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Neutrophil to Lymphocyte Ratio (NLR) to Predict Mortality in Patients with Sepsis

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ABSTRACT

Background: Sepsis, a leading cause of infection-related death, often results in high mortality despite advances in treatment. Early detection of high-risk patients is essential for improving outcomes. The Neutrophil-to-Lymphocyte Ratio (NLR) is a simple, inexpensive biomarker obtained from a complete blood count (CBC) that reflects the balance between inflammation and immune response. While NLR has been shown to predict outcomes in various conditions, its prognostic value in sepsis remains debated. **Objective:** This study aims to assess the predictive value of NLR for mortality in sepsis patients, determining whether higher NLR at hospital admission correlates with worse outcomes. **Material and Methods:** A retrospective analysis was conducted from July 2024 to December 2024 at tertiary care hospital in Quetta with 200 sepsis patients. NLR was calculated from CBC results at the time of admission, and patients were categorized based on survival and clinical outcomes. The relationship between NLR, disease severity, length of stay, and comorbidities was also examined. **Results:** Higher NLR values were significantly associated with increased mortality, prolonged hospital stays, septic shock, and higher mechanical ventilation requirements. Patients with NLR >10 had the highest mortality rate (83.3%). **Conclusion:** This study concludes that Neutrophil to Lymphocyte Ratio (NLR) has strong predictive value in sepsis severity and mortality. Higher NLR correlates with increased mortality, longer hospital stays, and more septic shock, with values above 10 being significant. It serves as a cost-effective biomarker, especially in resource-limited settings, aiding early detection and intervention. Future research should validate NLR thresholds and explore its role in sepsis monitoring and clinical protocols.

INTRODUCTION

Despite a decrease in mortality, there is still a widespread lack of awareness, delayed identification, and inadequate management (K.-M. Kaukonen et al., 2014; K. Reinhart, et al., 2013). The prompt and accurate identification of patients at high risk of mortality is an essential part of effective sepsis treatment (R. P. Dellinger, M. M. Levy, A. Rhodes et al., 2013). The most common cause of death among infected individuals is a septovirus infection. In spite of advancements in antibiotic treatment and haemodynamic management, it continues to rank among the top causes of death in the ICU. That year, 2008, Vincent J.L. Failure to adequately regulate the host's response to infection can lead to sepsis, a potentially fatal organ failure. It was over $20 billion in 2011 alone, making it a huge public health risk (Torio CM; 2019). (Author Iwashyna, 2010). Severe and persistent new cognitive impairment and functional handicap are common among sepsis survivors, placing a heavy cost on healthcare systems and society around the world. Sepsis, a complex condition, is still a big issue in both developed and developing nations. Globally, septic shock and severe sepsis remain top killers, and the reported morbidity of sepsis has been steadily rising. S. Vera et al. (2015) noted that while many clinical biomarkers have been extensively studied, only a few numbers have actually been implemented in clinical practice. (Et al., 2016; Dong Yun Hong, Kim Jong-Wook, Paik Jong-Han)In 2015, Leder, Hanson, Arnold, and Boy published Researchers are always trying to find better infection markers to utilize for predicting sepsis outcomes, according to a 2015 study by Hur, Kim, and Kim et al. A complete blood count can be used to determine the neutrophil-to-lymphocyte ratio (NLR), which is one of the easily accessible biomarkers. There is still no agreement on how NLR levels relate to clinical prognosis in sepsis patients, even though there is mounting evidence that NLR is a predictor of poor survival in other clinical contexts, like patients with

