

Frequency of In-Hospital Mortality in Patients Presenting with Acute Heart Failure with Elevated Neutrophil to Lymphocyte Ratio at Tertiary Care Hospital, Karachi

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ABSTRACT

Background: Patients admitted with acute heart failure (AHF) have in-hospital mortality rates of great concern, and a complex cascade of hemodynamic, neurohormonal, and inflammatory responses contribute to this. High NLR in hospital on admission could indicate the aggravated inflammatory state, which could result in poor clinical outcomes, such as increased in-hospital mortality.

Methodology: A cross-sectional study targeted 135 patients with their admission causes being acute heart failure and elevated NLR ratio. The variables were collected; the age, gender, residence status, diabetes mellitus type II, hypertension, dyslipidemia, smoking status, obesity status, anemia status and duration of heart failure. The patients were monitored and assessed with in-hospital mortality. The control of the effect modifiers was done by stratification and post stratification chi square test/ Fischer test was used with p value of 0.05 set as statistically significant.

Results: Mean age of the participants was 55.14 ± 12.49 years, and the mean duration of heart failure was 18.72 ± 10.24 hours. The mean BMI was 27.41 ± 2.56 kg/m², height was 158 ± 7.28 cm, weight was 78.7 ± 9.87 kg, and the neutrophil-to-lymphocyte ratio (NLR) was 2.21 ± 1.41 . Among the participants, 74 (54.81%) were female and 61 (45.19%) were male. In-hospital mortality occurred in 43 (31.9%) patients, while 92 (68.1%) survived during hospitalization.

Conclusion: NLR is a low cost, simple to use clinical applicable value that forecasts prognosis in the short-term and classifies the risk of AHF patients. Accordingly, there should be close surveillance of the patients with regular follow up in all patients.

Keywords: Acute Heart Failure; Mortality; Neutrophil to Lymphocyte Ratio, Prevalence

Authors' Contribution:

^{1,2}Conception; Literature research; manuscript design and drafting; ^{3,4}Critical analysis and manuscript review; ^{5,6}Data analysis; Manuscript Editing.

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Introduction

Acute heart failure (AHF) can be defined as the exacerbation or the development of symptoms and clinical manifestation (heart failure (HF)) within the heart.¹ The prevalence of the condition is currently on the increase and influenced by the rising incidence of coronary artery disease and ageing

population. Furthermore, there are high mortality and morbidity rates associated with acute heart failure.² It is important to identify those who are at high risk of acute heart failure in advance. A wide range of prognostic factors related to AHF has been discovered based on previous studies with a large percentage of those factors being inflammatory related. Besides, there is also evidence of specifically

investigating whether, inflammation is an underlying mechanism in AHF patients.³

An important reason is inflammation, which contributes to the occurrence and the evolution of the cardiovascular conditions. Several inflammatory biomarkers have been reported to be related to the severity and the prognosis of heart failure (HF).⁴ The number of white blood cells (WBC) and subtypes is firmly established as an inflammatory marker of cardiovascular disorders.⁵ Although the causes or effects of such an elevated level of white blood cells are unclear, it has been associated with the risk of increased chances of heart failures due to hospitalization, and increased mortality. Moreover, neutrophilia predicts an increased risk of acute decompensated heart failure in those who have faced acute myocardial infarction, and lymphopenia shows poorer patient results in heart failure.⁶⁻⁷

Heart failure causes imbalance of the inflammatory and anti-inflammatory pathways and leads to diminishing neutrophil apoptosis. This decline is a factor that leads to increased neutrophil count and more heart failure cases.⁸⁻⁹ The opposite is seen with decompensated heart failure whereby a lymphopenia is present and lymphopenia also acts as an independent predictor of mortality in cases of heart failure.¹⁰ This simple and inexpensive tool can be used as a prognostic indicator in the clinical field. Nevertheless, available data are not consistent. As an example, a study by Song et al. and Angkananard et al. found that there was a significant correlation between the neutrophil-to-lymphocyte ratio (NLR) and clinical outcomes in heart failure.¹¹⁻¹² Conversely, Kundnani et al and Che and his colleagues implied that this biomarker may not be independently relevant to the prognosis of heart failure. This means we need a rigorously conducted study in view of these inconsistencies.¹³⁻¹⁴

