Association of Serum Creatinine and NT-ProBNP Levels with the Length of Hospital Stay in Patients with Decompensated Heart Failure

Samir Kumar Poudel[1], **Prakash Bogati**[1], **Sudip Lamsal**[1], **Nirmal Ghimire**[1], **Binayak Gautam**[1], **Kunjang Sherpa**[1], **Prabha Chapagain Koirala**[1], **Deepak Kumar Mishra**[1], **Lata Gautam Poudel**[2]

[1]Department of Cardiology, National Academy of Medical Sciences, Kathmandu, Nepal, [2]Department of Psychiatry, National Academy of Medical Sciences, Kathmandu, Nepal.

ABSTRACT

Background: Despite the increasing arsenals in the basket of heart failure armamentarium, the management of acute decompensated heart failure still remains a partly resolved mystery with high morbidity and mortality. This study seeking correlation between serum NT-ProBNP, and serum creatinine at presentation in acute decompensated heart failure (ADHF) patients with the length of hospital stay (LOS) will give an idea about prioritizing ADHF patients for further management and proper downstream resource utilization.

Methods: This was a hospital-based prospective observational study conducted at National Academy of Medical Sciences, Bir Hospital, Kathmandu, Nepal. The study duration was from August 2023 to July 2024. Seventy-three consecutive patients above 18 years of age with ADHF were enrolled in the study. Patients underwent NT=ProBNP and serum creatinine tests from the routine lab within 24 hours of presentation to emergency department. The correlation between LOS and NT-ProBNP/ serum creatinine was assessed by Spearman correlation.

Results: Out of the 73 patients, females were higher in number (56.16%). The mean age of the population was (64.68 ± 16.19) years and the mean hospital stay was (9.89 ± 4.3) days. There was a moderately strong correlation between LOS and serum NT-ProBNP level ($r = 0.419$, $p = 0.027$). However, the correlation between LOS and serum creatinine was weak ($r = 0.245$, $p = 0.037$).

Conclusion: Serum NT-ProBNP taken within first 24-hours of admission in ADHF patients has moderately strong correlation with LOS in hospital; however, serum creatinine is a weak predictor of LOS in this cohort of patients.

Keywords: *acute decompensated heart failure; NT-ProBNP; serum creatinine; length of hospital stay; prognosis.*

INTRODUCTION

Heart failure (HF) is a clinical syndrome caused by structural and/or functional cardiac dysfunction that is clinically manifested by signs and symptoms of low cardiac output and/or congestion. Heart failure is associated with high rates of morbidity and mortality and patients may need frequent hospital admissions.[1] Every hospital admission has additive effect on poor future clinical outcome of the disease.[2] NT-ProBNP with a cut-off value of 300 pg/ml has 99% sensitivity, 60% specificity and 98% negative predictive value for exclusion of acute heart failure[3.] Moreover, NT-ProBNP has a strong prognostic value of predicting mortality in both acute and chronic heart failure. It has a half-life of 2 hours.[4] Baseline renal function is an independent prognostic factor in heart failure with both diastolic and systolic dysfunction.[5,6] Baseline serum creatinine reflects the severity of heart failure at the time of presentation if other concomitant factors have been ruled out.[7] We sought to see the association of baseline NT-ProBNP and serum creatinine levels with the length of hospital stay.

METHOD

This was a hospital-based prospective observational study. Seventy-three consecutive patients above 18 years of age with acute decompensated heart failure were enrolled in the study. The study duration was from August 2023 to July 2024. Patients with liver cirrhosis, concomitant infection, pulmonary embolism within one month, those undergoing peritoneal or hemodialysis, those planned for CABG, PCI, CRT and valvular surgery and those with life-threatening conditions with an expected survival of <6 months were excluded from the study. Correlation of serum creatinine with length of hospital stay in ADHF patients being extremely variable in different studies,

Correspondence: Dr. Samir Kumar Poudel, Department of Cardiology, National Academy of Medical Sciences, Bir Hospital, Kathmandu, Nepal. Email: poudelsamir@gmail.com, Phone: +977-9852026631.

