



Role of the Neutrophil-Lymphocyte Count Ratio in the Differential Diagnosis between Pulmonary Tuberculosis and Bacterial Community-Acquired Pneumonia

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Introduction

Globally there were an estimated 8.6 million new cases of tuberculosis (TB) in 2013 and 1.3 million deaths. India and China alone accounted for 26% and 12% of total cases, respectively.¹ Community-acquired pneumonia (CAP) is one of the most important infectious causes of death. Early diagnosis and appropriate administration of antibiotics are essential for reducing pneumonia-related morbidity and mortality.² Many studies conducted in high-tuberculosis (TB) burden countries have shown that *Mycobacterium tuberculosis* is a frequent cause of CAP; however, it is difficult to distinguish pulmonary TB from bacterial CAP during the initial diagnostic stage.^{3,4} The clinical and radiographic features of TB are often nonspecific, and the sensitivity of microscopic examination of expectorated sputum for acid-fast bacilli is as low as 50-60%.⁵ 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 percent of microbiologically confirmed

pneumonias, the incidence being higher in the HIV-positive subgroup of patients.^{6,7} *Mycobacterium tuberculosis* was not an uncommon cause of CAP requiring hospitalization in Malaysia. A longer duration of symptoms, history of night sweats, upper lobe involvement, cavitary infiltrates, lower total white blood cell count and lymphopenia were predictive of PTB.⁸ Nosocomial transmission of pulmonary TB to other hospitalized patients and healthcare workers can occur. Recently, some studies have suggested that biomarkers such as C-reactive protein (CRP), procalcitonin and soluble triggering receptor expressed on myeloid cells may play a role in discriminating pulmonary TB from bacterial CAP.^{9,10,11} However, not all of these biomarkers are available in countries with a high TB burden. The neutrophil-lymphocyte count ratio (NLR) is a readily calculable laboratory marker used to evaluate systemic inflammation. The NLR obtained at the initial diagnostic stage is a useful laboratory marker to discriminate patients with pulmonary TB from patients with bacterial CAP

in an intermediate TB-burden country.² Ratio of monocytes to lymphocytes 25% is predictive of active tuberculosis.¹ Delta neutrophil index was lower in PTB compared with CAP, and an initially elevated DNI (>1.0%) may be useful to rule out the possibility of PTB due to its high NPV.¹²

Hence this study was planned to investigate the role of the NLR in discriminating patients with active pulmonary TB from those with bacterial CAP and compare the diagnostic ability of the NLR.

Objectives

To compare neutrophil-lymphocyte count ratio (NLR) in patients with pulmonary tuberculosis and community acquired pneumonia and find out their diagnostic value in early stage of disease.

Material and Methods

This was a facility based retrospective record based analytical study which was conducted on patients attending the Department of General Medicine outpatient section and inpatient of R.L. Jalappa Hospital and Research Centre, Tamaka, Kolar. Patients who fulfilled the inclusion and exclusion criteria were included in this study. A Semi-Structured Questionnaire was prepared which included detailed history, clinical examination and requisite investigations which were performed and the data was captured from the Hospital Records. The study included all the cases which had documented findings which were available in the Hospital Records for a period of one year from Jan 2017 to Dec 2017.

Inclusion Criteria

- Patients of either sex aged more than 18 years
- Clinically or radiologically or microbiologically proven patients with pulmonary tuberculosis and community acquired pneumonia

Exclusion Criteria

- Patients with use of antibiotics for more

than 24 hours at the time of enrollment

- Conditions known to affect total and differential WBC counts such as hematologic disorders, chronic inflammatory conditions and current steroid therapy
- History of steroid use within 3 months before admission

All the Consecutive Patients who were eligible were enrolled and divided into 2 groups .Group 1 consisted of patients with pulmonary tuberculosis and group 2 consisted of patients with community acquired pneumonia who were matched for age, gender and locality.

Patients were assigned to the pulmonary TB group when M. tuberculosis was demonstrated in Auramine stain in the Smear from sputum or bronchial lavage fluid or the concentration of adenosine deaminase was ≥ 70 IU/dL according to lymphocyte-dominant exudative pleural effusion combined with a lung parenchymal lesion suggesting pulmonary TB. Patients were considered to have Bacterial CAP when clinical signs and new infiltration on chest radiograph were evident and completely resolved after treatment with the appropriate antibiotics.

Microbiological detection in patients with bacterial CAP was performed by sputum Gramstains, cultures and blood cultures. WBC differential count and CRP were determined before antibiotic treatment. Total WBC, Neutrophil, and Lymphocyte counts were determined using Hematology Analyzer. NLR was defined as absolute neutrophil count divided by absolute lymphocyte count. CRP levels were measured using an automated latex-enhanced Turbidimetric immunoassay.

Statistical Analysis

Continuous data are presented as the mean \pm standard deviation. Differences in continuous variables between groups were determined using Student's t-test or the Mann-Whitney U-test. Categorical data are presented as frequencies. Differences between categorical variables were analyzed using Pearson's chi-square test or

Fisher's exact test.

Ethical Considerations: Prior to the onset of the study, ethical approval was obtained from Institutional Ethics Committee (IEC), Kolar. All the collected information was kept confidential, and it is being used for research purpose only.