A study identified in-hospital mortality among individuals with acute heart failure as 5.9 percent among patients with high Neutrophil to Lymphocyte Ratio.¹⁵

AHF is highly dynamic clinical entity and most dangerous in the first few hours. Hence, very crucial is early risk stratification. Those patients that are identified early and found to be of high-risk levels are steered towards advanced and quite deeper treatment alternatives. This way, mortality and morbidity can be limited. Neutrophil-to-lymphocyte ratio (NLR) is a factor that can be easily accessed. A higher number of neutrophils could be a sign of inflammation and lymphopenia is an example of physiologic stress. Information on the capacity of the NLR to forecast cardiovascular risk within disparate patient populations has been described but lacks in this population. Moreover, this kind of data can add to the existing evidence about the involvement of inflammation in cardiovascular issues.

Methodology

A cross-sectional study was conducted at the Department of Cardiology, Tabbha Heart Institute, Karachi, for a duration of six months. The sample size of 135 patients was calculated using the WHO sample size calculator, considering an in-hospital mortality prevalence rate of 5.9%, a margin of error of 4%, and a 95% confidence level.⁵ Patients were enrolled in the study through a non-probability consecutive sampling technique after obtaining written informed consent. All patients aged 40-85 years of either gender who presented with acute heart failure and had an elevated neutrophil-to-lymphocyte ratio (NLR) at the time of admission, according to the operational definition, were included. Raised NLR defined as: An elevated neutrophil-to-lymphocyte ratio (NLR) was defined as an NLR value greater than 5.0, based on previously established literature cutoffs indicating increased systemic inflammation in patients with acute heart failure¹⁻². Patients with acute myocardial ischemia, cardiogenic shock, hematological disorders, neoplastic metastases to bone marrow, sepsis, pregnancy, severe arthritis, inflammatory bowel disease, other chronic

inflammatory or autoimmune diseases, those on active glucocorticoid therapy or who had received it within the past 3 months, and patients with extracellular fluid-increasing conditions such as hypothyroidism or hepatic cirrhosis were excluded from the study. All patients presenting with acute heart failure who met the inclusion criteria and demonstrated elevated NLR values were included in the study. No patient with normal or low NLR values was enrolled.

Patient demographic data (age, gender, and residence), clinical characteristics (comorbidities, duration of heart failure, smoking, obesity, anemia), and laboratory parameters were collected. NLR was measured at admission using blood samples drawn at the time of presentation to the emergency department. Patients were followed up during their hospital stay, and in-hospital mortality was recorded. Data were analyzed using SPSS Version 20.0. Continuous variables, including age, height, weight, BMI, NLR, and duration of heart failure, were presented as mean $\pm$ standard deviation (SD) for normally distributed data and as median with interquartile range (IQR) for non-normally distributed data, as determined by the Kolmogorov–Smirnov test. Categorical variables, such as gender, residence status, diabetes mellitus, hypertension, dyslipidemia, smoking status, obesity, anemia, and in-hospital mortality, were expressed as frequencies and percentages. Stratification was performed for age, gender, residence status, diabetes mellitus, hypertension, dyslipidemia, smoking status, obesity, anemia, and duration of heart failure to control for potential effect modifiers. Post-stratification analysis was carried out using the Chi-square test for variables with expected cell counts ≥ 5 and the Fisher’s exact test for variables with expected counts < 5 , to assess associations with in-hospital mortality. A p-value < 0.05 was considered statistically significant.

Ethical approval of the study was taken from the College of Physicians and Surgeons Pakistan (CPSP) and ethical approval from the Institutional Review

Board (IRB) of Tabba Heart Institute (Reference no: THI/IRB/SQ-04-04-2024/109).

