Relationship Between the Coma Scores and Hemogram Parameters Measured by New-generation Devices

Erdogan Duran[1], Basak Pehlivan[1], Ismail Koyuncu[2], Veli Fahri Pehlivan[1] and Ataman Gonel[2]

[1]*Department of Anaesthesiology and Reanimation, Medicine Faculty, University of Harran, Sanliurfa, Turkiye*
[2]*Department of Biochemistry, Medicine Faculty, University of Harran, Sanliurfa, Turkiye*

ABSTRACT

Objective: To investigate the relationship between the coma scores—Glasgow coma scale (GCS), Sequential Organ Failure Assessment (SOFA), and Acute Physiological and Chronic Health Assessment (APACHE-II)—in intensive care unit (ICU) patients and the percentage of macrocytosis (%MAC), immature granulocyte (IG), cellular haemoglobin concentration (cHGB), nucleated red blood cell (NRBC), nucleated red cell/ white cell ratio (NR/W), hyperchromic ratio (%HPR), and platelet distribution width (PDW) values.

Study Design: A descriptive comparative study.

Place and Duration of the Study: Medicine Faculty, University of Harran, Turkiye, from December 2020 to May 2022.

Methodology: The hemogram parameters of the patient groups with a GCS of 3-8 (n=51) and a GCS of 9-15 (n=43) and a control group of 55 healthy volunteers were measured using the new-generation hemogram autoanalyzer AlinityHQ (Abbott, USA). These parameters were compared with the coma scores (GCS, SOFA, and APACHE-II) of the patients.

Results: There was a statistically significant difference in IG, %MAC and PDW values (p-values were 0.025, 0.011, and 0.004, respectively) and an inverse correlation with GCS scores (correlation coefficients were -0.247, -0.264, and -0.297, respectively) was observed. There was also a significant correlation between the SOFA scores and %HPR and cHGB (correlation coefficients were 0.234, -0.358, p-values were 0.025, 0.001, respectively), and the APACHE-II scores and NRBC and NR/W values (correlation coefficients were -0.270, -0.247, p values were 0.009, 0.017, respectively).

Conclusion: While other haematological parameters other than PDW were not associated with coma scores, parameters measured using new-generation haematological devices (%MAC, IG, cHGB, NRBC, NR/W, and %HPR) were found to be associated with estimated coma scores. These parameters can therefore be used as simple, rapid prognostic biomarkers and assist researchers in the development of new scoring models.

Key Words: *ICU, Hyper, Coma, Sofa, Apache.*

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INTRODUCTION

The most frequently used predictive coma scoring systems in intensive care units (ICUs) are the Glasgow coma scale (GCS),[1,2] the sepsis-related Sequential Organ Failure Assessment (SOFA), and the Acute Physiological and Chronic Health Assessment (APACHE) II scales.[3]

Daily hemogram tests support the coma scoring systems and help guide treatment in ICU patients. There are studies that correlate the severity, prognosis, mortality risk, and complications of pathologies that may require ICU treatment with red blood cell distribution width (RDW),[4-7] and platelet distribution width (PDW) levels.[8]

Correspondence to: Dr. Erdogan Duran, Department of Anaesthesiology and Reanimation, Medicine Faculty, University of Harran, Sanliurfa, Turkiye
E-mail: dreduran@harran.edu.tr

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Sensitive and novel parameters such as the percentage of hypochromic red blood cells (%HPO), percentage of hyperchromic red blood cells (%HPR), percentage of immature granulocyte (%IG), percentage of macrocytic red blood cells (%MAC), percentage of microcytic red blood cells (%MIC), cellular haemoglobin concentration (cHGB), nucleated red blood cell (NRBC), and nucleated red cell/ white cell ratio (NR/W)—obtained using new-generation haematologic analyzers—are likely to be associated with morbidity and mortality.

In the literature, there was no study to investigate the correlation between the estimated coma scores used in the ICU and parameters that can be measured using new-generation haematology analyzers (e.g., %HPO, %HPR, IG, %MIC, %MAC, cHGB, NRBC, and NR/W). It was hypothesised that these parameters could be used to quickly predict or support the estimated coma score of patients evaluated for admission to the ICU and treated in the ICU. In addition, predictive scoring systems require periodic updating due to considerable number of clinical variables. Manual calculation creates a disadvantage due to data entry load.[9] Hence, there is ongoing research to develop a simpler, more reliable, and easy-to-apply estimation scoring system.[10,11]

The aim of this study was to investigate whether there is a relationship between coma scores (GCS, SOFA, and APACHE-II) and new blood count parameters of patients evaluated for admission to the ICU and treated in the ICU, and to standardise and facilitate the estimation of coma scores.

