Predictive Value of White Blood Cell Count and Neutrophil-to-Lymphocyte Count Ratio in Classifying the Severity of Community Acquired Pneumonia in Immunocompetent Patients

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Abstract

Introduction: White blood cell (WBC) count, from which neutrophil-to-lymphocyte count ratio (NLCR) can be derived, is commonly requested in the hospital setting among admitting patients with community acquired pneumonia (CAP). This study aims to establish the predictive value of WBC count and NLCR in classifying CAP which guides the clinicians in the choice of antibiotics and site-of-care. The researchers aim to evaluate the predictive value of WBC count and NLCR during consultation and admission in classifying patients with CAP based on the management-oriented risk stratification of the 2016 Philippine Clinical Practice Guidelines on CAP.

Methods: This was a prospective cross-sectional study conducted in St. Luke's Medical Center, Quezon City. Adult patients diagnosed with CAP were classified according to severity of infection based on the 2016 Philippine Clinical Practice Guidelines on CAP. WBC count of each patient was determined, and their corresponding NLCR was derived. The differences of WBC count and NLCR per risk were evaluated using chi-square and ANOVA test adjusted for the distribution of the outcome. Sensitivity and specificity of WBC and NLCR were determined for the following: (1) between CAP low risk (LR) versus CAP moderate risk (MR) and CAP high risk (HR) and (2) between CAP LR and CAP MR versus CAP HR. Receiver operating characteristic (ROC) curve was constructed to evaluate the sensitivity and specificity of WBC and NLCR in classifying. ROC curves displayed sensitivity versus 1-specificity such that area under the curve (AUC) ROC for WBC and NLCR.

Results: Two hundred eighty (280) CAP patients from June 2016 until April 2017 were studied. Among the CAP patients, 69 (24.6%) were classified as LR, 172 (61.5%) were classified as MR, and 39 (13.9%) were classified as HR. The mean WBC count was 11,725.8 (±5,205.82)/µl. The mean WBC per risk were as follows: 9,178/µl for LR; 12,251/µl for MR, and 13,916/µl for CAP HR. It showed that the higher the risk, the higher the mean of the WBC count (<0.00001). The mean NLCR was 8.9 (±8.4). The mean average of NLCR per risk were as follows: 5.4 for LR, 8.6 for MR, and 16.1 for HR. It showed that the higher the risk, the higher the NLCR (<0.00001). In predicting CAP patients with HR and MR from LR, the AUC of NLCR (0.700) was almost the same as that of the WBC count (0.698). In predicting CAP patients with HR from MR and LR, the AUC of NLCR (0.726) was higher than the WBC (0.621), indicating that NLCR is a fair predictive marker in distinguishing HR from MR and LR.

Conclusion: As the severity of CAP increases, the mean of the WBC count and NLCR increases. Between the two biomarkers, NLCR predicts CAP severity more than the WBC count. Furthermore, NLCR better predicts HR from MR and LR.

Keywords: white blood cell count, neutrophil-to-lymphocyte count ratio, community acquired pneumonia

Introduction

Pneumonia continues to be one of the top 10 leading causes of morbidity and mortality in the Philippines.[1] This potentially fatal infection remains to be a health burden especially in developing countries despite advances in both diagnosis and treatment.[2] Phlippine Clinical Practice Guideline in Diagnosis, Empiric Management, and Prevention of Community-Acquired Pnuemonia (CAP) in Immunocompetent Adults–2016 Update has been an effective guideline utilized by most clinicians in classifying the severity of CAP. This is used in the choice of antibiotics and decision to determine the site-of-care for patients whether they will be managed as outpatient, admitted at wards, or intensive care unit.[3]

Besides chest radiograph, complete blood count (CBC) is widely available and commonly requested laboratory test among CAP patients especially in resource-limited setting. Some clinicians are initially influenced by white blood cell (WBC) count as basis of the severity of CAP even with the availability of the guideline.

