

# Characteristics of the Neutrophil Lymphocyte Ratio in Patients with Neurological Disorders Against Infectious Disease Outcomes During Hospitalization in the Intensive Room of Prof. Dr. I.G.N.G Ngoerah Hospital, Denpasar, Bali from February 2019 to February 2022

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## ABSTRACT

**Introduction:** The neutrophil-lymphocyte ratio (NLR) biomarker is one of the biomarkers used to assess the possible outcome of infection in patients experiencing the acute phase of a disease. Patients with a diagnosis in the field of neurology tend to have the possibility of a long-extended stay, which is closely related to the risk of infection during treatment. Neutrophil-lymphocytes ratio (NLR) examination can provide a quick and easy prognostic estimation, especially in patients with an extended stay in the hospital.

**Methods:** This study is a descriptive analysis with a retrospective study that describes the characteristics of neurological patients with an infectious outcome through laboratory results of the serum neutrophil-lymphocyte ratio (neutrophil lymphocytes ratio). The data collected were gender, NLR (Neutrophil lymphocytes ratio) parameter sign, and outcome of infectious diseases such as pneumonia, sepsis, meningoencephalitis, and urinary tract infections during treatment with neurological diagnosis as the underlying illness caused the patient to be treated. Samples were taken based on the medical record data of treated patients. They meet the inclusion criteria, which are then

processed descriptively through the number and percentage.

**Results:** A total of 90 research sample data were included in the study, the number of male correspondents was 53 people (58.9%), and women were 37 people (41.1%). Analysis of the research sample data showed that the serum neutrophil-lymphocyte ratio level during treatment in the intensive room was 18.03%, with a standard deviation of 19.9. Of the total patients with pneumonia, 84 people (93.3%), ten people (11.1%) experienced meningoencephalitis during treatment in the intensive room, 66 people (73.3%) had sepsis, and 25 people (27.8 %) had a urinary tract infection with the mean ratio of neutrophil to lymphocyte for the outcome of the disease ranging from 2.3 to 75.1

**Conclusion:** Patients undergoing treatment in the intensive room of I.G.N.G Prof Ngoerah Hospital from February 2019 to February 2022 tend to experience an increase in the neutrophil-lymphocyte ratio above the average value, which is above 3.13, with an infection outcome during treatment.

This study uses a number of ethical exemptions as follows 2929/UN14.2.2.VII.14/LT/2022

**Keywords:** Infection Outcome, Neurological abnormalities, Neutrophil lymphocytes ratio (NLR)

## **INTRODUCTION**

Abnormalities in the field of neurology have many variations in incidence, ranging from the mildest to the most severe. Patients with neurological disorders tend to be treated for a more extended period. Prolonged treatment in the intensive care unit for patients with neurologic cases often results in poor outcomes and even death. [1,2] Diseases in the field of neurology are very diverse, ranging from acute to chronic phases with various symptoms that require clinicians to provide the best care. Biomarkers in blood tests are one method that is fast and accurate in giving. Leukocytes are biomarkers that clinicians have widely studied in the field of neuroscience. The neutrophil-lymphocyte ratio, known as the NLR, is the result of dividing absolute neutrophils with absolute lymphocytes, a marker for inflammatory and infectious processes. [2,3] Inflammation is a process that often occurs in the course of a disease, both in the field of neurology and other disease fields. Several studies illustrate the association between assessed biomarkers and clinical outcomes of patients treated in a hospital. In the last decades, NLR (Neutrophil lymphocyte ratio) has been known to be associated with the incidence of sepsis, death from infection, pneumonia, worsening of the condition of patients with acute stroke, head injury, cerebral hemorrhage, meningitis, and autoimmune diseases in the field of neurology. [2]