cardiovascular diseases (B. Ayc ¸a, F. Akln, O. Celiketal., 2015) and cancer patients (R. Zahorec, 2001). It was published in 2014 by M. H. Kang, S.-I. Go, H.-N. Song, and team. Despite prior research showing no correlation between NLR and mortality in sepsis patients, a new study (J.D. Salciccioli, D.C. Marshall, M.A. Pimentel et al., 2015) demonstrated that NLR reversed itself according to the date of death within the setting of infection. (Friedrich and colleagues, 2015) Thus, developing methods for earlier identification of patients at high risk for sepsis could be a straightforward approach to improving patient outcomes. Patients with sepsis have their treatment trajectories impacted by the diagnostic, theranostic, and prognostic capacities of plasma biomarkers. In the year 2018 the group headed by van Engelen T. Research has shown that C-reactive protein (CRP) and procalcitonin (PCT) can help assess the severity of sepsis, guide therapy recommendations for critically ill patients, and measure treatment efficacy. throughout the research conducted by Tschaikowsky et al. in 2011. But we must find a more powerful biomarker soon because they are not specific enough and do not have enough individual prognostic value. found in Lichtenstern et al.'s 2012 research. The balance between inflammation caused by neutrophils and the immunological response mediated by lymphocytes is reflected in NLR. Elevated NLR has been linked to systemic inflammation, immunological suppression, and poor outcomes in multiple illnesses, including sepsis, according to Zahorec (2001). This study seeks to analyse the predictive power of NLR in determining the likelihood of death in patients with sepsis, offering doctors a straightforward biomarker for gauging risk and making decisions.

LITERATURE REVIEW
It is one of the global main causes of death and is a potentially fatal organ failure due to a hyperdysregulated host response to infection (Singer et al., 2016). To improve patient outcome, early detection and risk assessment is required. Biomarkers such as the neutrophil to lymphocyte ratio (NLR) have recently become more important in the prognostic prediction in sepsis (Zhang et al., 2019). It is a very easy and relatively inexpensive marker of inflammation found in a regular CBC and used as a reflection of the balance of innate (neutrophils) and adaptive (lymphocytes) immune responses (Forget et al., 2017). This review of the literature will determine if NLR can add predictive mortality to the prediction of clinical outcomes and disease severity in sepsis patients.

Pathophysiology of Sepsis and the Role of NLR
However, for sepsis situation the pro-inflammatory and anti-inflammatory reaction occurs in combination. In this capacity as important components of the innate immune response to remove pathogens and promote

inflammation and tissue damage (Hotchkiss et al., 2016), neutrophils are important. However, during sepsis, the lymphocytes decrease and are linked to adaptive immunity whereas a bad prognosis is related to immunological suppression (Venet & Monneret, 2018). An indirect indicator of such an imbalance in the immune system is the NLR. The higher NLR has been associated with more type and more severe sepsis, and with sepsis mortality (Liu et al., 2020).

Clinical Utility of NLR in Sepsis Prognosis
There have been several researches on the predictive utility of NLR in patients with the sepsis. Liu et al., 2020, reported a meta-analysis of which higher NLR was greatly linked to better mortality of sepsis patients. The study found that NLR has a very powerful prediction of NLR, when compared to PCT and CRP." A retrospective analysis of 1,200 sepsis patients also found a high mortality of 28 days with NLR ≥ 10 in Jiang et al. (2019). The combination of NLR and the results of both Acute Physiology and chronic health evaluation II (APACHE II) and Sequential Organ Failure Assessment (SOFA) was suggested by the authors so that additional information can be used to achieve better risk classification. There has been multiple research regarding the prediction use of NLR in patients with sepsis. Liu et al., (2020) has conducted a meta-analysis, which has demonstrated a substantial link between the NLR levels and mortality in sepsis patients. The study included 14 observational studies with more than 3000 patients, the overall providing similar value for predicting NLR as to more conventional biomarkers like procalcitonin (PCT) and C-reactive protein (CRP). Jiang et al. (2019) in another retrospectively evaluated cohort of 1,200 sepsis patients reported that a 28-day mortality was strongly associated with an NLR greater than 10. The authors combine NLR with APACHE II and Sequential Organ Failure Assessment (SOFA) results in order to improve risk classification.

Comparison with Other Biomarkers
Currently, most traditional sepsis indicators used in clinical practice include lactate, PCT, and CRP. Although such acute phase protein CRP is frequently used to detect inflammation, it is not specific for the sepsis (Pepys & Hirschfield, 2003). PCT also is more targeted to bacterial infections and could be too expensive or hard to get as it could not be accessible in resource deprived environments (Rhee et al., 2017). It is, however, very attractive as a sepsis prognosis biomarker since it is an easy to measure "thing" that does not require additional testing than standard blood work (Zahorec, 2021), and compared NLR to traditional biomarkers in several studies. A study by Huang et al. (2020) has reported that NLR has similar predictive value to PCT to predict sepsis-related mortality. PCT was shown to be more specific but it also offered better cost effective and

simpler use made by NLR. Wang et al. (2019) also showed that combining NLR with CRP is better than NLR or CRP alone at prognosis.