Inflammatory markers and laboratory parameters, in combination with risk scores, are clinically useful in identifying

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severity and prognosis of CAP. These also guide antibiotic therapy.[4] WBC count plays an important role in the systemic inflammatory response to infection. Because it is widely available, WBC count is frequently requested when infection is suspected. But in a recent study, the area under the curve (AUC) of WBC count in diagnosing CAP is only 0.69 (0.62–0.77).[4]

In the differential count, neutrophilia and lymphopenia were both associated with bacteremia, the latter being more predictive based on several studies.[5] The combination of these parameters led to neutrophil-lymphocyte count ratio (NLCR) and studied in different clinical conditions. Initially, it was found to be correlated with severity and outcome of sepsis.[6,7]

In a prospective study, the NLCR proved to be a simple and even better marker in predicting bacteremia than routine parameters, like WBC count and C-reactive protein (CRP) level, in infectious admissions.[7] The NLCR was increased in all patients with bacteremia. It also predicted the adverse medical outcome and it consistently increased as the CURB-65 score increased. NLCR levels were significantly higher in non-survivors than in survivors with values of 23.4 and 13.0 respectively. The receiver-operating characteristic (ROC) curve for NLCR predicting mortality showed an AUC of 0.701. This was better than the AUC for the neutrophil count, WBC count, lymphocyte count and CRP level (0.681, 0.672, 0.630 and 0.565, respectively).[7]

In another prospective study, it showed that NLCR can be assessed simply and added to the assessment tools to determine the severity of pneumonia during emergency department admission. As the CURB-65 score increased from 0-1 (low risk), to 2-3 (moderate risk), and to 4-5 (high risk), the NLCR consistently increased (mean, 6.9, 8.9 and 16.2, respectively). The difference between the moderate and high risk groups was significant (p=0.008). The NLCR was high in patients with nosocomial hospital acquired pneumonia (10.28±8.81) and increased even more for patients admitted to the ICU (15.69±14.81) or who died within 72-hour (15.63±9.57). NLCR showed the trend of higher value in ICU admission (p=0.072), and CRP was significantly different between ICU and general ward admission (p=0.007).[8]

White blood cell (WBC) count, in which NLCR can be derived, is commonly requested in the hospital setting when admitting patients with CAP. This study aims to establish the predictive value of WBC count and NLCR in classifying CAP which guides the clinicians in the choice of antibiotics and site-of-care.

Methods

This is a cross-sectional prospective study. From June 2016 to April 2017, adult patients (19 years old and older) who consulted and admitted at St. Luke's Medical Center, Quezon City with admitting diagnosis of CAP were studied. St. Luke's Medical Center is a 544-bed academic tertiary institution in Quezon City, Philippines. CAP, based on the Phlippine Clinical Practice Guidelines: Diagnosis, Empiric Management, and Prevention of Community-Acquired Pnuemonia in Immunocompetent Adults–2016 Update, is defined as: (1) lower respiratory tract infection acquired in the community within 24 hours to less than two weeks, presents with an acute cough, abnormal vital signs of tachypnea (respiratory rate >20 breaths per minute), tachycardia (cardiac rate >100/minute) or fever (temperature >37.8°C) or at least one abnormal chest finding of diminished breath sounds, rhonchi, crackles, or wheeze and; (2) a new parenchymal infiltrate in the chest radiograph. Exclusion criteria are the following: patients diagnosed with hospital acquired pneumonia (HAP), ventilator associated pneumonia (VAP), and healthcare associated pneumonia (HCAP), active tuberculosis, patient with co-infection with other organ system, and patient with immunosuppressive state (patients with human immunodeficiency virus or acquired immunodefiency syndrome, uncontrolled diabetes mellitus, taking immunosuppresive or antineoplastic drug, solid organ and hematologic malignancy, organ transplant recipient).

The institutional review board approved the study and gave the investigator-initiated trial code of CT16050. Written informed consent was obtained from the patient or their legal representative.

The recruitment sites were the emergency department (ED) and wards. Collaborating doctors (ED and ward residents) referred and guided the investigator to the status and location of the subjects. Having met the inclusion/exclusion criteria, informed consent was given to the patient or the patient's representative for perusal and signature.

Sample size was calculated based on the comparison of the incidence of MR & HR patients with high NLCR versus low NLCR. Assuming that the incidence of MR & HR among those with high NLCR is 22%[9] and incidence among those with low NLCR is hypothesized to be lower by 50%, with an α error of 5%, power of 80%, and 1-tailed alternative hypothesis, the sample size calculated is 140 per group for a total of 280 for two groups.

Data were gathered once the informed consent form was signed. Patient's baseline characteristics, clinical features, and laboratory data were collected using data collection form and entered in an electronic database. The following data were gathered: age, sex, co-morbidity, smoking history, symptoms (such as fever, cough, sputum production, difficulty of breathing, mental status), vital signs, oxygen saturation, oxygen saturation, chest auscultation, white blood cell count, neutrophil count, lymphocyte count, official results of the chest radiographs, antibiotics started to the subjects, and disposition.