## **METHODS**

This research is descriptive with a retrospective study. Namely, the study describes the characteristics of patients with neurological complaints while being treated

in the intensive room (ICU) at Prof I.G.N.G Ngoerah Hospital. It has a high laboratory value of neutrophil-lymphocyte ratio with secondary infection outcomes such as pneumonia, intracranial infections, sepsis, and urinary tract infections. Samples were collected from February 2019 to February 2022. The data collected were demographic data on the distribution of the research sample, which included primary diseases in the field of neurology, gender, and the patient's external conditions during hospitalization, regardless of the return condition. Examination results include parameters of a high neutrophil-lymphocyte supporting an infectious state. The research sample was taken based on the patient medical record data, where all patients who met the inclusion criteria were included in this study. In this study, the number of samples was 90 patients. The inclusion criteria for the patients were as follows:

1. Neurological diagnosis:  
The patient was diagnosed with a neurological disorder from the initial admission to the intensive care unit
2. Identification of the neutrophil-lymphocyte ratio during intensive care
3. Outcome Infections such as pneumonia, central nervous system infections, sepsis, and urinary tract infections

## **RESULT**

This study used a sample of patients with underlying disorders in the neurology field at Prof I.G.N.G Ngoerah Hospital, Denpasar, Bali, from February 2019 to February 2022. A total of 90 patients were included in this study. The respondents in this study have age, sex, the ratio of neutrophils and lymphocytes, and the external conditions of patients who experience an infectious process during treatment in the intensive room.



The figure above shows the mean neutrophil-lymphocyte ratio. The average of 90 correspondents obtained serum neutrophil-lymphocyte ratio (NLR) levels during treatment in the intensive room was 18.03%, with a standard deviation of 19.9.

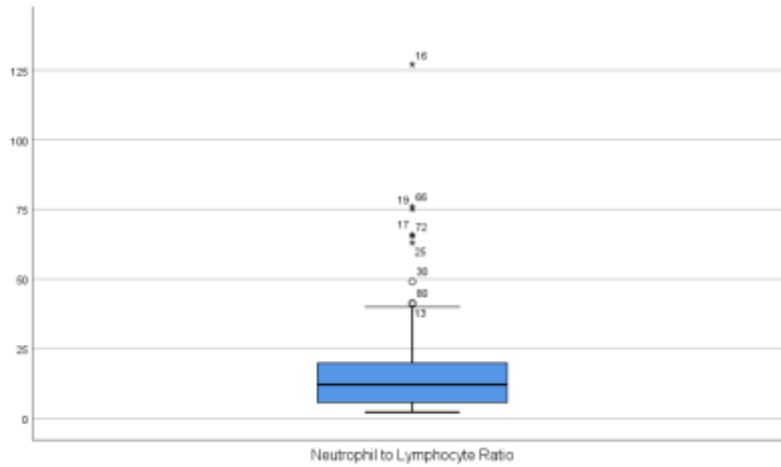


Figure 4. The plot of neutrophil to lymphocyte ratio

Patients treated in the intensive ward of I.G.N.G Prof. Ngoerah Hospital from February 2019 to February 2022 have varying neutrophil-to-lymphocyte ratios, with a tendency to increase the value of the neutrophil ratio during treatment.

Table 2. Outcome diagram of pneumonia and neutrophil-lymphocyte ratio (NLR)

| Pneumonia |           |         |               |                    |
|-----------|-----------|---------|---------------|--------------------|
|           | Frequency | Percent | Valid Percent | Cumulative Percent |
| Valid     | Yes       | 84      | 93.3          | 93.3               |
|           | No        | 6       | 6.7           | 100.0              |
| Total     | 90        | 100.0   | 100.0         |                    |

