

Utility of platelet- to lymphocyte ratio as an inflammatory biomarker in major burns. our experience

Abstract

Background: Burn injuries are a major cause of morbidity and mortality, because of the severe local and systemic response developed, affecting organics functions. A decline in platelets and lymphocyte count compromise the immune response and patient's outcome. To evaluate the usefulness of platelet to lymphocyte ratio as a biomarker of mortality in severely burned patients, the present research was performed.

Methods: A descriptive, longitudinal, prospective study was carried out at the Burn Department of Calixto García Hospital, La Habana, from January 2022 to December 2023. All admitted patients with major burns, ages between 19 and 60 years old, and less than 24 hours since the beginning of the trauma, were included. Blood samples were taken on days 3 and 6 after injury, to determine platelet to lymphocyte values, and a relationship between the mortality rate and presence of complications was established.

Results: 143 burned patients were included, males were predominant (63 %), flame (98.2 %) was the first causal agent and accidents (89.6 %) were the main production mode. 90 % of patients survived. Platelet-to-lymphocyte ratio values were lower in patients who developed complications and in the nonsurvivors group.

Conclusions: Platelet to Lymphocyte ratio is an effective biomarker for predicting mortality in severely burned patients.

Keywords: Burns, inflammation, lymphocytes, platelets

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Introduction

Burn injuries are a major cause of morbidity and mortality, representing a global health problem, affecting not only the skin, but besides developing an important local and systemic inflammatory response, with harmful effects in most of the organs and system of organs.¹ The severity of the burn injury is a determining factor for patient's prognosis. Despite the advancement in therapeutic protocols, including hydric resuscitation, early debridement of burned tissue, skin grafting, and enteral nutrition, the incidence of mortality rates and complications are still remarkable.²

Major Burn causes significant changes in haematological parameters marking the final evolution of the disease.³ White blood cells are the first defense line against injuries, and are seriously affected after a thermal trauma.^{4,5} Disorders in leukocytes, mainly in lymphocyte count and functions have been described.^{5,6} Lymphocytes (B and T), are one of the main immune cells with essential function for a normal host response, originating in the bone marrow, and circulating in peripheral blood and lymphatic tissue, playing a determinant role in both, innate and humoral immune response.⁷ A decline in lymphocyte count, (lymphopenia), suggests an Inflammatory process and immunosuppression.^{6,7} A redistribution of lymphocyte cells following an extensive burn injury, with a disruption of the balance between T cells (helpers and suppressive) seems to produce disturbances of the adaptative immune response.⁸

Platelets or Thrombocytes are anucleated small blood cells, that originated in bone marrow from the megakaryocytes series, having a crucial role in thrombus formation, hemostasis and wound healing.⁹ They have been recognized to be closely involved in the burn injury physiopathology, by inducing cytokines and epidermal growth factor

(EGF) release, and several Inflammatory mediators.⁸ Platelets count are useful as an acute biomarker for predicting sepsis, thrombotic complications and mortality in the major burn. Thrombocytopenia is considered a risk factor for septic shock in burns. Platelets are consumed in the endothelium of the damaged burned skin, affecting the function (margination), hemostasis and healing.^{5,6}

During the last decades numerous researches have been developed to find out non-invasive and effective diagnostic tools for the early detection of complications in severely burned patients. Utility of different Inflammatory biomarkers as Protein C Reactive (PCR), Procalcitonin, and Neutrophil to Lymphocyte Ratio (NLR), have been widely studied in burn trauma.⁹⁻¹²

Platelets to lymphocytes ratio (PLR) is defined as the ratio of platelets count to lymphocytes count, and can be calculated quickly and inexpensively from a routine complete blood count,^{13,14} which is performed in most the locations of the medical, using automated equipment for haematic cytometry.¹⁵ PLR has been demonstrated to play a role as a marker of acute inflammation in different conditions as: Breast and Lung cancer, Covid – 19 infection, neonatal sepsis, Cardiovascular diseases and traumas.¹⁶⁻²¹

As a new biomarker, PLR has been described as the combination of two hematological parameters, providing the concept of Inflammatory cascade and platelet aggregation.²² An improvement in the understanding of changes in blood cell series and derivated indexes as PLR, following a burn trauma, provides a tool for a rational and effective use of immunomodulator drugs.^{22,23}

There are no previous published studies in the country reporting the determination of PLR levels in burned patients; and being the

Inflammation is the physiopathological axis of the burn disease, there is a requirement to identify accessible biomarkers to predict the earliest clinical manifestations of complications or mortality in severe immunocompromised burned patients. To evaluate the usefulness of platelet to lymphocyte ratio in the evolution of the major injury, the present study was performed.