The severity of CAP was classified based on the management-oriented risk stratification of the Phlippine Clinical Practice Guidelines: Diagnosis, Empiric Management and Prevention of Community-Acquired Pnuemonia in Immunocompetent Adults–2016 Update.

The WBC count, neutrophil and lymphocyte counts were determined by the Sysmex XE-2100 hematology analyzer (Sysmex Corporation, Kobe, Japan). WBC count was expressed in counts/ul and NLCR was expressed in number (neutrophil count in % divided by lymphocyte count in %). In our institution, the upper limit of the normal range of the WBC count is set at 10,800 counts/ul. As previously used in a study for predicting bacteremia and severity of CAP, we used the cut-off point of 10.0 for the NLCR.[7]

Numerical data were summarized using mean and standard deviation. Categorical variables were expressed using frequency and percentage distribution. The differences in WBC count and NLCR were evaluated using chi-square and ANOVA test adjusted for the distribution of the outcome. ROC curve was constructed to evaluate the sensitivity and specificity of WBC and NLCR in classifying CAP based on the management-oriented risk stratification of CAP 2016 Guidelines. ROC curves displayed sensitivity versus 1-specificity such that AUC ROC for WBC and NLCR was determined for the following: (1) between CAP LR versus CAP MR and CAP HR, and (2) between CAP LR and CAP MR versus CAP HR.

Results

Baseline characteristics of patients (Table I)

During the study period, 405 consecutive patients with the clinical suspicion of CAP presented at the ED and wards. Because of alternative diagnoses, 56 patients were excluded. In 280 (80.2%) out of the initially included 349 patients, new infiltrates were visible on chest radiography and were diagnosed with CAP. Among the CAP patients, 69 (24.6%) were classified as LR, 172 (61.5%) were classified as MR, and 39 (13.9%) were classified as HR.

The mean age was 68.9 (±18.54). One hundred twenty three (43.9%) were males, while 157 (56.1%) were females. Most common co-morbidity was hypertension seen in 147 (52.5%) patients, followed by diabetes mellitus seen in 86 patients (30.7%), chronic obstructive pulmonary disease (COPD) seen in 30 (10.7%) patients, bronchial asthma seen in 28 patients (10.0%), and cerebrovascular disease seen in 25 (8.9%) patients. All of the co-morbidities had no significant differences among the different risk classification. Seventy-seven (27.5%) were smokers and 56 (72.7%) of them smoked 10 or more pack years.

Cough was the predominant symptom seen in 213 (76.1%) patients and 172 (80.8%) of them produced phlegm. As the CAP severity increases, the percentage of cough among patients decreases (*p*-value <0.00001). Fever was seen in 161 (57.5%) patients. Dyspnea was seen in 62 (22.1%) patients and mostly encountered in HR patients (n=23, 59.0%), compared with MR and LR (*p*-value <0.00001). Altered sensorium was seen in nine (3.2%) patients seen both in the HR and MR group.

The mean systolic blood pressure (SBP) was 133.6 mmHg (±24.2), mean diastolic blood pressure (DBP) was 77.9 (±14.9) mmHg, mean heart rate (HR) was 94.6 (±19.1) bpm, mean respiratory rate (RR) was 21.6 (±3.53) cpm, mean temperature was 37.6 (±0.96) °Celcius, mean oxygen saturation was 96.9 (±4.3) %. There were no significant differences among the SBP, DBP, and temperature among the risk classifications. However, it showed that as the CAP severity increased, the mean HR (*p*-value is 0.001) and mean RR (*p*-value <0.00001) increased while mean oxygen saturation decreased (*p*-value <0.00001).

Abnormal breath sounds were seen in 200 (71.4%) patients, of which HR patients had the highest percentage (*p*-value <0.00001). Crackles was the major adventitious breath sounds exhibited in 151 (75.5%) patients and mostly seen among HR and MR patients (<0.00001). Other adventitious sounds included wheezing and rhonchi seen in 26 and 21 patients, respectively.

For the oxygen requirement, 69 (100%) and 124 (72.1%) patients among CAP LR and CAP MR respectively did not require any oxygen supplementation upon consultation and admission. Thirty five (89.1%) patients with CAP HR required oxygen supplementation, of which, 14 (35.9%) patients required mechanical ventilatory support (*p*-value <0.00010).

For the radiographic findings, based on classification, multilobar involvement were seen in MR and HR patients; HR had a higher percentage of these findings (*p*-value <0.00001). Other findings included pleural effusion and consolidation seen in 25 and 12 patients, respectively. As to the location of the infiltrates, bibasal was the most common location. One hundred seventy three (61.8%) and 148 (59.2%) patients showed infiltrates on the right lower and left lower lobe respectively.