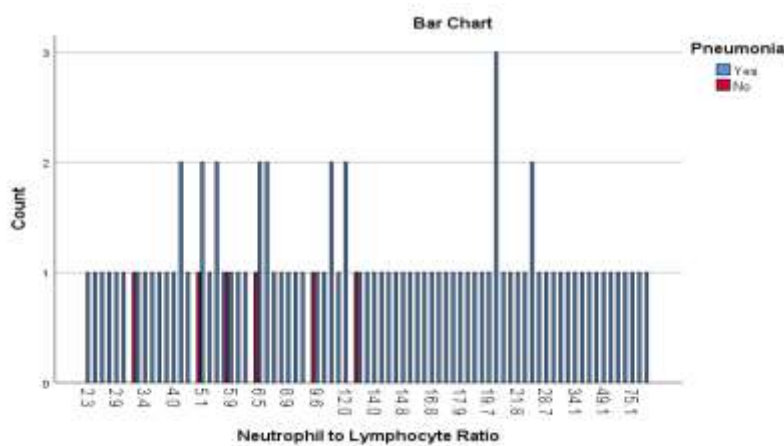


Figure 5. Outcome diagram of pneumonia and neutrophil-lymphocyte ratio (NLR)

In the diagram above, it can be seen that the total number of patients with pneumonia was 84 people (93.3%) of the total number, the respondents were 90 people, and the bar chart shows that most of the correspondents who underwent treatment had an output or clinical outcome with pneumonia during therapy in the intensive room. The lowest ratio of neutrophils to lymphocytes obtained during treatment was 2,3, with the highest percentage of 75,1. In addition to having pneumonia infection outcomes, patients

undergoing intensive care also experience sepsis conditions that occur with clinical pneumonia and other clinical conditions such as meningoenkephalitis and urinary tract infections. In the diagram above, it can

be seen that a low neutrophil ratio can also experience the outcome of sepsis during intensive care, with as many as 66 people (73.3%) out of a total of 90 correspondents.

Table 3. Percentage of sepsis outcome in correspondence

| Sepsis |       |           |         |               |                    |
|--------|-------|-----------|---------|---------------|--------------------|
|        |       | Frequency | Percent | Valid Percent | Cumulative Percent |
| Valid  | Yes   | 66        | 73.3    | 73.3          | 73.3               |
|        | No    | 24        | 26.7    | 26.7          | 100.0              |
|        | Total | 90        | 100.0   | 100.0         |                    |

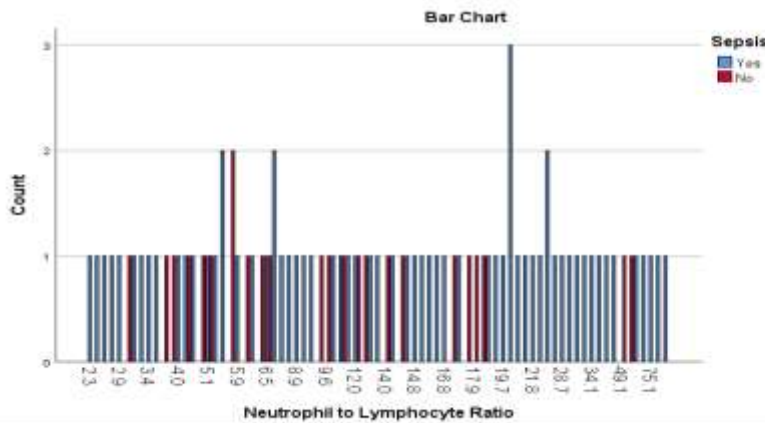


Figure 6. Percentage of sepsis outcome in correspondence on the bar chart

Table 4. Outcome of patients with meningoenkephalitis

| Meningoenkephalitis |       |           |         |               |                    |
|---------------------|-------|-----------|---------|---------------|--------------------|
|                     |       | Frequency | Percent | Valid Percent | Cumulative Percent |
| Valid               | Yes   | 84        | 93.3    | 93.3          | 93.3               |
|                     | No    | 6         | 6.7     | 6.7           | 100.0              |
|                     | Total | 90        | 100.0   | 100.0         |                    |