METHODOLOGY

This descriptive comparative study was conducted from 1st December 2020 to 31st May 2022 in Harran University Faculty of Medicine general ICU, in accordance with the Declaration of Helsinki, with the approval of the Ethics Committee of Harran University Faculty of Medicine (HRU/20.19.08), and with the informed consent of the participating patients (or first-degree relatives of the patient) and the volunteers who comprised the control group. The minimal sample size for each group for hemogram parameters was estimated as 42 using the one-way ANOVA test assuming a 0.50 effect size with a 0.05 margin of error and 0.80 power. G*Power was used to do the Power Analysis (version 3.1.9.7). This study involved three groups, with a total of 145 participating individuals. Participants who received sedation, had brain death, and were <18 years of age were excluded from the study. The study groups comprised two patient groups hospitalised in a mixed-type tertiary ICU: GCS 3–8 (n = 51) and GCS 9–15 (n = 43), and a control group comprising 55 healthy volunteers. Participants in the control group had no systemic disease, nor were they on any regular medication. Every morning the coma scores (GCS, SOFA, APACHE-II) were calculated. At the same time venous samples were taken from the ICU patient. Hemogram parameters including the percentage of macrocytosis (%MAC), immature granulocyte (IG), cellular haemoglobin concentration (cHGB), nucleated red blood cell (NRBC), nucleated red cell/ white cell ratio (NR/W), hyperchromic ratio (%HPR), and platelet distribution width (PDW) were measured using Alinity HQ (Abbott, USA), a fully automated next-generation hemogram autoanalyzer. Biochemical parameters were assessed using an Architect c16000 (Abbott, USA), a fully automated biochemistry autoanalyzer.

Windows-compatible IBM SPSS Statistics software (IBM, Chicago, IL, USA), version 25.0, for statistical analysis, was used. The normal distribution of the data was evaluated using the Shapiro–Wilk test. Numerical data conforming to the normal distribution were expressed as the mean ± standard deviation, and numerical data that did not conform to the normal distribution were expressed as the median and interquartile range of values. Categorical variables were expressed as numbers (n) and percentages (%). Between groups, data that did not fit the normal distribution were evaluated using the Kruskal–Wallis H test, while the Bonferroni correction was used for within-group comparisons. For normally distributed data, the authors used a one-way analysis of variance for between-group analysis and Tukey's test for within-group comparisons. The relationship between the variables was evaluated using Spearman's rank-order correlation analysis. The confidence interval was accepted as 95% for the analyses, and $p < 0.05$ was considered statistically significant.

RESULTS

Cardiac arrest, the need for ICU after COVID-19, stroke, and pneumonia were the most common reasons for ICU admission among patient groups. There was no statistically significant difference between the patient groups and the control group in terms of gender or mean age. Significant differences were found in the IG ($p<0.001$), MAC% ($p=0.002$), and PDW ($p<0.001$) parameters between the two patient groups and between the control and patient groups (Table I).

In the correlation analysis, a negative correlation was found between GCS scores and participants' MAC%, IG, and PDW values. A positive correlation was found between SOFA and HPR, and a negative correlation with cHGB. Negative correlation was found between APACHE-II and NRBC, NR/W (Table II).

DISCUSSION

This study is the first to investigate the relationship between the commonly used predictive coma scoring systems and the new--generation parameters such as %MIC, %MAC, IG, %HPO, %HPR, cHGB, NRBC, and NR/W. In this study, a negative correlation was found between GCS scores and participants' MAC%, IG, and PDW values. A positive correlation was found between SOFA and HPR, and a negative correlation with cHGB. Negative correlation was found between APACHE-II and NRBC, NR/W.

In addition to counting and measuring the distribution of blood cells, advances in automated haematology instruments also allow the authors to analyse the morphology of these cells, *e.g.*, %MIC, %MAC, %HPR, %HPO, anisocytosis.[12,13] Many diseases (*e.g.* coronary artery disease, diabetes mellitus) are tried to be associated clinically with these tests and parameters, which are cheap and easy to find. In the studies carried out, an increase in PDW has been found to be associated with a worsening clinical status and elevated risk in diabetic patients, as well as an increased risk of mortality in ICU patients.[14,15] In the study by Dubey *et al*., changes in the size of blood cells, and PDW were found to be associated with SOFA and APACHE scores of patients admitted to the ICU, and crucial indicators of sepsis, the need for mechanical ventilation, and an estimate of morbidity and mortality.[16] During the rapid evaluation of the coma scores of patients to be admitted to the ICU or who are undergoing treatment in the ICU—in addition to the routine hemogram parameters—parameters such as %MAC, %MIC, %HPR, and %HPO, which are measured using new-generation analyzers, can be useful for predicting the condition of the patient (in supporting coma scores) and making quick treatment decisions. These predictive biomarkers are critical for early diagnosis and treatment guidance, especially in diseases such as sepsis where even short-term delays in treatment increase mortality.