sample size was calculated based on the correlation between NT-ProBNP and length of hospital stay in systolic heart failure [correlation coefficient (r) = 0.49] in a study from New York Methodist Hospital;[8] keeping the value of α at 5% and β at 10%, sample size was calculated at 40. Heart failure was defined as per the standard definition given by ESC guidelines.[9] Reduced LVEF was defined as LVEF ≤40%, i.e. those with a significant reduction in LV systolic function; this was designated as HFrEF. Mildly reduced LV systolic function, i.e. HFmrEF was LVEF in the range of 41% - 49%. Those with symptoms and signs of HF, with evidence of structural and/or functional cardiac abnormalities and/or raised natriuretic peptides (NPs), and with an LVEF ≥50% were placed under heart failure with preserved ejection fraction (HFpEF). Acute Decompensated Heart Failure (ADHF) was defined as a clinical syndrome of new or worsening signs and symptoms of HF that often lead to hospitalization or an emergency department visit.[10] All the patients admitted in the cardiac wards with the diagnosis of acute decompensated heart failure were enrolled in the study. Patients were advised for blood tests for NT-ProBNP and Serum creatinine in addition to other routine blood tests. These tests were done from the routine lab within 24 hours of presentation to emergency department. The admitted patients were followed up. Their length of hospital stay was noted. Statistical analysis was performed using SPSS version 23. Descriptive statistics were computed. The association between two continuous variables was demonstrated in simple scatter plot. The correlation between the variables was assessed by Spearman correlation. p- value ≤ 0.05 was taken as statistically significant.

RESULTS

Out of the 73 patients with acute decompensated heart failure most were females (56.16%). The mean age of the population was (64.68 ± 16.19) years. Elderly population outnumbered other age-groups (Table 1).

More than half 53.42% of the cases presented in NYHA class IV (Figure 1).

Most of the patients had heart failure with reduced

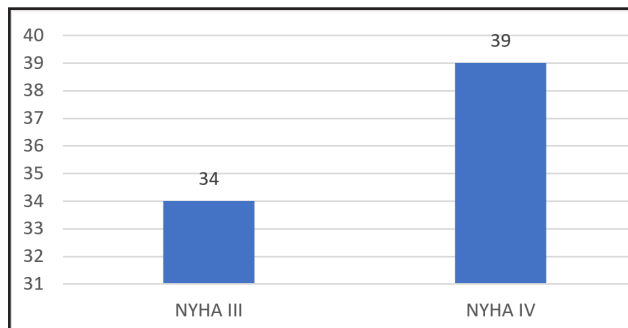| Table 1. Demographics of patient population.	
Variable	**Frequency (%)**
Range = 21 - 90 (in years)	
Mean = (64.68 ± 16.19) years	
Age-Groups	
18 - 44 (Adults)	11
45 - 64 (Middle-aged)	21
65 - 79 (Elderly)	27
>80 (Very elderly)	14
Sex	
Male	32 (43.83%)
Female	41 (56.16%)
Hospital Stay (Mean+SD) = (9.89± 4.3) days	

Figure 1. Patient distribution as per NYHA class.

ejection fraction (HFrEF) followed by those with heart failure with preserved ejection fraction (HFpEF) (Figure 2).
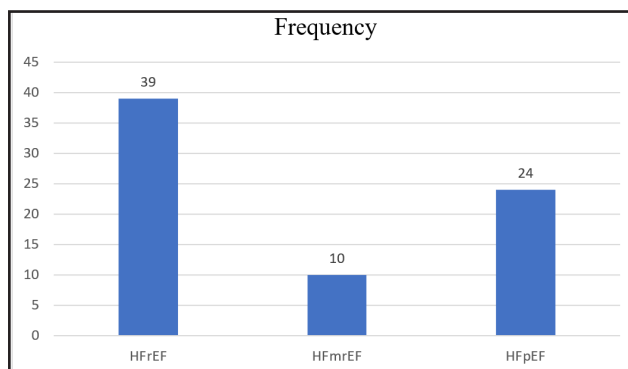

Figure 2. Heart failure category in ADHF patients.

The scatter plot between length of hospital stays and NT-ProBNP showed moderately strong correlation between the two (r = 0.419, p = <0.05) (Figure 3). The scatterplot between serum creatinine and length of hospital stay showed very weak association (r = 0.245, p = 0.037) (Figure 4).
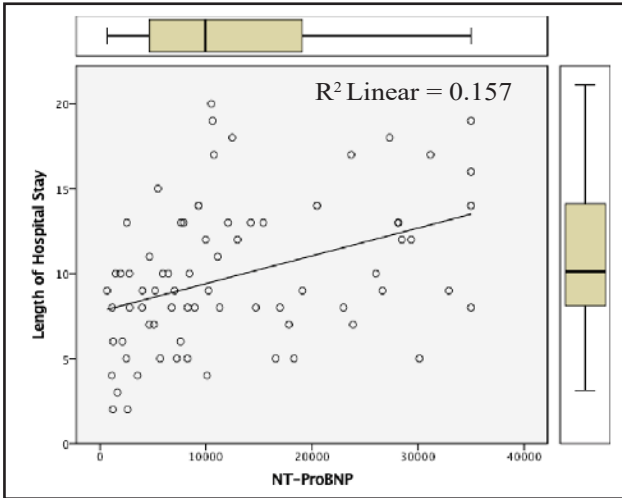
When patients were grouped into two as per the length

