Prognostic value of red cell distribution width-to-platelet ratio in mortality of major burn in Sanglah Hospital Bali

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ABSTRACT

Introduction: The mortality rate in Sanglah Hospital due to major burns is quite high. The ratio of red cell distribution width (RDW) and platelet (PLT) (RPR) as a prognostic marker of mortality in major burns has never been studied in Indonesia. Calculations of RPR are easy, widely available and cost-efficient.

Method: This study was retrospective observational case-control, with 60 patients with major burns consisting of 30 cases and 30 controls. Samples were taken from the Sanglah Hospital Medical Record Unit from April 2019 to April 2021. Cases were samples with mortality after day seven, while controls were samples that survived. RDW and PLT value on day seven are associated with the incidence of mortality.

Results: The mean of RPR in the case group was higher than in the control group. RPR mean of the control group was 0.0559, and the case group was 0.0947 (p<0.001). The increase of RPR in the case group was 40.97%. Statistical analysis showed that high RPR was a significant mortality risk factor in patients with major burns (OR = 21.36; p < 0.001).

Conclusion: High RPR is a prognostic marker of mortality in major burns at Sanglah Hospital.

Keywords: major burns, mortality, red cell distribution width (RDW), platelet (PLT), the ratio of RDW and PLT (RPR).

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INTRODUCTION

The mortality rate caused by major burn injuries is relatively high. In the past two years, there have been 90 patients treated for major burn injuries in the Burn Unit of Sanglah General Hospital, with a mortality rate reaching 50%. WHO estimates that 11 million burn injury cases occur worldwide, with 180,000 cases resulting in death.[1] Major burn are an emergency, depending on the individual's response. Often patients with the same area and depth of burns have different outcomes.[1] Given that the body's response to burns varies, many studies have explored the parameters to track these responses and their relationship to inflammatory status and patient prognosis.

The ratio of red cell distribution width (RDW) and platelet (PLT) (RPR) is considered an inflammation biomarker associated with the poor prognosis of a number of diseases. There are two studies about RPR related to the prognosis of major burn injury. Results indicate that RPR-as an inflammatory index-can be used as a biomarker for the prognosis of adult patients with major burn injuries.[2,3] Thus, RPR has caught our attention as an intriguing prognostic biomarker to investigate mortality in major burn injuries. Some other underlying reasons were that RPR has not yet been studied in Indonesia, despite its simplicity in calculation, wide availability, and efficiency in terms of its cost. This study aims to determine that a high RPR is a prognostic marker of mortality in major burns at Sanglah Hospital, Denpasar.

METHOD

This study employed a retrospective, case-control observational analytic study design. The samples in this study comprised all patients with major burn injuries who both fulfilled the inclusion and exclusion criteria and were treated at the Burn Unit of Sanglah General Hospital, Denpasar, from April 2019 to April 2021. The inclusion criteria were patients with major burn injuries (TBSA[3] 20%) who were 18 or older and undergoing treatment for more than seven days. The exclusion criteria were heart disease, chronic kidney disease, and diabetes mellitus. The data that has been collected is processed using the SPSS for windows version 22.0 program. The data obtained in this study were analyzed descriptively, then through a comparison test and the relationship between variables.

RESULTS

This study obtained patients' medical records treated for burn injuries between April 2021 at the Sanglah General Hospital, Denpasar. Of the total 267 medical records, 81 patients fulfilled both the inclusion and the exclusion criteria,

where 46 patients experienced mortality, while the remaining 35 patients did not. The consecutive sampling method was used to obtain 30 cases and 30 controls.

This study observed that the average RDW in the case group is higher than that of the control group. The average RDW in the control group is 12.65% ± 1.66%, whereas the average RDW in the case group is 13.37% ± 0.90% (p < 0.001). In the case group, RPR is higher than that of the control group, with a cut-off point of 0.0713. The average RPR of the control group is 0.0559 ± 0.0219, whereas the average RPR of the case group is 0.0947 ± 0.0213 (p < 0.001).

Furthermore, this study also determined that high RPR is a risk factor of mortality 21 times higher in patients with major burn injury (OR = 21.36; CI 95% 5.53 – 82.43; p < 0.001). RPR is deemed optimal in predicting mortality with a cut-off value of ≥ 0.0713. The sensitivity value of predicting mortality with this cut-off value is 86.7% and a specificity of 76.7%.

