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STUDY OF HEMATOLOGICAL INDICES IN HEART FAILURE WITH REDUCED EJECTION FRACTION AND THEIR ASSOCIATION WITH IN-HOSPITAL OUTCOME.

General Medicine

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ABSTRACT

Background And Objectives: In heart failure with reduced ejection fraction, various hematological parameters are known to be of prognostic significance. This study aimed to correlate these parameters with in-hospital outcome in patients. **Methods:** Patients hospitalized heart failure were enrolled. Hematological indices, including white blood cell counts, neutrophil counts, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio and monocyte to lymphocyte ratio were recorded. **Results:** The study considered 55 patients out of which 29 were male and 26 were female.mean duration of stay in hospital was 5.29 + 3.12.). Patients with NLR > 3.74 & with MLR > 0.49 had a 8.41 & 3.33 times higher risk of in-hospital mortality **Interpretation And Conclusion:** In this study ,NLR, MLR and PLR were independent predictors of in hospital mortality with NLR > 3.74 having the highest independent predictor power in prediction of in-hospital mortality.

KEYWORDS

heart failure, Nuetrophil to Lymphocyte ratio,Monocyte to Lymphocyte ratio, platelet to Lymphocyte ratio.

INTRODUCTION

Many intricate pathophysiological pathways, systemic inflammation being one of significant importance play a role in development and progression of heart failure.[1]HF progression is associated with leucocytosis mainly neutrophilia.[2].

The pro-inflammatory roles of lymphocytes and monocytes contribute to myocardial remodeling or negative inotropy.[3]Inflammation delays the neutrophils' apoptosis, causes increase in numbers. [4]

Whereas, lymphocyte apoptosis is activated by the severity of congestion in HF.[5] Increased left ventricular (LV) filling pressures, LV dilation and augmented shear stress forces induce monocyte activation, while chemokine secretion, end-organ hypoxia and systemic congestion may trigger monocyte mobilization and recruitment to the myocardium. [6].

MATERIALS AND METHODS

The prospective study was carried out between November 2021 TO February 2023 at Victoria hospital attached to Bangalore Medical College and Research Institute.Approval and clearance were obtained from institutional ethics committee.The study included patients aged >18years with heart failure with reduced ejection fraction(<40%) and excluded patients <18y and those with active infection. Case record form with follow up chart was used to record the demographic data , clinical features of the disease and blood investigations. The demographic and clinical data were collected.complete hemogram and 2d echo were obtained.all patients were followed up until discharge or death in hospital.

Study Design:

Based on the previous study conducted by C.DELCEA et al, by considering the sensitivity of NLR in predictors of In-hospital mortality, the sample size is calculated as follows,

Formula,

$$n = \frac{Z^2 Sen(1-Sen)}{d^2 \times p}$$

Where,

n = sample size

Z_α = Standard table value for 95% confidence interval(CI) = 1.96

Sen= Sensitivity of NLR in predictors of In-hospital mortality= 78.38%

d = Clinically expected precision = 7

p = proportion of In-Hospital mortality = 2.9%

On substitution,

$$n = \frac{1.96^2 \times 78.38(100-78.38)}{7^2 \times 2.9}$$

$$n = 45.8$$

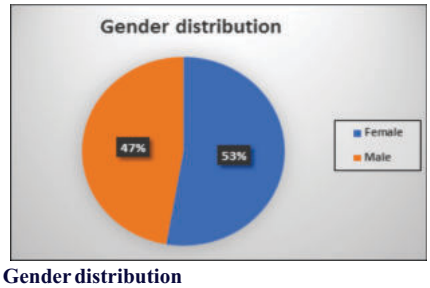
Therefore the samples size is approx. 46

RESULTS

The study considered 55 patients admitted to our centre and were diagnosed as heart failure with reduced ejection fraction. The demographic and clinical characteristics are given in table 1 and 2.Duration of hospital stay and haematological indices are given in table 3 and 4.

i) Table No-1: Gender distribution of study Participants (Total = 55)

Gender	Frequency(n)	Percentage (%)
Female	29	52.7
Male	26	47.3
Total	55	100



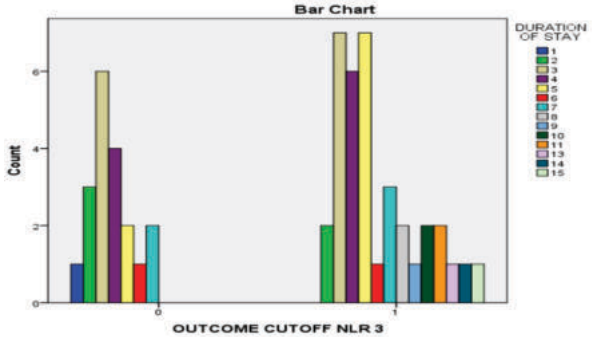
ii) Fig 1: Gender distribution

iii) Table No-2: Age distribution (Total=55)

