Prognostic Value of Neutrophil to Lymphocyte Ratio Marker in Chest Infection in Pediatric Intensive Care Unit

Rasha M. Zakria [a], Effat H. Assar [a], Yasser M. Ismael [b],

Samira S. Mohamed [a], Nouran R. Badr [a]

[a] Pediatrics Department, Faculty of Medicine Benha University, Egypt.

[b] Clinical and Chemical Pathology Department, Faculty of Medicine Benha University, Egypt.

Corresponding to:
Dr. Samira S. Mohamed.
Pediatrics Department, Faculty of Medicine Benha University, Egypt.
Email:
samira.shehata92@gmail.com

Abstract:

Background: Acute respiratory failure in children, often due to pneumonia and bronchiolitis, commonly leads to acute lung injury (ALI) and pediatric acute respiratory distress syndrome (PARDS) in Pediatric Intensive Care Units (PICUs). The neutrophil-to-lymphocyte ratio (NLR) is a potential prognostic marker for these conditions. This study aimed to evaluate NLR as a predictor of disease severity and outcomes, including mechanical ventilation and mortality, in pediatric chest infections in the PICU. **Methods:** This cross-sectional study included 100 children admitted to the PICU at Benha University Hospital for chest infections. Clinical data, lab results, and outcomes were assessed for each patient. **Results:** Of the 100 children (56 males, 44 females), pneumonia was diagnosed in 70%. NLR was significantly higher in patients needing mechanical ventilation (p<0.001) and those who died (p<0.001). NLR correlated positively with CRP, CO2, and hospital stay duration, and negatively with platelets, pH, and HCO3. ROC analysis showed an AUC of 0.876 for predicting mechanical ventilation and 0.950 for predicting mortality, with high sensitivity and specificity at cutoffs of >5.1 and >5.9, respectively. Conclusion: NLR is a valuable, rapid, and cost-effective prognostic marker for predicting the need for mechanical ventilation and mortality in children with chest infections in the PICU.
Keywords: NLR, Chest Infection, PICU.

Introduction

Acute respiratory failure in children, often caused by pneumonia and bronchiolitis, frequently meets criteria for acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) during their ICU stay [1]. Pediatric acute respiratory distress syndrome (PARDS) is prevalent in PICUs globally, affecting approximately 1 in 100 children admitted, with an incidence ranging from 1.4 to 9.5 cases per 100,000 annually [2].

Pediatric pneumonia, a leading cause of morbidity and mortality worldwide, poses significant diagnostic challenges, particularly in developing countries, and accounts for 18% of all deaths in children under five years old [3].

Respiratory disorders are often linked to inflammatory reactions involving cytokines such as interleukin-1, interleukin-6, interleukin-8, and tumor necrosis factor α [4]. Early-stage pneumonia can progress to severe pneumonia (SP) due to inadequate empirical antibiotic treatment [5].

The neutrophil-to-lymphocyte ratio (NLR), derived from the complete blood count, reflects the balance between neutrophils, indicative of innate immune response, and lymphocytes, representing adaptive immunity [6]. Neutrophils, key players in the systemic inflammatory response syndrome (SIRS), are critical in host defense mechanisms such as chemotaxis, phagocytosis, and cytokine production [7].

NLR has been associated with increased mortality from chronic lower respiratory diseases, influenza, and pneumonia [8]. Lymphocytes, including various subsets like B cells and T cells, are central to adaptive immunity and the host response to pathogens and SIRS [9].

However, factors such as age, steroid intake, and hematological disorders can falsely elevate NLR, highlighting the delicate balance in immune response [10].

The purpose of this study was to evaluate NLR as a predictor of disease severity and outcomes, including mechanical ventilation and mortality, in pediatric chest infections in the PICU.

Patients and methods:

Patients:

This cross-sectional study was conducted at Benha University Hospital, during the period from January 2023 to October 2023, and included 100 children admitted to PICU of Benha University Hospital due to chest infection.

The study was done after being approved by IRB, Faculty of Med, Benha University (**Approval code: MS 32-4-2023**). Informed consent was obtained from all parents of children included.

Inclusion criteria were pediatrics aged > 1 month to 18 years old of both sexes.

Exclusion criteria were children with active pulmonary tuberculosis, noninfectious interstitial pulmonary disease, malignant tumor, used immunosuppressive drugs, had other medical condition as immunodeficiency, metabolic or endocrinal disorders, cardiac and renal comorbidity and refusal to participate.

Methods:

All the infants were subjected to the following:

Full medical and demographic history taking: This included personal details (age, sex, residence), past medical history (antenatal, natal, postnatal), developmental history, current symptoms and their duration, any comorbidities or medications, past hospital admissions or surgeries, and family history, including consanguinity.

General examination: This included assessing the level of consciousness, complexion (pallor, jaundice, cyanosis), and vital signs (heart rate, respiratory rate, blood pressure, temperature). Anthropometric measurements such as weight, height, and BMI were recorded according to WHO percentiles. A systematic examination was conducted, covering the cardiovascular system

(abnormal heart sounds or murmurs), gastrointestinal tract and abdomen (organomegaly or ascites), and central nervous and musculoskeletal systems (Glasgow coma score, pupillary reaction, motor system power, tone, and reflexes) [11].