DISCUSSION

The results of this study are in line with a retrospective study conducted in 2016. That study asserted that mortality risk increases linearly as age increases in patients with burn injury. They recommended that health workers who handle burn injury cases be cautious when they are elderly. Patients aged > 60 with burn injury of larger than 30% TBSA have a mortality risk of 50% despite optimal burn injury management.[4] Research undertaken in Egypt in 2016–2017 regarding analysis on hospital stay in relation to mortality due to major burn injuries suggested that the length of stay correlates significantly with the depth or degree of burn injury. The deeper the burn injury, the more it plays a role in mortality, though the study did not find any significant relationship between the length of stay and mortality. Factors affecting the length of stay consist of infection, depth of burn injury, area of burn injury, and inhalation trauma.[5] A study by the Faculty of Medicine, Gadjah Mada University/Dr. Sardjito General Hospital, Yogyakarta, in 2018, concluded that albumin level, percentage of burn injury, inhalation trauma, and arrival time are prognostic factors that determine the mortality of patients with burn injury. Their data showed that 17 mortalities are found in burn injuries with an area of > 50%, compared to 11 mortalities in burn injuries with an area of < 50%. Compared to this study, fire-related burn injury was the predominant cause of burn injuries, accounting for 47 cases (39.5%), with mortality found in 17 cases (36.2%).[6]

Table 1. Basic characteristics of the samples.

Variable	Control n = 30	Case n = 30	p
Sex, n (%)			
Male	18 (60.0)	19 (63.3)	1.000[a]
Female	12 (40.0)	11 (36.7)	
Age (years), mean ± SD	38.87 ± 14.45	49.53 ± 19.70	0.034[b]*
Area of burn injury (%), mean ± SD	29.10 ± 8.59	46.22 ± 19.11	< 0.001[c]**
Length of hospitalization (days), mean ± SD	25.87 ± 14.08	14.97 ± 10.71	< 0.001[b]**
Cause of burn injury, n (%)			
Fire	17 (56.7)	27 (90.0)	
Low-voltage electricity	1 (3.3)	0 (0.0)	0.033*
High-voltage electricity	9 (30.0)	2 (6.7)	
Hot water	3 (10.0)	1 (3.3)	

[a]Chi-square test; [b]Mann-Whitney test; [c]Independent t-test;
*p < 0.05; **p < 0.001

Table 2. RDW, PLT, and RPR characteristics in the case and control groups.

Variable	Control n = 30	Case n = 30	p
RDW (%), mean ± SD	12.65 ± 1.66	13.37 ± 0.90	< 0.001[a]**
PLT (10^6/mL), mean ± SD	264.70 ± 112.45	149.33 ± 40.56	< 0.001[a]**
RPR, mean ± SD	0.0559 ± 0.0219	0.0947 ± 0.0213	< 0.001[b]**

[a]Mann-Whitney Test; [b]Independent T-test; **p < 0.01

Table 3. Cross-Tabulation of the RPR group and mortality.

Variable	Control n = 30	Case n = 30	OR (CI 95%)	p
RPR category, n (%)				
Low (< 0.0713)	23 (76.7)	4 (13.3)	21.36 (5.53 – 82.43)	< 0.001**
High (≥ 0.0713)	7 (23.3)	26 (86.7)		

**p < 0.01

Red cell distribution width (RDW) is a parameter that expresses the heterogeneity of red blood cell volume. An increase in RDW indicates inflammation, and poor prognosis of several diseases, including heart disease and acute kidney failure.[7,8] Severe inflammatory conditions also occur in major burn injuries. A retrospective study in the United States reported that, in major burn injury cases, RDW is significantly higher in patients who did not survive, and this trend persisted for one week.[9] This study observed that the average RDW in the case group is higher than that of the control group. The average RDW in the control group is 12.65% ± 1.66%, whereas the average RDW in the case group is 13.37% ± 0.90% (p < 0.001). It can be seen that there is an increase in RDW of 5.7% in the case group. The increased RDW is due to the disruption to erythrocyte homeostasis, leading to increased red blood cell (RBC) deaths and oxidative stress, which interfere with RBC production. The increase in DW indicates elevated RBC fragility and induces RBC death, resulting in decreased HGB, HCT, and RBC in patients who do not survive. RDW also reflects the increase in oxidative stress in patients with major burn injury who are deceased, which can act as a marker for poor prognosis.[9] In addition, in critical patients with sepsis, increased RDW has proven to be a more successful marker for predicting mortality than the established clinical score. A retrospective review of patients with trauma suggested that the RDW value when they first came to the hospital is an independent predictor of mortality.[9] ARDS is a fatal and serious condition emerging after major burn injuries. The RDW value correlates with increased risk of ARDS, and RDW is an independent risk factor in predicting ARDS occurrence after major burn injuries.[10]