From the correlation analysis in this study, a negative correlation was found between GCS scores and participants' MAC%, IG, and PDW values. A positive correlation was found between SOFA and HPR, and a negative correlation with cHGB. A negative correlation was found between APACHE-II and NRBC, NR/W. IG, PDW, and %MAC, as predictors of neurological deterioration in a patient, may contribute to determining the direction of treatment.

Table I: Laboratory findings of patient and control groups according to age, gender and coma scores.

Variables	GCS 3-8 (n:51)	GCS 9-15 (n:43)	Control group (n:55)	ANOVA p
Age*	67.00 (17.0)	65.00 (33.0)	63.00 (8.0)	0.073
Female gender ***	17(33.3%)	20(46.5%)	21 (38.2%)	0.422
SOFA*	8.00 (4.00)	6.00 (4.00)	-	-
APACHE-II*	32.00 (27.10)	15.0 (21.00)	-	-
IG* (10e3/µL)	0.202 (0503)	0.128 (0.160)	0.044 (0.059) η,δ	<0.001
%MAC*	3.64 (4.19)	2.03 (3.06) ¥	2.24 (3.34) η	0.002
PDW** (10GSD)	14.23± 1.12	13.57 ± 0.83 ¥	13.38 ± 0.58 η	<0.001
%MIC*	1.58 (1.82)	1.46 (2.46)	0.77 (0.66) η,δ	<0.001
%IG*	1.51 (2.74)	1.07 (0.87)	0.48 (0.74) η,δ	<0.001
%HPO*	3.77 (5.34)	2.12 (4.61)	0.35 (0.32) η,δ	<0.001
%HPR*	0.05 (0.13)	0.03 (0.05)	0.90 (0.11) δ	0.004
cHGB* (g/dl)	9.94 (1.63)	10.95 (3.55)	16.10 (1.90) η,δ	<0.001
MCV** (fL)	92.00 ± 5.37	89. 98 ± 7.63	93.18 ± 4.84 δ	0.031
MCH* (pg)	31.15 (1.72)	31.15 (1.57)	29.30 (2.10) δ	0.018
RDW* (%)	15.30 (1.60)	15.10 (3.20)	12.80 (1.50) η,δ	<0.001
HDW* (%)	7.03 (1.80)	6.84 (2.16)	4.98 (0.61) η,δ	<0.001
PCT* (%)	0.19 (0.15)	0.16 (0.10)	0.23 (0.07) η,δ	<0.001
CHCM* (g/dl)	33.30 (1.90)	33.60 (1.90)	35.20 (1.40) η,δ	<0.001
Platelet*	251.50 (186.50)	222.50 (148.25)	291.0 (90.00) δ	0.020
MPV** (fL)	7.90 ± 1.38	7.63 ± 1.15	8.17 ± 0.94 δ	0.064
NRBC** (10e3/µl)	0.45 ± 0.12	0.32 ± 0.09	-	0.003
NR/W**	0.26 ± 0.61	0.32 ± 1.39	-	0.004

APACHE-II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment; GCS, Glasgow Coma Scale; ¥, there is a significant difference between GCS 3-8 and 9-15; η, there is a significant difference between GCS 3-8 and Control group; δ, there is a significant difference between GCS 9-15 and Control group; %HPO, hypochromic ratio; %HPR, hyperchromic ratio; %MIC, percentage of microcytosis; %MAC, percentage of macrocytosis; MCV, mean corpuscular volume; MCH, mean corpuscular haemoglobin; RDW, red blood cell distribution width; MCH, mean corpuscular haemoglobin; PDW, platelet distribution width; cHGB, cellular haemoglobin concentration; IG, immature granulocyte; %IG, percentage of Immature Granulocyte; HDW, haemoglobin distribution width; CHCM, cellular haemoglobin concentration mean; MPV, mean platelet volume; PCT, plateletocrit; NRBC, nucleated red blood cell; NR/W, nucleated red cell/ white cell ratio * Kruskal–Wallis H test and, One-Way Analysis of Variance, Pearson chi-square test.*

Table II: Correlation analysis according to coma scores.