Methods

A descriptive, longitudinal and prospective investigation was carried out at the Burn Department, of "Calixto García University Hospital", La Habana, Cuba, from January 2022 to December 2023, to evaluate the predictive value of the Platelet to Lymphocyte ratio as a biomarker, in severely burned patients. All admitted patients fulfilling the selection criteria, were studied.

Inclusion criteria

- a) Burned patients with body surface area affected $\geq 20\%$ (Major Burns).
- b) Ages between 19 – 60 years old.
- c) Admitted patients with less than 24 hours since the beginning of injury.

Exclusion criteria

- a) Burns associated with other's traumas.
- b) Immunodeficiencies conditions and coagulopathies, cancer.
- c) History of medication intakes: aspirin, warfarin.
- d) Patients who died before the 6 th day of evolution.

Data collection

Medical records were fulfilled, and clinic findings were closely measured. Vital Signs were taken daily, including: Blood Pressure, Urine output, Cardiac and breathing rhythm.

Treatment of the Burn Wound: Extension and deepness of the burn were diagnosed. Burn Extension (Total Body Surface Area) $\geq 20\%$ were considered major burns. Change of dressing and wound swabs were performed daily.

Complete Blood Counts, Platelets Counts, Chest X-rays, microbiological cultures, and Electrocardiographics studies were performed 3 times per week, to detect complications.

To determine PLR values, blood samples (10 ml of venous blood) were taken at days 3rd and 6th after burn trauma, (considering that a calculated fluid reposition is performed during the first 6 days). Samples were centrifugated at 3000 rpm for 15 minutes. All were analyzed at the Central Laboratory of Calixto García Hospital. The cut-off value for PLR was: 71.4.

A relation between PLR values and the discharge status was established.

Statistical analysis

Data were collected from medical records. Analysis of data was carried out using Excel and SPSS software versión 20.0 for Windows, with 95 % CI. The non parametric test (Wilcoxon) was performed to find statistical significance ($p < 0.005$) of quantitative variables. The Media Values (X) and Standards Derivation. (SD) were calculated.

Ethics aspects

The present study was carried out following the standards ethics issues for human research, according to the Helsinki Declaration, Fortaleza, Brasil, 2013. The consent signature of every patient was confirmed by researchers.

Results

Of a total of 216 admitted burned patients, 143 were included. Table # 1 shows the demographic distribution of the sample.

Table 1 Demographic Distribution. Burned Patients. January 2022-December 2023

Ages	Male	Female	Total	%
19 -29	20	11	31	21.7
30-49	36	35	71	49.6
50-60	34	7	41	28.7
Total	90	53	143	100
	0.63	0.37		

n=143

Males were the predominant group. (63 %). Aged group between 30 and 49 years old is the most affected. (71 = 49.6 %). Accidents were the main production mode (128= 89.6 %), followed by 14 suicides (9.8 %) and 1 homicide (1 = 0.6 %).

Figure # 1 shows the etiological agents found.

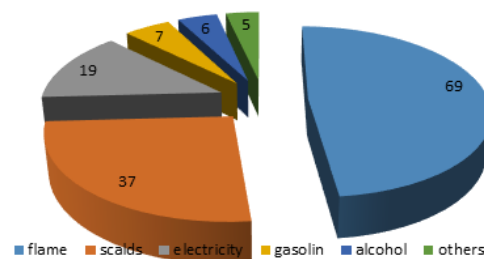


Figure 1 Etiology of Burns. January 2022-December 2023.

Flame was the first causal agent (69 = 98.2 %), followed by scald burns (37 = 25.8 %). Figure 2 shows media (X) values of Platelet to Lymphocyte Ratio at day 3rd after burn injury, and its relation with the discharge status.

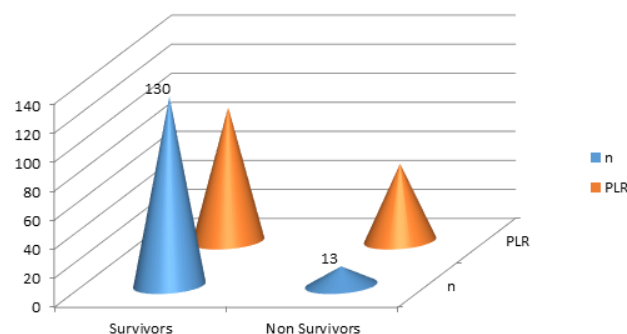


Figure 2 Discharge Status and PLR. Day 3rd after burn injury.

