

Study of Absolute Neutrophil Absolute Lymphocyte count ratio in Community Acquired Pneumonia patients as a prognostic indicator at a tertiary care centre



Dyaneshwar Nirgude¹, Mahadev Hanmantappa Malge², Swetha Rajoli³, Avinash Hanbe Rajanna⁴

¹Senior Resident, Department of Medicine, BMCRI, Bangalore, Karnataka, India, ²Assistant Professor, Department of Medicine, Gulbarga Institute of Medical Science Kalburgi, Karnataka, India, ³Assistant Professor, Department of Anaesthesia, ESIC PGIMSR, Bangalore, Karnataka, India, ⁴Assistant Professor, Department of Medicine, ESIC PGIMSR, Bangalore, Karnataka, India

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ABSTRACT

Background: Community acquired pneumonia refers to pneumonia contracted by a person with little or no contact with health care system. Following endotoxemia the number of circulating neutrophils increases while lymphocyte counts decrease. Combining both parameters seems a logical step and the ratio of neutrophil and lymphocyte counts is increasingly used in several clinical circumstances. Initially, this so-called neutrophil-lymphocyte count ratio (NLCR) was studied as an infection marker in ICU patients and found to correlate well with disease severity and outcome, according to APACHE-II and SOFA scores. In the current study, we explored the value of the NLCR in patients admitted with Community acquired pneumonia. **Aims and Objectives:** 1) To find out the value of Neutrophil-Lymphocyte Count Ratio (NLCR) in Community Acquired Pneumonia (CAP). 2) To study Neutrophil-Lymphocyte Count Ratio (NLCR) as prognostic indicator in Community Acquired Pneumonia (CAP). **Materials and Methods:** This prospective study was conducted on minimum of 100 patients admitted to hospitals from November 2015 to September 2017 from Bangalore. After admission of cases based on CURB-65 scores, a detailed history and clinical examination was done along with chest x-ray to establish the diagnosis. Before taking into the study all patients had signed the informed consent. Routine haematological investigations done on day 1,3 & 7 were carried out. Serum c-reactive protein levels, Urea nitrogen levels, Sputum for culture and sensitivity and Acid-fast bacilli (AFB) was done on the same day of admission. ANC (Absolute neutrophil count), ALC (Absolute lymphocyte count) and NLCR were calculated. **Results:** Our study included age groups above 18yrs. Majority of the patients in the study were between 58-67 years (30%) followed by 48-57 years (27%). As the CURB-65 score increased from score 0 to score 4-5, the NLCR consistently increased, while the lymphocyte counts consistently decreased. In patients who died there was a significantly higher NLCR at presentation compared to patients that survived (15.18 ± 3.55 versus 11.73 ± 3.01 , p-value, 0.003). **Conclusion:** In our study increased NLCR carried poor prognosis which correlated with high CURB65 score and ICU admission. In patients who died there was a significantly higher NLCR at presentation compared to patients those survived.

Key words: Community acquired pneumonia; CURB65; COPD; Absolute neutrophil count

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Address for Correspondence:

Dr. Swetha Rajoli, Department of Anaesthesia, ESIC PGIMSR, Rajajinagar Bangalore, Karnataka, India, Pin-560064.
Mobile: +91-9739020801. E-mail: swethasaritha1091@gmail.com

INTRODUCTION

Community acquired pneumonia refers to pneumonia contracted by a person with little or no contact with health care system. Groups with highest risk of morbidity and mortality with CAP include infants, elderly and ICS. Predisposed by COPD, smoking, diabetes and structural lung disease etc. The risk factors for early deterioration in community acquired pneumonia are hypoalbuminemia, neutropenia, thrombocytopenia, hyponatremia, hypoglycemia, multilobar infiltrates, severe hypoxemia (SPO₂ <90), mental confusion, severe tachypnea.¹

Severity scores like CURB65 severity score¹ are useful in estimating the outcome. Chest X ray is a useful tool in diagnosis of pneumonia with its correlation with clinical findings and laboratory values. Tests include sputum smear Gram staining, AFB, Sputum and blood culture. >50% cases, specific etiology is not identified.² Identified pathogens in community acquired pneumonia are *Streptococcus pneumoniae* (most common), *Haemophilus influenzae*, *Staphylococcus aureus*, gram negative bacilli, *Legionella* species, *Mycoplasma pneumoniae*, *Chlamydia*, viruses, aspiration.

Immuno-competent white blood cell populations play an important role in the systemic inflammatory response to infection. Following endotoxemia the number of circulating neutrophils increases while lymphocyte counts decrease. Neutrophilia is well recognized as infection marker whereas the clinician is less familiar with absolute lymphocytopenia as a possible marker in infectious disease management.

