# The Neutrophil Percentage-to-Albumin Ratio (NPAR) is Associated with In-Hospital Mortality in Patients with Liver Cirrhosis

*Ni Made Putri Lastiana[**], Ketut Mariadi[*], Dwijo Anargha Sindhughosa[*], Manoj Kumar[***]*

*Division of Gastroentero-Hepatology, Department of Internal Medicine, Faculty of Medicine, Udayana University/Prof. Dr. I.G.N.G. Ngoerah General Hospital, Denpasar, Bali, Indonesia
**Residency Program of Internal Medicine, Faculty of Medicine, Udayana University/Prof. Dr. I.G.N.G. Ngoerah General Hospital, Denpasar, Bali, Indonesia
***Department of Hepatology and Liver Transplantation, Institute of Liver & Biliary Sciences D1 Vasant Kunj, New Delhi 110070 India

***Corresponding author:***
*Ni Made Putri Lastiana, Residency Program of Internal Medicine, Faculty of Medicine, Udayana University/Prof. Dr. I.G.N.G. Ngoerah General Hospital, Denpasar, Bali, Indonesia, Email: putrilastiana.92@gmail.com, Telp: 081298582579*

## ABSTRACT

***Background:*** *Studies show that the Neutrophil Percentage-to-Albumin Ratio (NPAR) predicts mortality in a number of illnesses. On the other hand, there is currently limited clinical support for using NPAR in liver cirrhosis patients. Investigating the associated of NPAR and hospital mortality outcome patients with liver cirrhosis is the goal of this study.*

***Methods:*** *All cirrhosis patients who were admitted to the hospital were included in this retrospective cohort analysis. The percentage of neutrophils and albumin levels on the first day of hospitalization were compared to determine the NPAR. Data were analyzed using the Mann-Whitney test, operating curve (ROC) analysis, and Kaplan-Meier survival curves. P-value < 0.05 was considered statistically significant*

***Results:*** *This study included 98 patients with liver cirrhosis. It was found that NPAR had a high incidence of patient mortality compared to surviving patients who were hospitalised (35.13 vs. 25.33, p < 0.001). The median overall survival for all subjects was 10 days, indicating that 50% of the subjects had died within 10 days. According to ROC analysis, NPAR has an ideal cutoff value of 29.63 and can be utilized as a predictor of in-hospital mortality (sensitivity 74.1%, specificity 72.7%, AUC 0.8, p < 0.001). Survival analysis stratified by NPAR showed that patients with NPAR ≥ 29.63 had a lower median survival compared to those with NPAR < 29.6.*

***Conclusion:*** *In patients with liver cirrhosis, the Neutrophil Percentage-to-Albumin Ratio (NPAR) is a metric that can be used to assess in-hospital mortality outcomes.*

***Keywords:*** *Neutrophil Percentage-to-Albumin Ratio (NPAR), mortality, liver cirrhosis*

## ABSTRAK

***Latar Belakang:*** *Studi menunjukkan bahwa proporsi neutrofil albumin (NPAR) adalah prediktor kematian beberapa penyakit. Namun, sejauh ini bukti klinis untuk penggunaan NPAR terbatas pada pasien dengan sirosis. Penelitian ini bertujuan untuk menilai hubungan antara NPAR dan luaran mortalitas di rumah sakit pada pasien dengan sirosis hati.*

***Metode:*** *Penelitian ini adalah studi kohort retrospektif yang melibatkan semua pasien dengan sirosis yang dirawat di rumah sakit. NPAR dihitung berdasarkan rasio antara proporsi neutrofil dan albumin pada hari pertama pasien dirawat di rumah sakit. Data dianalisismenggunakan uji Mann-Whitney, analisis receiver operating curve (ROC), dan Kurva Kaplan Meier.P-value < 0,05 dianggap bermakna secara statistik.*