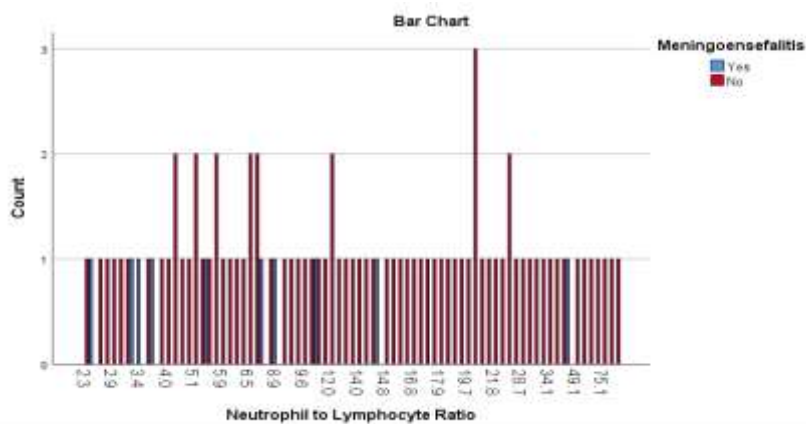


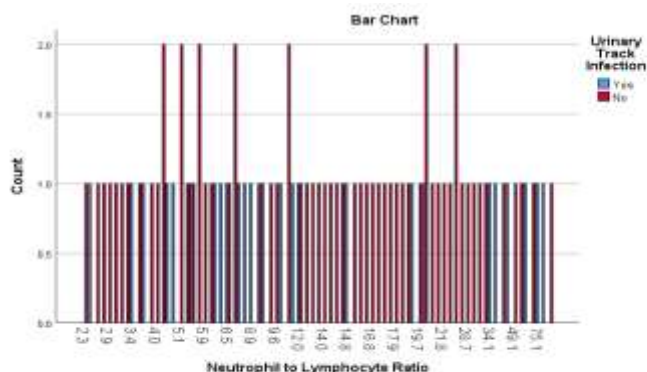
Figure 7. Outcome of patients with meningoenkephalitis

Figure 7 and Table 4 above shows that of 90 correspondents, 10 (11.1%) experienced meningoenkephalitis during treatment in the intensive room. Patients with

meningoenkephalitis during treatment tend to have a neutrophil ratio that varies from 2.9 to 40.

**Table 5. Urinary tract infection with neutrophil to lymphocyte ratio**

| Urinary tract infection |     | Frequency | Percent | Valid Percent | Cumulative Percent |
|-------------------------|-----|-----------|---------|---------------|--------------------|
| Valid                   | Yes | 25        | 27.8    | 27.8          | 27.8               |
|                         | No  | 65        | 72.2    | 72.2          | 100.0              |
| Total                   |     | 90        | 100.0   | 100.0         |                    |



**Figure 8. Urinary tract infection with neutrophil to lymphocyte ratio**

Patients undergoing intensive care tend to develop urinary tract infections during treatment. From the above data obtained from 90 correspondents, as many as 25 people (27.8%) had urinary tract infections, with an average ratio of neutrophils to lymphocytes above 2.3 to 75.1. From the data above, it can be concluded that during treatment in the intensive care unit, patients with neurological disorders can experience other disease outcomes such as pneumonia, sepsis, intracranial infections, and urinary tract infections. Patients with infectious effects during treatment tend to have an increased neutrophil-to-lymphocyte ratio (NLR).

## DISCUSSION

Findings biomarkers related to infection markers, such as NLR (neutrophil-lymphocyte ratio), can be checked quickly through peripheral blood sampling. Patients with neurological complaints treated in the intensive care unit (ICU) often experience worsening clinical conditions with various causes, thus increasing the amount of hospital financing. Before recognizing NLR as a predictor of infection outcome, several markers such as C-Reactive protein (CRP) and procalcitonin were also evaluated for clinical outcomes in patients at risk of infection during treatment.<sup>[1,2,3]</sup> Patients