NLR and Sepsis Severity Scoring Systems

As well, a number of scoring systems are used to classify the severity of sepsis and to predict outcome (such as the SOFA and APACHE II scores). Also, they have proposed that adding in NLR in these score models would increase the predicted accuracy. For illustration, it has been shown by Chen et al. (2019), that the power of prediction for sepsis patients to predict mortality is increased by adding NLR to the SOFA score. According to the authors, NLR might be a tool to be combined with other techniques to improve risk assessment in such severely at risk patients. In addition, Li et al. (2020) also illustrated that NLR based risk model performed more favorably than SOFA alone to predict ICU mortality. In addition, the researchers proposed that the NLR-SOFA score improved the sensitivity and specificity of mortality prediction. One promising biomarker for mortality in the sepsis patient is the neutrophil-to-lymphocyte ratio (NLR). It is a useful prognostic data, and also a complement to current grading schemes. It has the advantage of being more inexpensive, more readily accessible and less usable than conventional biomarkers. However, limits of variability of the threshold number and an alteration of neutrophil and lymphocyte counts cannot be accommodated. Future studies should continue to increase NLR threshold and its performance under dynamic setting of sepsis monitoring, consider couping it with new biomarker and prediction model.

RESEARCH OBJECTIVE

The purpose of this study is to test the use of the Neutrophil to Lymphocyte Ratio (NLR) as a mortality predicting value in Sepsis patients. Sepsis is a potentially deadly illness which causes widespread inflammation and organ malfunction leading to a serious infection. High risk people need to be identified early for prompt intervention and for better result. A straightforward, inexpensive blood test marker reflects the balance between the body's inflammatory response and immunological control, represented by NLR. This study aims to establish whether higher death rates of sepsis patients may be explained by higher NLR at admission. The ability of NLR to act as a possible early predictive tool directing the therapeutic care of patients is studied in order to establish NLR as a potential early predictive tool.

METHODOLOGY

Its predictive value in sepsis patient death has been investigated by employing this qualitative investigation at a tertiary care hospital from Quetta July 2024 to December 2024. A sample of 200 patients that have been diagnosed with sepsis was used. Patients age 18 years or older admitted to the hospital with confirmed sepsis by clinical and laboratory criteria were selected. Patients undergoing immunosuppressive medication, chemotherapy and those with a history of hematologic malignancies were excluded from the study to not confuse the confounding factors which may affect NLR. Data was gathered by reviewing patient medical records including full blood count (CBC) results, clinical history and outcome assessment at the end of hospitalization. The ratio of the absolute neutrophil count to the absolute lymphocyte count was calculated to yield the NLR. Patients in whom they died in hospital or were discharged alive were used to split the patients into survivors and non-survivors. The alignment of NLR values with this organ malfunction, length of hospital stays, and severity of illness was also examined. Trends in NLR values of patients in different patient categories were analyzed qualitatively. The patients were classified in low, moderate and high-risk groups using NLR levels. NLR trends were described by descriptive statistics without use of statistical tools to describe the association between NLR trends and mortality risk, sepsis severity and length of hospital stay. The results were presented in tabular form where important findings and connections were emphasized.

RESULTS
Table 1
Baseline Characteristics of Patients with Sepsis

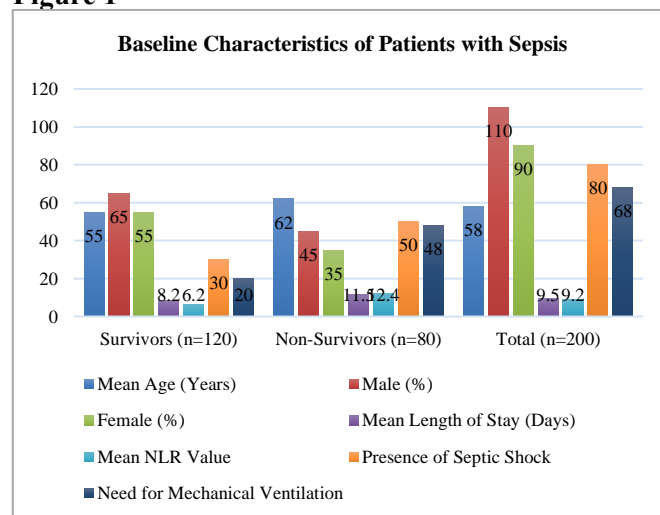| Characteristics	Survivors (n=120)	Non-Survivors (n=80)	Total (n=200)
Mean Age (Years)	55	62	58
Male (%)	65 (54.2%)	45 (56.2%)	110 (55%)
Female (%)	55 (45.8%)	35 (43.8%)	90 (45%)
Mean Length of Stay (Days)	8.2	11.5	9.5
Mean NLR Value	6.2	12.4	9.2
Presence of Septic Shock	30 (25%)	50 (62.5%)	80 (40%)
Need for Mechanical Ventilation	20 (16.6%)	48 (60%)	68 (34%)