Local examination: This included checking for adventitious sounds (wheezes, crepitation), decreased air entry, and signs of respiratory distress, graded as: Grade II (tachypnea, intercostal retraction), Grade III (tachypnea, intercostal retraction, grunting), and Grade IV (tachypnea, intercostal retraction, grunting, cyanosis) [12].

Laboratory Investigations: This included a complete blood count (CBC), arterial blood gases (ABGs), C-reactive protein (CRP), and blood culture. Blood samples were collected from peripheral veins, with 4 ml taken from each subject: 1 ml for CBC (EDTA), 1 ml for CRP (serum), 1 ml for ABGs (heparinized), and 1 ml for blood culture [13].

Complete blood count was analyzed by flow cytometry (Beckman LH 780; Beckman Coulter, Brea, CA, USA). C-reactive protein was measured by scattering immunoturbidimetry (Beckman Coulter AU5800). Arterial blood gases were analyzed using a heparinized needle and at least 0.2 ml of capillary blood, with analysis performed on an ABL 80 FLEX analyzer within 5 minutes, recording pH, pCO_2, base excess, and bicarbonate levels.

Blood Culture: One mL of blood was aseptically collected and placed in BACT/ALERT culture bottles to grow aerobic and anaerobic microorganisms. The BACT/ALERT 3D system, using BioMerieux culture media, employs colorimetric technology and algorithms to detect microbial growth by monitoring pH-induced color changes every ten minutes. This minimizes false negatives and false positives. Positive cultures were sub-cultured on blood and MacConkey agar for species identification and antimicrobial susceptibility testing.

Imaging: May be needed including chest X-ray and CT chest.

Follow up: The outcome included follow up until discharge or death, length of stay, complications or need of assisted ventilation was recorded.

Statistical analysis

The data were analyzed using IBM SPSS Statistics (Version 25.0). Normality was tested with the Shapiro test. Descriptive statistics included mean and standard deviation for parametric data, and median and range for non-parametric data, with frequencies and percentages for categorical data. Analytical statistics included the Student T Test for comparing two means, ANOVA for more than two means, Chi-Square and Fisher's exact tests for relationships between qualitative variables, and correlation analysis for associations between quantitative variables. ROC curve analysis was used to evaluate diagnostic sensitivity and specificity, with AUC values indicating accuracy.
(SPSS Inc., Chicago, Illinois, USA)

Results:

This study included 100 children (56 males, 44 females) with a mean age of 3.5±2.7 years. Diagnoses were pneumonia (70%), bronchiolitis (16%), pleural effusion & pneumonia (10%), empyema (3%), and lung abscess (1%). The history of NICU admission was noted in 30%, word hospital admission in 16%, and PICU admission in 14%. The mean weight was 27.5±25.7 kg, mean height 118.1±21.1 cm, and mean BMI 19.7±5.3. Table 1

In the study, 100% of cases had shortness of breath, 17% had grunting, 15% had cyanosis, 57% had fever, 85% had cough, 7% had vomiting, 19% had diarrhea, 45% had rhinorrhea, and 36% had refusal of feeding. Severity grades were distributed as 68% grade II, 17% grade III, and 15% grade IV. Table 2

The mean hemoglobin was 10.6±1.0 mg/dl, WBCs 11.2±4.0 x10^3/L,

neutrophils 65.56±12.49%, lymphocytes 30.61±10.31%, NLR 4.59±3.01, platelets 179±94 x10^3/L, CRP 45.29±45.40 mg/L, pH 7.27±0.07, CO2 50.22±7.46 mmHg, and HCO3 18.13±3.05 mmol/L. Blood cultures showed *Klebsiella* in 3%, *Strep-pneumococci* in 8%, *Coagulase-negative Staphylococcus* in 4%, *Haemophilus influenzae* in 4%, *Acinetobacter* species in 3%, and no growth in 78%. Radiological findings included consolidation in 50%, collapse in 21%, air trapping in 18%, pleural effusion in 10%, and cavitation in 1%. Table 2

About 11% of patients required nasal Oxygen, 30% needed high flow nasal nannula, 15% needed CPAP and 44% required MV, the mean duration of MV was 4.7±1.7 days, the mean duration of O2 support was 5.9±2.7 days, and the mean duration of hospital stay was 8.3±3.6 days. 14% died during the study. Table 2

There was a statistically significant difference in NLR as regards to cause of hospital admission, while there was no significant in NLR regarding to sex, history of Neonatal Intensive Care Unit (NICU) or history of hospital admission. Table 3

There was a statistically significant difference in NLR concerning dyspnea grade, cyanosis, chest X-ray, and blood culture, but not with fever. NLR was significantly higher in patients requiring mechanical ventilation and those who died. Additionally, NLR was higher in deceased patients with DIC, and sepsis compared to those with respiratory failure. Table 4

Table 1: Sociodemographic data and cause of admission in the studied group.

		N=100	%
Sex	**Male**	56	56.0%
	Female	44	44.0%
Age (years)	**Mean ± SD**		3.5±2.7
	Range		0.4-11
Cause of admission	**Pneumonia**	70	70.0%
	Bronchiolitis	16	16.0%
	Pleural effusion & pneumonia	10	10.0%
	Empyema	3	3.0%
	Lung abscess	1	1.0%
History of previous hospital admission	**No**	40	40.0%
	Neonatal Intensive Care Unit (NICU)	30	30.0%
	Word	16	16.0%
	Pediatric intensive care unit (PICU)	14	14.0%
Weight (Kg)	**Mean ± SD**		27.5±25.7
	Range		6-45
Height (cm)	**Mean ± SD**		118.1±21.1
	Range		77-155
BMI	**Mean ± SD**		19.7±5.3
	Range		16.5-25.5

NICU: Neonatal Intensive Care Unit, PICU: Pediatric Intensive Care Unit

Table 2: Clinical examination, investigations and outcome of the studied group.