***Hasil:*** *Sebanyak 98 pasien dengan sirosis hati dilibatkan pada penelitian ini. Diperoleh hasil NPAR yang tinggi pada luaran mortalitas dibandingkan dengan pasien yang bertahan hidup (35,13 vs 25,33, p < 0,001). Median kesintasan seluruh subjek adalah sebesar 10 hari. Hal ini menandakan bahwa sebanyak 50% subjek telah meninggal dalam 10 hari. Analisis ROC menunjukkan bahwa NPAR dapat digunakan sebagai prediktor mortalitas di rumah sakit dengan titik potong optimal NPAR 29,63 (sentivitas 74,1%; spesifisitas 72,7%; AUC 0,8; p < 0,001). Analisis kesintasan yang dibagi berdasarkan NPAR menunjukkan bahwa pada kelompok pasien dengan NPAR ≥ 29,63 memiliki median kesintasan yang lebih rendah dibandingkan NPAR < 29,63 (8 hari vs 15 hari).*

***Kesimpulan:*** *Neutrophil Percentage-to-Albumin Ratio (NPAR) merupakan parameter yang dapat digunakan untuk menentukan luaran mortalitas di rumah sakit pada pasien sirosis hati.*

***Kata Kunci:*** *Neutrophil Percentage-to-Albumin Ratio (NPAR), mortalitas, sirosishati*

## INTRODUCTION

Liver cirrhosis is defined as the final stage of chronic liver disease that is characterized by fibrosis and scarring of liver tissue with an irreversible replacement of liver parenchyma with regenerative nodules surrounded by fibrotic bands.[1,2] The natural history of cirrhosis is divided into two distinct stages; the compensated and the decompensated stage. The compensated stage is an asymptomatic period with a median survival of 10 or more years. The second stage, known as decompensated cirrhosis, is characterized by the presence of symptoms and a median survival of 1–2 years. The term "decompensated cirrhosis" is typically used to describe the presence or history of specific conditions, such as ascites, bleeding, hepatic encephalopathy (HE), or jaundice.[3]

The transition from compensated to decompensated cirrhosis leads to increased mortality risk. Further decompensation leads to further increased mortality risk.[4] In recent years, increasing attention has been given to new entities namely, acute decompensation (AD), Non- AD (NAD), pre-acute-on-chronic liver failure, and acute-on-chronic liver failure with an increased mortality rate with the increasing stage.[1-4] Every patient who is admitted with liver cirrhosis should be evaluated for the presence of acoompanying complications/decompensations like variceal bleeding, AKI, infections, HE etc. There are several scoring systems for mortality risk prediction in hospitalized cirhosis patients like MELD, MELD-Na, CTP, and ACLF specific scores like AARC-ACLF score and CLIF-C ACLF score. Although various scoring systems can be used to predict the mortality risk, they still have limitations.[1,3]

A common clinical sign in patients with liver cirrhosis is hypoalbuminemia. The most common protein found in human plasma is albumin, a medium-sized molecule, plays a vital role in several physiological processes. These include acting as the primary buffer, serving as an extracellular antioxidant, functioning as an immunomodulator, detoxifying, and transporting substances in the plasma.[4] Low levels of albumin are linked to organ failure and systemic inflammation. Additionally, numerous studies show that poor clinical outcomes and prognosis are linked to lower albumin levels.[5,6]

Inflammation has a significant role in liver cirrhosis. Neutrophil is one of the classic inflammation factors that release a wide range of cytokines and reactive oxygen species, leading to liver injury. On the other hand, albumin has anti-inflammatory properties and maintains plasma osmotic pressure. Neutrophil Percentage-to-Albumin Ratio is calculated as the ratio of neutrophil (%) to serum albumin concentration (g/dL).[7]As a potential biomarker, the NPAR is an inflammation-based predictor linked to mortality in various diseases. However, clinical evidence for the use of NPAR in patients with admitted liver cirrhosis remains limited to date. Therefore, the purpose of this research is to assess the relationship between NPAR and the mortality rates of hospitalized patients with liver cirrhosis.