This study identified a lower PLT count in the case group than in the control group. Peak PLT count in patients with a burn injury is explained by the increased thrombopoietin (TPO) circulation level following a decrease in overall PLT mass after injury. This induces PLT production from the bone marrow and may explain rebound thrombocytosis. Inflammatory cytokines, such as IL-6, can exacerbate this condition during the SIRS response after injury.[11] A study investigated massive burn injuries (> 70% TBSA) on 102 adults and discovered that severe thrombocytopenia (PLT count < $20x10^9$/L) is an independent predictor of mortality in the 30 days of hospitalization (p < 0.05).[12] Another study also pointed out that a PLT count decreasing more than 65% of its original level predicts 30-day mortality in patients with burn injury (p = 0.028).[2] There may be a difference in response to the decrease in original PLT count by the bone marrow between patients experiencing mortality and patients who do not. This may be attributable to the elevated inflammatory response in these individuals, which spurs bone marrow activities.[13]

The ratio of red cell distribution width (RDW) and platelet (PLT) (RPR) is acknowledged as an inflammatory biomarker associated with the poor prognosis of some medical conditions. A cohort study conducted in China taking place in 2020 concluded that RPR is an independent biomarker of poor prognosis in patients with sepsis (cut-off point 0.134).[14] RPR is an index that simultaneously reflects RBC and PLT's statuses. A meta-analysis study in 2019 summarized that RPR is a predictor of hepatic fibrosis and cirrhosis with a cut-off point from 0.06 to 0.14.[15] The categorization based on Angulo et al. (2022) cut-off point, 0.0726, is nearing the research data. ROC analysis was conducted to observe RPR's ability as a predictor of mortality in this study's data. The result suggests that RPR can predict mortality with an area under the curve (AUC) of 0.893 (CI 95% 0.814 – 0.973). Additionally, this study also noted that the RPR in the case group is higher than that of the control group, with a cut-off point of 0.0713. The average RPR of the control group is 0.0559 ± 0.0219, whereas the average RPR of the case group is 0.0947 ± 0.0213 (p < 0.001). There is an increase in RPR of 40.97% in the case group. Furthermore, this study also determined that high RPR is a risk factor of mortality 21 times higher in patients with major burn injury (OR = 21.36; CI 95% 5.53 – 82.43; p < 0.001).

The results of this study are supported by a retrospective study on 580 patients with STEMI in 2016, which asserted that RPR increases in patients with no-reflow phenomenon secondary to primary percutaneous coronary intervention, in which the groups are at high risk of mortality.[16] Inflammation and oxidative stress are observed in patients with sepsis, hepatic cirrhosis, and myocardial infarction, same with patients with major burn injuries. There are two studies related to RPR and the prognosis of major burn injuries. A retrospective study in 2017 in China described that an increase in RPR (cut-off point of 0.108) on day three and day 7 is an independent predictor of mortality in major burn injury cases. That study also discussed that RDW and PLT could not predict mortality in major burn injury cases.[2] Another retrospective study undertaken in Uruguay in 2020 remarked that RPR, as an inflammatory index, can be employed as a prognostic biomarker in adult patients with major burn injury.[3] The limitation of this study is that we took research samples from 1 center, so it cannot be generalized nationally. And also, we only took the data on the 7th day, so we could not see the PRP trend from the previous day in the first week.

CONCLUSION

A high RPR is a prognostic marker of mortality in major burn injuries in Sanglah General Hospital, Denpasar. RPR can be used on the 7th day after a major burn case as a prognostic marker of mortality. It is necessary to conduct a multicenter study from Burn Units throughout Indonesia so that there to generalize the research results.

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ETHICAL CLEARANCE

This study has obtained ethics approval from the Ethics Committee of Universitas Udayana No. 2715/UN14.2.2.VII.14/LT/2021 prior to the study conducted.

CONFLICT OF INTEREST

We declare that there were no conflicts of interest in this study.

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