Figure 3. Scatterplot between NT-ProBNP level and length of hospital stay in ADHF patients.
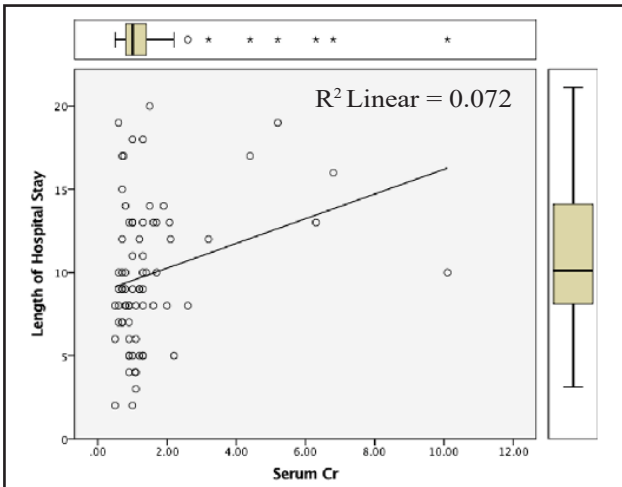

Figure 4. Scatterplot between serum creatinine and length of hospital stay in ADHF patients.

Figure 5. Boxplot showing the relation between NT-ProBNP values and length of hospital stay in patients of ADHF.

Figure 6. Length of hospital stay in patients of ADHF grouped as per the NT-ProBNP values.
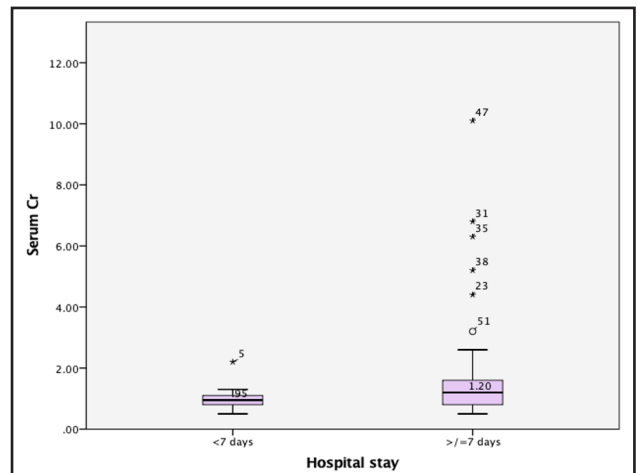
Figure 7. Serum creatinine values as per hospital stay in patients with ADHF.

of hospital stay, there was overlap in the values of NT-ProBNP but the median value was higher in those staying longer i.e. $\geq$ 7 days as shown by the boxplot (Figure 5).

When patients were grouped as per the values of NT-ProBNP, the length of hospital stay was longer for those with higher values though there was considerable overlap (Figure 6).