## METHOD

### Study Design:

Retrospective cohort research was used in this investigation.

### Setting:

The study was done at RSUP Prof. Ngoerah Hospital, Bali, Indonesia (Department of Medicine). This research has received approval from the Medical Research Ethics Committee at the Faculty of Medicine, UniversitasUdayana (registration number: 0739/UN14.2.2.VII.14/I.T)

### Participants:

The study was conducted on patients with cirrhosis admitted to the Department of Medicine at the Hospital. Period of data collection was from Jan 2022 to Dec 2024The inclusion criteria were the following: Adult patients (>18 years) with cirrhosis admitted to the hospital.Exclusion criteria were the following: Pregnant patients, patients with autoimmune illnesses (including autoimmune liver diseases) and patients with hepatocellular carcinoma (HCC) or extra hepatic malignancy.

### Variables assessed:

The following data was collected at baseline at the time of admission:Neutrophil, albumin, and the Neutrophil-to-albumin ratio; and other relevant clinical, biochemical, haematological, and imaging parameters were collected. . We also assessed the survival rateof the patients. . The data were obtained from medical records at the date of admission. Survival was assessed from September 2024 to April 2025.

### Definitions and methods of assessments (measurements):

**Cirrhosis:** Cirrhosis was diagnosed by clinical, radiological criteria or liver biopsy (if required).

Neutrophil Percentage-to-Albumin Ratio (NPAR): NPAR was the percentage of neutrophils to albumin levels on the first day of hospital admission.

**Survival:** The time from the admission dateto death (days)

In-hospital mortality: The death during hospitalization, regardless of its cause and length. The data was obtained from medical records.

**Cause of mortality:** Death by hypovolemic shock due to ongoing uncontrolled bleeding was considered as bleed related mortality. Other causes of deaths were categorized as follows: death by shock associated with sepsis was attributed to infection (septic shock); death by coma, acute kidney injury, or multiorgan failure was attributed to terminal liver failure**Sample size and statistical methods:** Version 27.0 of the Statistical Program for Social Science (SPSS) for Windows was used to process the data. Continuous variables in a normal distribution were expressed as mean ± standard deviation and in non-normal distribution as median with inter quartile range (IQR). Frequencies (percentages) were used to express categorical variables. Kaplan-Meier curves for survival were plotted. Receiver operating curves (ROCs) was plotted for NPAR and assessed the NPAR categories (> 29.63, < 29.63, and overall) for sensitivity, specificity, and optimal cut-off point of NPAR to predict in-hospital mortality of our participants. Interpretation was based on clinically meaningful values.

## RESULTS

This study involved 98 samples, comprising 71 (72.4%) males and 27 (27.6%) females. The basic characteristics of the study subjects can be observed in **Table 1.**

**Table 1. Baseline Characteristic of the Patients**

| Characteristics | N : 98 |
|---|---|
| **Age, mean ± SD** | 55.95 ± 11.26 |
| **Sex** | |
| - Male, n (%) | 71 (72.4) |
| - Female, n (%) | 27 (27.6) |
| **Albumin, mean ± SD** | 2.4 ± 0.78 |
| **Neutrophil (%), mean ± SD** | 73.16 ± 13.49 |
| **Etiology** | |
| - Hepatitis B (%) | 49 (50) |
| - Hepatitis C (%) | 24 (24.5) |
| - Unknown (%) | 25 (25.5) |

98 patients fulfilling the inclusion and exclusion criteria were analyzed for this study **(Figure 1).** 54 patients died during the current hospitalization, while 44 patients survived and were discharged. The NPAR was significantly higher in patients who died in hospital vs those who survived (P<0.001). The mean NPAR was 35.13 for those who experienced mortality and 25.33 for those who survived.