Mean age	Median age	Minimum	Maximum
54.91	57	23	75

iv) Table No-3: Duration of stay in the hospital (in days):

Mean + SD	Median(IQR)	Min	Max
5.29 + 3.12	4 (3-7)	1	15

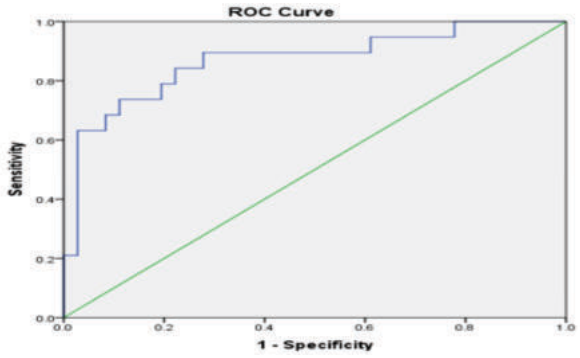


v) Fig 2: Duration of stay in the hospital

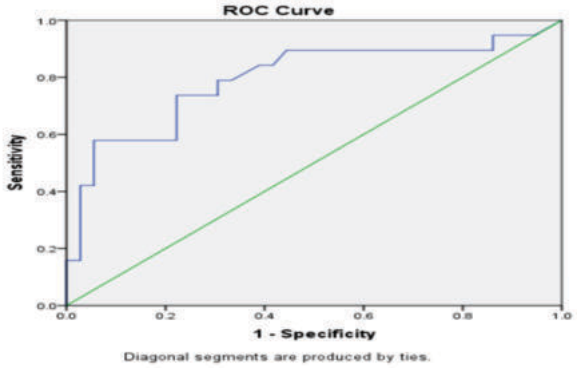
In this graph on x-axis: 0 = DEATH, 1 = DISCHARGE

vi) Table No-4: Hematological indices (One sample t-test)

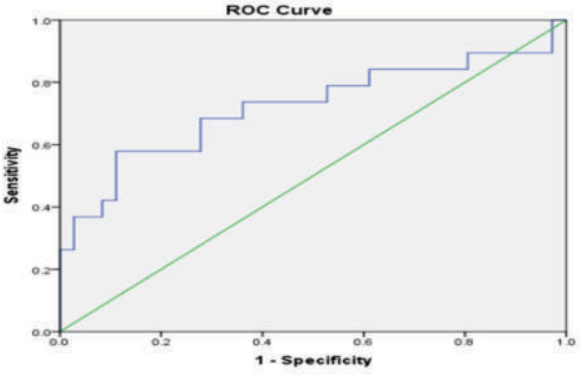
Indices	Mean + SD	Median(IQR)	SE	95% CI (LL-UL)	P value
NLR	8.05 + 6.13	6.18(3.33-10.49)	0.83	6.39 – 9.71	<0.001
MLR	0.598 + 0.43	0.50(0.34-0.81)	0.06	0.48 – 0.72	<0.001
PLR	256.81 + 237.99	208.33(112.57-288.89)	32.09	192.48 – 321.15	<0.001



1) NLR



2) MLR



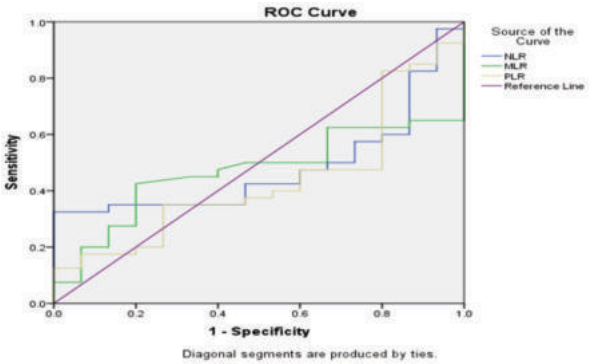
3) PLR

vii) Fig3: ROC Curves (Hematological indices and in-hospital mortality):

viii)Table 5: Hematological indices – Predictors of in-hospital mortality:

Indices	AUC	95% CI	p-value	Cut off	Sen	Spe	OR
NLR	0.868	0.761 – 0.976	<0.001	> 3.74	94.7%	38.9%	8.41
MLR	0.795	0.656 – 0.933	<0.001	> 0.49	84.2%	61.1%	2.87
PLR	0.722	0.563 – 0.881	0.007	> 153.92	78.9%	38.9%	3.33

All the indices are significant predictors of in-hospital mortality (p<0.05). Patients with NLR > 3.74 & with MLR > 0.49 had a 8.41 & 3.33 times higher risk of in-hospital mortality. Therefore NLR > 3.74 has the highest independent predictor power of hematological indices in prediction of in-hospital mortality.



ix) Fig 4;ROC (Hematological indices and duration of stay):

x) Table 6:Hematological indices – Predictors of duration of stay in hospital:

Indices	AUC 95% CI	p-value	Cut off	Sen, Spe	OR	Probability
NLR	0.480 (0.324 – 0.636)	0.821	> 3.74	67.5%,13.3%	0.45	31%
MLR	0.469 (0.318 – 0.620)	0.727	> 0.49	50%,33.3%	0.37	27%
PLR	0.435 (0.272 – 0.598)	0.461	> 153.92	62.5%,20%	0.40	28%

None of the indices are significant predictors of duration of stay in hospital (p>0.05).
Since ODD's ratio of all 3 indices were <1, hence none of them are independent predictors of duration of stay in the hospital.