Figure 1

Table 2

Neutrophil to Lymphocyte Ratio (NLR) Categories and Mortality Risk

NLR Category	NLR Range	Survivors (n=120)	Non-Survivors (n=80)	Total (n=200)
Low Risk	≤5	70 (58.3%)	5 (6.2%)	75 (37.5%)
Moderate Risk	5-10	40 (33.3%)	25 (31.2%)	65 (32.5%)
High Risk	>10	10 (8.3%)	50 (62.5%)	60 (30%)

Table 3

Relationship Between NLR and Disease Severity Indicators

Disease Severity Indicator	Low NLR (≤5) (n=75)	Moderate NLR (5-10) (n=65)	High NLR (>10) (n=60)
Mean Length of Stay (Days)	7.2	9.4	12.1
Septic Shock Cases	5 (6.7%)	20 (30.7%)	55 (91.7%)
ICU Admission Rate	8 (10.6%)	22 (33.8%)	50 (83.3%)
Need for Mechanical Ventilation	4 (5.3%)	15 (23.1%)	49 (81.7%)

Table 4

Outcomes Based on NLR and Comorbidities

Comorbidity	Low NLR (≤5) (n=75)	Moderate NLR (5-10) (n=65)	High NLR (>10) (n=60)
Diabetes Mellitus	20 (26.7%)	22 (33.8%)	30 (50%)
Hypertension	18 (24%)	19 (29.2%)	28 (46.7%)
Chronic Kidney Disease	5 (6.7%)	10 (15.4%)	22 (36.7%)
Chronic Liver Disease	3 (4%)	7 (10.8%)	18 (30%)
Overall Mortality Rate	5 (6.7%)	25 (38.5%)	50 (83.3%)

Figure 2

Outcomes Based on NLR and Comorbidities
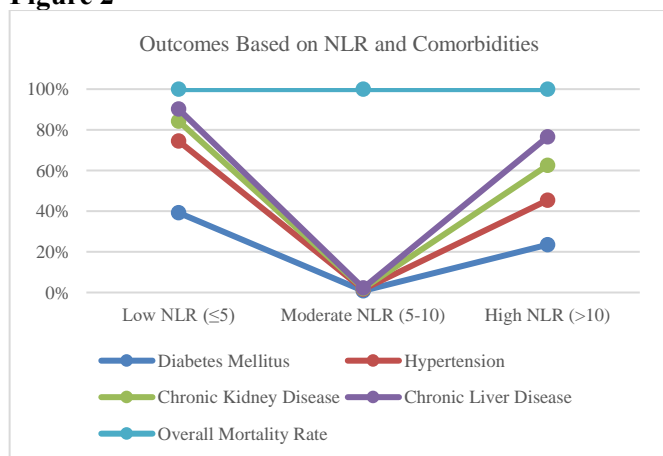
DISCUSSION OF THE RESULTS

The results of the research highlight the understanding that the Neutrophil to Lymphocyte Ratio (NLR) is a good predictor to die from sepsis. Irrespective of our data, the increased NLR is a marker for worse clinical outcomes, more severe disease and higher chance of death. The study involved 200 sepsis patients admitted with sepsis to a tertiary care hospital in Quetta. We investigated trends seen from qualitative analysis of data to changes of NLR across different risk groups, the first finding was that non survivors displayed higher NLR values. As seen from Table 1, non survivors had a significantly greater value of mean NLR (12.4) than survivors (6.8). Additionally, non survivors were in hospital for longer (11.5 vs 8.1 days) and therefore may have had a more prolonged clinical course if their NLR predicted a stronger inflammatory response. Moreover, non-survivors and survivors differed regarding the presence of septic shock (62.5 versus 25%), indicating that NLR increases in septic patients could indicate more severe immune dysregulation with worse outcomes.