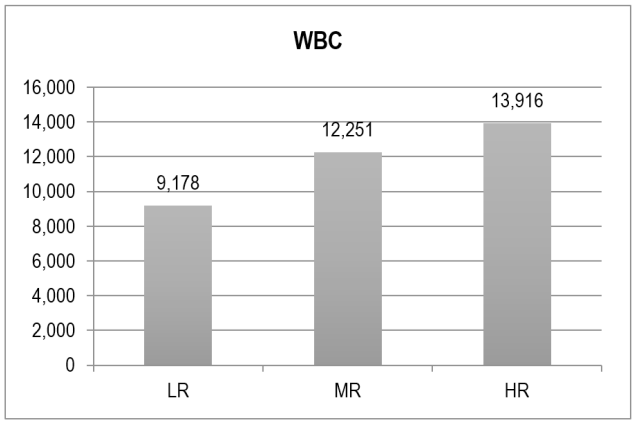
Among the LR studied patients, 47 (68.1%) of them were admitted at the wards and 22 (31.9%) were managed on an outpatient basis. Among MR patients, 167 (97.1%) of them were admitted at the wards and five (2.9%) were manged on an outpatient basis. Among the HR patients, 37 (94.9%) of them were admitted at intensive care unit (ICU).

The most prescribed regimen for LR was cefuroxime with azithromycin given in 35 (50.7%) patients. This was followed by ceftriaxone with azithromycin (n=6, 8.7%), cefuroxime (n=4, 5.8%), and co-amoxiclav (n=4, 5.8%).

Table I. Baseline characteristics CAP patients upon presentation at the emergency department and wards

	CAP LR N=69	CAP MR N=172	CAP HR N=39	*p*-value
Age	68.8 (±19.1)	68.5 (±18.2)	70.5 (±19.0)	0.840
Gender				
Male	26 (37.7%)	76 (44.2%)	21 (53.8%)	0.265
Female	43 (62.3%)	96 (44.2%)	18 (53.8%)	
Co-morbidity				
Hypertension	35 (50.7%)	92 (53.7%)	20 (51.3%)	0.915
Diabetes mellitus	18 (26.1%)	59 (34.3%)	9 (23.1%)	0.246
Chronic obstructive pulmonary disease	3 (4.3%)	22 (12.8%)	5 (12.8%)	0.144
Bronchial asthma	9 (13.0%)	17 (9.9%)	2 (5.1%)	0.419
Cerebrovascular disease	9 (13.0%)	14 (8.1%)	2 (5.1%)	0.323
Coronary artery diseases	4 (5.8%)	15 (8.7%)	1 (2.6%)	0.356
Dyslipidemia	5 (7.2%)	8 (4.7%)	2 (5.1%)	0.719
Cronic kidney disease	3 (4.3%)	7 (4.1%)	3 (7.7%)	0.619
Alzheimer's disease	1 (1.4%)	4 (2.3%)	1 (2.6%)	0.896
Congestive heart failure	0 (0%)	4 (2.3%)	2 (2.3%)	0.202
Parkinson's diseases	0 (0%)	4 (2.3%)	1 (4.2%)	0.433
Smoking	18 (26.1%)	49 (28.5%)	10 (25.6%)	0.895
≥10 pack years	12 (66.7%)	36 (73.5%)	8 (80.0%)	0.736
Symptoms				
Fever	41 (59.5%)	99 (57.6%)	21 (53.8%)	0.853
Cough	59 (85.5%)	134 (77.9%)	20 (51.3%)	<0.0001
Productive	48 (81.4%)	107 (79.9%)	17 (85.0%)	0.854
Dyspnea	7 (10.1%)	32 (18.6%)	23 (59.0%)	<0.00001
Altered sensorium	0 (0%)	5 (2.9%)	4 (10.3%)	0.014
Vital signs				
Systolic blood pressure (mmHg)	133.6(± 22.7)	135.48 (± 23.7)	125.2 (± 28.0)	0.058
Diastolic blood pressure (mmHg)	77.8 (± 13.6)	78.26 (± 14.7)	76.3 (± 17.6)	0.756
Heart rate (bpm)	8.5 (± 15.4)	95.2 (± 19.1)	102.6 (± 21.9)	0.001
Respiratory rate (cpm)	20.1 (± 1.6)	21.7 (± 3.5)	23.7 (± 4.9)	<0.00001
Temperature (° celcius)	37.7 (± 0.9)	37.6 (± 1.0)	37.6 (± 0.9)	0.899
Oxygen saturation	98.8% (± 1.3)	97.0% (± 4.0)	93.1% (± 6.1)	<0.00001
Abnormal breath sounds	37 (53.6%)	129 (75.0%)	26 (92.3%)	<0.00001
Crackles	28 (40.6%)	97 (56.4%)	28 (71.8%)	0.006
Rhochi	5 (7.2%)	8 (4.7%)	5 (12.8%)	0.163
Wheezes	6 (8.7%)	16 (9.3%)	4 (10.3%)	0.965
Decreased breath sounds	0 (0%)	17 (9.9%)	4 (10.3%)	0.024
Oxygen support				
Room air	69 (100%)	124 (72.1%)	4 (10.3%)	<0.00001
Nasal canula	0 (0%)	37 (21.5%)	11 (28.2%)	
Face mask	0 (0%)	6 (3.5%)	6 (15.4%)	
BIPAP	0 (0%)	5 (2.9%)	4 (10.3%)	
Mechanical ventilator	0 (0%)	0 (0%)	14 (35.9%)	
Radiographic findings				
Lobar	69 (100%)	45 (26.2%)	6 (15.4%)	<0.00001
Multilobar	0 (0%)	127 (73.8%)	33 (84.6)	
Pleural effusion	0 (0%)	21 (12.2%)	4 (10.3%)	0.010
Consolidation	0 (0%)	9 (5.2%)	3 (7.7%)	0.102
Dispostion				
Outpatient	22 (31.9%)	5 (2.9%)	0 (0%)	<0.00001
Wards	47 (68.1%)	167 (97.1%)	2 (5.1%)	
ICU	0 (0%)	0 (0%)	37 (94.9%)	