with a high neutrophil-lymphocyte ratio tend to have a poor prognosis when admitted to the neutrophil-lymphocyte. A cohort study in China concluded that high NLR was closely associated with patient mortality. Neutrophils are biomarkers that show the quality of a person's resistance to pathogens such as bacteria and are part of white blood cells as much as 40-60%.<sup>[4,5]</sup> In the circulation of healthy people, neutrophils in the body undergo a resting phase, where neutrophils become active if induced by bacterial products and cytokines or chemokines such as TNF-, gm-CSF, IL-8 and IFN- $\gamma$ , and activated neutrophils move from the site of infection or inflammation by activating signals to kill bacteria.<sup>[4,5,6]</sup> NLR (Neutrophil lymphocyte ratio) is an inflammatory marker for systemic inflammation, where the number of absolute neutrophils is divided by the number of absolute lymphocytes.<sup>[7]</sup> Neutrophil to lymphocyte ratio is one of the most studied biomarkers to diagnose sepsis.<sup>[7,8,9]</sup> These markers can be divided into risk prediction or prognosis, diagnosis and monitoring, and outcome of a disease. As an inflammation marker, lymphocytes protect from components of the adaptive immune system (Adaptive immune response).<sup>[9,10]</sup> The relationship between NLR and several disease outcomes is as follows:



- The neutrophil-lymphocyte ratio in patients with chronic diseases such as diabetes and hypertension increase due to normal inflammatory processes. This relationship between the percentage of neutrophils and lymphocytes in metabolic syndrome tends to grow in the inflammatory phase. NLR can predict the prognosis of metabolic diseases such as type 2 diabetes mellitus and malignancy, especially on the outcome of the given therapy. From a high neutrophil to lymphocyte ratio, it can determine the staging of metabolic disorders in patients with chronic disease.
- In diseases with cardiac symptoms also associated with a severe inflammatory process. Endothelial dysfunction associated with atherosclerotic plaques often reflects neutrophilia and lymphopenia. Neutrophils will be active in the early stages of heart damage until atherosclerosis occurs. This is mediated by the release of lipid mediators in the blood until atherosclerosis and infiltration of atherosclerotic arteries appear. Under some conditions, this increased neutrophil activity is

associated with cell maturation, which inhibits nuclear segmentation. From this, it can be concluded that neutrophilia originates from segmental cells since the atherosclerosis process in chronic inflammation occurs. Neutrophils will activate macrophages; this requires lipid mediation. Macrophages will express IL-6, CD40, and CD80 in forming foam cells, whereas neutrophils will also express atherogenic factors such as chemokines and cytokines. [12,13] When there is damage to the myocardial tissue, inflammation will occur, so the number of neutrophils in the blood will increase.

- The ratio of neutrophil lymphocytes to the incidence of head injury is also closely related, namely in the primary (early) stage of damage and a secondary stage involved in decreased blood and oxygen flow, edema, ischemia, metabolic and endocrine dysfunction, oxidative stress, and failure of homeostatic processes. All of these processes lead to activation and accumulation of cells that play a role in the inflammatory process.