Combining both parameters seems a logical step and the ratio of neutrophil and lymphocyte counts is increasingly used in several clinical circumstances. Initially, this so-called neutrophil-lymphocyte count ratio (NLCR) was studied as an infection marker in ICU patients and found to correlate well with disease severity and outcome, according to APACHE-II and SOFA scores.^{3,4}

In the current study, we explored the value of the NLCR in patients admitted with Community acquired pneumonia.

AIMS AND OBJECTIVES

To find out the value of Neutrophil-Lymphocyte Count Ratio (NLCR) in Community Acquired Pneumonia (CAP).

To study Neutrophil-Lymphocyte Count Ratio (NLCR) as prognostic indicator in Community Acquired Pneumonia (CAP).

MATERIALS AND METHODS

This prospective study was conducted on minimum of 100 patients admitted to hospitals from November 2015 to September 2017 from Bangalore. After admission of cases based on CURB-65 scores, a detailed history and clinical examination was done along with chest x-ray to establish the diagnosis. Before taking into the study all patients had signed the informed consent. Routine haematological investigations done on day 1, 3 and 7 were carried out. Serum c-reactive protein levels, Urea nitrogen levels, Sputum for culture and sensitivity and AFB also done on the same day of admission. ANC, ALC and NLCR were calculated using following formulae

- ANC = % of Neutrophils divided by 100 and multiplied by Total WBC Count
- ALC = % of Lymphocytes divided by 100 and multiplied by Total WBC Count
- NLCR = ANC divided by ALC.

Inclusion criteria

1. Patients of either sex aged 18 years and above
2. Patients willing to written consent
3. Patients with clinically suspected Community Acquired Pneumonia.

Exclusion criteria

1. Age less than 18 years
2. Immunocompromise individuals
3. Coexisting malignancy.

Method of statistical analysis

Based on previous study Cornelis P. C. de Jager et al NLCR in patient was 13.6±12.0.

The sample size calculated as

$$n = \frac{z_{\alpha}^2 \sigma^2}{d^2}$$

Where z_{α} = standard table value for 95% CI.

=1.96

σ = standard deviation

=12

d= precision

=2.4

$$n = \frac{(1.96)^2 \times (12)^2}{2.4^2}$$

$n \approx 100$

Method of statistical analysis

The data was entered in Microsoft excel sheet and was analysed using SPSS version 22 software. The categorical data was represented in the form of frequency and

percentage. Chi square test/Fisher’s exact test was used to test the significance for qualitative data. Continuous data was represented as mean and standard deviation. p value <0.05 was considered as significant.

RESULTS

Age distribution of patients studied

Most common age group in our study was 58-67 years comprising 30 % followed by 48-57 years comprising 27 %.

Gender distribution among study group were 40 females and 60 males i.e. 40 % and 60 % respectively (Figure 1).

Among the patients studied 62% had no comorbidities 17% had diabetes,15% had COPD and 6% had hypertension (Table 1).

Among the patients studied 35% are smokers and the patients studied 39% required ICU admission and care (90%) required mechanical ventilation.

Among the studied patients 62% had Right lower zone consolidation (Table 2).

Among the studied patient’s majority 56% were in high CURB-65 score (>4), followed by 41% were in intermediate (2-3) (Figure 2).

Distribution of sputum culture in study population

Among the studied patients Streptococcus pneumoniae is the most common organisms found on sputum culture (41%), followed by Normal commensals (32%), Klebsiella organisms found in 21% of the patients.

Table 1: Co morbidities Distribution of patients studied

Co morbidities	Numer	Percentage
Never	62	62
T2DM	17	17
COPD	15	15
HTN	06	06
Total	100	100

Table 2: Chest X-ray Distribution of patients studied

Chest X-ray	Number	Percentage
Bil lower zone	1	1
Left lower zone	30	30
Right lower zone	62	62
Right middle zone	7	7
Total	100	100

Outcome

In our majority of patients show 68% radiological and clinical improvement(resolving), followed by 11% resolved, and 8% patients were died during the study.

In the study patients on the day of admission mean ± SD valves of CRP, WBC, ANC, ALC, NLCR with respect to high values of CURB 65 were 181.01±49.39, 19732.04±1327.47, 15579.30±1282.51, 1202.02±267.12, 13.45±2.52 respectively (Table 3).

In the study patients NLRCR on day 1 (12.01±3.18), day 3 (7.21±1.96) and day 7 (1.84±0.97) respectively (Table 4). In those needed ICU care mean ± SD valves of WBC, ANC, ALC, NLCR were 19654.36±1236.44, 1618 7.56±2668.93,1203.00±280.34, 13.93±2.79 respectively (Table 5).

