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Utility of Neutrophil-To-Lymphocyte Ratio as Prognostic Marker of Dilated Cardiomyopathy in Children

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ABSTRACT

Background: Dilated cardiomyopathy (DCM) is a frequent form of cardiomyopathy exhibiting systolic and/or diastolic dysfunction, leading to varying degrees of heart failure (HF). The present research was aimed at assessing the utility of the neutrophil-to-lymphocyte ratio (NLR) as a prognostic marker of DCM in children.

Methods: This cohort study was conducted at the Department of Pediatrics, Rai Teaching Hospital, Sargodha, Pakistan, from October 2022 to September 2024. Seventy-four children of both genders aged up to 18 years with an established diagnosis of DCM and taking treatment for chronic HF were analyzed. Non-probability, consecutive sampling technique was adopted. The NLR for each patient was determined by dividing the total count of neutrophils by the total count of lymphocytes. Children were advised a bi-monthly follow-up and outcomes were recorded after 6 months. The chi-square test was applied to compare categorical data whereas an independent sample t-test was employed for comparing numeric data. P<0.05 was labeled as the level of significance.

Results: This cohort study was conducted at the Department of Pediatrics, Rai Teaching Hospital, Sargodha, Pakistan, from October 2022 to September 2024. Seventy-four children of both genders aged up to 18 years with an established diagnosis of DCM and taking treatment for chronic HF were analyzed. Non-probability, consecutive sampling technique was adopted. The NLR for each patient was determined by dividing the total count of neutrophils by the total count of lymphocytes. Children were advised a bi-monthly follow-up and outcomes were recorded after 6 months. The chi-square test was applied to compare categorical data whereas an independent sample t-test was employed for comparing numeric data. P<0.05 was labeled as the level of significance.

Conclusion: The study demonstrated that NLR may hold promise as a prognostic marker for pediatric DCM. The significant association between lower NLR and survival highlights the potential utility of this simple and cost-effective biomarker in risk stratification and clinical decision-making.

Keywords: Biomarker, Dilated Cardiomyopathy, Heart Failure, Neutrophil, Lymphocyte.

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INTRODUCTION

Heart failure (HF) is a persistent inflammatory condition characterized by unclear hormonal and immunological processes[1]. Dilated cardiomyopathy (DCM) is a frequent form of cardiomyopathy exhibiting into systolic and/or diastolic dysfunction, leading to varying degree of HF[2]. Despite treatment efforts, the prognosis remains unfavorable, with a substantial risk of mortality, hospital readmissions, or the necessity for cardiac transplantation[3]. Several factors that impact the prognosis include age, HF severity, occurrence of arrhythmias, and the extent of ventricular function impairment[4,5].

Literature suggests that inflammation plays a key role in the onset and development of cardiovascular diseases (CVD)[6]. Chronic inflammation is also prevalent among HF patients. Two relatively new inflammatory biomarkers, namely "Neutrophil-to-Lymphocyte Ratio (NLR)" and "Platelet-to-Lymphocyte Ratio (PLR)", have been employed as prognostic indicators in numerous diseases. Researchers have revealed that higher NLR exhibited raised death rates in individuals with coronary artery disease (CAD)[7,8,9].

Biomarkers like "B-type natriuretic peptide (BNP)", highly sensitive troponins, and soluble protein ST2 have proven valuable for assessing the severity of HF and the risk of both short-term and long-term mortality[10]. However, these biomarkers are often expensive and not widely available. On the other hand, routine hemogram tests are readily accessible and routinely ordered for patients during follow-up. The potential for a cost-effective biomarker derived from hemogram data is highly beneficial in clinical practice. The NLR is emerging as a relatively newer inflammatory biomarker and is being adopted in the prognosis and staging of numerous chronic diseases. As the inflammatory process is an important consideration behind HF, evaluation of NLR may hold prognostic value and marker of dilated cardiomyopathy in children. This study aimed to assess the utility of NLR as a prognostic marker of DCM in children.

