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Red Cell Distribution Width versus Procalcitonin as A Marker for Severe Sepsis

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Abstract: Background: Sepsis is a systemic, deleterious host response to infection leading to severe sepsis (acute organ dysfunction secondary to documented or suspected infection) and septic shock (severe sepsis plus hypotension not reversed with fluid resuscitation). **Objectives:** The aim of the study was evaluation the red cell distribution width as a prognostic marker of sepsis and as a predictor of mortality compared with procalcitonin. **Patients and Methods:** Type of Study: observational study, study Setting: Ain Shams University Hospital, Misr University For science and technology hospital. Study Period: 6 months (from 1 October 2018 till 31 of Mars 2019). **Results:** Procalcitonin was non-significantly high among died cases. RDW was significantly higher among died cases. Demographic and sources of infection among the studied cases. Mortality was less than three quarters of the studied cases (73.3 %). Males, pneumomia and bed sores were significantly more frequent among died cases while wound infection was significantly less frequent. SOFA mortality was significantly high among died cases. APACHE mortality was significantly high among died cases. **Conclusion:** This study revealed that the red cell distribution width (RDW) was a significant prognostic marker of sepsis and a significant predictor of mortality compared with procalcitonin.

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1. Introduction

Sepsis is a systemic, deleterious host response to infection leading to severe sepsis (acute organ dysfunction secondary to documented or suspected infection) and septic shock (severe sepsis plus hypotension not reversed with fluid resuscitation) ***(Bernard et al., 1997).***

Severe sepsis and septic shock are major healthcare problems, affecting millions of individuals around worldwide each year, killing one in four (and often more), and increasing in incidence ***(Annane et al., 2005).***

Sepsis is defined as the presence (probable or documented) of infection together with systemic manifestations of infection. Severe sepsis is defined as sepsis plus sepsis-induced organ dysfunction or tissue hypoperfusion ***(Levy et al., 2003).***

It is very important that clinicians have the tools to identify and diagnose sepsis promptly because early diagnosis and treatment may lead to improvement in both mortality and morbidity. Gold standards for the diagnosis of infection do not exist, but procalcitonin is known to be among the most promising sepsis markers in critically ill patients, can complement clinical signs and routine laboratory variables that are suggestive of sepsis ***(Tang et al., 2007).***

The use of procalcitonin in developing countries such as Egypt, however, remains very expensive and hardly accessible in all ICUs. The red blood cell distribution width (RDW) represents an index of the heterogeneity of the erythrocytes (anisocytosis), which is calculated by dividing the standard deviation of erythrocyte volume by the mean corpuscular volume and multiplying by 100 to express the result as a percentage ***(Morris et al., 2001).***

Although it has been postulated that systemic inflammation, malnutrition, and impaired renal function play a significant role in the underlying pathological processes, the mechanism of the association between increased RDW and mortality remains unclear ***(Förhécz et al., 2009).***

Studies by electronic microscopy have founded important alterations in RBC shape during the refractory phase of shock. They also showed morphologic and functional changes during sepsis in the RBC population. This led to the hypothesis that RBC alterations during shock and sepsis may contribute toward multiple organ dysfunction syndrome. It has been reported previously that the flexibility of RBC may be dysfunctional because of the endotoxins of bacteria in septic shock. The RBC exposed to endotoxin decreased their deformability

and showed increased hidromiristic acid content, which is a component of bacterial endotoxins, suggesting a relationship ***(Pöschl et al., 2003).***

Aim of the Work

The aim of the study was evaluation the red cell distribution width as a prognostic marker of sepsis and as a predictor of mortality compared with procalcitonin.

2. Patients and Methods

- **Type of Study:** observational study
- **Study Setting:** Ain Shams University Hospital
- Misr University For science and technology hospital
- **Study Period:** 6 months (from 1 Octobar 2018 till 31 of Mars 2019).
- **Study Population**
  - Inclusion Criteria: Patients who fulfilled the criteria of sepsis and severe sepsis according to the criteria of International Sepsis Definitions Conference were included in this study.
  - Exclusion Criteria:

(1) Patients younger than 18 years old.

(2) Patients with other causes associated with increased red cell distribution width. Patients with congestive heart failure, acute myocardial infarction, pulmonary embolism, and patients after cardiac arrest.

(3) Patients with previous history of diseases primarily affecting RBCs, blood loss >10% of blood volume, blood product transfusion one week prior to admission, use of drugs known to change morphology and rheology of RBCs and pregnant patients were excluded from the study.