Results

A total of 135 patients admitted to Department of Cardiology, Tabba Heart Institute, Karachi were included in the study. Mean age of the participants was 55.14 ± 12.49 years, with an age range of 40–85 years. Mean duration of heart failure was 18.72 ± 10.24 hours, while the mean BMI was 27.41 ± 2.56 kg/m². The average height and weight were 158.00 ± 7.28 cm and 78.70 ± 9.87 kg, respectively. The mean neutrophil-to-lymphocyte ratio (NLR) at admission was 2.21 ± 1.41 . Regarding clinical outcomes, in-hospital mortality occurred in 43 patients (31.85%), while 92 patients (68.15%) survived to discharge. Among the total participants, 61 (45.19%) were males and 74 (54.81%) were females. In terms of age distribution, 46 (34.07%) patients were between 40–65 years, and 89 (65.93%) were between 66–85 years. Most participants were from urban areas (110; 81.48%), while 25 (18.52%) belonged to rural regions. The prevalence of comorbidities showed that 93 (68.89%) patients had type 2 diabetes mellitus, 103 (76.30%) had hypertension, and 85 (62.96%) had dyslipidemia. Smoking was reported in 45 (33.33%) patients, obesity was observed in 58 (42.96%), and anemia was found in 67 (49.63%) participants. Although variations were noted between groups, none of the demographic or clinical factors showed a statistically significant association with in-hospital mortality ($p > 0.05$). Mortality was higher among patients aged 40–65 years (18/46; 39.1%) than those aged 66–85 years (25/89; 28.1%).

Among females, 23 out of 61 (37.7%) died, compared to 20 out of 74 (27.0%) males (Table I). Table II presents the analysis of demographic and clinical factors associated with in-hospital mortality among 135 study participants.

Table I: Baseline Characteristics and Clinical Distributions of Study Participants (N=135)	
Variable (N=135)	Mean $\pm$ SD n(%)
Age (Years)	55.14 $\pm$ 12.49
Duration of Heart Failure (Hours)	18.72 $\pm$ 10.24
BMI (Kg/M ²)	27.41 $\pm$ 2.56
Height (Cm)	158 $\pm$ 7.28
Weight (Kg)	78.7 $\pm$ 9.87
NLR Ratio	2.21 $\pm$ 1.41
In-Hospital Mortality Distribution	
Yes	43(31.85)
No	92(68.15)
Gender Distribution	
Male	61 (45.19)
Female	74 (54.81)
Age Distribution (Years)	
40-55	46 (34.07)
66-85	89 (65.93)
Residence Status Distribution	
Urban	110 (81.48)
Rural	25 (18.52)
Type 2 Diabetes Mellitus Distribution	
Yes	93(68.89)
No	42(31.11)
Hypertension Distribution	
Yes	103 (76.30)
No	32 (23.70)
Dyslipidemia Distribution	
Yes	85 (62.96)
No	50 (37.04)
Smoking Status Distribution	
Yes	45 (33.33)
No	90 (66.67)
Obesity Status Distribution	
Yes	58 (42.96)
No	77 (57.04)
Anemia Status Distribution	
Yes	67 (49.63)
No	68 (50.37)

Table II: Analysis of demographic and clinical factors associated with in-hospital mortality among study participants, including corresponding p-values for statistical significance.				
Variable	Total	In-Hospital Mortality Yes	In-Hospital Mortality No	P value
Age (Years)				0.082
40-65	46	18 (39.1)	28 (60.9)	
66-85	89	25 (28.1)	64(71.9)	
Gender				0.152
Male	74	20 (27)	54(73)	
Female	61	23(37.7)	38 (62.3)	
Residence Status				0.982
Urban	110	35(31.8)	75(68.2)	
Rural	25	8(32)	17(68)	
Type 2 Diabetes Mellitus				0.091
Yes	93	31(33.3)	62(66.7)	
No	42	12(28.6)	30(71.4)	
Hypertension				0.930
Yes	103	33(32)	70(68)	
No	32	10(31.2)	22(68.8)	
Dyslipidemia				0.683
Yes	85	26 (30.6)	59 (69.4)	
No	50	17 (34)	33(66)	
Smoking Status				0.791
Yes	45	15 (33.3)	30 (66.7)	
No	90	28 (31.1)	62 (68.9)	
Obesity Status				0.192
Yes	58	15 (25.9)	43 (74.1)	
No	77	28 (35.4)	49 (63.6)	
Anemia				0.906
Yes	67	21(31.3)	46(68.7)	
No	68	22(32.4)	46(67.6)	

The data are expressed as numbers with corresponding percentages for categorical variables and as mean $\pm$ standard deviation (SD) for continuous variables. Patients aged 40–65 years showed a higher mortality rate (39.1%) compared to those aged 66–85 years (28.1%), though the difference was not statistically significant ($p = 0.082$). Mortality was slightly higher among females (37.7%) than males (27%) ($p = 0.152$). Urban and

rural participants exhibited similar mortality rates (31.8% vs. 32%, $p = 0.982$). Likewise, mortality among patients with type 2 diabetes mellitus (33.3%) and those without diabetes (28.6%) did not differ significantly ($p = 0.091$). No significant associations were found between in-hospital mortality and hypertension ($p = 0.930$), dyslipidemia ($p = 0.683$), smoking status ($p = 0.791$), obesity ($p = 0.192$), or anemia ($p = 0.906$). Overall, none of the demographic or clinical characteristics demonstrated a statistically significant relationship with in-hospital mortality ($p > 0.05$).