METHODS

This prospective observational cohort study was performed at the Department of Pediatric Medicine, Rai Teaching Hospital, Sargodha, Pakistan from October 2022 to September 2024. Approval was obtained from "Institutional Ethical Committee" (ERC/2020/095). A sample size of 64 was calculated using the OpenEPI online sample size calculator considering the mortality in pediatric cardiomyopathy as 12.0%,[11] with 95% confidence level, and 8% margin of error. Anticipating 15% drop-out, another 10 patients were added to the sample size, and this study finally analyzed 74 children. The inclusion criteria for this research were children aged up to 18 years having an established diagnosis of DCM and taking treatment for chronic HF. Exclusion criteria consisted of children who had congenital heart disease or other forms of cardiomyopathy (like diabetic cardiomyopathy). Children were also excluded if they had chronic inflammatory conditions or severe infections. Children reporting a history of any kind of cardiac procedures were also not included. Informed consents from the participants or their parents/guardians were also required. Non-probability, consecutive sampling technique was adopted.

Age, gender, residence, and "left ventricular ejection fraction (LVEF)" were noted at the time of inclusion. The NLR for each patient was determined by dividing the total count of neutrophils by the total count of lymphocytes. Treatment advised included an appropriate dose of diuretics (if congestive symptoms present), "angiotensin-converting enzyme inhibitors", β-blockers, spironolactone (if LVEF<30%), and digoxin (if presence of refractory symptoms). The contact number of the legal guardians of the children enrolled was taken and a reminder for the scheduled follow-up was sent using phone calls. Children were advised a bi-monthly follow-up and outcomes were recorded after 6 months. The outcome was noted in terms of life or mortality. Need for the hospitalization during the follow-up period was also recorded. Data of children missing the mandatory minimum follow-up period of six months were excluded from the analysis. A special format was formed to record all the study data.

Data analysis was performed using "IBM-SPSS Statistics", version 26.0. Mean and standard deviation were calculated for variables of numeric nature. Frequency and percentages were chosen for the representation of data categorical in nature. The chi-square test was applied to compare categorical data whereas an independent sample t-test was employed for comparing numeric data. P<0.05 was labeled as the level of significance.

RESULTS

Table-1: Baseline Parameters (n=74)

Characteristics		Frequency (%) / Mean±SD
Gender	**Boys**	43 (58.1%)
	Girls	31 (41.9%)
Age (years)	**≤5**	51 (68.9%)
	6-12	15 (20.3%)
	13-18	8 (10.8%)
Residence	**Urban**	29 (39.2%)
	Rural	45 (60.8%)

Serum creatinine (mg/dl)	0.8±0.2
Oxygen saturation (%)	95.0±4.8
C-reactive protein (mg/L)	4.8±1.15
Left ventricular ejection fraction (%)	39.28±12.63
Hemoglobin (g/dl)	11.4±1.6
Leukocytes (/mm^3)	9428±4658
Platelets (10^9/L)	321±162
Neutrophils (/uL)	5274±4239
Lymphocytes (/uL)	3414±1645
Neutrophil-to-lymphocyte ratio	1.6±2.2

In a total of 74 patients, 43 (58.1%) were boys, representing a boy-to-girl ratio of 1.4:1. The mean age was 4.61±4.37 years while 51 (68.9%) patients were aged ≤ 5 years. The residential status of 45 (60.8%) children was rural. **Table 1** shows details of the baseline demographic, clinical, and laboratory parameters.

By the end of the mandatory period of 6-month follow-up, mortality was reported among 18 (24.3%). Need for readmission was noted in 13 out of 18 children who died while this was 15 out of 56 children who survived (72.2% vs. 26.8%, p=0.030). The mean NRL among children who survived was significantly lower than those who died (p<0.001), and the details are shown in **Figure 1.**

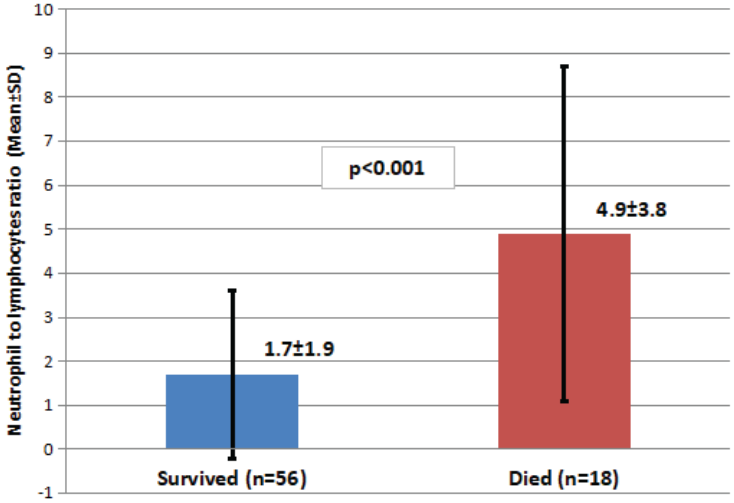

Figure 1: Comparison of NLR with respect to outcome

Table 2: Comparison of baseline characteristics with respect to final outcome (N=43)

