0.842, sensitivity was 89%, specificity was 85%, and accuracy was 86%, and there was significant correlation between presepsin and CBC indices combination ($r = 0.417$, $p = 0.001$).

The current study had some limitations. First, single-center study and these results might not be generalizable to other medical institutions. Second, relatively small sample size did not allow in-depth analysis of relationships between the studied biomarkers and disease characteristics. So, further multi-center studies with large patients' number to maximize the accuracy of statistical analyses of results.

However, the present treatise might have strengths. First, the prospective study nature, all the analyzed data and variables were from the patients' charts and direct clinical measurements. Second, patients' transfusion records were available. Third, a comparison with already proven strength marker "Presepsin". Fourth, data were measured initially on ICU admission, so the measurement time was uniform. Fifth, patients with serial measurements were included only. Sixth, Patients who required blood products or died before day 3 were excluded to avoid bias of results. Finally, use of mortality as an unbiased end point and of much greater clinical significance than surrogate end points such as length of ICU and/or hospital stay.

6. Conclusion

This study revealed that combination of RDW, MPV, and NLR is obtained from routine CBC – which is easily evaluated, less time-consuming, radially available, and do not incur additional costs – had strong correlation concerning septic shock prognosis and could be integrated into early prognostication tools with sensitivity, specificity, and accuracy similar to presepsin.

Disclosure statement

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References

[1] Fleischmann C, Scherag A, Adhikari NK, et al. Assessment of global incidence and mortality of hospital-treated sepsis. Current estimates and limitations. Am J Respir Crit Care Med 2016;193(3):259–72.
[2] Rhodes A, Evans LE, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock: 2016. Crit Care Med 2017;45(3):486–552.
[3] Singer M, Deutschman CS, Seymour CW, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA 2016;315(8):801–10.
[4] Pierrakos C, Vincent J. Sepsis biomarkers: a review. Crit Care 2010;14(1):R15.
[5] Chenevier-Gobeaux C, Borderie D, Weiss N, et al. Presepsin (sCD14-ST), an innate immune response marker in sepsis. Clin Chim Acta 2015;450:97–103.
[6] Wu J, Hu L, Zhang G, et al. Accuracy of presepsin in sepsis diagnosis: a systematic review and meta-analysis. PLoS One 2015;10(7):e0133057.
[7] Wu CC, Lan HM, Han ST, et al. Comparison of diagnostic accuracy in sepsis between presepsin, procalcitonin, and C-reactive protein: a systematic review and meta-analysis. Ann Intensive Care 2017;7(1):91.
[8] Behnes M, Bertsch T, Lepiorz D, et al. Diagnostic and prognostic utility of soluble CD 14 subtype (presepsin) for severe sepsis and septic shock during the first week of intensive care treatment. Crit Care 2014;18(5):507.
[9] Yang HS, Hur M, Yi A, et al. Prognostic value of presepsin in adult patients with sepsis: systematic review and meta-analysis. PLoS One 2018;13(1):e0191486.
[10] Rajagopal P, Ramamoorthy S, Jeslin AG. Utility of haemogram parameters in mortality risk prediction of critically ill patients. J Evol Med Dent Sci 2018;7(8):1024–29.
[11] Orfanu AE, Popescu C, Leustean A, et al. The importance of haemogram parameters in the diagnosis and prognosis of septic patients. J Crit Care Med 2017;3(3):105–10.
[12] Salvagno GL, Sanchis-Gomar F, Picanza A, et al. Red blood cell distribution width: A simple parameter with multiple clinical applications. Crit Rev Clin Lab Sci 2015;52(2):86–105.
[13] Farzanegan B, Zangi M. Predictor factors for sepsis diagnosis, length of ICU stay and mortality in ICU. J Cell Mol Anesth 2017;2(2):55–62.
[14] Ju XF, Wang F, Wang L, et al. Dynamic change of red cell distribution width levels in prediction of hospital mortality in chinese elderly patients with septic shock. Chin Med J (Engl) 2017;130(10):1189–95.