		IG	%MAC	PDW	%HPR	cHGB	NRBC	NR/W
GCS	rho	-0.247	-0.264	-0.297	-.0169	0.186	0.010	-0.026
	p	0.025	0.011	0.004	0.108	0.075	0.922	0.080
SOFA	rho	-0.040	0.033	0.173	0.234	-0.358	-0.68	-0.080
	p	0.722	0.751	0.095	0.025	0.001	0.517	0.445
APACHE-II	rho	-0.049	0.010	0.144	0.156	-0.129	-0.270	-0.247
	p	0.665	0.927	0.167	0.139	0.218	0.009	0.017

MONO, monocyte; IG, immature granulocyte; RBC, red blood cell; HCT, Hematocrit; MAC%, percentage of macrocytosis; PDW, platelet distribution width; GCS, Glasgow Coma Scale; SOFA, Sepsis-related Organ Failure Assessment; APACHE-II, Acute Physiology and Chronic Health Evaluation; %HPR, hyperchromic ratio; cHGB, cellular haemoglobin concentration; NRBC, nucleated red blood cell; NR/W, nucleated red cell/ white cell ratio; rho, Spearman's ranking correlation coefficient.

Similarly, %HPR and cHGB can be useful in calculating SOFA scores and predicting the course of sepsis. NRBC and NR/W values can contribute to the estimation of APACHE-II scores and the risk of morbidity and mortality. Studies have shown that predictive values of %MAC, IG (an indicator of bone marrow activation and severe infection),[17] and PDW can be used as indicators of morbidity and mortality in patients with low GCS scores.[14,15,18] Macrocytosis, heart failure, pregnancy, end-stage renal disease, and malignancies indicate inflammation by increasing acute phase reactants. Advanced age, anaemia, macrocytosis, and high ambient temperature are counted as non-inflammatory factors that increase the erythrocyte sedimentation rate.[19] The results of this study (negative correlation between MAC and GCS) suggest that the increase in the %MAC may contribute to the increase in the levels of acute phase reactants, indicating the worsening of GCS in ICU patients. Therefore, the %MAC ratio may contribute to future studies in scoring the estimated coma scores of patients evaluated for admission to ICU or treated in ICU, and in the development of these scoring systems.

One of the limitations of this study is that it was conducted in a single centre in a mixed ICU, and participating patients did not have a single diagnosis. In addition, it should be considered that %MAC and PDW may give misleading results in patients with diseases that may disrupt haemoglobin and platelet structure.[17]

CONCLUSION

Changes in the %MAC and IG values measured using new-generation technological methods can be used as simple, rapid prognostic biomarkers that will support the GCS. Similarly, %HPR and cHGB can support the SOFA score, and NRBC and NR/W can support the APACHE-II score. These parameters can assist researchers in the development of predictive coma-scoring models.

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ETHICAL APPROVAL:
This study was approved by the Medicine Faculty, University of Harran, Clinical Research Ethics Committee (Approval Date: 09 November 2020, Session No. 19, HRU/20.19.08).

PATIENTS' CONSENT:
Informed consent were obtained from all the participants.

COMPETING INTEREST:
The authors declared no competing interest.

AUTHORS' CONTRIBUTION:
ED: The analysis and interpretation of data for the work, drafting the work, and revising it critically for important intellectual content.
BP: Drafting the work and revising it critically for important intellectual content.
IK: Obtaining data for the study and recording the data.
VFP: Review of the study and statistical analysis of data.
AG: Significant contribution in the manuscript write-up.
All the authors have approved the final version of the manuscript to be published.