Baseline characteristics		Survived (n=56)	Died (n=18)	P-value
Gender	**Boys**	35 (62.5%)	8 (44.4%)	0.177
	Girls	21 (37.5%)	10 (55.6%)	
Age (years)	**≤5**	42 (75.0%)	9 (50.0%)	0.136
	6-12	9 (16.7%)	6 (33.3%)	
	13-18	5 (8.9%)	3 (16.7%)	
Residence	**Urban**	22 (39.2%)	7 (38.8%)	0.976
	Rural	34 (60.8%)	11 (61.2%)	
Serum creatinine (mg/dl)		0.8±0.1	0.8±0.2	1

Oxygen saturation (%)	95.8±3.9	93.4±5.6	0.046
C-reactive protein (mg/L)	4.61±1.38	5.19±1.07	0.108
LVEF (%)	42.64±11.05	32.98±10.71	0.002
Hemoglobin (g/dl)	11.5±1.7	11.2±1.2	0.4901
Leukocytes (/mm^3)	8972±3281	9902±4273	0.336
Platelets (10^9/L)	316±130	332±169	0.675

Among patients who died, oxygen saturation (p=0.046), and LVEF were significantly lower at the time of enrollment when compared to those who survived (p=0.002). The details about the comparison of baseline characteristics of children with respect to final outcomes are shown in **Table 2**.

DISCUSSION

The main objective of this research was to assess the prognostic value of NLR in pediatric DCM. Our results indicated that the mean NLR was significantly lower among children who survived (1.7±1.9) compared to those who died (4.9±3.8) (p<0.001). This finding suggests that NLR may indeed serve as a valuable prognostic marker in pediatric DCM. The observed linkage between NLR and outcomes may reflect the inflammatory nature of DCM[12,13]. Elevated NLR could signify a heightened inflammatory response, which has been linked to cardiac remodeling and adverse cardiac outcomes[14,15]. Pediatric DCM may involve immune dysregulation, and NLR, as a marker of the innate immune response, could be reflective of this imbalance. A study from Brazil explored NLR and its potential utilization as a prognostic marker for poor outcomes among children with DCM[16]. Similar to our findings, they also noted significantly higher NLR among children with DCM who died in comparison to those who survived (1.9±4.6 vs. 5.5±7.9, p=0.034). The present findings along with others exhibit that high NLR is linked with poor prognosis and enhances the chances of poor outcomes among children with DCM[16].

A study from Turkey revealed that NLR was significantly raised among patients with hypertrophic cardiomyopathy and it was related to a significantly higher risk of sudden cardiac death[17]. In another research, the authors found that NLR was raised among patients of HF when compared to age and gender-matched controls, although that study was conducted among the adult population[18]. The same study also concluded that NRL can be utilized to predict death during follow ups of HF patients. Another study highlighted high NLR among acute heart failure patients at the time of admission to be an independent predictor of in-hospital and post-discharge 3-year mortality[19]. Another research found that NLR was linked with the existence of subclinical diabetic cardiomyopathy which further suggests that NLR can be used as a biomarker to predict diabetic cardiomyopathy[20]. A comprehensive review concluded that increased NLR among HF cases is an important biomarker regarding the severity and poor prognosis[21].

Importantly, most studies evaluating the utilization of NLR have been conducted among adult populations, and there is a scarcity of data about the utility of NLR as a prognostic marker among children with DCM[22,23]. Still, whatever relevant literature is present, it supports the utilization of NLR for predicting poor outcomes among children with DCM[24,25]. The precise NLR thresholds and associations may vary among different cardiac conditions, so more research is needed to further add to what is already known in these aspects.