PLR cut off value =71.4, $p = 0.02$

130 patients (90 %) were discharged live, and 13 (9,09 %) did not survive. PLR Media (X) \pm SD values at day 3rd after burn, were lower (40.5 ± 18.6) in non survivors than in survivors (89.92 ± 22.9). $p < 0.05$

Table 2, exhibits the PLR values (Media \pm Standard Derivation) on day 6 th after burn trauma and its relation with the discharge status. A permanent decline of PLR was observed in patients who died. ($p < 0.05$).

Table 2 Discharge Status and PLR. Day 6th after burn injury

Discharge Status	X	\pm SD
Non survivors n= 13	53.4	25.5
Survivors n= 130	92.3	45.2

Cut off value: PLR =71.4, $p=0.002$, SD (Standard Derivation), X, Media

Table 3 exposes the incidence of complications and its relation with the discharge status. A 100 % of studied patients developed wound infection. The incidence of complications was higher in nonsurvivors.

Table 3 Incidence of complications and Discharge Status

Complications	Survivors (130)	Non Survivors (13)	%
Wound infection	130	13	100
Systemic infection	85	13	68.5
Urinary Infection	12	4	11.1
Pneumonia	8	1	6.3
Digestive Bleeding	1	1	1.4
Multiple Organ Dysfunction	-	10	6.7

n=143

Discussion

Different biomarkers have been described to predict complications and mortality in severe burn trauma, but during the last decades, a new group of hematological indexes has been recognized as the earliest and useful inflammation markers, including Platelets to Lymphocyte ratio and Neutrophil to Lymphocyte ratio.⁹ Systemic Inflammation in severely burned patients can lead to a decline in platelet count and a neutrophilic sequestration in organs with suppression of an immune response, causing lymphopenia.^{24,25} In the present research, low values of platelet to lymphocyte ratio were found since the first 72 hours after trauma, in all burned patients studied, being lower in those who did not survive. On the day 6 th after injury recovery of the PLR levels was not obtained in patients who died ($p < 0.05$).

A similar correlation was demonstrated by Angulo et al.,¹³ in a retrospective study of 88 adult burned patients, with a Media PLR value lower than 60.28 in non-survivors, suggesting that PLR can predict survival in adults with thermal injuries.

According to Del Carpio Orantes,²⁶ PLR is a useful parameter for predicting prognosis in diseases affecting immune response. Hussein et al.,²⁷ described the role of platelet count in predicting outcome in a sample of 30 burned patients, finding thrombocytopenia since the first hours after trauma in dead patients. In the present study, a permanent decline in platelet counts associated with lymphopenia in non survivors patients, was a crucial factor in obtaining a low PLR level even after an adequate hydric reposition.

Djordjevic²⁸ claims that PLR, NLR and Monocyte to lymphocyte ratio may help to identify mortality in critically ill patients, revealing

the absence of a proinflammatory state in immunocompromised conditions.

Aggarwall et al.,²⁹ carried out a prospective investigation in a group of 90 pediatric burned patients, finding lower levels of PLR in children who developed sepsis and in those who did not survive. Their results confirm our findings.

A low PLR was associated with high short-term mortality in severe trauma patients, according to Kim et al.,³⁰ who reported in their study of 139 adults no- burned patients, lower PLR values in the expired group, in comparison to the survivor group.

According to Cato et al.,³¹ an important diminish in platelets count occurs on the 3rd day after an extensive burn, and a slight recovery of the values can be seen a month after trauma.

Nhorigheimasi and colleagues,³² in a review article claim that PLR helps indicate a shift in platelets and lymphocyte counts in acute inflammation.

In some other conditions the values of PLR remain high,^{20,33} revealing differences in the type of Inflammatory response in comparison to the major burn. Infection remains the main cause of mortality and complication of burn injury.³⁴ Most of the published investigations of burn diseases confirm the growth of germens in the wound.^{11,12,34} Our results also exhibit a higher incidence of complications, including systemic infections in patients who died.

Extensive burns are still a therapeutic challenge because of the important immunosuppression secondary to the systemic Inflammatory response and releasing of several mediators.³⁵ Understanding the pathophysiology behind these biomarkers, including PLR, could result in earlier intervention and improve outcome among burn patients.