The most prescribed regimen for MR was also cefuroxime with azithromycin given in 59 (34.3%) patients, followed by piperacillin-tazobactam (n=29, 16.9%) and ceftriaxone with azithromycin (n=16, 9.3%). The most prescribed regimens for HR was piperacillin-tazobactam alone (n=10, 25.6%) and piperacillin-tazobactam with azithromycin (n=10, 25.6%), followed by meropenem (n=7, 17.9%) and ceftriaxone with azithromycin (n=3, 7.7%).



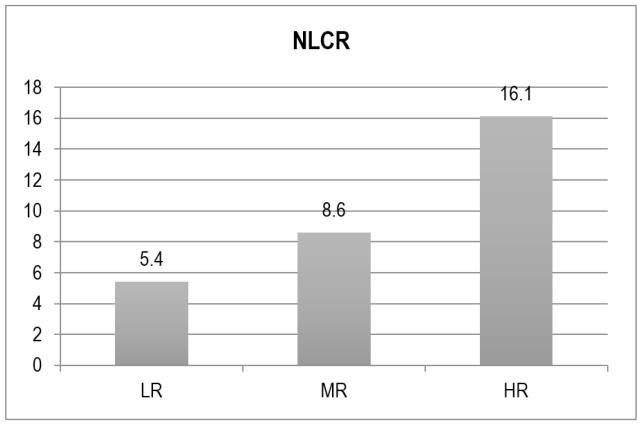


Figure 1A and 1B. Trend of the mean WBC (1A) and mean NCR (1B) per risk assessment

WBC and NLCR of patients

The mean WBC count among CAP patients was 11,725.8 (±5,205.82)/ul. The mean WBC per risk were as follows: 9,178 (±3,930)/ul for LR; 12,251 (±5,022)/ul for MR, and 13,916 (±6314)/ul for CAP HR. It showed that the higher the risk, the higher the mean of the WBC count (<0.00001). The mean NLCR among CAP patients was 8.85 (±8.4). The mean of NLCR per risk were as follows: 5.4 (±4.4) for LR, 8.6 (±7.1) for MR, and 16.1 (±13.3) for HR. It showed that the higher the risk, the higher the NLCR (<0.00001) (Figure 1A and 1B)

The cut-off of normal WBC count in our instution was equal or less than 10,800/µl. One hundred forty one (50.1%) patients had elevated WBC. Among LR patients, only 17 (24.6%) had WBC of >10,800/ul. Among MR patients, 100 (58.1%) have WBC of >10,800/ul. Among HR patients, 24 (61.5%) have WBC of >10,800/ul. It showed that the higher the risk, the higher the percentage of elevated WBC (<0.00001). (Figure 2)

Eighty three (29.6%) patients had NLCR >10. Among LR patients, only 10 (10.1%) had NLCR >10. Among MR patients, 53 (30.8%) had NLCR >10. Among HR patients, 23 (59.0%) had NLCR >10. It showed that, the higher the risk, the higher the percentage of patients with NLCR >10 (<0.00001). (Figure 3)