			N=100	%
Presenting symptoms		**Shortness of breath**	100	100.0%
		Grunting	17	17.0%
		Cyanosis	15	15.0%
		Fever	57	57.0%
		Cough	85	85.0%
		Vomiting	7	7.0%
		Diarrhea	19	19.0%
		Rhinorrhea	45	45.0%
		Refusal of feeding	36	36.0%
Dyspnea Grade		**II**	68	68.0%
		III	17	17.0%
		IV	15	15.0%
Respiratory rate/min.	**<1 year old**	**Mean ±SD**	58.2±11.3	
		Range	41-79	
	1-6 years	**Mean ±SD**	51.4±8.7	
		Range	35-61	
	>6 years old	**Mean ±SD**	39.3±4.3	
		Range	21-46	
Heart rate/min.	**<1 year old**	**Mean ±SD**	125.6±11.1	
		Range	86-168	
	1-6 years	**Mean ±SD**	110.2±10.2	
		Range	81-124	
	>6 years old	**Mean ±SD**	98.7±8.7	
		Range	76-109	
		Mean ± SD	**Min.**	**Max.**
Hemoglobin (mg/dl)		10.6±1.0	8.4	13.2
WBC (x10³/L)		11.2±4.0	5.2	19.3
Neutrophils (%)		65.56±12.49	24.10	90.20
Lymphocytes (%)		30.61±10.31	6.50	69.20
NLR		4.59±3.01	0.80	13.80
Platelets (x10³/L)		179±94	25	325
CRP (mg/dl)		45.29±45.40	3.00	192.00
ABGs	**pH**	7.27±0.07	7.14	7.37
	CO2	50.22±7.46	41.00	66.00
	HCO3	18.13±3.05	4.10	22.50
Blood culture	*No growth*	78	78.0%	
	Klebseilla	3	3.0%	
	Strep.pneumococci	8	8.0%	
	Coagulase-negative Staphylococcus	4	4.0%	
	Haemophilus influenzae.	4	4.0%	
	Acinetobacter species	3	3.0%	
Chest X ray	**Consolidation**	60	60.0%	
	Pleural effusion	13	13.0%	
	Pneumonthorax	2	2.0%	
	Cavitation	1	1.0%	
	Collapse	8	8.0%	
	Hyperinflation	14	14.0%	
Need Oxygen support		**Nasal Oxygen**	11	11.0%
		High flow nasal canula	30	30.0%
		CPAP	15	15.0%
		MV	44	44.0%
Duration of MV /days		**Mean ± SD**	4.7±1.7	
		Range	2-7	
Duration of O2 support /days		**Mean ± SD**	5.9±2.7	
		Range	2-12	
Duration of hospital stay /days		**Mean ± SD**	8.3±3.6	
		Range	3-16	
Death		**No**	86	86.0%
		Yes	14	14.0%
Cause of death		**Sepsis**	11	11.0%
		Respiratory failure	5	5.0%
		DIC	3	3.0%

WBC: white blood cells, NLR: neutrophil-to-lymphocyte ratio, CRP: C-reactive protein, ABGs: arterial blood gases, CPAP: continuous positive airway pressure, MV: mechanical ventilation, PH: potential of hydrogen, CO2: carbon dioxide, HCO3: bicarbonate.

Table 3: Neutrophils / Lymphocytes ratio according to primitive data and cause of admission.

		NLR			Test	P value
		Mean±SD	Min.	Max.		
Sex	Male	4.81±3.21	1.80	13.80	t=0.23	0.730
	Female	4.42±2.75	0.80	10.30		
Cause of admission	Pneumonia	4.87±3.21	1.10	13.80	F=3.9	0.006*
	Bronchiolitis	3.09±1.90	0.80	7.40		
	Pleural effusion	5.41±2.10	3.50	9.70		
	Empyema	8.57±2.48	5.70	10.00		
	Lung abscess	7.90	7.90	7.90		
History of hospital admission	No	4.55±2.97	0.80	13.80	t=0.33	0.653
	Yes	4.78±3.30	1.50	10.30		

t: Student t-test, F: F-value of one-way ANOVA, *: significant, NLR: Neutrophils / Lymphocytes ratio.

Table 4: Neutrophils / Lymphocytes ratio according to clinical assessment, chest X ray and outcome.