Serum creatinine values did not show any association with the length of hospital stay (Figure 7). However, those with serum creatinine values>1.5 gm/dl were more likely to have prolonged hospital stay (Figure 8).
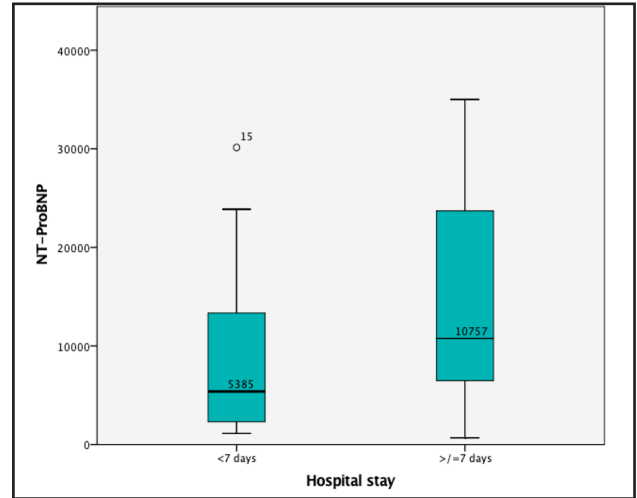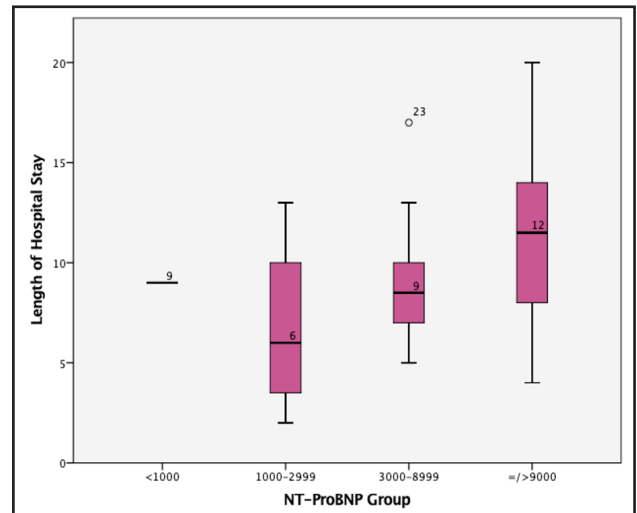
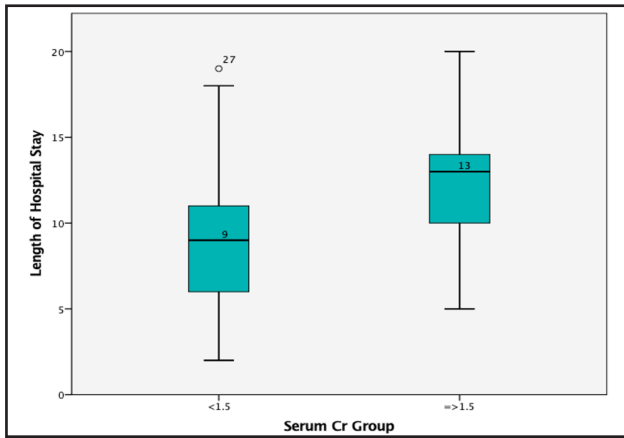The correlation between length of hospital stay

Figure 8. Length of hospital stay as per serum creatinine values in patients with ADHF.

and serum NT-ProBNP level within 24 hours of presentation was assessed using Spearman's test. The correlation was statistically significant (p = <0.05) and the coefficient (r = 0.419) indicates moderately strong correlation. On the other hand, the correlation between length of hospital stays and serum creatinine within 24 hours of hospital presentation was weak (r = 0.245) but statistically significant (p = 0.037). NT-ProBNP and serum creatinine values were assessed using independent samples T-test in patients with shorter (<7days) and prolonged hospital stays (≥7 days). This cut-off point was based on previous publications in the scientific literature.[11] It was statistically significant with NT-ProBNP (p= 0.027) but not with serum creatinine (p=0.087) (Table-2).

Table 2. Independent samples T-test.					
Variables	Hospital stay	Number of patients	Mean	Std Deviation	p-value (2-tailed)
NT-ProBNP	<7 days	20	8568.3	8381.809	0.027
	≥7 days	53	14550.3	10692.36	
Serum Cr	<7 days	20	0.9935	0.36879	0.087
	≥7 days	53	1.6928	1.77924	

DISCUSSION

Despite the growing horizon in the management of decompensated heart failure, the morbidity and mortality due to this entity is still high.[12] Each successive hospital admission due to decompensated heart failure increases the chance of earlier readmissions.[13] and higher mortality in the future.[2] Serum NT-ProBNP and serum creatinine at

the time of admission or within twenty-four hours of presentation were assessed in ADHF patients so as to find out the prognostic significance of these parameters in our population. In our study, the mean age of the population was (64.68 ± 16.19) years and female were higher in number (56.16%). Elderly population outnumbered other age-groups. Mean length of hospital stay was (9.89 ± 4.3) days. In a study from the Persian registry of heart failure, the mean age of participants was (66.13 ± 13.2) years and the mean length of hospitalization was 6.35 ± 5.46 days, male comprising of 66.5% of the population.[14] In a similar study of ADHF done in Brazil, the mean age of the population was 69 ± 16 years and males were more in number (55%); the mean length of hospitalization was 5 days.[15] As of 1st January, 2024, the sex ratio of the total population in Nepal was 0.984 (984 males per 1,000 females) which is lower than the global sex ratio. This might explain the higher number of females in our study. Our patients had longer hospital admissions than these studies most likely because of multiple co morbidities which had to be addressed during admission. In our study, most of the patients presented in NYHA class-IV(53.42%) and the rest were in class III. In a similar study done in Japan, patients admitted with ADHF had NYHA class IV symptoms at baseline in 44.3%, where patients with NYHA class II symptoms were also included (17.3%).[16] In a Malaysian heart failure MY-HF) registry, only 10.4% of acute heart failure patients at admission were in NYHA class IV, 45.3% in class III and the rest in class II.[17] So the NYHA class at admission in acute heart failure patients differ in different studies. However, it shows that our patients with heart failure present late to the medical facilities. In our study, most of the patients had heart failure with reduced ejection fraction (HFrEF) [53.4%] followed by those with heart failure with preserved ejection fraction (HFpEF) [32.8%]. The prevalence of HFrEF (64.6%) was higher than that of HFpEF (21.6%) and HFmrEF (11.4%) in the cohort of patients with acute heart failure in the Malaysian study. Similar study