Among 8 patients died during the study mean ± SD values of WBC, ANC, ALC, NLCR were 20033.32 ± 1505.78, 15848.88 ± 1256.13, 1455.92 ± 449.29, 15.18 ± 3.55 respectively and the p- values of the same parameters were 0.901, 0.256, 0.126, 0.003 respectively. This shows NLCR with p valve 0.003 is statistically significant (Table 6).

DISCUSSION

The present study of Absolute neutrophil lymphocyte count ratio in community acquired pneumonia patients

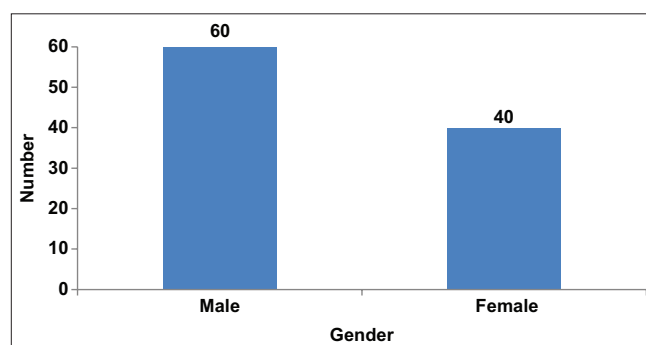


Figure 1: Gender distribution of the patients

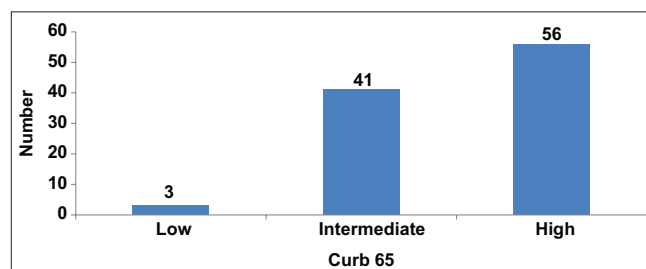


Figure 2: CURB 65 score Distribution of patients studied

Table 3: Distribution between CURB-65 for different Parameter on Day 1

Parameter	Low	Intermediate	High	P-Value
CRP	136.6±84.3	148.76±66.75	181.01±49.39	0.02
WBC	19670.33±708.93	20457.59±1747.28	19732.04±1327.47	0.064
ANC	14808.67±1498.73	16755.59±2534.88	15579.30±1282.51	0.007
ALC	1827±465.97	1727.1±440.96	1202.02±267.12	<0.001
NLCR	8.46±2.17	10.29±3.03	13.45±2.52	<0.001

Table 4: Descriptive Statistics of different parameters for different days

Parameter	Day 1 (n=100)	Day 3 (n=100)	Day 7 (n=96)
WBC	20027.66±1533.79	16165.85±2046.6	6658.96±2585.69
ANC	16038.46±1983.29	11538.78±2184.92	3695.24±1914.02
ALC	1436.05±439.65	1680.09±444.47	2077.05±491.48
NLCR	12.01±3.18	7.21±1.96	1.84±0.97

Table 5: Comparison of different parameters with ICU Group

Parameter	ICU		P
	Yes	No	
WBC	19654.36±1236.44	20266.33±1662.82	0.038
ANC	16187.56±2668.93	15943.13±1398.27	0.550
ALC	1203.00±280.34	1585.05±469.65	<0.001
NLCR	13.93±2.79	10.77±2.80	<0.001

Table 6: Comparison of different parameters with Mortality

Parameter	Mortality		P
	Yes	No	
WBC	20033.32±1505.78	19962.63±1946.89	0.901
ANC	15848.88±1256.13	18218.63±5404.93	0.256
ALC	1455.92±449.29	1207.50±210.99	0.126
NLCR	15.18±3.55	11.73±3.01	0.003

as a prognostic indicator was conducted on 100 patients at Bangalore.

Our study included age groups above 18yrs. Majority of the patients in the study were between 58-67 years (30%) followed by 48-57 years (27%).

Majority of the patients were males which constitutes 66% (60 patients).

When patients were enquired/examined about comorbidities they were having, most of them had no comorbidities (62), 17% had type2 DM, 15% had COPD. About 2/3rd patients in the study group were non-smokers (65%).

Evaluation of vital data at the time of admission showed most patients had pulse rate of 90-110 bpm (67%), respiratory rate of 20-30 (95%) SBP of <120 mm/hg

(99%) DBP of <80 (99%) and temperature of 100-105F (58 %).

The above parameters along with clinical status of the patient were used to calculate CURB-65 score during admission. Majority of the patients admitted had scores of >4 (56%) followed by 2-3(41 %) and 1-2 scores (3 %). this score was simple, easy to calculate and was used for bed side assessment of pneumonia patients.

Among the patients in the study admitted 39% patients required ICU care among the patients sifted to ICU, 90% required mechanical ventilation(35patients).

