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Review Article

Platelet-to-lymphocyte ratio as a prognostic predictive marker on adults with traumatic brain injury: Systematic review

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ABSTRACT

Background: The platelet-to-lymphocyte ratio (PLR) has emerged as a prognostic predictive marker in various diseases, but its role in traumatic brain injury (TBI) has not been fully elucidated. This study aims to evaluate the role of PLR as a prognostic predictive marker in adults with TBI.

Methods: This systematic review was conducted according to the Preferred Reporting Items in the Systematic Review and Meta-analysis Guidelines 2020. A comprehensive search was performed using PubMed, Google Scholar, Scopus, Crossref, OpenAlex, Semantic Scholar, Library of Congress, and Jisc Library Hub Discover database to identify relevant studies published up to February 2023. Both prospective and retrospective observational studies written in English or Indonesian were included in the study. No restrictions were placed on the year and country of publication and duration of follow-up. Study quality was evaluated using the Newcastle-Ottawa Scale (NOS), and the risk of bias was estimated using the Cochrane Risk of Bias Assessment Tool for Nonrandomized Research (Ro-BANS) tool. A narrative synthesis was also conducted to summarize the findings.

Results: We retrieved 1644 references using the search strategy, and 1623 references were excluded based on screening the title and abstract. The full text was retrieved for 20 articles and subjected to the eligibility criteria, of which 16 were excluded from the study. Four papers with a total of 1.467 sample sizes were included in the review. The median of NOS for study quality was 8–9, with the risk of selection bias using the Ro-BANS tool being low in all studies except for the blinding outcome assessments, which are all unclear. The study finding suggests that the PLR has the potential as an independent prognostic predictive marker in adult patients with TBI. In three studies, a high level of admission PLR may independently predict an increasing mortality risk in 30 days and adverse outcomes measured by the Glasgow outcome scale in 6 months following TBI. However, one study shows that PLR may have limited value as a predictor of mortality or favorable neurological outcomes compared to other hematological parameters. Further studies were needed to establish the clinical utility of PLR and fill the present gaps.

Conclusion: This systematic review provides evidence supporting the utilization of PLR as a prognostic predictive marker in adult patients with TBI. The PLR can mainly be utilized, especially in rural practice, as PLR is a simple, low-cost, and routinely performed hematological examination.

Keywords: Marker, Platelet-lymphocyte ratio, Prognosis, Systematic review, Traumatic brain injury

INTRODUCTION

The Centers for Disease Control and Prevention defines traumatic brain injury (TBI) as brain damage produced by a bump, blow, or jolt to the head or a penetrating head injury that disrupts normal brain function.[5] TBI is considered one of the leading causes of death not only in lower- to middle-income countries but also in high-income countries.[36] TBI is more common in underdeveloped nations than in most industrialized countries; for example, the incidence rate in Asia is 344/100.000 people, whereas Europe's is 235/100.000 people. Data obtained in Indonesia from 2009 to 2013 indicated that the average number of persons suffering from brain damage was 1178 each year, with fatality rates reaching 11.22%, compared to the international benchmark of 3–8%. Based on severity, severe TBI mortality ranges from 25.13% to 37.14%; this statistic is also relatively high when compared to the known research, which is 22%.[17,35]

TBI has a wide range of classifications based on macroscopic modes of injury (e.g., mass compression, contusion, and diffuse axonal injury) as well as a range of mechanisms by which neuronal injury can be inflicted (e.g., "classical" ischemia, apoptosis, mitochondrial dysfunction, cortical spreading depression, and microvascular thrombosis), each of which differs in proportions and clinical courses.[21] TBI severity can be divided into mild, moderate, and severe based on the Glasgow coma scale (GCS) on the first 24 h, duration of consciousness lost period of consciousness alteration, imaging result, and period of posttraumatic amnesia.[5] Numerous prognostic assessments, including IMPACT and CRASH, might guide the care and predict the fate of TBI patients; however, it is not always simple to acquire all of the features in the prognostic tools in diverse hospital settings. As a result, researchers tried to develop simple biomarkers that may be used to predict outcomes.[29]

While primary brain damage is nearly irreversible, secondary brain injury caused by trauma-induced oxidative stress, edema, ischemia, and other systemic reactions related to inflammation can be controlled.[28] The present study demonstrates that trauma patients exhibit an immunoinflammatory response following injury related to platelet activation and the coagulation system.[3,31] At sites of injury, damaged cells release factors that trigger the inflammatory cascade, along with chemokines and growth factors, which will attract neutrophils, monocytes, lymphocytes, and mast cells to the injury site.[14,25]

