



## Does hemogram biomarkers predict mortality in intensive care population?

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### ABSTRACT

**Aim:** To compare hemogram-mediated inflammatory markers such as mean platelet volume (MPV), red cell distribution width (RDW), platelet distribution width (PDW), neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), MPV to platelet ratio (MPR) and RDW to platelet ratio (RPR) in predicting outcome in the intensive care units (ICU) population.

**Methods:** After obtaining approval of intuitional board the patients whom were treated in the Anesthesiology and Reanimation ICU of Bolu Abant Izzet Baysal University Hospital between March 2017 and December 2018 were evaluated retrospectively and enrolled to the study. The above-mentioned laboratory parameters of the deceased and survivors were compared.

**Results:** The PDW, MPV, C-reactive protein (CRP), RPR and MPR values were significantly different between deceased and survived subjects. Moreover, MPV and PDW values were significantly and positively correlated with serum CRP level.

**Conclusion:** We suggest that PDW, MPV, MPR and RPR could be used in determining the severity of the disease in ICU patients along with CRP. Since these hemogram results could be obtained in a much shorter time period compared to CRP, they could be useful in this population; in which hours and even minutes are important in the treatment in ICU.

**Keywords:** Intensive care unit, biomarkers, hemogram-mediated inflammatory markers, outcome.

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### Introduction

Intensive care units (ICU) make an important part of the sophisticated hospitals by the patients residents demand attentive care.

Despite careful and elaborating care in ICU, mortality of these patients are far higher than other patients receive inpatient treatment.

Various scoring systems are used to determine the clinical course with less invasive method and to predict the risk of mortality in ICU patients. Several inflammatory biomarkers, including, C- reactive protein (CRP) and procalcitonin, suggested to be predictors of mortality in these patients [1]. In addition, recent studies emphasized the role of

hemogram indices in predicting morbidity and mortality in ICU. These indices include mean platelet volume (MPV), red cell distribution width (RDW), platelet distribution width (PDW), and neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), MPV to platelet ratio (MPR) and RDW to platelet ratio (RPR) [2-6].

In present retrospective analysis, we aimed to study hemogram derived inflammatory indices (MPV, RDW, MPR, RPR, PLR and NLR) in intensive care population and to compare them in the groups consisted of deceased and survived subjects to investigate whether they could predict mortality in ICU.

## Methods

After approval of the local ethics committee, the patients whom were treated in the Anesthesiology and Reanimation ICU of Abant İzzet Baysal University Hospital between March 2017 and December 2018 were evaluated retrospectively and enrolled to the study. Patients who were hospitalized within the last month were excluded from the study. The indications for admission to ICU, age and gender of the subjects, comorbid diseases, and duration of hospitalization were recorded. The indications for intensive care were classified as systemic disease and malignancy. The treatment results of the patients were determined as survived or deceased and the study population was grouped accordingly. Biomarkers to predict mortality were calculated from blood samples taken at the time of hospitalization in ICU.

Parameters viewed from hemogram measurements; Fasting blood glucose (FPG), CRP, leukocyte count (WBC), neutrophil count (NC), lymphocyte count (LC), hemoglobin (Hb), hematocrit (Htc), platelet count (PltC), RDW, platelet distribution width (PDW), MPV

values were obtained from database and recorded. NLR was calculated by simply dividing of NC to LC. PLR was calculated by division of PltC to LC. MPR calculated by division of MPV to PltC. Finally, RPR calculated by division of RDW to PltC.

Statistically analyses performed by SPSS software (SPSS 15.0 for Windows, IBM Inc, Chicago, IL, USA). Comparison of the variables in study groups were conducted by Mann-Whitney U Test or by independent samples t test. Categorical variables were conducted with Chi-Square test. Pearson's correlation test was used to evaluate correlation between study variables and CRP. The significance were set on a p value less than 0.05.

## Results

A total of 174 patients were included in the study (99 male and 75 female). Gender was not significantly different between deceased and survived patients in terms of gender ( $p=0.27$ ). Median ages of the survived and deceased patients were 68 (16-96) years and 73 (33-94) years, respectively. The age difference between survived and deceased subjects was statistically significant ( $p=0.03$ ). 149 patients were admitted to the ICU with the diagnosis of systemic disease and 25 patients with malignancy. 42% of the patients hospitalized because of systemic diseases were deceased, while this rate was 32% in the patients hospitalized because of malignancy. The incidence of systemic disease and malignancy in deceased and survived patients groups was not statistically different ( $p=0.16$ ).

The hospitalization period of the survived and deceased patients were 3 (1-118) days and 6 (1-97) days, respectively ( $p=0.003$ ). Comorbidity rate in survived and deceased patients were 63% and 78%, respectively ( $p=0.03$ ).

**Table 1.** Laboratory data of the study population.

Parameters	Survived group	Deceased group	<i>p</i>
Age (years)	68 (16-96)	73 (33-94)	0.03
PDW (%)	18 (16-23)	18 (15-23)	0.01
MPV (fL)	8 (5-15)	8.5 (6-15)	0.02
CRP (U/mL)	32.5 (1-333)	117 (1-336)	<0.001
RPR (%)	8 (3-42)	9 (2-96)	0.03
MPR (%)	3 (1-24)	5 (1-63)	0.02

PDW: platelet distribution width; MPV: mean platelet volume; CRP: C-reactive protein; RPR: red cell distribution width to platelet ratio; MPR: mean platelet volume to platelet ratio.