		NLR			Test	P value
		Mean±SD	Min.	Max.		
Dyspnea	II	4.22±3.36	1.10	10.20	F=3.56	0.041*
	III	4.94±3.27	0.80	13.80		
	IV	5.99±2.37	1.50	13.30		
Cyanosis	No	4.95±3.11	0.80	13.80	t=4.1	<0.001*
	Yes	7.21±2.13	1.10	7.50		
Fever	No	4.58±3.05	1.10	10.30	t=0.26	0.88
	Yes	4.59±3.00	0.80	13.80		
Chest X ray	Consolidation	4.80±2.98	0.80	10.30	F=2.7	0.036*
	Pleural effusion	6.36±2.57	3.50	10.00		
	Pneumonthorax	4.57±3.83	1.90	13.80		
	Cavitation	7.90	7.90	7.90		
	Collapse	3.70±1.66	1.30	6.80		
	Hyperinflation	3.10±1.74	1.14	5.24		
Blood culture	No growth	2.4±1.74	1.14	5.24	F=2.7	0.036*
	Klebseilla	6.36±2.57	3.50	10.00		
	Strep.pneumococci	4.57±3.83	1.90	13.80		
	Coagulase-negative Staphylococcus	4.80±2.98	0.80	10.30		
	Haemophilus influenzae.	3.10±1.74	1.14	5.24		
	Acinetobacter species	3.70±1.66	1.30	6.80		
Oxygen support	Nasal Oxygen	3.21±1.73	0.80	9.70	F=6.1	<0.001*
	High flow nasal canula	4.23±2.11	1.10	10.2		
	CPAP	5.74±2.31	1.22	11.5		
	MV	7.51±3.09	1.10	13.80		
Death	No	3.83±2.35	0.80	10.00	t=8.1	<0.001*
	Yes	9.27±2.30	6.80	13.80		
Cause of death	Sepsis	9.3±1.92	7.2	12.5	F=3.5	0.031*
	Respiratory failure	8.4±1.87	7.10	11.5		
	DIC	10.9±2.32	6.80	13.80		

NLR: neutrophil-to-lymphocyte ratio, MV: mechanical ventilation, DIC: disseminated intravascular coagulation, t: Student t-test, F: F-value of one-way ANOVA, *: significant, NLR: Neutrophils / Lymphocytes ratio.

There was a statistically significant positive correlation between NLR and (CRP, CO2, duration of hospital stays, duration of O2 support and duration of

MV) and there was a statistically significant negative correlation between NLR and (Platelets, PH, Hco3), while here was no significant correlation between NLR and (respiratory rate, heart rate, hemoglobin and WBCs). Figure 1

ROC analysis was done to assess the performance of NLR to predict need of mechanical ventilator; AUC was 0.876 (95% confidence interval: 0.783-0.970), p<0.001. At a cutoff point $\geq$ 5.1, the sensitivity was 83.1% and specificity was 91.2%. Figure 2

ROC analysis was done to assess the performance of NLR to predict mortality; AUC was 0.950 (95% confidence interval: 0.909-0.991), p<0.001. At a cutoff point $\geq$ 5.9, the sensitivity was 100% and specificity was 88.4%. Figure 3
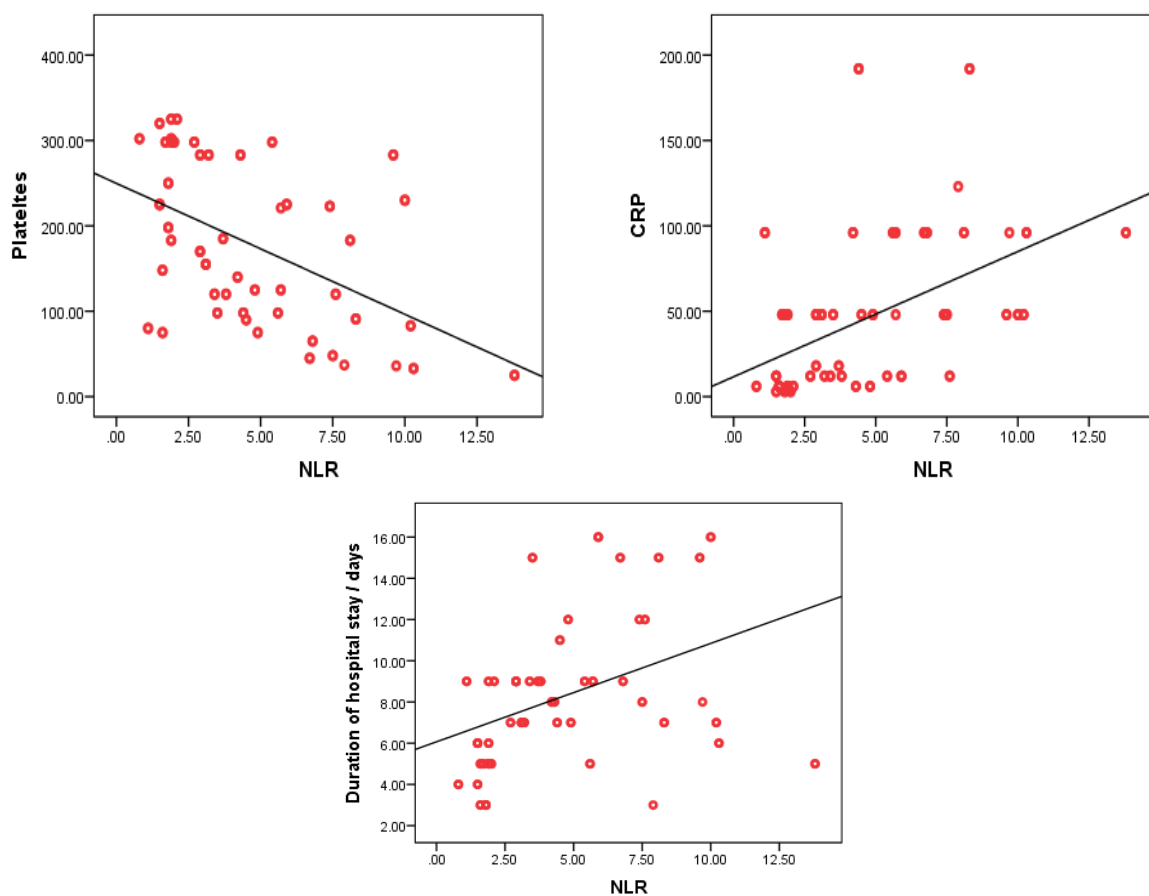
Figure 1: Correlation between Neutrophils / Lymphocytes ratio and platelets, CRP and duration of hospital stay.
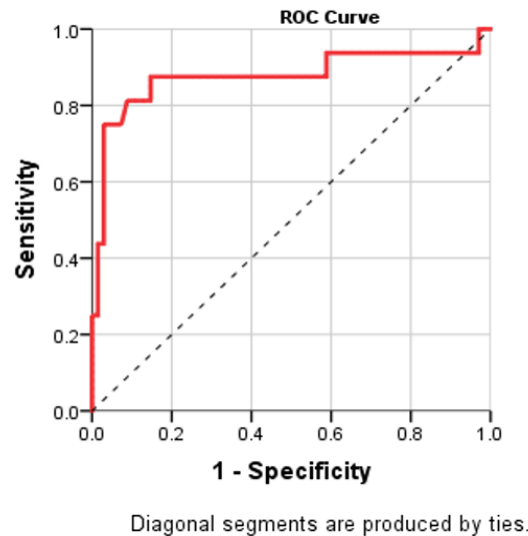
Figure 2: ROC curve of performance of Neutrophils / Lymphocytes ratio (NLR) to predict need of mechanical ventilator.
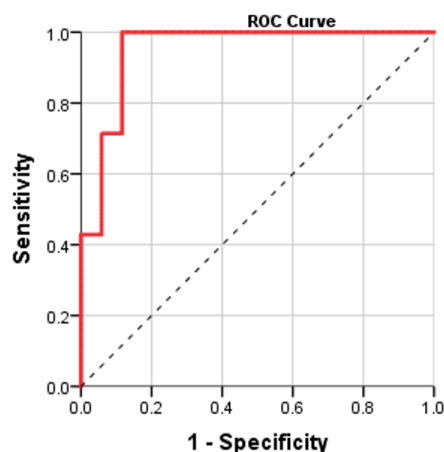
Figure 3: ROC curve of performance of Neutrophils / Lymphocytes ratio (NLR) to predict mortality.