- **Sampling Method** All patients included in the study were subjected to the following:

(1) Demographic data: age and sex.

(2) Complete assessment of medical history, including family history and drug history.

(3) Comprehensive physical examination.

(4) Vital signs.

(5) The following laboratory investigations and clinical scores were performed:

(a) On admission

(i) Blood culture: on admission and before administration of antibiotics.

(ii) Culture from the suspected source of infection such as urine, sputum, and cerebrospinal fluid on admission.

(iii) The Acute Physiology and Chronic Health Evaluation II (APACHE II) score.

(b) Daily:

(i) Complete blood count: microtubes containing the EDTA anticoagulant. The red cell distribution width was assessed using the auto hematology analyzer mindray BC-5500.

(ii) Blood urea (mg/dl), serum creatinine (mg/dl), serum sodium (mg/dl), and serum potassium (mg/dl).

(iii) Bilirubin, total and direct (mg/dl), alanine aminotransferase, and aspartate aminotransferase (μ/l).

(iv)Arterial blood gases: when needed. (v) The Glasgow Coma Scale.

(v) The SOFA score.

(c) On days 1, 5 and 10.

(i) Procalcitonin level (ng/ml): procalcitonin (PCT) levels (normal range 0–0.5 ng/ ml) were determined using a stat fax– 2100 ELISA (Awareness Technology, Inc. New York, USA) reader.

(d) radiological examination: when needed.

- **Sample Size** 45 patient.
- Ethical Considerations informed consent
- **Study Tools:** CBC, PROCALCITONIN
- **Study Procedures:** Non- invasive

Statistical method

The collected data were coded, tabulated, and statistically analyzed using IBM SPSS statistics (Statistical Package for Social Sciences) software version 18.0, IBM Corp., Chicago, USA, 2009. The level of significance was taken at P value < 0.050 is significant, otherwise is non-significant.

3. Results

Table (1): Comparison according to fate regarding demographic characteristics

Characteristics		Death (N=33)	Survival (N=12)	p
Age (years)		67.1±6.5	66.8±10.2	^0.936
Sex	**Male**	23 (69.7%)	4 (33.3%)	**#0.041***
	Female	10 (30.3%)	8 (66.7%)	
Source of infection	**Pneumomia**	24 (72.7%)	4 (33.3%)	**#0.034***
	UTI	14 (42.4%)	4 (33.3%)	#0.735
	Sores	12 (36.4%)	0 (0.0%)	**#0.020***
	Wound infection	3 (9.1%)	8 (66.7%)	**#<0.001***
	SBP	6 (18.2%)	0 (0.0%)	#0.171

^Independent t-test. #Fisher's Exact test. *Significant

Table (1) showed that: **Males, pneumomia** and **bed sores** were significantly more frequent among died cases while **wound infection** was significantly less frequent.

Table (2): Comparison according to fate regarding Procalcitonin (ng/mL)

Time	Death (N=33)	Survival (N=12)	p
Day-1	8.2 (4.3–17.6)	3.2 (1.5–11.3)	0.063
Day-5	4.9 (2.9–12.4)	2.0 (0.8–7.6)	0.079
Day-10	8.3 (5.8–14.8)	1.1 (0.1–9.8)	0.051

Mann Whitney test. *Significant

Table (2) showed that: **procalcitonin** was non-significantly high among died cases.

Table (3): Comparison according to fate regarding RDW (%)

Time	Death (N=33)	Survival (N=12)	p
Day-1	17.1 (16.7–21.0)	14.9 (14.1–15.3)	**<0.001***
Day-5	17.3 (16.4–17.6)	14.5 (13.9–15.3)	**<0.001***
Day-10	17.8 (16.8–18.1)	14.3 (14.2–14.6)	**<0.001***

Mann Whitney test. *Significant

Table (3) showed that: **RDW** was significantly higher among died cases.

Table (4): Comparison according to fate regarding SOFA mortality (%)

Time	Death (N=33)	Survival (N=12)	p
Day-1	52.5 (42.0–92.4)	15.4 (6.6–18.2)	**<0.001***
Day-5	53.7 (45.2–59.2)	12.3 (7.2–19.0)	**<0.001***
Day-10	43.7 (38.8–82.9)	9.2 (8.3–17.7)	**<0.001***

Mann Whitney test. *Significant

Table (4) showed that: **SOFA mortality** was significantly high among died cases.