A limitation of the present research was the short time studied. We consider that further investigations and comparative studies should be performed to obtain more efficient results. Conclusions: Since the first 72 hours after trauma, a diminish in PLR values was found in burned patients who did not survive, and a recovery of the values was not seen at day 6th of evolution. Platelet to Lymphocyte ratio is an effective biomarker for predicting mortality in severely burned patients.

Acknowledgment

None.

Conflict of interest

None.

References

- Reynoso Trujillo KA, Herrera Lozada AE, Suárez Concha EG, et al. Actualización en el manejo del paciente quemado. *RECIMUNDO*. 2022;6(4):123–131.
- Andrade Ponce AC, Soria Álvarez CE, Aguirre Esparza KL, et al. Calvo-piña Álvarez CD y cols. Actualización en el manejo de las quemaduras: Artículo de Revisión. *LATAM Revista Latinoamericana de Ciencias Sociales y Humanidades*. 2024;5(4):3324–3337.
- Carrillo E R, Tamez C A, Garnica E MA, et al. Alteraciones de la homeostasia en el enfermo con quemaduras. *Med crit (Col Mex Med Crit)*. 2018;32(1):42–49.
- Patiño Gómez K, Moya Rosa EJ, Tapia Mesa G. Alteraciones hematológicas en el paciente gran quemado. *Arch Méd Cam*. 2024;28:e9822.