Discussion:

Acute respiratory failure in children, mainly from pneumonia and bronchiolitis, often leads to ALI and PARDS in PICUs. NLR is a promising marker for predicting disease severity and outcomes in these cases [14]. We included 100 children admitted to the PICU for chest infections to evaluate NLR as a predictor of disease severity and outcomes, including mechanical ventilation and mortality, in pediatric chest infections in the PICU.

The study comprised 56 males and 44 females with a mean age of 3.5 years. The majority had pneumonia, followed by bronchiolitis, pleural effusion with pneumonia, empyema, and lung abscess. A significant proportion had previous admissions to the Neonatal Intensive Care Unit (NICU), other hospitals, and the PICU.

Our results agreed with a study included 303 medical records of hospitalized children and infants with LRTI and found that majority of patients were males (59.4%), and 40.6% were females, The mean age was 29.09±38.96 months (ranging from one month to 15 years). Pneumonia (74.6%) and bronchitis (17.2%) were the most common LRTIs among patients [15].

Similar to our results; a study assessed clinical features and outcome of 265 children with severe lower respiratory tract infection and revealed total of 265 patients (median [interquartile range, IQR] age = 4 months [2–12 months]) were admitted with ALRTI; 157 (59.3%) were male [16].

However, in another study, the mean age of patients was 17.4±26.8 months, and the majority of patients were younger than 6 months of age (n=27, 42.9%). Most of the patients were diagnosed with acute bronchiolitis (57.1%), while 31.7% had pneumonia and 11.1% had asthma crisis or recurrent wheezing [17].

In the present study, more boys compared to girls were admitted to the hospital for LRTI, which was similar to other studies that were carried out among children with LRTI hospitalization in PICU [18, 19].

In the current study, pneumonia and bronchitis were the most common LRTIs among patients, which was reported in other similar studies [20, 21].

In the present study, the mean weight in the studied group was 27.5±25.7 kg, the mean height was 118.1±21.1 cm and the mean BMI was 19.7±5.3

In the same way, a study reported that of the 303 patients, 65 (21.5%) and 33 (10.9%) patients were severely (<−3 - score) and moderately underweight. In addition, 54 (17.8%) and 37 (12.2%) patients were severely (<−3 -score) and moderately stunted. There were no significant differences in weight and height (cm) between the two genders [15].

In the current study, 100% had shortness of breath, 17% had grunting, 15% had cyanosis, 57% of children had fever, 85%

had cough, 7% had vomiting, 19% had diarrhea, 45% had rhinorrhea, 36% had refusal of feeding. 68% had grade II, 17% had grade III, 15% had grade IV.

Our results were matched with a study which reported that the most common symptoms were cough (77.2%), tachypnea (56.4%), fever (50.8%), and tachycardia (37.9%) at the time of admission [15].