[15] Choi DH, Kang SH, Song H. Mean platelet volume: a potential biomarker of the risk and prognosis of heart disease. Korean J Intern Med 2016;31(6):1009–17.
[16] Budak YU, Huysal K, Demirci H. Correlation between mean platelet volume and B-type natriuretic peptide concentration in emergency patients with heart failure. Biochem Med (Zagreb) 2015;25(1):97–102.
[17] Ileri M, Kanat S, Orhan G, et al. Increased mean platelet volume in patients with infective endocarditis and embolic events. Cardiol J 2015;22(1):37–43.
[18] Kovacs S, Csiki Z, Zsori KS, et al. Characteristics of platelet count and size and diagnostic accuracy of mean platelet volume in patients with venous thromboembolism. A systematic review and meta-analysis. Platelets 2019;30(2):139-47.
[19] Sanchez-Calzada A, Navarro JL, Delgado L, et al. Mean platelet volume as a marker of sepsis in patients admitted to intensive therapy. Intensive Care Med Exp 2015;3(1):A871.
[20] Kim CH, Kim SJ, Lee MJ, et al. An increase in mean platelet volume from baseline is associated with mortality in patients with severe sepsis or septic shock. PLoS One 2015;10(3):e0119437.
[21] Nakamura Y, Watanabe R, Katagiri M, et al. Neutrophil/lymphocyte ratio has a prognostic value for patients with terminal cancer. World J Surg Oncol 2016;14:148.
[22] Angkananard T, Anothaisintawee T, McEvoy M, et al. Neutrophil lymphocyte ratio and cardiovascular disease risk: a systematic review and meta-analysis. Biomed Res Int 2018;2018:2703518.
[23] Kayrak M, Erdogan HI, Solak Y, et al. Prognostic value of neutrophil to lymphocyte ratio in patients with acute pulmonary embolism: a restrospective study. Heart Lung Circ 2014;23(1):56–62.
[24] Song SY, Zhao XX, Rajah G, et al. Clinical significance of baseline neutrophil-to-lymphocyte ratio in patients with ischemic stroke or hemorrhagic stroke: an updated meta-analysis. Front Neurol 2019;10:1032.
[25] Akilli NB, Yortanli M, Mutlu H, et al. Prognostic importance of neutrophil-lymphocyte ratio in critically ill patients: short- and long-term outcomes. Am J Emerg Med 2014;32(12):1476–80.
[26] Liu X, Shen Y, Wang H, et al. Prognostic significance of neutrophil-to-lymphocyte ratio in patients with sepsis: a prospective observational study. Mediators Inflamm 2016;2016:8191254.
[27] Masson S, Caironi P, Spanuth E, et al. Presepsin (soluble CD14 subtype) and procalcitonin levels for mortality prediction in sepsis: data from the Albumin Italian outcome sepsis trial. Crit Care 2014;18(1):R6.
[28] Carpio R, Zapata J, Spanuth E, et al. Utility of presepsin (sCD14-ST) as a diagnostic and prognostic marker of sepsis in the emergency department. Clin Chim Acta 2015;450:169–75.
[29] Punekar J, Jain N, Yawalkar V, et al. Role of red blood cell distribution width as a prognostic marker in patients with severe sepsis and septic shock. J Evol Med Dent Sci 2016;5(21):1111–5.
[30] Lorente L, Martin MM, Abreu-Gonzalez P, et al. Red blood cell distribution width during the first week is associated with severity and mortality in septic patients. PLoS One 2014;9(8):e105436.
[31] Sadaka F, O'Brien J, Prakash S. Red cell distribution width and outcome in patients with septic shock. J Intensive Care Med 2013;28(5):307–13.
[32] Gao Y, Li Y, Yu X, et al. The impact of various platelet indices as prognostic markers of septic shock. PLoS One 2014;9(8):e103761.
[33] İşgüder R, Ceylan G, Agin H, et al. Increased mean platelet volume in children with sepsis as a predictor of mortality. Turk J Pediatr 2016;58(5):503–11.
[34] Okashah AS, El-Sawy MM, Beshay BN, et al. Ratio of neutrophil to lymphocyte counts as a simple marker for sepsis and severe sepsis in Intensive Care Unit. Res Opin Anesth Intensive Care 2014;2:39–45.
[35] Meng Y, Lijuan L, Nan S, et al. Dynamic monitoring of the neutrophil/lymphocyte ratio could predict the prognosis of patients with bloodstream infection. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue 2015;27(6):471–6.
[36] Spanuth E, Ebelt H, Ivandic B, et al. Diagnostic and prognostic value of presepsin (soluble cd14 subtype) in emergency patients with early sepsis using the new assay PATHFAST Presepsin. In: Renz H, Tauber R, editors. Advances in clinical chemistry and laboratory medicine. Birlin: Walter de Gruyter; 2012. p. 128–33.
[37] Jo YH, Kim K, Lee JH, et al. Red cell distribution width is a prognostic factor in severe sepsis and septic shock. Am J Emerg Med 2013;31(3):545–8.
[38] Kim S, Lee K, Kim I, et al. Red cell distribution width and early mortality in elderly patients with severe sepsis and septic shock. Clin Exp Emerg Med 2015;2(3):155–61.
[39] Zhang Z, Xu X, Ni H, et al. Platelet indices are novel predictors of hospital mortality in intensive care unit patients. J Crit Care 2014;29(5):885e1–6.
[40] Mandal RK, Valenzuela PB. Neutrophil–lymphocyte count ratio on admission as a predictor of bacteremia and in Hospital mortality among sepsis and septic shock in patients at Rizal Medical Center. Asian J Med Sci. 2018;9(3):36–40.