5. Herrera Aguilar L. Cambios clínicos tempranos en el hemograma completo en lesiones por quemaduras severas. *Rev Argent Quemaduras*. 2024;34(1):5–10.
6. Osuka A, Ishihara T, Shimizu K, et al. Natural kinetics of blood cells following major burn: Impact of early decreases in white blood cells and platelets as prognostic markers of mortality. *Burns*. 2019; 45(8):1901–1909.
7. Burgess M, Valdera F, Varon D, et al. The Immune and Regenerative response to Burn Injury. *Cells*. 2022;11:3073.
8. Kim M, Kym D, Park J. Big data insights into the diagnostic values of CBC parameters for sepsis and septic shock in burn patients: a retrospective study. *Sci Rep*. 2024;14:800.
9. Bordeanu–Diaconescu EM, Grosu–Bularda A, Frunza A, et al. Diagnostic and Prognostic Value of Trombocytopenia in Severe Burn Injuries. *Diagnostic*. 2024;14:582.
10. El Ayadi A, Herndon DN, Finnerty CC. 21– Biomarkers in Burn Patient Care. *Total Burn Care*. 2018:232–235.
11. Li AT, Moussa A, Gus E, et al. Biomarkers for the early diagnosis of Sepsis in Burns: Systematic Review and Meta–analysis. *Ann Surg*. 2022;275(4):654–662.
12. Juárez GU, Sánchez MJ. Asociación entre Índice Neutrófilos linfocitos como marcador de mortalidad en pacientes con quemaduras mayores durante el período del 01 febrero de 2020 al 28 de enero de 2022. *Med Crit*. 2023;37(1):17–20.
13. Zaldívar Castillo D, Palacios Alfonso I. Evaluación del Índice Neutrófilos–Linfocitos en lesionados severamente quemados. *An Fac Cienc Méd*. 2024;57(2):59–66.
14. Angulo M, Moreno L, Aramendi I, et al. Complete blood count and derived indices: evolution pattern and prognostic value in adult burned patients. *J Burn Care Res*. 2020;41(6):1260–1266.
15. Vélez Paez JL. Mean platelet volumen and mean platelet volumen–to–platelet count ratio as predictor of severity and mortality in sepsis. *PLOS ONE*. 2022;17(1):e0262356.
16. Lee SM, Russell A, Hellawell G. Predictive value of pre–treatment inflammation based prognostic scores (Neutrophil–to–lymphocyte ratio, platelet–to–lymphocyte ratio, and neutrophils–to–monocyte ratio) for Invasive bladder carcinoma. *Korean J Urol*. 2015;56:749–755.
17. Koh CH, Bhoo–Pathy N, Jabir RS, et al. Utility of pre–treatment Neutrophil–to–lymphocyte–ratio and platelet–to–lymphocyte ratio as prognostic factors in breast cancer. *Br J Cancer*. 2015;113:150–158.
18. Camacho Sosa K, Ramos Suzarte M, Viada González CE. Índice neutrófilos–linfocitos e índice plaquetas–linfocitos: herramientas pronósticas del cáncer de pulmón. *Rev medica electron*. 2023;45(6).
19. Toprak E, Bozuert M, Carma BD, et al. Platelet–to–lymphocyte ratio: a new Inflammatory marker for the diagnosis of premature ruptura of membranas. *J Turk Gynecol Assoc*. 2017;18:122–126.
20. Zhai G, Wang J, Liu Y, et al. Platelet –lymphocyte ratio as a new predictor of in– hospital mortality in cardiac intensive care unit patients. *Scientific Reports*. 2021;11:23578.
21. Valga F, Monzón T, Henríquez F, et al. Índice plaquetas–linfocitos y neutrófilos–linfocitos como marcadores de resistencia a la eritropoyetina en pacientes en hemodiálisis crónica: estudio transversal–multicéntrico. *Nefrolgía*. 2020;40(3):320–327.
22. Ravindra R, Rammamurthy P, Kulkarni A, et al. Platelets Indices and Platelet–to–Lymphocyte ratio as markers for predicting Covid–19 Infection Severity. *Cureus*. 2022;14(8):e28206.
23. Lin HC, Wu GH, Zheng JJ, et al. Prognostic values of Platelet Distribution Width and Platelet Distribution Width–to– Platelet ratio in severe burns. *Shock*. 2022;57(8):494–500.
24. Llitjos JF, Carrol ED, Osuchowski MF, et al. Enhancing sepsis biomarkers development: key considerations from public and private perspectives. *Critical Care*. 2024;28:238.
25. Zielinsky M, Wroblewski P, Kozielski J. Prognostic factors in patients with burns. *Anaesthesiol Intensive Ther*. 2020;52(4):330–335.
26. Arslanagic S, Karamehic J. Analysis of peripheral blood lymphocytes in burns of varying degrees in the assesment of immune supression. *Sana-med*. 2020;15(3):255–264.
27. Del Carpio Orantes L, García Méndez s, Hernández Hernández SN. Neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, and systemic immune–inflammation index in patients with Covid–19–associated pneumonia. *Gac Med Mex*. 2020;156(6):527–531.
28. Hussein AI, Elsaka DM, Ammar MS, et al. Role of platelet count in predicting outcomes in major burn patients. *Menoufia Med J*. 2022;35(3):1600–1603.
29. Djordjevic D. Neutrophil to lymphocyte ratio, Monocyte to lymphocyte ratio , Platelet to Lymphocyte ratio and Mean Platelet value to Platelet Count Ratio as Biomarkers in Critically Ill and Injured patients: Which Ratio to Choose to predict Outcome and Nature of Bacteremia?. *Inflamm*. 2018.
30. Aggarwall N, Karki D, Gaind R, et al. Neutrophil to lymphocyte ratio and platelet to lymphocyte ratio as markers of early sepsis and mortality in paediatric burns: a prospective evaluation. *Int J Res Med Sci*. 2023;11:2531–2537.
31. Kim JK, Sun KH. Role of platelet –to–lymphocyte ratio at the time of arrival to the Emergency room as a predictor of short– term mortality in trauma patients with severe trauma team activation. *Acute and Critical Care*. 2024;39(1):146–154.
32. Cato L, Wearn CM, Bishop JRB, et al. Platelet count: A predictor of sepsis and mortality in severe burns. *Burns*. 2018;44(2):288–297.
33. Nourigheimas Sh, Yazdani E, Ghaedi A, et al. Association of Inflammatory biomarkers with overall survival in burn patients: A systematic Review and Meta–analysis. *BMC Emergency Medicine*. 2024; 24:76.
34. Lagos Castro JR, Lagos Castro KD, Ramírez Herrán W, et al. Relación de los Índices neutrófilo–linfocito y plaquetas–linfocito con desenlaces de severidad en isquemia aguda de miembros inferiores. *Angiología*. 2023;75(2):67–77.
35. Miranda Kretzschmar AK, Xavier Cartaxo F, Erastides Sánchez T, et al. Incidencia y factores asociados a sepsis en víctimas quemadas internadas en un hospital brasileño. *Rev Bras Quemaduras*. 2021;20(1):8–12.
36. Mulder P, Vlig M, Fasse E, et al. Burn–injured skin is marked by a prolonged local acute Inflammatory response of innate immune cells and pro–Inflammatory Cytokines. *Front Immunol*. 2022;13:1034420.