Studies have demonstrated that a considerable number of indicators may be found in cerebrospinal fluid after TBI, indicating that neuroinflammation is one of the key causes of subsequent damage in TBI. The identification of these markers, however, has a high technological and financial need.[10,25] Complete blood counts are a simple, low-cost standard examination procedure that provides doctors with information about a patient's blood composition and characteristics, such as platelet-lymphocyte ratio (PLR), associated with systemic nonspecific inflammation.[3,27] In multiple studies, elevated PLR was associated with a worse prognosis for non-small-cell lung cancer and colorectal cancer.[24,26]

Past research is abundant regarding whether PLR could be used as a prognostic measurement for patients with TBI, but the results vary between studies, and the quality of studies is still unknown; therefore, there is a need for systematic review and meta-analysis to be made to synthesize the best evidence regarding this matter. This systematic review aims to evaluate the role of PLR as a prognostic predictive marker in adults with TBI.

MATERIALS AND METHODS

Search strategy

The present study is a systematic review based on the Preferred Reporting Items in the Systematic Review and Meta-Analysis (PRISMA) 2020 checklist. The protocol of this study has been registered on the International Prospective Register for a systematic review with the number CRD42023465410. The search was conducted on February 19, 2023, in eight international databases, including PubMed, Google Scholar, Scopus, Crossref, OpenAlex, Semantic Scholar, Library of Congress, and Jisc Library Hub Discover, related to the study's objectives. We formulated the PICO question according to the following: Population: adult patients with TBI; intervention: the PLR; comparison: none; and outcome: patient outcomes including mortality, Glasgow Outcome Scale (GOS), and extended GOS (GOSE). The keywords used are as follows: (PLR OR "platelet#lymphocyte" OR "platelet#to#lymphocyte") AND (TBI OR "brain injury" OR "head injury" OR "cerebral injury" OR "intracranial injury" OR "cortical injury" OR "craniocerebral trauma" OR "brain trauma" OR "brain concussion" OR "commotion cerebral"), we conducted a systematic search to collect relevant research, followed by a manual search of references cited in the included studies to prevent missing any relevant publications.

Inclusion and exclusion criteria

The next step was to establish the inclusion and exclusion criteria. Both prospective and retrospective observational studies that evaluated the association between PLR and prognosis in adult patients (≥18 years old) with TBI were included in the study. Retrieved articles with a sample size of at least 50 patients and written in English or Bahasa Indonesia from any year publication were considered. No restrictions

were placed on the year and country of publication and duration of follow-up. On the other hand, studies that did not report relevant outcomes and different study designs, for instance, experimental animal studies, cross-sectional studies, case reports, reviews, and meta-analyses, were excluded from the study.

Selection process

Four reviewers (MFI, AL, EAB, and GPS) independently screened titles and abstracts to identify possibly suitable research during the selection process. Full-text papers were found and evaluated for eligibility using the inclusion and exclusion criteria. Any disagreements among the reviewers were handled through mutual discussion and then with the consensus of the fifth reviewer (GAR).

Quality assessment

The Newcastle-Ottawa Scale (NOS) was used to evaluate the quality of each study in this investigation.[42] It was a scale for assessing the quality of nonrandomized research, such as cohort and case–control studies. The NOS has three primary components: selection of the study groups (0–4 points), comparability of cases and control studies (0–2 points) or cohorts, and ascertainment of exposure/outcome (0–3 points). Research with six or more points is deemed high-quality. Using this tool, four reviewers separately assessed the quality of the study, and any conflicts in the assessment among the reviewers were also handled through mutual discussion and then with the consensus of the fifth reviewer.

Risk of bias assessment

The Risk of Bias Assessment Tool for Non-randomized Research (Ro-BANS) tool was used to assess the risk of bias in the included research.[22] The tool evaluates the risk of bias in six areas: selection of participants, confounding variables, measurement of exposure, blinding of outcome assessments, incomplete outcome data, and selective outcome reporting. Using this tool, four reviewers separately assessed the risk of bias, and any conflicts in the evaluation among the reviewers were also handled through mutual discussion and then with the consensus of the fifth reviewer.