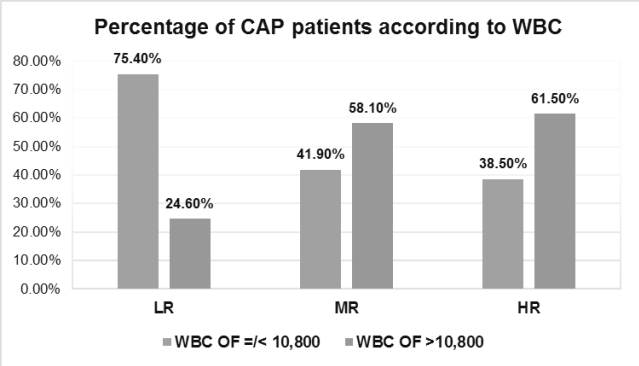


Figure 2. Percentage of CAP patients per risk assessment with normal and elevated WBC count

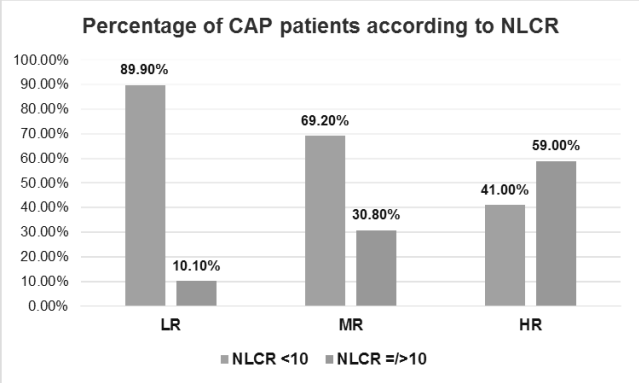


Figure 3. Percentage of CAP patients per risk assessment with <10 or >10 NLCR

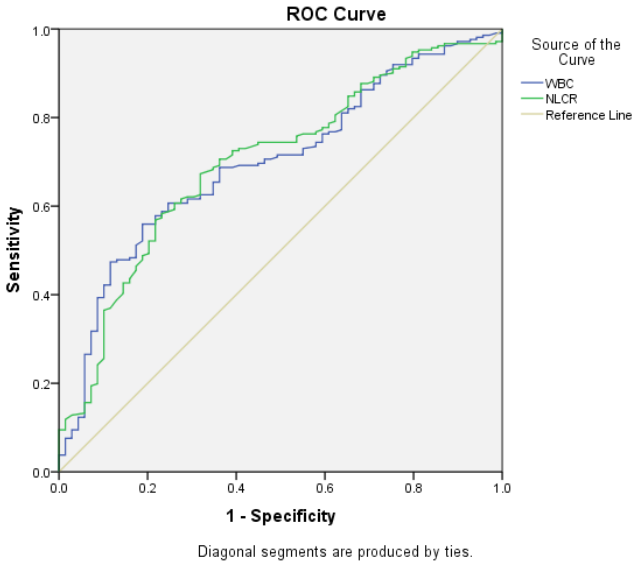


Figure 4. Receiver operating characteristic ROC of WBC (blue) and NLCR (green) in predicting MR and HR from LR

Diagnostic accuracy in predicting CAP MR and HR from LR

The WBC count cut-off of 10,350/ul (which is near the institution cut-off for elevated WBC) had a sensitivity of 58.8% and specificity of 76.8%. The established WBC cut-off of the study was 11,250/ul and had a sensitivity of 55.9% and specificity of 81.2%. To achieve a specificity of 90%, the WBC cut-off is 13,260/ul. But this only showed a sensitivity of 43.3% (Table II).

Table II. Multilevel sensitivity, specificity, and likelihood ratios in predicting CAP severity

	Sensitivity	Specificity	LR +	LR-
Prediciting MR and HR from LR				
WBC count/ul Cut-off				
≥10,350*	58.8%	76.8%	2.53	0.54
≥11,250**	55.9%	81.2%	2.97	0.54
≥13,260***	43.3%	89.9%	4.29	0.63
NLCR Cut-off				
≥ 5.07**	67.3%	68.1%	2.11	0.48
≥ 9.94****	36.0%	89.9%	3.56	0.71
≥ 10.24***	35.5%	89.9%	3.51	0.72
Predicting HR from MR and LR				
WBC count/ul Cut-off				
≥ 10,350*	51.5%	51.9%	1.07	0.93
≥ 16,390**	41.0%	83.8%	2.53	0.70
≥ 18,345***	23.5%	90.0%	2.35	0.85
NLCR Cut-off				
≥ 7.82**	71.8%	66.8%	2.16	0.42
≥ 10.24****	56.4%	75.1%	2.27	0.58
≥ 15.71***	33.3%	90.0%	3.33	0.74