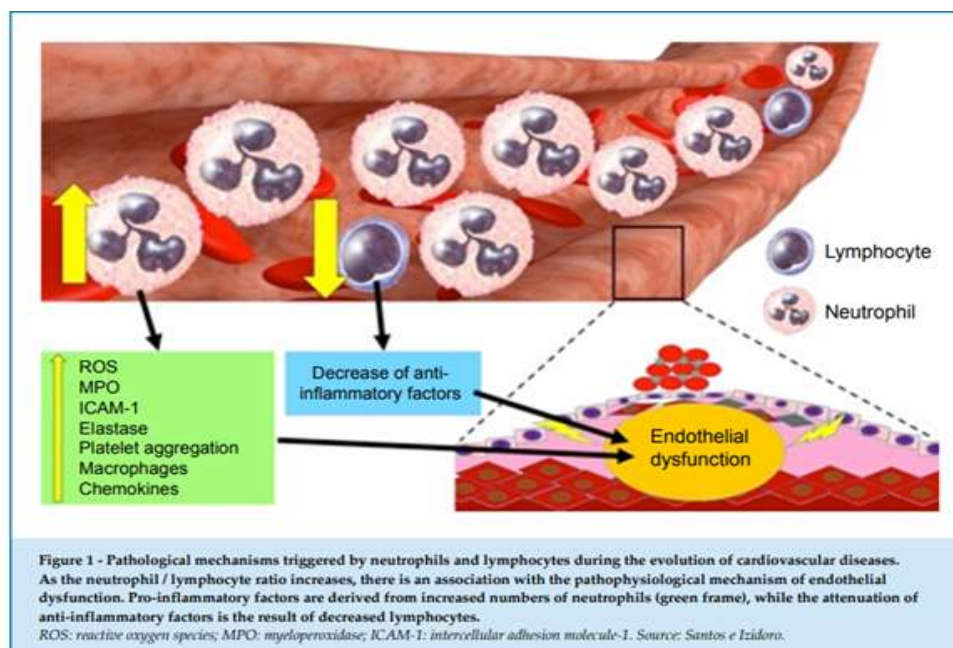


Figure 9. Mechanism of neutrophil activation in myocardial tissue damage.<sup>[1]</sup>

- Damage to the blood-brain barrier (BBB) will cause an increase in leukocytes that migrate to the inflamed area and cause significant secondary changes. Neutrophils enter the lesion site in the brain within one hour, damage the parenchyma and stimulate cellular damage in brain tissue. [13,14] Free radicals will induce membrane damage, and the presence of tight junction proteins such as occludin and claudin through P13K/AKT will damage the blood-brain barrier (blood-brain barrier).
- An elevated neutrophil-to-lymphocyte ratio may also be experienced in stroke patients undergoing thrombolysis and subsequent treatment. Based on the investigation of a retrospective cohort study conducted at the Taipei Veterans

General Hospital by Chung Ting Chen et al., it was found that out of 100 patients who underwent r-TPA as standard therapy for acute ischemic stroke, a high neutrophil-lymphocyte ratio was found in post-stroke patients undergoing r-TPA treatment where r-TPA affects the condition of the peripheral blood cell count. The affected peripheral blood cells include leukocytes, macrophages, lymphocytes, platelets, and fibrin. This study found that  $NLR > 5.9$  will affect the outcome of patients receiving r-TPA therapy for 90 days after stroke for stroke caused by large vessel ischemic stroke.

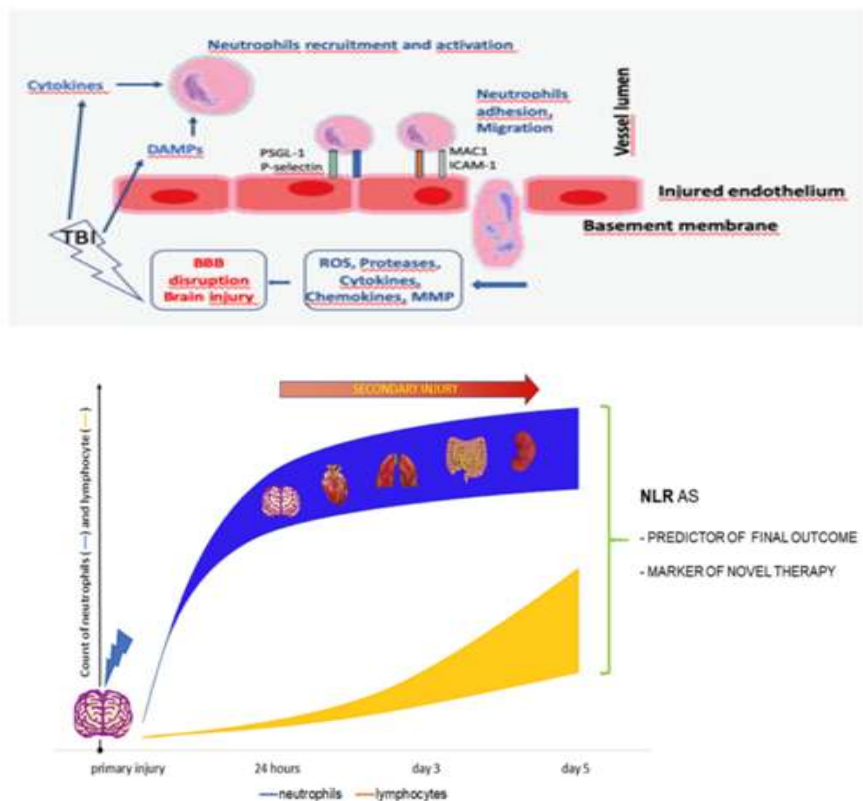


Figure 10. NLR activation process in head injury. [2]