Data analysis

The data analysis in this systematic review consisted of summarizing the findings of the included studies using a narrative synthesis approach. The extracted data were

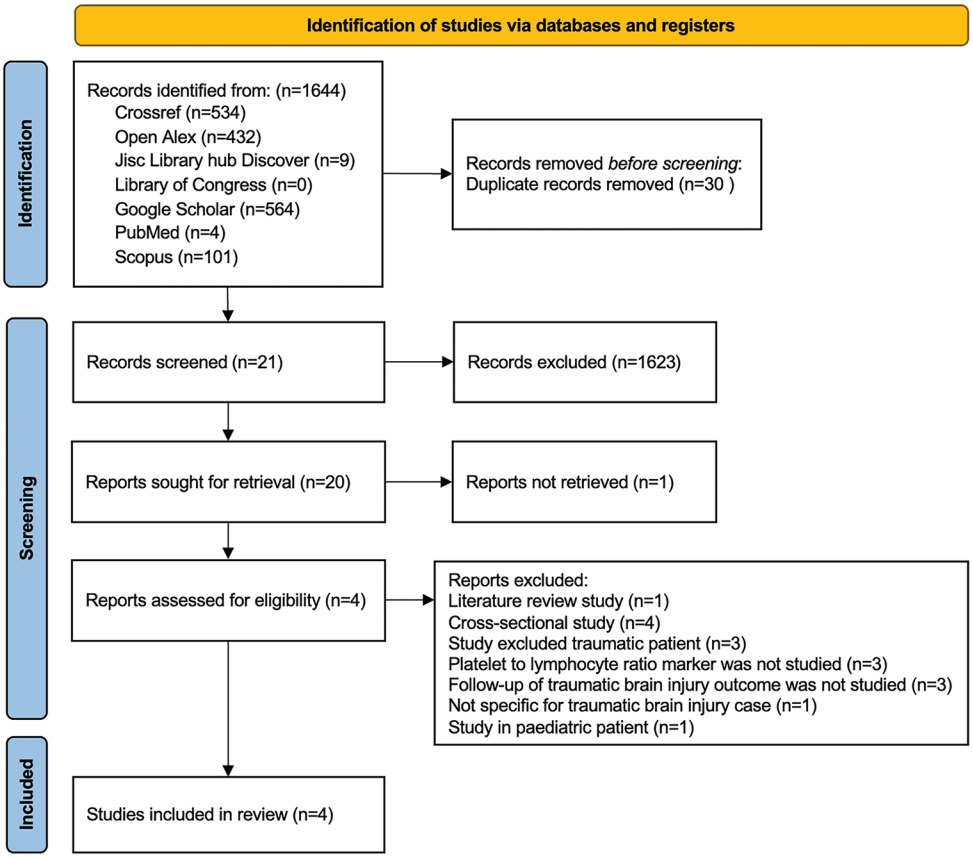

Figure 1: Preferred Reporting Items in the Systematic Review and Meta-Analysis 2020 flow diagram.

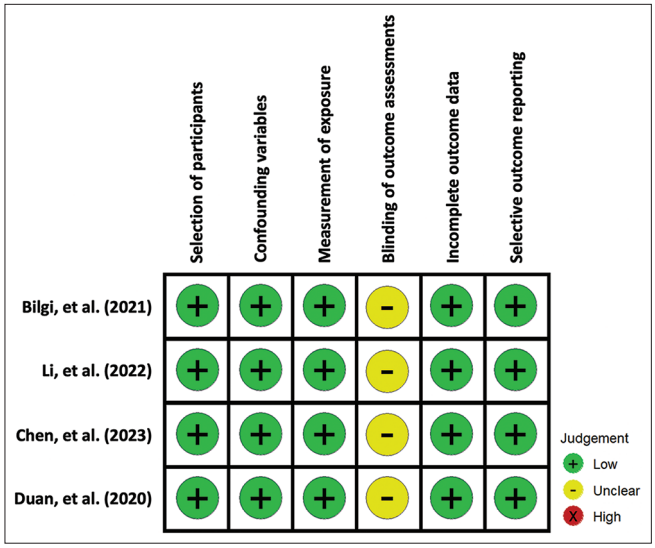

Figure 2: Graph summary of the risk of bias assessment tool for nonrandomized studies.

analyzed descriptively, with the mean and standard deviation used to describe continuous outcomes, while frequencies and percentages were used to describe categorical outcomes. A qualitative approach was used to identify patterns and themes across studies. Publication bias was not assessed in this review, as a meta-analysis was not conducted. However, the review's limitations section mentioned the likelihood of publication bias.

Ethical considerations

This systematic review is based on published studies that have already undergone ethics review and approval by the respective institutions where the research was conducted. As such, ethical considerations related to participant recruitment, informed consent, and data collection were the responsibility of the original authors of the included studies. No primary data collection or involvement of human subjects was conducted for this systematic review. We strictly adhered to ethical guidelines and maintained confidentiality throughout the review process.