But by considering probability, 31%, 27%, 28% of the patients with NLR > 3.74, MLR > 0.49 & PLR > 153.92 respectively had prolong hospital stay.

PEARSON's correlation:
Table 7:NLR and duration of stay in hospital:

	NLR	DURATION OF STAY			
	X	Pearson Correlation	Sig. (2-tailed)	Pearson Correlation	Sig. (2-tailed)
NLR	55	1		-0.147	0.284*
DURATION OF STAY	55	-0.147	0.284*	1	

*P>0.05 hence statistically not significant

Table 8: MLR and duration of stay in hospital:

	MLR	DURATION OF STAY			
	X	Pearson Correlation	Sig. (2-tailed)	Pearson Correlation	Sig. (2-tailed)
MLR	55	1		-0.141	0.306*
DURATION OF STAY	55	-0.141	0.306*	1	

*P>0.05 hence statistically not significant

Table 9: PLR and duration of stay in hospital:

	PLR	DURATION OF STAY			
	X	Pearson Correlation	Sig. (2-tailed)	Pearson Correlation	Sig. (2-tailed)
MLR	55	1		-0.161	0.239*
DURATION OF STAY	55	-0.161	0.239*	1	

*P>0.05 hence statistically not significant

Table 10:Duration of stay and Outcome:(Chi square test)

Duration of stay	DEATH	DISCHARGE
<7 days	17	23
> 7 days	2	13
TOTAL	19	36

The two-tailed P value equals 0.058, hence the association is statistically not significant(p>0.05)

Table 11:NLR cut off ratio and duration of stay in hospital:

	< 7 days	> 7days
> 3.74	28	13
< 3.74	12	2
Total	40	15

The two-tailed P value equals 0.3040, hence the association is statistically not significant(p>0.05)

Table12;MLR cut off ratio and duration of stay in hospital:

	< 7 days	> 7days
> 0.49	20	10
< 0.49	20	5
Total	40	15

The two-tailed P value equals 0.3656, hence the association is statistically not significant(p>0.05)

Table 13:PLR cut off ratio and duration of stay in hospital:

	< 7 days	> 7days
> 153.92	25	12
< 153.92	15	3
Total	40	15

The two-tailed P value equals 0.3353, hence the association is statistically not significant(p>0.05)

Limitations

1) The sample size was limited.
2) The study did not correlate prognostic index with various age population

DISCUSSION

In this study, three hematological indices derived from the leukocyte differential, NLR, MLR and PLR were compared for predicting in-hospital prognosis of HF patients.This study correlated all three indices in univariate analysis to both in-hospital mortality and prolonged hospitalization patients with heart failure with reduced ejection fraction.

Cox regression using the prediction parameters derived from this study identified increased MLR ,NLR,PLR as the l indices with independent prognostic value for in-hospital mortality. All the indices are significant predictors of in-hospital mortality ($p<0.05$). Patients with NLR > 3.74 & with MLR > 0.49 had a 8.41 & 2.87 times higher risk of in-hospital mortality. Therefore NLR > 3.74 has the highest independent predictor power of hematological indices in prediction of in-hospital mortality.

Regarding LOS, one prior study correlated dynamic improvement of NLR to longer hospitalization in HF [7]however, this study did not show any significant correlation between hematological indices and length of hospital stay. None of the indices are significant predictors of duration of stay in hospital ($p>0.05$).Since ODD's ratio of all 3 indices were <1, hence none of them are independent predictors of duration of stay in the hospital.

But by considering probability, 31%, 27%, 28% of the patients with NLR > 3.74, MLR > 0.49 & PLR > 153.92 respectively had prolong hospital stay.

HF and inflammation play a key role in stimulating genesis of blood cells and function. monocyte activation and recruitment is triggered by multiple pathways [8]which accumulate in myocardium causing fibrosis and worsening of heart failure.[9] increase in neutrophil lifespan in congestive heart failure patients is found to cause endothelial damage and worsen the outcome. [10]

Studies showed that, in pateints with heart failure with reduced ejection fraction lymphocytopenia was associated with worse in hospital outcome. [11] Increased neutrophil level was linked to lv dysfunction due to the effect of circulating MPO secreted by neutrophils. [12]

CONCLUSION

The haematological indices are cost effective biomarkers that can be used to predict in hospital mortality in heart failure with reduced ejection fraction.In our study,NLR,MLR and PLR were independent predictors of in hospital mortality with NLR > 3.74 having the highest independent predictor power in prediction of in-hospital mortality.

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