- Sepsis is a clinical condition often associated with an increased neutrophil-lymphocyte ratio in patients undergoing treatment in the ICU. The ratio of

neutrophil to lymphocyte can be used as an indicator of early diagnosis when a patient has symptoms of sepsis



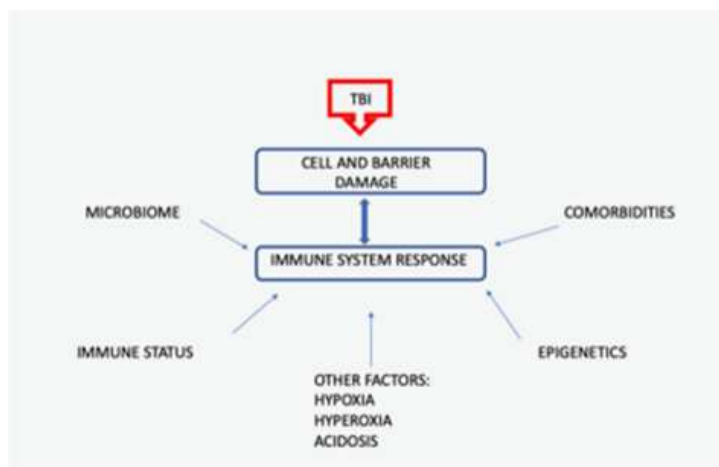


Figure 11. Immune system related to head trauma.<sup>[2]</sup>

Figure 3 shows that the damage to the barrier and cells will activate the immune system by activating neutrophils and lymphocytes in this process.<sup>[2]</sup> Immune cells, such as neutrophils, monocytes, astrocytes, and microglia, are crucial components of the inflammatory process. Inflammatory reactions in head injuries will be stimulated by molecular processes that occur rapidly after the head injury. In healthy people, tight junctions between endothelial cells will stop the penetration of neutrophils into the nervous system. Neutrophils in inflammatory conditions can be seen for several hours to five days.<sup>[14]</sup> As a result of the pathological process that occurs in head injury will result in the entry of large numbers of neutrophils at the lesion site and affect the blood-brain barrier damage secondarily. Neutrophils enter the lesion site in the brain within one hour, destroying the parenchyma and inducing cellular damage to brain tissue.<sup>[13,14]</sup> The number of neutrophils will increase dramatically in 24 hours; these cells invade arterioles and venules within 5 minutes. Under these conditions, the IL-23, IL-17, and G-CSF axis components that suppress death and neutrophil formation will increase. Free radicals will induce membrane damage, and the presence of tight junction proteins such as occludin and claudin through P13K/AKT will damage the blood-brain barrier (blood-brain barrier). As

a result of this damage, a vascular response can be observed within 4 to 8 hours after the head injury.<sup>[13]</sup>

## CONCLUSION

Patients with neurological disorders can experience worsening conditions and fall into other systemic disease conditions such as pneumonia, sepsis, intracranial infections, and urinary tract infections. To predict these outcomes, parameters from peripheral blood can be used, namely the examination of the neutrophil-lymphocyte ratio level. Patients undergoing treatment in the intensive room at I.G.N.G Prof Ngoerah Hospital from February 2019 to February 2022 tend to experience an increase in the neutrophil-lymphocyte ratio above the average value above 3.13. The most common infectious outcome conditions were pneumonia and sepsis, with the most common underlying disease being non-haemorrhagic stroke.