Being a single-center study and a relatively short follow-up period, there were some of limitations of this study. Further prospective studies employing long-term follow-ups and exploring the linkage of different thresholds of NLR with outcomes can provide valuable information

CONCLUSION

The study demonstrated that NLR may hold promise as a prognostic marker for pediatric DCM. The significant association between lower NLR and survival highlights the potential utility of this simple and cost-effective biomarker in risk stratification and clinical decision-making. However, further prospective studies with larger sample sizes and comprehensive consideration of treatment effects, comorbidities, and disease severity are necessary to validate these findings and to establish NLR as a robust prognostic tool in the management of pediatric DCM.

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CONFLICT OF INTEREST`
None

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ETHICAL APPROVAL
The study received ethical approval from the Institutional Ethics Committee of Rai Medical College Teaching Hospital, Sargodha, Pakistan, under reference number ERC/2020/095.

AUTHORS' CONTRIBUTIONS
SL did data collection, and drafting, was responsible for the data's integrity, and approved for publication. **SHS** designed conceived the idea, supervised, proofread, made critical revisions, and approved for publication

REFERENCES
1. Agrawal A, Janjua D, Alsayed AZAA, Taher EA. Heart failure in children and adolescents: an update on diagnostic approaches and management. Clin Exp Pediatr. 2024;67(4):178-190. doi: 10.3345/cep.2023.00528
2. Mallavarapu A, Taksande A. Dilated Cardiomyopathy in Children: Early Detection and Treatment. Cureus. 2022;14(11):e31111. doi:10.7759/cureus.31111
3. Mumbulu ET, Nkodila AN, Saint-Joy V, Moussinga N, Makulo JR, Buila NB. Survival and predictors of mortality in patients with heart failure in the cardiology department of the Center Hospitalier Basse Terre in Guadeloupe: historical cohort study. BMC Cardiovasc Disord. 2024;24(1):599. doi: 10.1186/s12872-024-04268-1
4. Jenča D, Melenovský V, Stehlik J, Stanek V, Kettner J, Kautzner J, et al. Heart failure after myocardial infarction: incidence and predictors. ESC Heart Fail. 2021;8(1):222-237. doi:10.1002/ehf2.13144
5. Chen S, Chen L, Duru F, Hu S. Heart Failure in Patients with Arrhythmogenic Cardiomyopathy. J Clin Med. 2021;10(20):4782. doi:10.3390/-jcm10204782
6. Alfaddagh A, Martin SS, Leucker TM, Michos ED, Blaha MJ, Lowenstein CJ, et al. Inflammation and cardiovascular disease: From mechanisms to therapeutics. Am J Prev Cardiol. 2020;4:100130. doi:10.1016/j.ajpc.2020.100130
7. Karaca G, Ekmekci A, Kimiaei A, Safaei S, Özer N, Tayyareci G. The Impact of the Neutrophil-to-Lymphocyte Ratio on In-Hospital Outcomes in Patients With Acute ST-Segment Elevation Myocardial Infarction. Cureus. 2024;16(2):e54418. doi: 10.7759/cureus.54418
8. Bagyura Z, Kiss L, Lux Á, Csaba C, Jermendy AL, Polgar L, et al. Neutrophil-to-Lymphocyte Ratio Is an Independent Risk Factor for Coronary Artery Disease in Central Obesity. Int J Mol Sci. 2023;24(8):7397. doi:10.3390/ijms24087397
9. Wang W, Liu L, Ning Z, Che L, Li X. The neutrophil-lymphocyte ratio to predict poor prognosis of critical acute myocardial infarction patients: a retrospective cohort study. Biochem Med (Zagreb). 2023;33(1):010702. doi:10.11613/BM.2023.010702
10. Kantor FP, Rusconi P. Biomarkers in pediatric heart failure: their role in diagnosis and evaluating disease progression. Prog Pediatr Cardiol. 2011;33:53-7. doi: 10.1016/j.ppedcard.2011.06.003
11. Tsirka AE, Trinkaus K, Chen SC, Lipshultz SE, Towbin JA, Colan SD, et al. Improved outcomes of pediatric dilated cardiomyopathy with utilization of heart transplantation. J Am Coll Cardiol. 2004 Jul 21;44(2):391-7. doi: 10.1016/j.jacc.2004.04.035
12. Zhang JL, Yang R, Zhu Y, Shao Y, Ji Y, Wang FF. Association between the neutrophil-to-lymphocyte ratio and risk of in-hospital heart failure and arrhythmia in patients with acute myocardial infarction. Front Cardiovasc Med. 2023 Oct 20;10:1275713. doi: 10.3389/fcvm.2023.1275713
13. Qi B, Yang ZJ, Huang N, Zheng WB, Gui C. Exploring the diagnostic and prognostic value of the C-reactive protein/lymphocyte ratio for dilated cardiomyopathy based on a real-world study. Sci Rep. 2023;13(1):18889. doi: 10.1038/s41598-023-46338-y
14. Vakhshoori M, Nemati S, Sabouhi S, Yavari B, Shakarami M, Bondariyan N, et al. Neutrophil to lymphocyte ratio (NLR) prognostic effects on heart failure; a systematic review and meta-analysis. BMC Cardiovasc Disord. 2023;23(1):555. doi: 10.1186/s12872-023-03572-6
15. Lillo R, Graziani F, Franceschi F, Iannaccone G, Massetti M, Olivotto I, et al. Inflammation across the spectrum of hypertrophic cardiac phenotypes. Heart Fail Rev. 2023;28(5):1065-1075. doi: 10.1007/s10741-023-10307-4
16. Araújo FDDR, Silva RMFDL, Oliveira CAL, Meira ZMA. Neutrophil-to-lymphocyte ratio used as prognostic factor marker for dilated cardiomyopathy in childhood and adolescence. Ann Pediatr Cardiol. 2019;12(1):18-24. doi:10.4103/apc.APC_47_18
17. Ozyilmaz S, Akgul O, Uyarel H, Pusuroglu H, Gul M, Satilmisoglu MH, et al. The importance of the neutrophil-to-lymphocyte ratio in patients with hypertrophic cardiomyopathy. Rev Port Cardiol. 2017;36(4):239-246. doi:10.1016/j.repc.2016.09.014
18. Durmus E, Kivrak T, Gerin F, Sunbul M, Sari I, Erdogan O. Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio are Predictors of Heart Failure. Arq Bras Cardiol. 2015;105(6):606-613. doi:10.5935/abc.20150126
19. Cho JH, Cho HJ, Lee HY, Ki Y, Jeon E, Hwang K, et al. Neutrophil-Lymphocyte Ratio in Patients with Acute Heart Failure Predicts In-Hospital and Long-Term Mortality. J Clin Med. 2020;9(2):557. Published 2020 Feb 18. doi:10.3390/jcm9020557
20. Huang X, Qin Z, Xu M, Zhang F, Jiang X, Hua F, et al. Neutrophil: lymphocyte ratio is positively associated with subclinical diabetic cardiomyopathy. BMC