In the same way, a study reported that the most frequently reported symptoms among patients diagnosed with acute bronchitis or pneumonia were cough, fever, dyspnoea, and increased purulent sputum [22].

In our study, the mean hemoglobin was 10.6 mg/dl, WBCs 11.2 x10^3/L, neutrophils 65.56%, lymphocytes 30.61%, NLR 4.59, platelets 179 x10^3/L, CRP 45.29, pH 7.27, CO_2 50.22, and HCO_3 18.13. Blood cultures showed no growth in 78% of cases, with the remainder having various bacterial infections. Radiological findings included consolidation in 50% of children, collapse in 21%, air trapping in 18%, pleural effusion in 10%, and cavitation in 1%.

Our results were matched with a study observed that the median WBCs was 7.22 x10³/L, the median neutrophils was 5.09, the median lymphocytes was 1.14, the median NLR was 4.67, and the median CRP was19.40 mg/dl [23].

A study reported that raised ESR and leukocytosis were found in 261 and 88 patients, respectively. In addition, 66 patients were neutrophil predominant. A C-reactive protein (CRP) test had been performed and was increased in 150 of the cases. Abnormal CRP levels were significantly associated with longer length of stay (LOS) in hospital ($p<0.05$) [15].

In the current study, 11% of patents required nasal Oxygen, 30% needed high flow nasal nanulla, 15% needed CPAP and 44% required MV, the mean duration of MV was 4.7±1.7 days, the mean duration of O2 support was 5.9±2.7 days, and the mean duration of hospital stay was 8.3±3.6 days. 14% died during the study.

Similarly, a study reported that most children were successfully managed with NIV support (52.4%), while 47.6% required IMV support at admission, and 25.4% transitioned from NIV to IMV. The mean duration of MV was 10.3 days, and the mean time from PICU admission to IMV initiation was 28.8 hours. The average hospital stay was 20.4 days, with 90.5% staying in the PICU for over 3 days. The mortality rate was 12.7% [17].

In another study, 40 patients (13.2%) required mechanical ventilation. The mean length of hospital stay was days (range 1-57), and the overall mortality rate was 11.6%. The mortality rates caused by pneumonia and bronchitis were 10.23% and 0.66%, respectively [15].

In contrast, similar studies among children with LRTI in Mexico and Morocco reported that the mortality rate of children was 1.04% [24] and 4%, respectively [25].

The high mortality in this study likely resulted from severe LRTI in critically ill patients, with 32% needing mechanical ventilation. Differences in patient populations and additional clinical factors may have also contributed to the increased mortality rate.

Our study found that NLR was significantly higher in patients with empyema and lung abscess, followed by pleural effusion, pneumonia, and lowest in bronchiolitis. NLR also varied significantly with dyspnea grade, cyanosis, chest X-ray findings, and blood culture results but not with sex, fever, or hospital admission history.

Our results agreed with a study reported that there was no difference between males and females in NLR values (P = 0.78) [26].

NLR has been noted for its diagnostic accuracy in sepsis, pneumonia, and bacteremia [27]. However, its effectiveness in determining underlying microbiological etiology is limited. A study found NLR inferior to WCC in distinguishing between viral and bacterial pneumonia [28]. Pediatric studies also showed NLR's poor discriminatory power in this context [29, 30].

This may be because NLR reflects physiological stress in critically ill patients, regardless of the microbial cause.

In the present study, NLR was statistically higher in patients needed MV and in patients who died. Moreover, there was statistical difference between died cases as regards to cause of death, as it was higher in patients with DIC and patients with sepsis compared to patients with respiratory failure.

Our results were in agreement with a study reported that NLR was significantly higher among patients who died in hospital (11.96, IQR 7.26–30.68) than among those who survived (4.19, IQR 2.39–7.52, P < 0.001) [23]. And another one reported that NLR of the death group were higher than those of the survival group (P < 0.05) [31].

Similarly, a study reported that patients with poor prognosis (died) had higher NLR compared to patients with good prognosis (improvement and discharge from the pediatric ICU), (3.05 ± 0.99 vs 0.83 ± 0.69, p < 0.001) [32].

The calculated NLR is a sensitive biomarker to reflect the balance between inflammatory response and immune status in patients [33].

During stress, catecholamine and cortisol increase neutrophils and decrease lymphocytes rapidly, faster than leukocytosis and pandemia. This makes NLR a useful early marker of critical illness [34].

In the current study, there was a significant positive correlation between NLR and CRP, CO_2, hospital stay duration, oxygen support duration, and MV duration. There was a significant negative correlation between NLR and platelets, pH, and HCO_3. No significant correlation was observed between NLR and respiratory rate, heart rate, hemoglobin, or WBCs.

In the same line, a study reported that the NLR correlated positively with serum levels of C-reactive protein (r = 0.239, P < 0.001) [23].

In accordance with our results, a study revealed positive correlations of NLR with

prolonged ICU stay (<0.001), mechanical ventilation (<0.001), and fatality (<0.001) [35]. However, another one reported that there were no correlation among mechanical ventilation time and the length of intensive care stay and NLR- values [26]. In the present study, ROC analysis showed NLR's performance in predicting the need for mechanical ventilation had an AUC of 0.876, with 83.1% sensitivity and 91.2% specificity at a cutoff >5.1. For predicting mortality, NLR had an AUC of 0.950, with 100% sensitivity and 88.4% specificity at a cutoff >5.9.