RESULTS

Study selection

The PRISMA diagram that follows Figure 1 gives an overview of the gathering procedure. A total of 1624 studies were retrieved from the databases below: Google Scholar: 564 records; Crossref: 534 records; Open Alex: 432 records; Jisc Library Hub Discover: 9 records; Library of Congress: 0 records; PubMed: 4 records; and Scopus: 101 records. Before the screening was done, 33 duplicate records were removed. One thousand six hundred and twenty-three studies were eliminated from the study after the title and abstract were screened. Twenty papers' full texts were examined for eligibility after one's full text could not be obtained. One study was a literature review; four studies were cross-sectional; three excluded trauma patients; three did not examine PLR markers; three did not examine the outcomes of TBI follow-up; one did not focus on a particular TBI case; and one studied pediatric patients. The final four articles were selected as the conclusive studies for the qualitative synthesis.

Study characteristics

Two of the four articles included were retrospective studies, and the other two were prospective studies. The other three studies were from China, whereas one report was published in India. Each article's sample size ranged from 96 to 1.009 patients, for a total sample size of 1.467. The follow-up period they have lasted between 14 days and 6 months. The other two studies comprised individuals with moderate-to-severe TBI (GCS 12), whereas the third study included all TBI patients who underwent unilateral decompressive craniectomy. One study only included individuals with severe TBI (GCS 8). The entire study's characteristic description is visualized in Table 1.

Quality and risk of bias

The NOS instrument for the study quality and the Ro-BANS tool for the risk of bias were then used to evaluate the chosen articles for a more in-depth discussion. For nonrandomized research, two of them were chosen as instruments. The quality assessment result based on the NOS instrument is visualized in Table 1. All of the studies are considered high-quality since they score more than 6 points each, with three studies scoring a maximum of 9 points and the other scoring 8 points. Subsequently, in terms of risk of bias based on the 6-item Ro-BANS questionnaire (visualized in)[Figure 2], all of the studies included have a "low" risk of bias except for the blinding outcome assessments, which all of the studies are "unclear."

Results of synthesis

A retrospective study by Li and Deng (2022) in 170 patients with moderate-to-severe TBI assessed the prognostic ability of the PLR and Rotterdam computed tomography score on the patients' mortality rate. It was found that PLR can be an independent biomarker with a good level of prognostic ability in short-term mortality (30-day mortality), with hazard risk = 1.523 (95% confidence interval [CI] 1.110–2.090, $P = 0.009$) and area under the curve (AUC) 0.711 (95% CI 0.618–0.803, $P < 0.001$).[25]

Another significant result was also found in the prospective study by Duan *et al*. (2020) on 192 TBI patients, which stated

Table 1: Characteristic of study.

No.	Author (year)	Country	Study design	Aim of study	Sample size	Study duration	Population description and setting	Inclusion criteria	Exclusion criteria
1	Bilgi, *et al.* (2021)	India	Prospective observational study	1. To compare certain hematologic parameters assessed by GOSE with the IMPACT and CRASH prognostic model; 2. To evaluate the predictive ability of these parameters for mortality and morbidity	*n*=96	June–November 2019	Adults with moderate and severe isolated TBI patients attending a single institution	1. Age 18–60 years; 2. GCS≤12	1. Severe extracranial injuries; 2. Infection; 3. Autoimmune disease history; 4. Stroke and recent cardiovascular/cerebrovascular disease history; 5. Anticoagulant/antiplatelet drug use; 6. Previous systemic disorders
2	Li and Deng, (2022)	China	Retrospective observational study	To investigate the connection between PLR and short-term mortality in individuals with moderate to severe TBI.	*n*=170	January 2020–December 2021	Adults with moderate and severe TBI patients attending a single institution	1. Admission within 24 hours of injury; 2. GCS<12; 3. Confirmed by CT scan	1. AIS≥3 points in organs other than head and neck; 2. Diagnosed with pregnancy, heart failure, renal failure, tumor, and blood system disease; 3. Use of antiplatelet aggregation medications, glucocorticoids, contraception, and so on; 4. Hospitalization period of 24 h
3	Chen *et al.* (2023)	China	Retrospective observational study	1. To gather data on fundamental clinical features of patients with severe TBI; 2. To compare and analyze the predictive performance of these factors; 3. To investigate the roles of SII and coSII-CO_2 in the prognosis of TBI patients.	*n*=1009	January 2016–December 2021	Adults with severe TBI patients attending three institution	1. Primary TBI caused by car accidents, high fall injury, and external object strikes; 2. Admission within 12 h of injury with complete blood indicator tests; 3. GCS≤8	1. DOA; 2. A history of hematological malignancy, chronic inflammatory illness, or acute infection; and 3. Admission to our hospital following emergency surgery at another hospital.
4	Duan *et al.* (2020)	China	Prospective cohort study	To analyze the major risk factors of TCH and improve the clinical prognosis.	*n*=192	November 2017–November 2019	TBI patients who received unilateral decompressive craniectomy attending a single institution	1. Aged≥18 years; 2. A clear history of head trauma; 3. Admission is within 24 hours of injury and confirmed by a CT scan.	1. Patients who died in ICU or were discharged within 24 hours; 2. History of coagulation dysfunction; 3. Use of anticoagulant drugs.