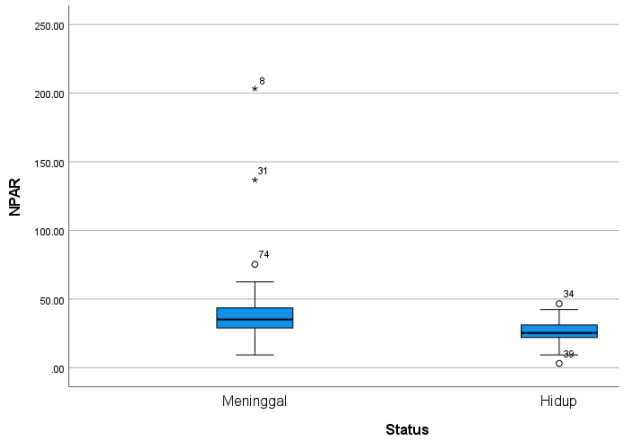


**Figure 1. The comparison of Neutrophil Percentage-to-Albumin Ratio (NPAR) in patients with liver cirrhosis with outcomes of in-hospital mortality and survival**

ROC analysis indicated that an optimal cutoff point of NPAR at 29.63 (sensitivity 74.1%; specificity 72.7%; AUC 0.8; $p < 0.001$) is associated with in hospital mortality **(Figure 2).**

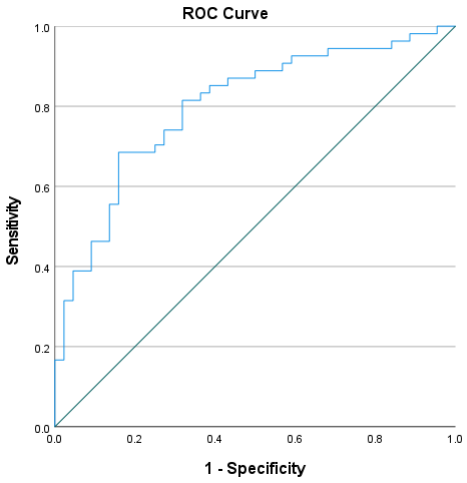


**Figure 2. The ROC curve of NPAR in predicting in-hospital mortality in patients with liver cirrhosis**

The median survival for all subjects is 10 days, indicating that 50% of the subjects had died within 10 days. Survival analysis stratified by NPAR reveals that in the group of patients with NPAR ≥ 29.63, the median survival is lower compared to those with NPAR < 29.63 (8 days vs. 15 days). This information is presented in **Table 2, Figure 3, and Figure 4**.

**Table 2. The survival values of patients based on NPAR**

| NPAR Category | Estimation of survival (days) |
|---|---|
| NPAR ≥ 29.63 | 8 |
| NPAR < 29.63 | 15 |
| Overall | 10 |