from the USA revealed that 61% of participants had HFrEF, 5.9% had HFmrEF, and 32% had HFpEF.[18] The distribution of heart failure types among patients is similar in all these studies. In our study,serum NT-ProBNP level showed moderately strong correlation (r = 0.419) with the length of hospital stay. Those having higher values were more likely to have prolonged hospital stay (> 7days) [p = 0.027]. The median value for prolonged stay was 10,757 pg/ml and that for shorter stay was 5,385 pg/ml. In a study from Spain, the median NT-ProBNP of patients with non-prolonged admission (<7 days) was close to 3500pg/dL, while when admission was prolonged (≥7 days) it was close to 6000 pg/mL.[12] In a similar study from Switzerland, patients with NT-proBNP levels ≥6096 ng/l had a 5-day longer length of hospital stay compared to patients with lower values, and these results persisted after adjustment for other co-variables.[19] In another study done in South Carolina, length of hospital stay in ADHF patients showed a positive linear association with increasing NT-proBNP levels with a p- value <0.0005.[20] Our study, however, revealed weak correlation (r = 0.0245) between serum creatinine and the length of hospital stay [p = 0.037]. Serum creatinine values > 1.5 gm/dl were more likely to have prolonged hospital stay but it was statistically not significant [p = 0.087]. The median value of serum creatinine in ADHF patients who had prolonged hospital stay was 1.2mg/dl; patients with shorter hospital stay had a median value of serum creatinine at 0.95 mg/dl. Regarding creatinine, the study from Spain witnessed that patients with non-prolonged admission had a median value of 1.0mg/dL, whilst in prolonged admission, it was 1.5 mg/dL (p < 0.0001).[21] Another paper from Iran showed that the presence of serum creatinine level of >1.5 mg/dl in ADHF patients on admission was associated with prolonged length of hospital stay (p < 0.027).[22] Similar study done by Mohammed W. Akhter et al. found that elevated serum creatinine (>1.5 mg/dl) on admission was common and found in almost half of patients hospitalized with decompensated heart failure; it was associated with prolongation

of length of stay and rate of rehospitalizations after discharge (p<0.001).[23] Statistical significance was not observed with the length of hospital stay and serum creatinine within twenty-four hours of admission in ADHF patients in our study. Our study comprised of a greater number of elderly populations, who have multiple co-morbidities and therefore need further stay in hospital after stabilization of heart failure. This could have been a confounding factor for unusual result in our study. In a study from Poland, a multivariate analysis after adjustment for significant covariates including age, sex, diastolic blood pressure and diabetes, renal impairment clinched its prognostic value [hazard ratio (HR)=2.43 at 95% confidence interval (CI), 1.52–3.89] in HFrEF patients, but its prognostic value was no longer significant in HFpEF patients [HR, 1.46 at 95% CI, 0.66–3.21].[24] About one-third (32.8%) of patients in our study had HFpEF, thus cutting the prognostic significance of serum creatinine with regard to length of hospital stay in ADHF patients.

CONCLUSION

Acute decompensated heart failure is a common cardiac emergency. There are many factors studied as prognostic indicators in patients with this disorder so far but the results are variable. The length of hospital stay (LOS) in these patients is one of the concerns to the treating physicians on the background of limited intensive care unit beds. Serum NT-ProBNP tested within 24-hours of presentation was found to have moderately strong correlation with the length of hospital stay. However, serum creatinine tested within the same time frame had weak correlation with the length of hospital stay but patients with higher values had a tendency of prolonged stay i.e. > 7 days.

Limitations: Our study had a relatively small sample size. Results would have been representative of general population had it included larger number of patients from different areas and ethnicities. Some of the patients were discharged on clinician's discretion so the length of hospital stay could have differed irrespective of their condition at the time of

discharge. Several other factors like socioeconomic status, hospital environment, counselling from treatment staff, cultural issues such as not going back home at 9th day, and lack of confidence on self-care might have been associated with prolonged LOS in some cases.

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