No.	Author (year)	Defined management	PLR measurement	Time of PLR measurement	Tools for outcome measurement	Outcomes measured	Subgroups reported	Follow-up duration	Quality assessment
1	Bilgi, *et al.* (2021)	Managed surgically as per the neurosurgical protocol for the diagnosed lesion.	Complete blood count, differential count, prothrombin time, INR, APTT, and biochemical markers were all obtained from blood samples.	At admission	Medical database and telephonic interviews	14-day mortality, 6-month mortality, and GOSE at 6 months	Age, gender, period of injury, vital statistics, oxygen saturation, GCS, pupil, localized neurological impairments, brain CT scan, and chest X-ray are all factors to consider. Hemodynamic and respiratory parameters, complete blood count, differential count, prothrombin time, INR, APTT, and biochemical parameters.	14 days and 6 months	9
2	Li and Deng, (2022)	Neurosurgery refers to decompression and/or removal of hematoma and ventricular drainage.	Immediately after admission, blood was collected and transported to the first affiliated Hospital of Zhengzhou University's emergency laboratory, where Coulter LH750 (Beckman-Coulter firm in California, USA) was utilized for testing.	Immediately after admission	Medical database	30-day mortality	Age, gender, hypertension, diabetes, time of injury, categories of injury, Rotterdam CT score, GCS, neurosurgery, blood transfusion, and the platelet and lymphocyte count	1 month	8
3	Chen *et al.* (2023)			At admission	Telephonic interviews and medical database	GOS at 6 months	Age, gender, SBP, pupil, SAH, GCS, CRP, PLT, SII, NLR, PLR, LMR, INR, D-dimer, Glucose, Alb, venous CO2, CK, Cr, Blood electrolytes, and LOS.	6 months	9
4	Duan *et al.* (2020)	received unilateral decompressive craniectomy	The clinical data of participants were investigated. The specific detection method was carried out according to the kit instructions.	Postdecompression surgery	Medical database	GOS at 6 months	Age, gender, GCS, cerebral hernia formation, FBG, Initial hematoma volume, PLT, and PLR	6 months	9

TBI: Traumatic brain injury, PLR: Platelet-to-lymphocyte ratio, GOSE: Extended Glasgow Outcome Scale, GCS: Glasgow Coma Scale, CT: Computed tomography, APTT: Activated partial thromboplastin time, ICU: intensive care unit, GOS: Glasgow Outcome Scale, AIS: Abbreviated injury scale, SBP: Systolic blood pressure, SAH: subarachnoid hemorrhage, CRP: C-reactive protein, INR: International normalized ratio, SII: Systemic immune-inflammation index, NLR: Neutrophil-lymphocyte ratio, LMR: Lymphocyte-Monocyte ratio, CO2: Carbon dioxide, coSII-CO2: systemic immune inflammation index combined with carbon dioxide , FBG: Fasting blood glucose, PLT: Platelet, CRASH: Corticosteroid Randomisation After Significant Head Injury, IMPACT: International Mission for Prognosis and Clinical Trials in Traumatic Brain Injury, TCH: Traumatic Cerebral Hemorrhage, GCS: Glasgow Coma Scale, CRP: C-reactive Protein, ALB: Albumin, DOA: Death on Admission, CK: Creatine Kinase, LOS: Length of Hospital Stay

that the clinical prognosis of TBI was significantly related to PLR levels, along with admission GCS score and PLT ($P < 0.005$). However, PLT and PLR cannot fully reflect the inflammatory state and immune response to TBI; they can only be used to assess inflammatory indicators of hemorrhage and affect coagulation function after TBI.[16]

Further, the significance of PLR-related outcomes as an independent predictor of prognosis in TBI patients was also demonstrated by the study of Chen *et al*. (2023) in 1009 patients assessed using GOS after 6 months with $P < 0.001$ and AUC 0.636 (95% CI 0.660–0.670).[7]