All patients were treated empirically according to guidelines. Most of them were given a beta lactam and a macrolide. Rest of them were treated with a combination of Piperacillin and Tazobactam.

Outcome of the study showed clinical signs of resolution in 68 % of the patients(resolving), 11% of patients were resolved,3 patients were discharged against advice, 7 patients did not show any features of resolution (resolving).8 patients were died during the study.

In the study patients, ANC, ALC and NLCR values were calculated for day 1, day and day7.

NLCR mean values was 13.45±2.52, 10.29±3.03, 8.46±2.17 in high, intermediate and low CURB-65 values respectively.

ALC mean values was 1202.02±267.12, 1727.1±440.96, 1827±465.97 in high, intermediate and low CURB-65 values respectively.

As the CURB-65 score increased from score 0 to score 4–5, the NLCR consistently increased, while the lymphocyte counts consistently decreased. Among patients in different CURB-65 categories there were no significant differences in CRP levels (p = 0.02). Overall, the NLCR (mean ± SD) was increased in patients with CAP when patients were admitted to the hospital (10.77±2.80) or ICU (13.93±2.79) or died in-hospital (15.18±3.55).

Mean NLCR values in ICU needed patients was 13.93±2.75 and those who doesn't need ICU was

10.77±2.80($p < 0.001$). Values of NLCR was categorised into ≤ 10 and > 10 .

Among 39 patients admitted to ICU, 33 patients NLCR values was > 10 which correlated well with the need for ICU and mechanical ventilation($p = 0.011$). which is statistically significant.

In patients with an adverse outcome defined as ICU admission and/or mortality ($n = 39, 39\%$), a NLCR > 10.0 was observed significantly more frequent (33/39 (84.61%) versus 6/39 (15.38%) NLCR ≤ 10 , p -value = 0.011.

In our study, out of 100 admitted patients 39 (39%) patients were admitted to the ICU. A total of 8 (8%) patients did not survive hospitalization. In patients who died there was a significantly higher NLCR at presentation compared to patients that survived (15.18±3.55 versus 11.73±3.01, p -value, 0.003).

The host inflammatory response in the development of pneumonia has gained growing interest and infection markers are increasingly used to facilitate treatment decisions and improve the accuracy of clinical severity scores in patients admitted with CAP “Old” markers like CRP, WBC count and neutrophil count are still the most frequently used infection markers in daily clinical practice.

In various stressful events the physiological response of circulating leucocytes is characterized by an increase in neutrophil counts and a decline in lymphocyte counts. Neutrophilia is caused by demarginating of neutrophils, delayed apoptosis of neutrophils and stimulation of stem cells by growth factors. Margination of lymphocytes, redistribution of lymphocytes and marked accelerated apoptosis are supposed mechanisms of the observed lymphocytopenia in infectious emergencies.^{5,6,7} In CAP patients it is hypothesized that depression of absolute peripheral blood T-cell counts represents the shift of these cells towards the lung in order to be sequestered in protective mechanisms.^{8,9}

Zahorec *et al.*, further explored its use as a marker of systemic inflammation.³ Recently, we showed that the NLCR proved to be a simple infection marker with discriminatory capacity in predicting bacteraemia in infectious emergency admissions as compared to CRP level, neutrophil count and WBC count.¹⁰

In another study reported by De Jager *et al.*, observed NLCR at the emergency department predicts severity and outcome of CAP with a higher prognostic accuracy as compared with traditional infection markers.¹¹

CONCLUSION

In our study increased NLCR carried poor prognosis which correlated with high CURB65 score, ICU admission and mortality. In patients who died there was a significantly higher NLCR at presentation compared to patients that survived. In our opinion the novelty of the NLCR is the possibility of implementing this parameter simply by using already available biomarkers (WBC-count, neutrophil count and lymphocyte count). Since calculating the NLCR is easy to do and does not require additional testing it may add to our ability to predict mortality.

Limitations of the study

Sample size was small and single centre study.

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Author's Contribution:

DN - Concept and design of the study; Interpreted the results; **MM** - reviewed the literature and manuscript preparation and revision of the manuscript; **SR** - Statistically analysed and interpreted, preparation of manuscript; **AHR** - Concept, coordination, review of literature and manuscript preparation.

Work Attributed to:

Bangalore Medical College and Research Institute, KR Road, Bangalore, Karnataka, India.

Orcid ID:

Dr. Dyaneshwar Nirgude - <https://orcid.org/0000-0003-2560-4145>

Dr. Mahadev Hanmantappa Malge - <https://orcid.org/0000-0003-4133-0367>

Dr. Swetha Rajoli - <https://orcid.org/0000-0002-0765-7959>

Dr. Avinash Hanbe Rajanna - <https://orcid.org/0000-0001-6484-5190>

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