In the same line, a study found that AUC (area under the curve) for NLR in predicting mortality was 0.617 (95% CI: 0.535–0.7). The cutoff value of NLR in predicting mortality was 2.18 with a sensitivity of 54% and specificity of 67% [35]. Research reported that in children with sepsis; NLR was found to be significantly higher in the group with sepsis and among the deceased septic children. The AUC for NLR in sepsis was 0.72. A high NLR had a 4.2 times higher risk of mortality [36]. Also, a study had similar results with a high NLR in the deceased group with AUC of 0.798 with the sensitivity of 56.25% and specificity of 89.83% [31].

The differences in the cutoff values between studies implies that the cutoff value may need to be defined by multicentric studies for each population.

This study suggests that NLR is a simple, promising marker for assessing the severity of chest infection and for identifying children at elevated risk of in-hospital mortality. These findings justify further work into the role of NLR in comprehensive management of patients.

However, this study has potential limitations including variable etiological investigations and difficulty attributing etiology in childhood ALRTI. The results may not be generalizable to less severe cases as the sample represents the sickest children in the PICU. Although the sample size was small, it covers a full year of PICU admissions, accounting for seasonal variability. Long-term outcomes were not assessed as children were only followed until discharge.

Conclusion:

NLR is a reliable, rapid, and cost-effective predictor for the need for mechanical ventilation and mortality in children with severe chest infections admitted to PICU.

Sources of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contribution

The authors contributed equally to the study.

Conflicts of interest

No conflicts of interest

References:

1. Pham H, Thompson J, Wurzel D, Duke T. Ten years of severe respiratory syncytial virus infections in a tertiary paediatric intensive care unit. J Paediatr Child Health. 2020;56:61-7.

2. Khemani RG, Smith L, Lopez-Fernandez YM, Kwok J, Morzov R, Klein MJ, et al. Paediatric acute respiratory distress syndrome incidence and epidemiology (PARDIE): an international, observational study. Lancet Respir Med. 2019;7:115-28.

3. Marangu D, Zar HJ. Childhood pneumonia in low-and-middle-income countries: An update. Paediatr Respir Rev. 2019;32:3-9.

4. Kany S, Vollrath JT, Relja B. Cytokines in Inflammatory Disease. Int J Mol Sci. 2019;20.

5. Mani CS. Acute pneumonia and its complications. J Pediatr Infect Dis. 2018;12:238.

6. Capitanio JP, Del Rosso LA, Spinner A. Variation in infant rhesus monkeys' (Macaca mulatta) neutrophil-to-lymphocyte ratio is associated with environmental conditions, emotionality, and cortisol concentrations, and predicts disease-related outcomes. Brain Behav Immun. 2023;109:105-16.

7. Buonacera A, Stancanelli B, Colaci M, Malatino L. Neutrophil to Lymphocyte Ratio: An Emerging Marker of the Relationships between the Immune System and Diseases. Int J Mol Sci. 2022;23.

8. Kourilovitch M, Galarza-Maldonado C. Could a simple biomarker as neutrophil-to-lymphocyte ratio reflect complex processes orchestrated by neutrophils? J Transl Autoimmun. 2023;6:100159.

9. Rosa Neto JC, Calder PC, Curi R, Newsholme P, Sethi JK, Silveira LS. The immunometabolic roles of various fatty acids in macrophages and

lymphocytes. International Journal of Molecular Sciences. 2021;22:8460.

10. Ruta VM, Man AM, Alexescu TG, Motoc NS, Tarmure S, Ungur RA, et al. Neutrophil-To-Lymphocyte Ratio and Systemic Immune-Inflammation Index-Biomarkers in Interstitial Lung Disease. Medicina (Kaunas). 2020;56.

11. Wiggermann N, Bradtmiller B, Bunnell S, Hildebrand C, Archibeque J, Ebert S, et al. Anthropometric Dimensions of Individuals With High Body Mass Index. Hum Factors. 2019;61:1277-96.

12. Heuer AJ. Wilkins' Clinical Assessment in Respiratory Care-E-Book: Elsevier Health Sciences; 2021;109:105-16.

13. Dawson S. Blood culture contaminants. J Hosp Infect. 2014;87:1-10.

14. Pujari CG, Lalitha AV, Raj JM, Kavilapurapu A. Epidemiology of Acute Respiratory Distress Syndrome in Pediatric Intensive Care Unit: Single-center Experience. Indian J Crit Care Med. 2022;26:949-55.

15. Mirkarimi M, Alisamir M, Saraf S, Heidari S, Barouti S, Mohammadi S. Clinical and Epidemiological Determinants of Lower Respiratory Tract Infections in Hospitalized Pediatric Patients. Int J Pediatr. 2020;2020:8844420.

16. Hutton HK, Zar HJ, Argent AC. Clinical Features and Outcome of Children with Severe Lower Respiratory Tract Infection Admitted to a Pediatric Intensive Care Unit in South Africa. J Trop Pediatr. 2019;65:46-54.

17. Duyu M, Karakaya Z. Viral etiology and outcome of severe lower respiratory tract infections among critically ill children admitted to the PICU. Med Intensiva (Engl Ed). 2021;45:447-58.