Discussion

Of the total 135 patients, 43 (31.9) died in hospital, whereas 92 (68.1) of them survived to go home. Hematologic biomarkers such as neutrophil-to-lymphocyte ratio (NLR) and percentage lymphocytes (%L) have become significant to foretell the results of severe cardiovascular diseases, including acute heart failure (AHF), and myocardial infarction (MI). Such biomarkers are indicators of systemic inflammation and an expression of stress, and provide an economical and generally available way of gauging patient risk and informing treatment approaches. The prognostic information in respect of elevated NLR indicated by several studies in cardiovascular conditions is highly promising. Ang et al. illustrated that increased numbers of neutrophils had a substantial adverse impact on the survival rate at three years and 30 days after an MI.⁴ Patients who had the highest tertile of NLR were found to be significantly worse off in terms of survival than those in the lowest tertile of NLR despite other factors, such as age, sex, and comorbidities. On the same note, Siraj et al. were able to demonstrate that NLR portends in-hospital death in AHF patients even in isolation of other factors.⁵ The patients with a high NLR were much more inclined to a negative experience in the hospital, which highlighted its accuracy as a risk indicator.² Relative lymphocyte count has also been a big diviner of cardiovascular

mortality. Basak et al. classified %L as a by definition not multifactorial critical risk factor of survival in patients with implantable cardioverter defibrillators (ICDs).⁸ The existence of lower %Ls imposed substantial risks of mortality to the patients even when adjusted to mutable factors, including left ventricular ejection fraction (LVEF) and underlying diagnoses.¹⁶ Davison et al. went further to determine %L as a useful prognostic indicator of AHF. When authors conducted a study and compared mortality rate at one year of patients with a %L below 25% at admission with patients with higher counts, they found a higher mortality rate among the former. Notably, lymphocyte percentage was also an independent prognosticator of death even when LVEF, age, and renal function were accounted.¹⁰

Such results lead to the application of NLR and lymphocyte percentage as a cardiovascular patient routine assessment measure. The two markers present easy and affordable ways to detect high-risk patients early enough to get a higher priority in terms of intensive monitoring and patient-specific interventions.¹⁷ Although NLR is sensitive to systemic inflammation, it is not only highly predictive of mortality, but lymphocyte percentage too provides information about neurohormonal and immune imbalance. Patient outcomes may be better predicted by combining these markers with more traditional risk factors.¹⁸⁻¹⁹ NLR has been found to provide insight into the prognosis of patients in acute cardiovascular diseases. There are chances that the perfection of risk assessment would raise patient outcomes as well as the allocation of resources in the event of their incorporation into the mainstream.²⁰

Limitations: The given study has several limitations that should be mentioned. Although the sample size was sufficient to provide insights into the entire population analysis, it was also possible that it was not sufficient to identify slight variation between the groups, especially when it comes to less prevalent variables. Being observational research, it does not

enable us to cause and effect relationships between the variables with the mortality in hospital. Confounders were probably at it; unmeasured confounding, e.g., differences in disease severity, availabilities of health care, or other comorbidities, can have underlain both the results and masked important trends. Moreover, the study performed in one center reduces the reasoning of such findings to other larger groups of people that might possess different culture in healthcare practices, differences in demographics, or disease incidences. Multicenter studies and bigger ones which consider the possible confounding factors need to be carried out to further investigate the determinants of in-hospital mortality.

Conclusion

Out of the patients, 43 (31.9) died in the hospitals and 92 (68.1) survived during their stay. This evidence demonstrates that NLR is affordable and readily available in predicting the prognosis of patients with acute heart failure (AHF) in the short term, as well as the risk stratification. Since it is a routinely available measure, it may be used when attempting to identify the patients that have an increased risk of dying, therefore, becoming a worthwhile addition to the clinical decision-making process.

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