However, opposite results were shown in a prospective study by Bilgi *et al*. (2021) on 96 patients who assessed hematological parameters using GOSE with the IMPACT and CRASH prognostic models and assessed the ability of predictors of mortality and morbidity and found that PLR was said to be less able to be used as a predictor of mortality or a good neurological outcome with AUC 0.58 (95%CI 0.42–0.73; $P = 0.110$), OR 1.01, $P = 0.11$; AUC 0.53 (95%CI 0.38–0.68; $P = 0.360$), respectively, compared to the international normalized ratio, total leukocyte count, and transfusion of blood products, which were considered statistically significant in predicting.[4]

DISCUSSION

The current systematic review examined the evidence for the predictive relevance of PLR measurement in predicting outcomes after TBI. In the qualitative synthesis, four studies were included. In regards to the outcomes measured and duration of follow-up, there was substantial heterogeneity between the included studies. The investigations are restricted to TBI in adults. The majority of studies use the PLR level at admission, and only one study used a blood sample after decompression surgery. GOSE at 6 months was used as a measure of outcome in two of the four investigations, whereas mortality follow-up spanning from 14 days to 6 months and GOSE at 6 months were used in the other two.

PLR clinical implication

PLR is a simple and routine laboratory test that can be performed and evaluated instantly in TBI patients. PLR is linked to systemic nonspecific inflammation and is associated with a bad prognosis for a variety of illnesses. Platelets play an essential part in malfunctioning the blood-brain barrier (BBB) after a TBI. Platelets cling to exposed sub-endothelium at sites of vascular damage through a bridge between coagulation factor in the sub-endothelium, resulting in the formation of microthrombi after TBI; if left untreated, platelet aggregation and microvascular blockage may occur in the brain.[20] In the early stages of moderate-to-severe TBI, an imbalance between coagulation and anticoagulation promotes platelet hyperactivation and a drop in platelet count. This spontaneous aggregation, followed by platelet misuse, resulted in secondary platelet depletion, increasing the risk of bleeding.[25]

The proportion and absolute quantity of T-cells reduced dramatically within 24 h after a TBI.[19] Severe TBI has been linked to significant decreases in the proportion and absolute quantity of circulating T-cells.[32,38,42] This decrease, which at first has been observed within the first 24 h of injury,[32,38] and on day four postinjury,[42] is attributable to a substantial decrease in each of CD4+ T helper cells and CD8+ cytotoxic T-cells. The exact processes underlying the aforementioned TBI-induced reduction of the circulating T-cell pool are not understood at this time, but a recent investigation on animal models provides a possible explanation. Nakai *et al*. discovered that administering B2-adrenergic receptor (B2AR) agonists resulted in an immediately noticeable decrease in the number of CD4+ and CD8+ T-cells in the blood, with additional research demonstrating that this lymphopenia was caused by B2AR stimulation inhibiting lymphocyte release from lymph nodes.[33] Due to the fact that TBI causes an increase in circulating catecholamines, lymphocyte retention in lymph nodes might account for the observed significant reduction in circulating T-cells subsequent to TBI.[11,18,19]

Platelets also stimulate the release of inflammatory mediators and interact with a variety of cells, including neutrophils, T lymphocytes, and macrophages, which promote the initiation or exacerbation of the inflammatory process.[2,8] Therefore, a high PLT could indicate an elevated production of cytokines and thrombocyte activation, both of which contribute to a deleterious inflammatory response. In addition, high levels of PLT have been associated with increased perihematomal edema and a poor prognosis at discharge.[45]

One investigation discovered that the PLR has the second-highest accuracy among inflammatory markers, such as the systemic immune-inflammation index, neutrophil-lymphocyte ratio (NLR), and lymphocyte-monocyte ratio. The proposed PLR cutoff value was 190.98×10^9, and a high PLR level indicates a poor prognosis at 6 months after discharge in patients with severe TBI.[7]

Mortality

TBI refers to an insult to the brain that is neither congenital nor degenerative but results from an external physical force. It may result in a lowered or altered state of consciousness and a loss of cognitive or physical function. Globally, TBI is a significant public health concern and remains the primary cause of death.[34] As a sentinel outcome indicator, mortality is utilized to evaluate the performance of healthcare systems and make necessary improvements.[30] In areas with limited

resources, recognizing the mortality risk factors for TBI patients would aid the healthcare provider in allocating resources appropriately and promptly, thereby reducing the mortality rate.[34]