18. Greenbaum AH, Chen J, Reed C, Beavers S, Callahan D, Christensen D, et al. Hospitalizations for severe lower respiratory tract infections. Pediatrics. 2014;134:546-54.

19. Zhong P, Zhang H, Chen X, Lv F. Clinical characteristics of the lower respiratory tract infection caused by a single infection or coinfection of the human parainfluenza virus in children. J Med Virol. 2019;91:1625-32.

20. Kwon JM, Shim JW, Kim DS, Jung HL, Park MS, Shim JY. Prevalence of respiratory viral infection in children hospitalized for acute lower respiratory tract diseases, and association of rhinovirus and influenza virus with asthma exacerbations. Korean J Pediatr. 2014;57:29-34.

21. Ujunwa F, Ezeonu C. Risk Factors for Acute Respiratory Tract Infections in Under-five Children in Enugu Southeast Nigeria. Ann Med Health Sci Res. 2014;4:95-9.

22. Hansen LS, Lykkegaard J, Thomsen JL, Hansen MP. Acute lower respiratory tract infections: Symptoms, findings and management in Danish general practice. Eur J Gen Pract. 2020;26:14-20.

23. Yang T, Wan C, Wang H, Qin J, Chen L, Shen Y, et al. The prognostic and risk-stratified value of neutrophil–lymphocyte count ratio in Chinese patients with community-acquired pneumonia. European Journal of Inflammation. 2017;15:22-7.

24. Vizcarra-Ugalde S, Rico-Hernández M, Monjarás-Ávila C, Bernal-Silva S, Garrocho-Rangel ME, Ochoa-Pérez UR, et al. Intensive Care Unit Admission and Death Rates of Infants Admitted With Respiratory Syncytial Virus Lower Respiratory Tract Infection in Mexico. Pediatr Infect Dis J. 2016;35:1199-203.

25. Jroundi I, Mahraoui C, Benmessaoud R, Moraleda C, Tligui H, Seffar M, et al. Risk factors for a poor outcome among children admitted with clinically severe pneumonia to a university hospital in Rabat, Morocco. Int J Infect Dis. 2014;28:164-70.

26. Mısırlıoğlu M, Yıldızdaş D, Horoz Ö, Ekinci F, Haytoğlu Z, Aslan N. Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio in Pediatric Acute Respiratory Distress Syndrome. Turk Thorac J. 2021;22:274-8.

27. Honda T, Uehara T, Matsumoto G, Arai S, Sugano M. Neutrophil left shift and white blood cell count as markers of bacterial infection. Clin Chim Acta. 2016;457:46-53.

28. Ng WW, Lam SM, Yan WW, Shum HP. NLR, MLR, PLR and RDW to predict outcome and differentiate between viral and bacterial pneumonia in the intensive care unit. Sci Rep. 2022;12:15974.

29. Bekdas M, Goksugur SB, Sarac EG, Erkocoglu M, Demircioglu F. Neutrophil/lymphocyte and C-reactive protein/mean platelet volume ratios in differentiating between viral and bacterial pneumonias and diagnosing early complications in children. Saudi Med J. 2014;35:442-7.

30. Gauchan E, Adhikari S. C-reactive Protein Versus Neutrophil/lymphocyte Ratio in Differentiating Bacterial and Non-bacterial Pneumonia in Children. J Nepal Health Res Counc. 2016;14:154-8.

31. Qi X, Dong Y, Lin X, Xin W. Value of Neutrophil to Lymphocyte Ratio, Platelet to Lymphocyte Ratio, and Red Blood Cell Distribution Width in Evaluating the Prognosis of Children with Severe Pneumonia. Evid Based Complement Alternat Med. 2021;2021:1818469.

32. Hassan ES, Ahmad SA, Mohamad IL, Ahmad FA. The value of modified Ross score in the evaluation of children with severe lower respiratory tract infection admitted to the pediatric intensive care unit. Eur J Pediatr. 2023;182:741-7.

33. Köse N, Yıldırım T, Akın F, Yıldırım SE, Altun İ. Prognostic role of NLR, PLR, and LMR in patients with pulmonary embolism. Bosn J Basic Med Sci. 2020;20:248-53.

34. Shenoy S, Patil S. Neutrophil Lymphocyte Ratio and Platelet Lymphocyte Ratio as Predictors of Disease Severity and Mortality in Critically Ill Children: A Retrospective Cohort Study. Journal of Pediatric Intensive Care. 2023;2023:412-8.

35. Domnicu AE, Boia ER, Mogoi M, Manea AM, Marcovici TM, Mărginean O, et al. The Neutrophil-to-Lymphocyte Ratio (NLR) Can Predict Sepsis's Presence and Severity in Malnourished Infants-A Single Center Experience. Children (Basel). 2023;10.

36. Pasaribu FM, Setyaningtyas A, Andarsini MR. Neutrophil to lymphocyte ratio, monocyte to lymphocyte ratio, platelet to lymphocyte ratio, mean platelet volume as a predictor of sepsis mortality in children at Dr. Soetomo General Hospital. Critical Care & Shock. 2021;24:312-9.

To cite this article: Rasha M. Zakria , Effat H. Assar , Yasser M. Ismael , Samira S. Mohamed , Nouran R. Badr. Prognostic Value of Neutrophil to Lymphocyte Ratio Marker in Chest Infection in Pediatric Intensive Care Unit. BMFJ XXX, DOI: 10.21608/bmfj.2024.308995.2155.