Endocr Disord. 2020;20(1):99. doi:10.1186/s12902-020-00571-y
21. Delcea C, Buzea CA, Dan GA. The neutrophil to lymphocyte ratio in heart failure: a comprehensive review. Rom J Intern Med. 2019;57(4):296-314. doi:10.2478/rjim-2019-0018
22.= Avci A, Alizade E, Fidan S, Yesin M, Guler Y, Kargin R, et al. Neutrophil/lymphocyte ratio is related to the severity of idiopathic dilated cardiomyopathy. Scand Cardiovasc J. 2014;48(4):202-8. doi: 10.3109/14017431.2014.932922
23. Wang Y, Zhuang Y, Lin C, Hong H, Chen F, Ke J. The neutrophil-to-lymphocyte ratio is associated with coronary heart disease risk in adults: A population-based study. PLoS One. 2024;19(2):e0296838. doi: 10.1371/journal.pone.0296838
24. Ahmed M, El Amrousy D, Hodeib H, Elnemr S. Neutrophil-to-lymphocyte ratio as a predictive and prognostic marker in children with dilated cardiomyopathy. Cardiol Young. 2023;33(12):2493-2497. doi: 10.1017/S1047951123000501
25. Gao P, Liu J, Wang X, Zhang P, Jin Y, Bai L, et al. The association between neutrophil-lymphocyte ratio and poor outcomes following infant cardiac surgery. BMC Cardiovasc Disord. 2021;21(1):529. doi: 10.1186/s12872-021-02345-3. Retraction in: BMC Cardiovasc Disord. 2024 Oct 26;24(1):596. doi: 10.1186/s12872-024-04285-0