Table (5): Comparison according to fate regarding APACHE mortality (%)

Time	Death (N=33)	Survival (N=12)	p
Day-1	84.5 (50.3–88.4)	35.5 (25.2–46.6)	**<0.001***
Day-5	54.1 (46.0–85.5)	19.8 (11.5–26.6)	**<0.001***
Day-10	73.0 (54.7–91.4)	16.5 (9.8–24.9)	**<0.001***

Mann Whitney test. *Significant

Table (5) showed that **APACHE mortality** was significantly high among died cases.

Table (6): Correlations of mortality day among died cases

Findings	N	r	p
Age	33	-0.094	0.603
Procalcitonin level, day-1	33	-0.737	**<0.001***
Procalcitonin level, day-5	25	-0.879	**<0.001***
Procalcitonin level, day-10	25	-0.594	**0.002***
RDW, day-1	33	-0.431	**0.012***
RDW, day-5	25	-0.072	0.733
RDW, day-10	25	-0.124	0.555
SOFA mortality, day-1	33	-0.661	**<0.001***
SOFA mortality, day-5	25	-0.564	**0.003***
SOFA mortality, day-10	25	-0.557	**0.004***
APACHE mortality, day-1	33	-0.636	**<0.001***
APACHE mortality, day-5	25	-0.697	**<0.001***
APACHE mortality, day-10	25	-0.649	**<0.001***

Spearman correlation. *Significant

Table (6) show that: There were significant negative correlations between mortality day and procalcitonin level, SOFA mortality and APACHE mortality at different days as well as RDW at day-1 only.

4. Discussion

In the current study, the red cell distribution width (RDW) was a significant prognostic marker of sepsis and a significant predictor of mortality compared with procalcitonin.

Patients in this study group were recruited from ICU, Faculty of Medicine, Ain Shams University Hospitals and Misr University for Science and technology hospital as teaching hospitals.

As regard demographic characters, our results showed that the males' source of infections (respiratory tract infections, UTI and bed sores) were significantly more frequent among the dead cases, these results were supported by studies carried on procalcitonin by ***(Jain et al., 2014), (Cui et al., 2019)*** and studies carried on red cell distribution width by ***(Jo et al., 2013).***

Moreover, and similar to the present study, ***(Karlson et al., 2010)*** found a significant difference between men, who accounted for 168 patients (68%) in their study population, and women, who accounted for 74 patients (32%) in their study population ($P < 0.001$).

In this study, it was found that procalcitonin level wasn't a good predictor of mortality; as procalcitonin was non-significantly higher among non-survivors on day 1, day 5, and day 10 ($P = 0.0063$, $P > 0.001$, $P > 0.001$), respectively, these results were supported by the studies of ***Jain*** and the colleagues, 20 whose results found that among the biomarkers, the levels of serum procalcitonin on admission or day1 were significantly higher among non-survivors compared with that of survivors ($P < 0.01$) ***(Jain et al., 2014).***

In agreement with the present study, (***Devran et al., 2010)*** found that the SOFA score for predicting mortality rates was significantly higher among dead cases on days 1, 5 and 10 with ($P<0.001$).

The RDW value in our study, was also significantly higher among the non survivors ($P<0.001$). these results go in concordant with the results of ***(Lorente et al., 2014)*** who found higher RDW in non-survivors ($n = 104$) than in surviving ($n = 193$) septic patients on day 1 ($P = 0.001$), day 5 ($P = 0.001$), and day 10 ($P = 0.002$) of ICU admission.

Also, ***(Esper et al., 2008)*** found in their study carried out to found that RDW was also statistically higher in patients with the highest SOFA values, which was similar to the present study.

Also, the procalcitonin levels showed no significant correlation between day 10 or the discharge day and other variables among survivors.

In the current study there were significant negative correlations between mortality day and procalcitonin, SOFA mortality and APACHE mortality at different days as well as RDW at day 1 only ***(Esper et al., 2008).***

The limitations of the study are that it was conducted in only two centers and was an observational study. However, it was adequate and generalizable and the results appear to have adequate effect size to suggest a reasonable strength of evidence but we need more clinical trials for more reliable results. Future studies with larger samples are also needed to confirm these findings.

5. Conclusion

This study revealed that the red cell distribution width (RDW) was a significant prognostic marker of sepsis and a significant predictor of mortality compared with procalcitonin.

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