International Journal of Contemporary Pediatrics
Mosleh T et al. Int J Contemp Pediatr. 2022 Nov;9(11):1022-1026
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291
DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20222761

Original Research Article

Role of neutrophil-lymphocyte ratio as a potential marker to differentiate between pulmonary tuberculosis and community-acquired pneumonia in children

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Received: 25 September 2022
Accepted: 14 October 2022

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ABSTRACT

Background: This is often creating challenge to differentiate pulmonary tuberculosis (TB) with community acquired pneumonia (CAP) particularly in children. The neutrophil-lymphocyte count ratio (NLR) as an indicator of inflammation has been used in various infectious diseases. The aim of this study was to investigate the role of NLR as a possible marker in differentiating pulmonary TB from CAP.
Methods: In this retrospective record based analytic study, conducted from July 2020 to Dec 2021, patient aged 2 months to 18 years diagnosed as pulmonary TB or CAP were enrolled in this study i.e., 155 children after exclusion. The diagnostic ability of NLR in differentiating between pulmonary Tb and CAP were assessed.
Results: Out of 155 children, 85 (54.8%) had CAP and 70 (45.1%) had pulmonary TB. Mean values of NLR were significantly lower in patients with TB than in pneumonia (3.16±1.9 vs 5.05±1.2, p<0.000). Total WBC, neutrophil, Hb and CRP were also significantly lower in patients with pulmonary TB. On the other hand, lymphocyte count was significantly higher in children with pulmonary TB in compare to children with pneumonia (p=0.04).
Conclusions: The NLR can be used as a useful simple laboratory marker in differentiating children with Pulmonary TB from CAP, especially in resource limited high TB disease burden countries.

Keywords: NLR, Lymphocyte, Neutrophil, Pneumonia, TB

INTRODUCTION

Around 2 billion people of the world has been infected with TB, which is a quarter of the world's population. Certain risk factors such as undernutrition, diabetes, smoking, alcohol consumption and HIV infection increases the disease burden. In 2020, most TB cases were estimated in Southeast Asia constituting around 43% of the global total with Bangladesh constituting 3.6% of the global total.[1]

In Bangladesh, the total estimated TB incidence rate per 100,000 population in 2019 was 221, accounting for one of the 30 high TB burden countries globally.[2]

There are studies showing *Mycobacterium TB* to be one of the causes of CAP, which may pose difficulty in differentiating pulmonary TB from CAP.[3,4]

Sputum smear examination for AFB (acid fast bacilli) can detect 50-60% of pulmonary TB cases in a good laboratory setup but in low-income countries with high prevalence of TB and HIV infection, it is difficult, owing to unavailability of services and also paucibacillary nature of TB in children.[5] As a result of the complexity in the differential diagnosis of pneumonia and TB in children, new markers for differentiation are being investigated as isolation and early initiation of treatment is a major public health concern in patient with TB. Some authors suggested expensive biomarkers like C-reactive

protein (CRP), prolactin and triggering receptor expressed on myeloid cell to differentiate pulmonary Tb from pneumonia.[6-8] But in resource limited set up with high TB burden countries like Bangladesh, some cheap and readily available biomarker will be more beneficial. The NLR has been found to be a useful laboratory marker for differentiating pulmonary TB from bacterial CAP at the initial diagnostic stage in adults by some authors.[9,10]

The NLR can be determined by dividing the absolute count of neutrophils by the number of lymphocytes in the complete blood count. The value of NLR has been studied in cardiovascular disease, chronic renal disease, malignancies, osteoporosis and Alzheimer's disease.[11-19] Few studies are available evaluating the value of NLR in infectious lung diseases. The NLR can also be used to determine the severity of both pulmonary TB and pneumonia & can also guide us towards the management of the patient.[10,20-22]

In this study, we aim to assess the role of NLR as a possible marker in differentiating pulmonary TB from CAP.

METHODS

This was a hospital based retrospective record based analytical study conducted on patients attending department of pediatrics, Bangabandhu Sheikh Mujib medical university (BSMMU), Dhaka, Bangladesh from July 2020 to December 2021. Patients aged 2 month to 18 years of both sex who were clinically or radiologically or microbiologically proven to be case of pulmonary TB or CAP with in this time period were included for the study. Exclusion criteria included use of antibiotics for >24 hours at the time of enrollment, patient having history of any hematological or chronic diseases that can affects total and differential WBC counts, and/or history of recent steroid therapy (within 3 months before admission).