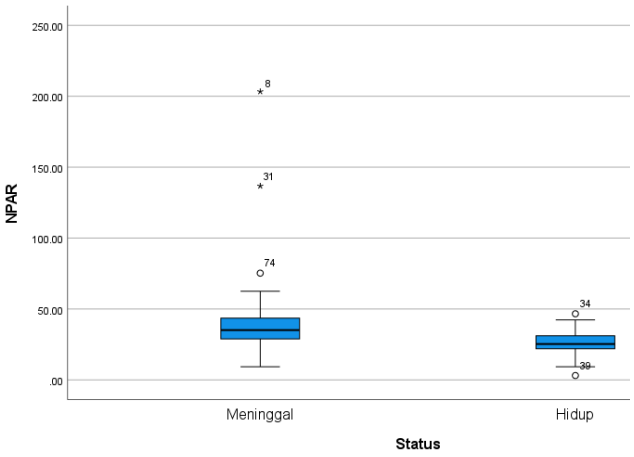


**Figure 3. The cumulative survival of hospitalized liver cirrhosis patients**

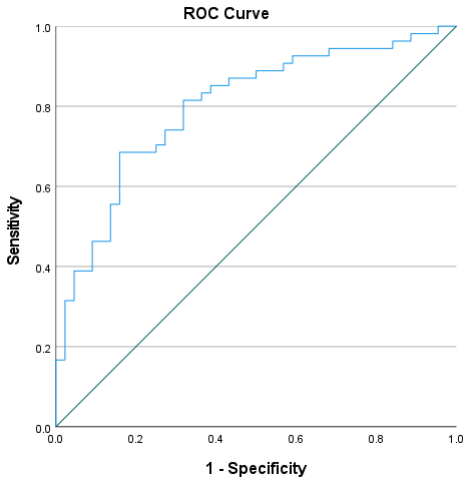


**Figure 4. The survival of liver cirrhosis patients based on NPAR**

## DISCUSSION

Liver cirrhosis represents the end stage of liver disease. Liver cirrhosis develops through the process of hepatocyte necrosis and regeneration, resulting in fibrosis and capillarization of the liver sinusoids. Decreasing liver parenchyma, impaired blood flow due to fibrosis and abnormal reconstruction, and the development of phylum erymentystemy shunts is associated with portal hypertension of lung, liver, liver, heart, steatosis, liver damage, dysfunction.[8] Liver cirrhosis is a complex and multifaceted pathological process. Studies have indicated that one of the independent risk factors for liver cirrhosis is inflammation.[9]

Liver fibrosis is a liver reaction to acute or chronic damage. Numerous processes, such as liver inflammation, fibrogenesis, and angiogenesis, contribute to the development of cirrhosis. Liver fibrosis process due to inflammation as a reaction to

the injury of the liver. For patients with cirrhosis, the barrier is a change due to the increase in the product of inflammatory cytokine and systemic inflammation.[10,11] The inflammatory response is characterized by neutrophil activation.

Since the liver synthesises proteins, inflammation in the liver affects the serum albumin concentration. Hypoalbuminemia has been reported as a poor prognostic indicator in liver diseases resulting from malnutrition and inflammation.[13,14] Albumin has roles as a antioxidant, buffer, antidote, immunomodulator, and transporter in plasma.[15] In previous studies, a relationship between NPAR and prognosis in various inflammatory diseases has been reported. Other studies have also demonstrated that NPAR levels are link to mortality rates in conditions like septic shock, cardiogenic shock, and kidney injury. In this current study, we examined the connection between mortality and NPAR in hospitalized patients with hepatic cirrhosis, and found that patients who died had higher NPAR values at admission. The optimal cutoff point of NPAR associated with mortality was 29.63 (sensitivity 74.1%; specificity 72.7%; AUC 0.8; $p < 0.001$). The median survival was also lower in patients with NPAR $\geq 29.63$, compared to those with NPAR $< 29.63$ (8 days vs. 15 days).

This research has several limitations. It did not account for comorbid factors that could affect patient mortality. Additionally, the study did not investigate the relationship between the specific causes of liver cirrhosis, specific stages of cirrhosis and the NPAR levels in patients. The findings of this study can be generalized to other liver cirrhosis patients, as the study participants were selected based on the additional work-up findings of liver cirrhosis commonly used in clinical practice, where NPAR can be applied as a predictor of in-hospital mortality in liver cirrhosis patients. Further studies may be required for further analysis regarding the NPAR application as the predictor of in-hospital mortality in liver cirrhosis patients with a larger sample size, more variables, comparing NPAR in liver cirrhosis patients with and without comorbid diseases, also comparing NPAR with other predictor of in-hospital mortality in liver cirrhosis to support the finding of this study and determine the best predictor of in-hospital mortality in liver cirrhosis patients.

## CONCLUSION

The study highlighted the finding of in-hospital mortality predictor in patients with liver cirrhosis. The Neutrophil Percentage-to-Albumin Ratio (NPAR) is a parameter that can be used to determine the outcome of in-hospital mortality in patients with liver cirrhosis.

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