When the presence of additional disease was examined as single or multiple, 35% of survivors had single additional disease and 65% had multiple additional diseases. In 46% of the patients who died, 56% had multiple additional diseases. The difference between the groups in terms of single or multiple additional disease was not statistically significant ( $p = 0.30$ ).

Wbc ( $p = 0.94$ ), NC ( $p = 0.84$ ), LC ( $p = 0.62$ ), MCV ( $p = 0.53$ ), RDW ( $p = 0.08$ ), Plt ( $p = 0.08$ ) were examined. Flow ( $p=0.66$ ), monocyte ( $p = 0.61$ ), pct ( $p = 0.68$ ), NLR ( $p = 0.94$ ), PLR ( $p = 0.29$ ), MLR ( $p = 0.28$ ), MOLR ( $p = 0.94$ ) values groups was not different between. Hb ( $p = 0.01$ ), Hct, ( $p = 0.02$ ) values were significantly higher in surviving patients than those who died.

The PDW values of the surviving and dying patients were 18 (16-23) % and 18 (15-23) %, respectively ( $p=0.01$ ). MPV values of surviving and dying patients were 8 (5-15) fL and 8.5 (6-15) fL, respectively ( $p=0.02$ ). CRP values of surviving and dying patients were 32.5 (1-333) units and 117 (1-336) units, respectively ( $p <0.001$ ). RPR values of surviving and dying patients were 8 (3-42) % and 9 (2-96) %, respectively ( $p=0.03$ ). MPR

values of surviving and dying patients were 3 (1-24) % and 5 (1-63) %, respectively ( $p=0.02$ ). Mean MPV ( $r=0.20$ ,  $p=0.009$ ) and PDW ( $r=0.24$ ,  $p=0.001$ ) values showed significant positive correlation with serum CRP level.

### Discussion

Present study showed that along with CRP, a well-defined inflammatory marker, PDW, MPV, RPR and MPR elevation could also be predictors of mortality in ICU population. Recent studies showed significant association between MPV and malignant and inflammatory diseases [7]. MPV has been suggested as an indicator of platelet activity, and there is strong evidence that MPV may have an important hemogram indice, which means that larger platelets are more active than normal platelets. [8]. MPV has role in both obesity and inflammation [9]. Since platelets have important role in angiogenesis of malignant masses, MPV could be involved in such reactions. Moreover it has been suggested to be associated with mortality in respiratory ICU population [10]. In a previous study of ours, we have found increased MPV in deceased ICU patients compared to survived patients [11].

In literature, elevated CRP has been found to be associated with decreased survival [12]. We shall speculate that as another inflammatory marker, MPV could be increased with greater inflammatory burden in mortal cases compared to non-mortal situations.

PDW is introduced as an associated hemogram marker with pulmonary tuberculosis [13]. Moreover, the authors reported that treatment of tuberculosis reduce the increased levels of PDW [14].

Elevated PDW levels have been reported in patients with obstructive sleep apnea syndrome [15].

There are also conflicting reports about PDW in literature, such as Ozdemir et al's study, which concluded that there was no change in PDW levels before and after treatment in subjects with acute rheumatic carditis [16]. Authors found elevated MPR in subjects with hepatosteatosis compared to those without hepatosteatosis [17]. In that study, increased MPR levels in hepatosteatosis reflect the burden of inflammation and was correlated with plasma glucose and LDL cholesterol, which are also associated with hepatosteatosis [17]. Authors suggested PDW as an inflammatory marker in type 2 diabetes mellitus [18]. In addition, it has been reported that MPR increased in patients with ST elevation myocardial infarction and with infective endocarditis [19,20]. MPR was considered as a marker of inflammatory burden in another study in literature [21]. Several studies in literature suggested the relation between MPR and inflammatory conditions. MPR was also associated with irritable bowel disease, a condition that associated with low grade inflammation [2]. Elevated RPR has been introduced as a marker of mortality by Qui et al. in 2017 [22]. Although RDW and platelet alone were not associated with prognosis, RPR was

significantly correlated with mortality in Qiu et al's study [22]. On the other hand, as a conflicting result, RPR of patients with and without irritable bowel syndrome were not different in a study by Atak et al. [2]. The role of RPR in inflammation is controversial. In a study it is reported that RPR was not associated with ovarian insufficiency, which could be an inflammatory process [23]. Elevated RPR was a marker in type 2 diabetes mellitus in Bilgin et al.'s study, too [21,24].

More importantly, both MPR and RPR were strongly and positively correlated with CRP levels in present study. They could substitute or may be used as additive to CRP in determining morbidity and mortality in ICU patients since the results of hemogram tests are accessible within minutes, which is much shorter assay duration compared to CRP assay.

Significant correlation between CRP, a well-established mortality marker of ICU population, and PDW and MPV, two important hemogram parameters, is a very striking result of present study. PDW and MPV could react inflammatory changes in bloodstream as quickly as CRP.

Limitations of present study are retrospective design and relatively small study population. Single center experience could be the third limitation of our work. However, to the best of our knowledge, this is the first study in literature that found significant correlation between CRP and hemogram parameters; MPR and RPR.

In conclusion, we suggest that PDW, MPV, MPR and RPR could be used in determining the severity of the disease in ICU patients along with CRP. Since these hemogram results could be obtained in a much shorter time period compared to CRP, they could be useful in this population; in which hours and even minutes are important in the treatment in ICU.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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