The detailed demographic information, history, clinical findings, laboratory findings and details of clinical course of enrolled patients obtained from hospital records were recorded in a predesigned data collection sheet. After enrollment patients were divided into 2 groups. Group1 included patients with CAP and group 2 included patients with pulmonary TB.

Patients were diagnosed to have pulmonary TB as per the Bangladesh revised national guides for management of TB in children (2nd Edition, 2016). Microbiological tests included direct microscopy by Ziehl-Nielsen stain for the presence of acid-fast bacilli (AFB), MTB culture and multiplex PCR/Gene expert of appropriate clinical samples including sputum, gastric lavage, plural fluid, stool etc. We also considered the histopathological finding of tissue specimen including lymph node. Patients were considered to have bacterial CAP when clinical signs and new infiltration on chest radiograph were evident and it completely resolved after treatment with the appropriate antibiotics. Sputum-Gram stains, cultures and blood cultures were done for microbiological detection of bacterial CAP in patients. Total WBC, neutrophil, and lymphocyte counts were determined before antibiotic treatment using hematology analyzer. NLR was defined as absolute neutrophil count divided by absolute lymphocyte count.

Data analysis was performed using SPSS version 20 (SPSS, Chicago, IL). The normality of continuous variables was tested with Kolmogorov-Smirnov test. The analysis of patient demographics and baseline outcome variables were summarized using descriptive summary measures: expressed as mean± standard deviation for continuous variables and frequencies and percentage for categorical variables. Appropriate statistical test (e.g., Chi-square test, unpaired t-test,) was applied for data analysis. $P<0.05$ was considered as significant.

RESULTS

Total 155 children were enrolled for the study (Figure 1). Among them 85 (54.8%) had CAP and 70 (45.1%) had pulmonary TB. The mean age of patients with pulmonary TB and CAP was 11.6±3.9 year. (range, 2-18 yearr.) and 4.3±3.6 year (range 1-16 year), respectively. Patients of TB were older than pneumonia patients ($p<0.001$). Baseline clinical characteristics of both groups are listed in Table 1. Among the patients with pulmonary TB, 33 (47.1%) had *M. TB* culture-positive respiratory specimens. The remaining patients had pleural effusion and lung infiltration on radiography compatible with TB.

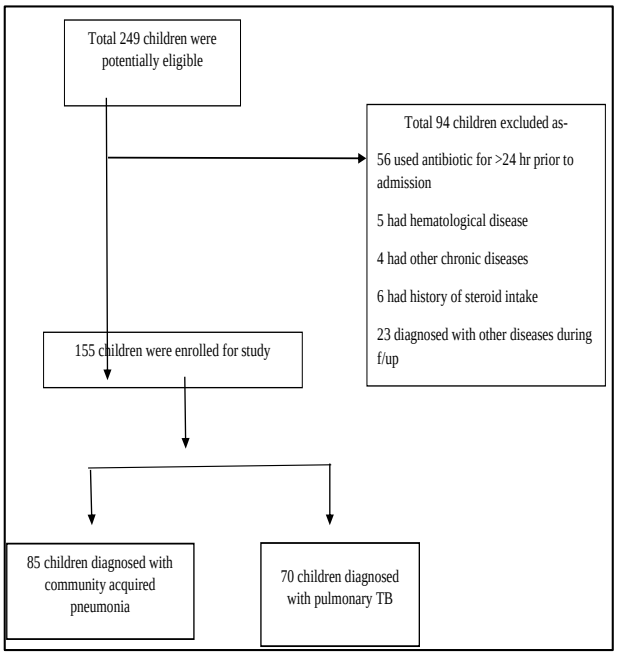

Figure 1: Study design.

When the TB and pneumonia groups were compared with each other, a statistically significant difference was found

between the groups in terms of leukocyte, neutrophil, lymphocyte counts, CRP and NLR. Mean values of NLR were significantly lower in patient with TB than in pneumonia (3.16±1.9 vs 5.05±1.2, p<0.000). Total WBC, neutrophil, Hb and CRP were also significantly lower in patients with pulmonary TB. On the other hand, lymphocyte count was significantly higher in children with pulmonary TB in compare to children with pneumonia (p=0.04).