The primary outcomes measured by Bilgi *et al*. were mortality at 14 days and 6 months. The web-based prognostic calculators of IMPACT (http://www.tbi-impact.org/?p14impact/calc.html) and CRASH (http://www.crash.lshtm.ac.uk/Risk%20calculator/index.html) were used to predict the probability of an unfavorable outcome at 6 months and death at 6 months (IMPACT) and 14 days (CRASH). At 14 days, the overall mortality rate was 32%; over the next 6 months, it increased to 44%. CRASH and IMPACT predicted respective mortality rates of 44% at 14 days and 48% at 6 months. A total of 59% of patients had a poor prognosis at 6 months, comparable to the 60% and 57% predicted by CRASH and IMPACT, correspondingly. According to Bilgi *et al*., neither the admission NLR nor the admission PLR were effective predictors of 6-month mortality.[4] Corbett *et al*. discovered that in severe TBI, the platelet count had a modest predictive value (AUC = 0.447, 95%CI = 0.387–0.505) and had no effect on the anticipated chance of a bad outcome at 18 months.[13] In the investigation conducted by Bilgi *et al*., the addition of PLR to IMPACT and CRASH can only marginally improve the prediction of mortality.[4]

PLR, on the other hand, was found by Li and Deng as an independent biomarker with strong diagnostic potential for 30-day all-cause mortality in people with moderate-to-severe TBI. Reduced PLR levels have an independent connection with increased mortality in short-term periods.[25] Low PLR is achieved mostly by lowering platelet count while increasing lymphocyte count. The fundamental mechanism of harm in TBI is capillary and vascular rupture and disruption of the BBB, which begins an interaction between platelets and endothelial cells or subendothelial matrix. This results in the stimulation of platelet adhesion and the formation of platelet emboli at the site of injury in order to maintain hemostasis. In patients with moderate-to-severe TBI, the equilibrium between coagulation and anticoagulation becomes disrupted, causing platelet overactivation and lower platelet counts in the early phase of injury. This sudden aggregation and subsequent excessive consumption of platelets increase the risk of hemorrhage due to secondary platelet depletion. Platelet counts below 175×10^9/L were associated with a greater chance of intracranial hemorrhage progression, and platelet counts below 100×10^9/L were associated with a 9-fold increase in mortality.[37]

PLR has been studied in the context of TBI and its connection with mortality. Multiple studies have investigated the association between PLR and mortality in TBI patients. Li and Deng conducted a study to determine the association between PLR and short-term mortality among individuals with moderate-to-severe TBI. The study of 170 patients revealed a correlation between elevated PLR levels and increased short-term mortality.[25] This study suggests that a high PLR might be used to predict poor outcomes in TBI patients. Anglin *et al*. conducted another trial to assess the impact of platelet and plasma transfusion on prognosis in TBI patients with mild bleeding diatheses. According to the study, platelet transfusion was associated with increased survival in TBI patients with moderate hemorrhage diatheses.[1]

Furthermore, Kleinveld *et al*. conducted a systematic review and meta-analysis of the link between platelet-to-red blood cell ratio and mortality in patients with bleeding trauma. The study discovered that a high platelet-to-red blood-cell ratio was related to better mortality rates in trauma patients.[23] Although this study did not specifically focus on TBI patients, it provides further evidence of the potential impact of platelet-related factors, such as the PLR, on mortality in trauma patients. It is crucial to keep in mind that the PLR is only one of the many factors that can affect TBI patient mortality. Other factors, such as injury severity, age, GCS score, and the presence of coagulopathy, serve crucial functions in determining patient outcomes.[14,44]

GOS

GOS has long been used to describe the outcome of head injury patients as a standard measure.[12] The traditional GOS consists of five categories, whereas the GOSE includes eight. The GOS severity levels are as follows: (1) death, (2) persistent vegetative state, (3) severe disability, (4) moderate disability, and (5) good recovery.[43] There are a variety of methods for specifying the GOS as the primary endpoint. The most common distinction has been between favorable outcomes, which include good recovery and moderate disability, and unfavorable outcomes, which include severe disability, persistent vegetative state, and death.[6]

It is crucial to take into account the expected, if not actual, time to recovery when determining the optimal time to evaluate the efficacy of a drug, as the selection of the time to assess the outcome can drastically alter the results of a clinical trial. Despite the fact that the 6-month GOS has typically been the preferred outcome, a 12-month score may be required. One study, however, examined the transition of GOS-based outcome states from 3 to 6 months post-injury.[9]

A retrospective investigation of TBI was carried out on 192 individuals who had undergone unilateral decompressive craniectomy.[16] After decompressive surgery, the PLR was calculated, patients were followed up 6 months after treatment, and GOS scoring was conducted. It was discovered that PLR, along with other parameters, was substantially correlated with the clinical prognosis of TBI, despite the fact

that PLR could not fully reflect the extent of inflammation and immune response to TBI. Another study evaluating the prognostic value of PLR in patients with severe TBI reveals that patients with a high PLR had an inferior GOS at 6 months compared to those with a low PLR.[7]