## Declaration by Authors

**Ethical Approval:** Approved

**Acknowledgement:** None

**Source of Funding:** None

**Conflict of Interest:** The authors declare no conflict of interest.

## REFERENCES

1. Santos, H.O. and Izidoro, L.F.M. (2018) 'Neutrophil-Lymphocyte Ratio in Cardiovascular Disease Risk Assessment',

- International Journal of Cardiovascular Sciences* [Preprint]. Available at: <https://doi.org/10.5935/2359-4802.20180038>.
- Siwicka-Gieroba, D. and Dabrowski, W. (2021) 'Credibility of the Neutrophil-to-Lymphocyte Count Ratio in Severe Traumatic Brain Injury', *Life*. Available at: <https://doi.org/10.3390/life11121352>
  - Liu, C.C. et al. (2019) 'Neutrophil-to-lymphocyte ratio as a predictive marker of metabolic syndrome', *Medicine (United States)*, 98(43). Available at: <https://doi.org/10.1097/MD.00000000000017537>.
  - Wright, H.L. et al. (2010) 'Neutrophil function in inflammation and inflammatory diseases', *Rheumatology*. Available at: <https://doi.org/10.1093/rheumatology/keq045>.
  - Martins, E.C. et al. (2019) 'Neutrophil-lymphocyte ratio in the early diagnosis of sepsis in an intensive care unit: A case-control study', *Revista Brasileira de Terapia Intensiva*, 31(1). Available at: <https://doi.org/10.5935/0103-507X.20190010>.
  - Dionisie, V. et al. (2021) 'Neutrophil-to-lymphocyte ratio, a novel inflammatory marker, as a predictor of bipolar type in depressed patients: A quest for biological markers', *Journal of Clinical Medicine*, 10(9). Available at: <https://doi.org/10.3390/jcm10091924>.
  - Imtiaz, F. et al. (2012) 'Neutrophil lymphocyte ratio as a measure of systemic inflammation in prevalent chronic diseases in Asian population', *International Archives of Medicine*, 5(1). Available at: <https://doi.org/10.1186/1755-7682-5-2>.
  - Salciccioli, J.D. et al. (2015) 'The association between the neutrophil-to-lymphocyte ratio and mortality in critical illness: An observational cohort study', *Critical Care*, 19(1). Available at: <https://doi.org/10.1186/s13054-014-0731-6>.
  - Song, S.Y. et al. (2019) 'Clinical Significance of Baseline Neutrophil-to-Lymphocyte Ratio in Patients With Ischemic Stroke or Hemorrhagic Stroke: An Updated Meta-Analysis', *Frontiers in Neurology*. Available at: <https://doi.org/10.3389/fneur.2019.01032>.
  - Liu, X. et al. (2016) 'Prognostic Significance of Neutrophil-to-Lymphocyte Ratio in Patients with Sepsis: A Prospective Observational Study', *Mediators of Inflammation*, 2016. Available at: <https://doi.org/10.1155/2016/8191254>.
  - Nam, K.W. et al. (2018) 'High neutrophil-to-lymphocyte ratio predicts stroke-associated pneumonia', *Stroke*, 49(8). Available at: <https://doi.org/10.1161/STROKEAHA.118.021228>.
  - Sari, R. et al. (2019) 'Neutrophil to lymphocyte ratio as a predictor of treatment response and mortality in septic shock patients in the intensive care unit', *Turkish Journal of Medical Sciences*, 49(5). Available at: <https://doi.org/10.3906/sag-1901-105>.
  - Giede-Jeppe, A. et al. (2021) 'Neutrophil-to-lymphocyte ratio is associated with increased cerebral blood flow velocity in acute bacterial meningitis', *Scientific Reports*, 11(1). Available at: <https://doi.org/10.1038/s41598-021-90816-0>.
  - Levochkina, M. et al. (2021) 'Neutrophil-to-lymphocyte ratios and infections after traumatic brain injury: Associations with hospital resource utilization and long-term outcome', *Journal of Clinical Medicine*, 10(19). Available at: <https://doi.org/10.3390/jcm10194365>.

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