Table 1: Baseline clinical characteristics of the study population.

Variables	Pneumonia, (n=85) (%)	TB, (n=70) (%)	P value
Age (years)	4.3±3.6 (1-16)	11.6±3.9 (2-18)	<0.001
Sex			
Male	32 (45.7)	32 (45.7)	
Female	38 (54.3)	38 (54.3)	0.297
Fever	82 (96.4)	68 (97.1)	0.40
Cough	76 (89.4)	53 (75.7)	0.01
Weight loss	3 (3.5)	38 (54.3)	<0.00001
Symptom duration >2 weeks	7 (8.2)	67 (95.7)	<0.0001

Table 2: Baseline laboratory characteristics of the study population.

Variables	Pneumonia, (n=85)	TB, (n=70)	P value
WBC (10^9 /l)	12.61±5.18	10.7±3.4	<0.0001
Hb (gm/dl)	10.2±1.63	9.5±1.5	0.001
Neutrophil (10^9 /l)	12.61±5.18	7.28±3.23	<0.001
Lymphocyte (10^9 /l)	2.41±0.88	2.77±1.33	0.045
ESR	45.27±30	120±33.6	<0.0001
NLR	5.05±1.2	3.16±1.9	<0.000

DISCUSSIONS

TB and pneumonia both has been a major public health concern in Bangladesh since decades. In other Asian countries with high burden of TB, like Singapore and Hong Kong, there is a high frequency of *Mycobacterium TB* identification in patients with suspected pneumonia.[3,23] The incidence of TB being diagnosed among patients presenting with clinical and radiological signs of a CAP has varied across series and can be as high as 35% of microbiologically confirmed pneumonias, the incidence being higher in the HIV-positive subgroup of patients.[24,25]

It is important in public health to discriminate TB at an early stage of disease evaluation because prompt isolation and treatment of TB can reduce its transmission. In children this situation is more critical and sometimes it is not even possible to distinguish through history, physical examination or radiologically. In this situation, a patient should be started on anti-TB therapy and closely monitored. Our study was conducted to determine that results of primary laboratory investigation like CBC can provide an impression for discriminating TB from pneumonia in children. In this study, we analyzed the differences in CBC characteristics between children with TB and pneumonia.

In infectious diseases particularly in bacterial diseases, the physiological immune response of peripheral leukocytes showed that patients had increased neutrophil counts and decreased lymphocyte counts.[26-29] The NLR has been shown to be a predictive marker for various infectious diseases by maximizing these CBC characteristics.

It has been established as a marker of inflammation and its relation with prognosis by many authors. In the present study, we observed relatively significant decreased neutrophil counts and increased lymphocyte counts in children with TB compared with those counts in children with pneumonia. Total WBC, neutrophil, Hb and CRP were also significantly lower in children with pulmonary TB in compare to children with pneumonia in the current study. These results were consistent with those from a previous study comparing patients having TB with patients having bacterial pneumonia.[9,30] But Veenstra et al, Park et al and Wang et al showed a decrease in lymphocyte count in TB and Yoon et al found no significant difference of lymphocyte count in addition to increase neutrophil count between two groups in their study.[31-33]

Two studies have suggested the MLR as a predictive marker of TB, to differentiate patients with TB from healthy populations based on these findings.[33,34] In this study mean values of NLR were significantly lower (p<0.000) in patient with TB than in pneumonia (3.16±1.9 vs 5.05±1.2). This result is consistent with the study done by Yoon et al, Kumar er al and Jeon et al.[9,30,35]

CONCLUSION

This study suggested that the NLR can be used an invaluable tool in differentiating pulmonary TB from CAP in a high TB disease burden country. The NLR as an useful simple laboratory marker was found to be supportive in differentiation of TB and pneumonia in children in resource limited high TB disease burden countries. This result suggests the need for further studies in this field.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Mosleh T, Das N, Mutanabbi M. Role of neutrophil-lymphocyte ratio as a potential marker to differentiate between pulmonary tuberculosis and community-acquired pneumonia in children. Int J Contemp Pediatr 2022;9:1022-6.