The GOSE

A tertiary neurological care center conducted a prospective observational investigation on patients with moderate and severe isolated head injuries. Six months after being admitted, laboratory and clinical parameters were recorded, and the GOSE was obtained for each patient. The GOSE is a widely used tool for assessing the outcome of patients after a brain injury or other neurological events. It comprehensively evaluates a patient's cognitive, physical, and functional abilities. The GOSE score ranges from (1) death, (2) vegetative state, (3) lower severe disability, (4) upper severe disability, (5) lower moderate disability, (6) upper moderate disability, (7) lower good recovery, and (8) upper good recovery, with higher scores indicating better outcomes.[41] A telephone conversation with the patient or caregiver was used to determine the patient's GOSE 6 months after the diagnosis. An undesirable result was determined at 6 months as a GOSE of 4 (upper severe impairment or worse). According to Bilgi *et al*., the admission NLR and PLR were not highly predictive of unfavorable outcomes at 6 months, either when used separately or in conjunction.[4]

There is insufficient research examining the significance of the PLR on the GOSE score. Nonetheless, studies have demonstrated that PLR is associated with a variety of clinical outcomes in various medical conditions. For instance, elevated PLR has been associated with an unfavorable prognosis and decreased survival in patients with gastric cancer.[15] Comparably, an elevated PLR has been found to be an unfavorable prognostic factor in patients with multiple myeloma.[39] These findings indicate that the PLR may have implications for patients with TBI's overall functional outcomes, including the GOSE score.

These findings imply the possibility that PLR may serve as a marker of systemic inflammation and disease burden, which may influence the functional outcomes of a variety of medical conditions. In conclusion, while there is minimal research on the influence of the PLR on the GOSE score in patients with TBI, studies have demonstrated that the PLR is connected with numerous clinical outcomes in diverse medical situations. Consequently, it is plausible that the PLR may have implications for overall functional outcomes, such as the GOSE score, in patients with TBI. Additional research is required to establish a direct correlation between the PLR and the GOSE score in this population. The study about the correlation between GOSE and PLR is worth knowing because it can provide additional information about a patient's overall health and prognosis. By understanding the correlation between GOSE and PLR, healthcare professionals can better understand a patient's condition and tailor their treatment accordingly.

Therefore, the PLR should be viewed as a component of a comprehensive evaluation of TBI patients and not as a predictor of mortality and prognostic factor in its own right. In a broader sense, the PLR in relation to TBI patient mortality and patient outcomes has been studied. According to studies, a higher PLR is associated with an increase in short-term mortality and less favorable results in patients with moderate-to-severe TBI. When evaluating TBI patients' mortality risk and clinical prognosis, it is crucial to consider the PLR in addition to other clinical factors. Despite the limited number of evidence regarding PLR in TBI patients, current evidence suggests that a higher PLR ratio correlates with a poor prognosis in TBI patients. In addition to the foregoing, drawing solid conclusions is difficult due to the variability of the included studies in terms of measurement intervals, sites of follow-up, and definitions of differing findings. Additional research is necessary to corroborate the association between the PLR ratio and TBI prognosis.

Limitation of study

The included studies in this systematic review varied in study design, sample size, outcome measures, and methodologies. Several studies included in the review were retrospective, which may introduce inherent limitations such as recall bias, incomplete data, and selection bias. Retrospective studies rely on existing medical records, which may lack standardized assessments and measurements. Although efforts were made to conduct a comprehensive search, the number of studies included in the review was relatively small. There is a possibility of publication bias in systematic reviews, where studies reporting significant associations between PLR and outcomes are more likely to be published, while studies with null or nonsignificant findings may be underrepresented.

CONCLUSION

The study finding suggests that the PLR has the potential as an independent prognostic predictive marker in adult TBI patients. PLR levels have been linked to a variety of negative clinical outcomes, including short-term mortality and functional outcomes, in both retrospective and prospective investigations. However, one study shows that PLR may have limited value as a predictor of mortality or favorable neurological outcomes compared to other hematological parameters.

Despite the conflicting results, the majority of studies included in this systematic review support the potential of PLR as a prognostic marker in adult TBI patients. The use of PLR may mainly be used in rural practice due to

the advantages of being simple, low-cost, and routinely performed hematological examination. Incorporating PLR into clinical practice may aid in identifying patients at higher risk of adverse outcomes, enabling more vigilant monitoring and targeted interventions. However, it is essential to note that further prospective studies with larger sample sizes, standardized methodologies, and consideration of other relevant variables are necessary to establish the clinical utility of PLR in TBI management.

Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent was not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that they have used artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript or image creations.

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