LR – Likelihood Ratio
**- Nearest cut-off of our institution*
***- Best Cut-off determined by current study*
****- Cut-off having a specificity of 90%*
*****- Nearest Cut-off set by a study[7]*

The established NLCR cut-off of the study was 5.07 and had a sensitivity of 67.3% and specificity of 81.2%. To achieve a specificity of 90%, the NLCR cut-off were 9.94 and 10.24 but these only had a sensitivity of 36.0% and 35.5% respectively. (Table II)

In predicting CAP patients with HR and MR from LR, the AUC of NLCR (0.700) was almost the same as that of the WBC count (0.698). However, in reference to the AUC, NLCR was a fair predictive marker, while WBC count was poor predictive marker in distinguishing CAP MR and HR from LR. (Figure 4)

Diagnostic accuracy in predicting CAP HR from MR and LR

The WBC cut-off of 10,350/ul (which is near our institution's cut-off for elevated WBC) had a sensitivity of 51.5% and specificity of 51.9%. The established WBC cut-off of the study was 16,390/ul and had a sensitivity of 41.0% and specificity of 83.8%. To achieve a specificity of 90%, the WBC cut-off is 18,345/ul. But this only had a sensitivity of 23.5%. (Table II)

The established NLCR cut-off of the study was 7.82 and demonstrated a sensitivity of 71.8% and specificity of 66.8%. The NLCR cut-off of 10.24 (cut off established for predicting bacteremia) had a sensitivity of 56.4% and specificity of 75.1%.To achieve a specificity of 90%, the NLCR cut-off was 15.71. But this only demonstrated a sensitivity of 33.3%. (Table II).

In predicting CAP patients with HR from MR and LR, the AUC of NLCR (0.726) was higher than the WBC (0.621), indicating that NLCR is a fair predictive marker in

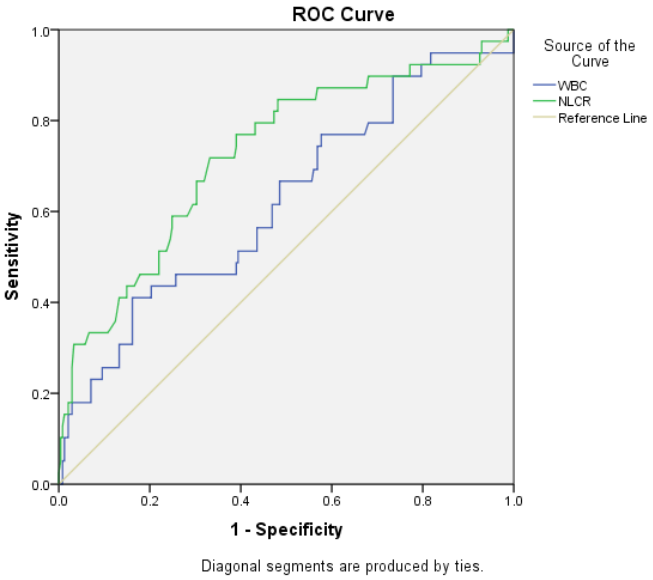


Figure 5. Receiver operating characteristic ROC of WBC (blue) and NLCR (green) in predicting HR from MR and LR

distinguishing HR from MR and LR. (Figure 5)

Discussion

Between the two biomarkers, NLCR predicts CAP severity more than the WBC count. Furthermore, NLCR can better predict HR from MR and LR. This study is the first to evaluate the predictive capability of WBC count and NLCR in classifying the CAP risk set by our local guidelines. One of the features of the study is it involved only immunocompetent patients and did not include leukocytosis-related conditions such as malignancy and steroid use which may influence the increase in WBC count.