REFERENCES

1. Bastos PG, Sun X, Wagner DP, Wu AW, Knaus WA. Glasgow coma scale score in the evaluation of outcome in the intensive care unit: findings from the acute physiology and chronic health evaluation III study. *Crit Care Med* 1993; **21(10)**: 1459-65. doi:10.1097/00003246-199310000-00012.
2. Zhang JB, Zhu JQ, Cao LX, Jin XH, Chen LL, Song YK, *et al*. Use of the modified glasgow coma scale score to guide sequential invasive-noninvasive mechanical ventilation weaning in patients with AECOPD and respiratory failure. *Exp Ther Med* 2020; **20(2)**:1441-6. doi:10.3892/etm. 2020.8884.
3. Eddahchouri Y, Peelen R V., Koeneman M, van Veenendaal A, van Goor H, Bredie SJH, *et al*. The effect of continuous *versus* periodic vital sign monitoring on disease severity of patients with an unplanned ICU transfer. *J Med Syst* 2023; **47(1)**:43. doi:10.1007/s10916-023-01934-3.
4. Fava C, Cattazzo F, Hu Z-D, Lippi G, Montagnana M. The role of red blood cell distribution width (RDW) in cardiovascular risk assessment: useful or hype? *Ann Transl Med* 2019; **7(20)**:581. doi:10.21037/atm.2019.09.58.
5. Mohindra R, Mishra U, Mathew R, Negi NS. Red cell distribution width (RDW) index as a predictor of severity of acute ischemic stroke: A correlation study. *Adv J Emerg Med* 2020; **4(2)**:e24. doi:10.22114/ajem.v0i0.257.
6. Naga AA, Fattah MIA, Nofal WH, AlMenshawe MA. Evaluation of red cell distribution width (RDW) as a septic marker in comparison with clinical scores and C-reactive protein. *QJM An Int J Med* 2021; **114(Supplement_1)**. doi:10.1093/qjmed/hcab086.014.
7. Li X, Chen Q, Bi X, Zhao J, Li Z, Zhou J, *et al*. Preoperatively elevated RDW-SD and RDW-CV predict favorable survival in intrahepatic cholangiocarcinoma patients after curative resection. *BMC Surg* 2021; **21(1)**:105. doi:10.1186/ s12893-021-01094-6.
8. Efe S, Asker I, Inal V. Karma yogun bakımda takip edilen kritik hastalarda platelet indekslerinin prognostik degeri. Dahili ve cerrahi bilim. *Yogun Bakım Derg* 2019; **10(1)**: 13-7. doi:10.33381/dcbybd.2019.1877.
9. Kuzniewicz MW, Vasilevskis EE, Lane R, Dean ML, Trivedi NG, Rennie DJ, *et al*. Variation in ICU risk-adjusted mortality: impact of methods of assessment and potential confounders. *Chest* 2008; **133(6)**:1319-27. doi:10.1378/chest. 07-3061.
10. Granholm A, Perner A, Krag M, Hjortrup PB, Haase N, Holst LB, *et al*. Simplified mortality score for the intensive care unit (SMS-ICU): Protocol for the development and validation of a bedside clinical prediction rule. *BMJ Open* 2017; **7(3)**: e015339. doi:10.1136/bmjopen-2016-015339.
11. Ermens AAM, Hoffmann JJML, Krockenberger M, Van Wijk EM. New erythrocyte and reticulocyte parameters on CELL-DYN Sapphire: Analytical and preanalytical aspects. *Int J Lab Hematol* 2012; **34(3)**:274-82. doi:10.1111/j.1751-553X. 2011. 01391.x.
12. Khodaiji S. Newer CBC parameters of clinical significance. In: Hematopathology. Singapore: *Springer Singapore*; 2019. pp. 3-25.
13. Philipsen JP, Madsen KV. Hypo- and hypernatremia results in inaccurate erythrocyte mean corpuscular volume measurement in vitro, when using sysmex XE 2100. *Scand J Clin Lab Invest* 2015; **75(7)**:588-94. doi:10.3109/0036 5513.2015. 1062534.
14. Samuel D, Bhat AN, Prabhu VM. Platelet indices as predictive markers of prognosis in critically ill patients: A prospective study. *Indian J Crit Care Med* 2020; **24(9)**:817-22. doi:10. 5005/jp-journals-10071-23574.
15. Zhang Z, Xu X, Ni H, Deng H. Platelet indices are novel predictors of hospital mortality in intensive care unit patients. *J Crit Care* 2014; **29(5)**:885.e1-85.e6. doi:10. 1016/j.jcrc.2014. 04.020.
16. Dubey A, Kumar S, Acharya S, Wanjari AK, Bawankule S, Agrawal S, *et al*. Impact of red cell and platelet distribution width in patients of medical intensive care unit. *J Lab Physicians* 2021; **13(4)**:309-16. doi:10.1055/s-0041-1730883.
17. Bedel C, Korkut M, Avcı A, Uzun A. Immature granulocyte count and percentage as new predictors of mortality in patients with upper gastrointestinal bleeding. *Indian J Crit Care Med* 2020; **24(9)**:794-8. doi:10.5005/jp-journals-10071-23563.
18. Karon BS, Tolan NV, Wockenfus AM, Block DR, Baumann NA, Bryant SC, *et al*. Evaluation of lactate, white blood cell count, neutrophil count, procalcitonin and immature granulocyte count as biomarkers for sepsis in emergency department patients. *Clin Biochem* 2017; **50(16–17)**:956-8. doi:10. 1016/j.clinbiochem.2017.05.014.
19. Hacimustafaoğlu M. Acute phase reactants (erythrocyte sedimentation rate, CRP). *Cocuk Enfeksiyon Derg* 2017; **11(1)**: 53-5. doi:10.5578/ced.201701.