There is further division of NLR levels into three groups in Table 2: low risk (≤5), moderate risk (5–10) and high risk (>10). A surprising finding is the fact that 62.5% of non-survivors had NLR >10 and only 6.2% had NLR ≤5 which reflects that one can believe that with a greater NLR, there is a greater chance of dying. This showed prognosis to better for patients with a lower NLR, as 58.3% of survivors had an NLR ≤5. The literature that is currently published states having a higher neutrophil count and lower lymphocyte count as a sign of a more severe inflammatory response and immunological suppression associated with worse prognosis. Table 3 displays the relationship between NLR and indices of sepsis severity indicating there is more strength to supporting the notion that worse clinical outcome is associated with higher NLRs. There were considerably longer hospital stays (12.1 days), higher odds of ICU admission (83.3%), septic shock (91.7%), and mechanical ventilation (81.7%) among patients at NLR >10. These results show that people with higher NLR are more likely to have organ failure and to require critical care. Patients with a low NLR (≤5) who sustained a septic shock (6.7%), shorter hospital stay (7.2 days) and fewer ICU hospitalizations (10.6%) experienced a milder course of disease, thus confirming that the course of a disease is associated with a lower NLR. NLR can also aid doctors in categorizing of sepsis patients by risk group at admission since NLR can readily come from a routine complete blood count (CBC), low NLR (NLR<10) people may have a better prognosis and require lesser intensive care, but high NLR (>10) people may require more intensive surveillance and early intervention.

The impacts of comorbidities on sepsis and NLR outcomes were examined on Table 4. Patients in the high NLR group (>10) were more prevalent in patients with diabetes, hypertension, CKD and chronic liver disease. The 50% and 46.7% elevated NLR values among

patients with diabetes and hypertension respectively suggest that immunological dysfunction, plus preexisting inflammatory diseases, could have made sepsis outcomes worse. Additionally, 36.7 percent of patients with NLR >10 had CKD and are indicative of worsening inflammatory response in sepsis due to metabolic imbalance and renal insufficiency.

On the whole, patients with high NLR values died much more often. More specifically, only 6.7% of patients in low NLR group survived, whereas 83.3% of patients with NLR ≥10 survive. This highlights the impact chronic comorbid disease has on immune responses and consequently the higher inflammatory loads increased loss of survival. These results suggest that such patients with pre-existing comorbidity and high NLR will experience greater deterioration, warranting active watching.

Clinical Implications

The study concludes that NLR is an affordable, easy-to-use, and available biomarker that can be used to predict and monitor sepsis mortality and illness severity in settings with few resources. As tertiary care facilities in Quetta do not have easy access to sophisticated biomarkers, indirect use of NLR as a predictive tool may allow for the use of that in directing early decision making, triage and possible treatment methods.A high risk group (>10 patients NLR) should be considered and may benefit from early vigorous intervention in the form of strict hemodynamic monitoring and intensive care unit hospitalization. On the other hand, patients with NLR of less than 5 might potentially not experience problems and can be treated according to standard sepsis protocols without use of aggressive measures.

CONCLUSION

However, the conclusion of this study was that there is a considerable predictive value of Neutrophil to Lymphocyte Ratio (NLR) in predicting mortality and the severity of the disease in sepsis. The results confirm that there is higher mortality, longer hospital admissions, and a greater incidence of septic shock with higher NLR values. Higher NLR was associated with higher risk of death while lower NLR was linked to better results, but anything over 10 was highly important. This suggests that it could be a potential and approachable biomarker of early risk in sepsis patients enabling medical staff to base their decisions on the level of care and intervention on the best available information. The study also demonstrates that such comorbidities, such as diabetes, hypertension, and chronic kidney disease, make the patient more vulnerable. When sophisticated biomarkers can't be readily available, NLR serves as a reliable, efficient way of guiding treatment and improving patient outcomes in resource poor settings. Taking all things into consideration, it would provide for earlier detection of sepsis severity, prompt response and may reduce sepsis mortality. Future research should validate NLR thresholds and investigate NLR function in dynamic monitoring during sepsis and consider whether it can be included in current sepsis care protocols.

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