The majority of the subjects were elderly with mean age of 68.9 which is at par with other studies having mean ages of 63 and 67.1.[4,5] The most common co-morbidities included elderly-related conditions such as hypertension, diabetes mellitus, and COPD. Cough was a predominant symptom (76.1%) like other studies.[4,7,8] Fever was only seen in 57.5% of patients. This may be attributed to a majority of the patients who were old. Diminished thermoregulatory responses during aging and abnormalities in both the production and response to endogenous pyrogens, such as IL-1, IL-6, and TNF, may be the possible explanations for the differences between elderly and young patients in fever response to infection.[11,12] Respiratory and nonrespiratory symptoms were also less commonly reported by elderly patients with pneumonia.[12] Vital signs, as expected, worsen as the severity increased except for the blood pressure and temperature. Abnormal auscultation was appreciated in 71.4% compared with one study with 86.1%.[4] With the variation of clinical signs and symptoms of the different studies, their use as screening and establishing the diagnosis of CAP are of limited value.[4] This study also revealed the site of care of the patients. Among LR patients, around 68.1% were admitted at the wards instead being discharged. Reasons behind include clinical judgement by the physician and patients's prerogative since most of the cases were seen at the ED. Ninty-seven percent of MR were admitted at wards, while 94.9% were admitted at the ICU. In terms of choice of antibiotics, those classified as LR patients were influenced by the site of care hence were given MR regimen treatment.[2]

An elevated WBC is a common sign of infection, particularly bacterial, hence it is a commonly requested laboratory examination.[9] In this study, the mean WBC count is 11,725.7/ul. For other studies, the mean WBC count was 13,500/ul and 12,900/ul respectively.[4,5] However for these latter studies, leukocytosis-associated conditions were included. These studies also included patients who were all admitted. Using our institution's cut-off, half of the patients (50.4%) with CAP had elevated WBC count. Although it was postulated that total WBC decrease slightly in the elderly, it increases in acute infection and in sepsis, and the increase is very dramatic.[14] As exhibited, as the severity of CAP increases, the mean WBC count increases. In other studies, the difference of WBC count per risk was not significant in determining the severity.[4,8] But the risk assessment used for these studies was CURB 65. The AUC of WBC count in predicting severity of CAP was poor and these results are comparable to other studies.[4,7] WBC counts may help identify complications in those with severe pneumonia but reliance on the WBC count to help guide management decisions should not be encouraged.[15]

NLCR has been widely studied biomarker of different infections because it can be easily derived with the differential count. For pneumonia patients, increased NLCR values were seen in patients with increased CURB-65 scores, bacteremia, and predicting mortality.[7] The mean NLCR of this study was 8.85. Like WBC, it is lower compared to other studies because other studies included mostly admitted CAP patients.[5,7] As exhibited, as the severity increases, the mean NLCR increases. In one study, in which the subjects were diagnosed with HCAP, they studied NLCR in relation to CURB 65 risk assessment (LR 6.6, MR 8.9, HR 16.2). Results were comparable to our study. NLCR of 10 and above was used as cutoff to establish bacteremia.[7] In this study, as the severity increased, the percentage of NLCR of >10 increased. The AUC of NLCR in predicting severity of CAP was fair. The highest AUC was seen in predicting HR patients from MR and LR with a value of 0.726. In another study, the AUC of NLCR was also fair: 0.73, 0.70 and 0.76, but measured parameters were predicting bacteremia, in-hospital moratlity, and 30 day mortality respectively.[7,15] The physiological response of circulating WBC in infection is characterized by increase in neutrophil counts. Production of neutrophils can be increased in the presence of an inflammatory stimulus, such as bacterial infection. Neutrophilia is caused by demargination of neutrophils, delayed apoptosis of neutrophils and stimulation of stem cells by growth factors.[7] Another response is lymphopenia. Margination of lymphocytes, redistribution

of lymphocytes and marked accelerated apoptosis are supposed mechanisms of the observed lymphopenia in infectious emergencies.[5,7] Lymphopenia has shown results in the prediction of bacteremia in infectious emergency.[5]

Comparing both, NLCR was more superior than WBC in predicting the severity of CAP. In other studies, the NLCR was superior than WBC in diagnosing ang predicting mortality of CAP patients. Since this ratio is a combination of two infectious responses–neutrophilia and lymphopenia, its predictive ability is higher when combined.

As proven in this study, the use of the NLCR may allow clinicians to stratify patients with CAP based on the severity. The findings could lead to the exploration of adding the NLCR to our local risk assessment thereby guiding the site-of-care and choice of antibiotics for CAP patients.

However, this study has some limitations. First, the percentage of LR patients may not reflect the actual percentage of LR patients since the patients included were those consulted at ER and admitted at wards and ICU. Second, this is a single center study, the results can be validated by other institutions.

Conclusions

As the severity of CAP increases, the mean of WBC count and NLCR increases. Between the two biomarkers, NLCR predicts CAP severity more than the WBC count. Furthermore, NLCR can better predict HR from MR and LR.

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