Results

The study included 30 subjects each who had had pulmonary TB and Bacterial CAP. The median age of patients with pulmonary TB and bacterial CAP was 58yr (range, 18-76yr) and 54yr (range, 20-71 yr), respectively. Baseline clinical characteristics are described in Table I.

Among the patients with pulmonary TB, 27 had

Smear Positive M Tuberculosis and 3 were diagnosed clinically or radiologically. 24 patients were under Cat- I treatment and 6 were under Cat-II treatment regimens, all of whom were treated at R L Jalappa RNTCP Unit. None of the patients had MDR and XDR.

The causative pathogens were determined in 18 patients with Bacterial CAP. Streptococcus pneumoniae was detected in 10 patients using respiratory specimen culture or blood culture. Other pathogens identified were Klebsiella pneumonia (n=2), Escherichia coli (n=3), Methicillin-Sensitive Staphylococcus aureus (n=2) and Methicillin-Resistant S. aureus (n=1).

Table I: Baseline clinical characteristics of the study population

	Bacterial CAP (N=30) (%)	Tuberculosis (N=30) (%)	P value
Age (yr)	58 (Range= 18-76)	54 (Range= 20-71)	0.056
Male	21 (70)	25 (83.3)	0.321
History of tuberculosis	04(13.3)	12 (40)	0.654
Symptom duration >2 weeks	2 (6.6)	23 (76.6)	<0.001
Hemoptysis	01(3.3)	07(23.3)	0.024
Fever	27 (90)	19 (63.3)	<0.001
Cough	18 (60)	28 (93.3)	0.130
Night sweats	03 (10)	11 (36.6)	0.21
Weight loss	01 (3.3)	07 (23.3)	<0.001

Values are presented as median (range) or number (percentage). Abbreviation: CAP, community-acquired pneumonia.

Total WBC and Neutrophil count, NLR and CRP were significantly lower in patients with pulmonary TB than in patients with Bacterial CAP, whereas lymphocyte count was

significantly higher in patients with pulmonary TB than in patients with Bacterial CAP (Table II).

Table II. Baseline laboratory characteristics of the study population

	Bacterial CAP (N=30)	Tuberculosis (N=30)	P value
WBC ($10^9/L$)	13.81±5.99	7.03±2.19	<0.001
Neutrophil ($10^9/L$)	11.93±6.81	4.91±2.03	<0.001
Lymphocyte ($10^9/L$)	1.03±0.45	1.47±0.53	<0.001
NLR	14.43±9.23	3.73±2.32	<0.001
CRP (mg/dL)	18.31±9.46	6.73±6.91	<0.001

Values are presented as mean ± standard deviation.

Abbreviations: CAP, community-acquired pneumonia; WBC, white blood cell; NLR, neutrophil- lymphocyte count ratio; CRP, C-reactive protein.

Discussion

India is a high TB-burden country with 27% of all the TB cases globally reported. The frequency of

Mycobacterium Tuberculosis identification in patients with suspected CAP is as high as 12% in Hong Kong¹³ and 21% in Singapore¹⁴ the

prevalence of TB in these countries is similar to that in India. Distinguishing Pulmonary TB from CAP is important in public health; immediate isolation and early treatment with anti-TB agents is essential for patients with pulmonary TB. However, differentiating between pulmonary TB and CAP based only on history, physical examination, and radiological findings is frequently difficult. Therefore, a rapid and readily available test to distinguish pulmonary TB from CAP is necessary.

The response in our body to various stressful events are characterized by an increased neutrophil count and decreased lymphocyte count. An increase in total WBC and neutrophils is an inflammatory reaction, particularly when caused by a bacterial infection.¹⁵ Lymphocytopenia has also been described as a diagnostic marker of bacterial infection.¹⁶ Therefore, the NLR is thought to have stronger discriminative power for predicting bacteremia compared to discrimination based on neutrophilia or lymphocytopenia alone.

In a study conducted on patients with tuberculosis and sarcoidosis, Iliaz et al. demonstrated that the NLR was higher in patients with tuberculosis compared to the patients with sarcoidosis.¹⁷

In a study conducted on patients with Behcet disease, Rifaioglu et al. demonstrated that the NLR was higher in cases when compared to controls and a similar observation was made on patients with Sjogren's syndrome by Z D Hu et al.^{18,19}

In a study conducted on patients with tuberculosis and bacterial community-acquired pneumonia, Yoon et al. showed that NLR levels were significantly lower in patients with pulmonary tuberculosis than in patients with bacterial community-acquired pneumonia the findings of which are persistent with our study findings.²

Conclusion

The Neutrophil Lymphocyte Ratio which was derived from a single blood sample during the initial diagnostic stage can be a very useful

laboratory marker for discriminating patients with pulmonary TB from patients with bacterial CAP. The diagnostic ability of the NLR is superior to that of CRP, and WBC, neutrophil and lymphocyte counts alone. Hence the Clinician should always derive NLR and the necessary investigations required to be incorporated into routine evaluation in patients with an ambiguous diagnosis between pulmonary TB and bacterial CAP.

Limitations

- 1) Selection bias could not be eliminated, as it was a non-randomized retrospective record based study and it was carried out in Single Tertiary care Hospital.
- 2) Etiology in Community Acquired Pneumonia was not available for all the patients.

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