

# Neutrophil to lymphocyte count ratio as a biomarker of bacterial infections

## Research Article

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**Abstract:** The implementation of new markers of bacterial infection into clinical practice is hindered by their costs. We assessed the potential use of the neutrophil to lymphocyte count ratio (NLCR) to discriminate between bacterial and viral infections. NLCR was evaluated in 45 patients with bacterial infections: 24 patients with viral infections and 18 healthy adults. The medians of NLCR were 11.73 in bacterial infections, 2.86 in viral infections and 1.86 in controls. The NLCR cut-off value of 6.2 exhibited a sensitivity value of 0.91 and a specificity value of 0.96 for bacterial infection. These results suggest a diagnostic potential for NLCR.

**Keywords:** Bacterial infection • Viral infection • Laboratory diagnosis • Marker • Neutrophil to lymphocyte ratio

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## 1. Introduction

The ideal marker for rapid discrimination between bacterial and viral infection has not been determined for routine use. Currently, C-reactive protein (CRP), white blood cell (WBC), and neutrophil counts are the most frequently used parameters for early diagnosis of bacterial infection [1]. However, these parameters do not always reliably differentiate among bacterial, fungal, and severe viral infections [2]. Therefore, other parameters have been recommended, including serum levels of procalcitonin (PCT), interleukin (IL)-6, and IL-8 [3,4]. PCT has become a widely used marker in recent years. The superiority of PCT over CRP, WBC and neutrophil counts for predicting the bacterial etiology of infection was also shown in our previous study [5].

Neutrophilia and lymphocytopenia are well-established markers of severe bacterial infection. Zahorec et al. [6] have documented the neutrophil to lymphocyte count ratio (NLCR) as an easily measurable parameter that indicates the severity of systemic inflammation and sepsis in 90 oncology patients. Moreover, NLCR is a useful parameter for predicting bacteremia in

emergency care settings [7]. However, there is a lack of information about the potential use of NLCR to discriminate severe bacterial from viral infections. Therefore, the aim of our study was to assess the sensitivity and specificity of NLCR for the diagnosis of community-acquired bacterial infections in patients who were hospitalized with febrile illness.

## 2. Methods

In all, 87 adults were enrolled in the prospective study. The study was approved by the ethics committee, and the patients signed informed consent forms before enrollment. The cohort with bacterial infection comprised 45 patients (22 females and 23 males) with a mean age of 45 yrs spanning 18–80 yrs. The following clinical diagnoses were established in the patients: community-acquired pneumonia (19), urosepsis (10), pyelonephritis (9), cellulitis (2), erysipelas (1), invasive meningococcal disease – IMD (3) and sepsis (1). The bacterial etiology was confirmed in 24 patients (53.9%). The following etiological agents were detected by culture: *Escherichia*

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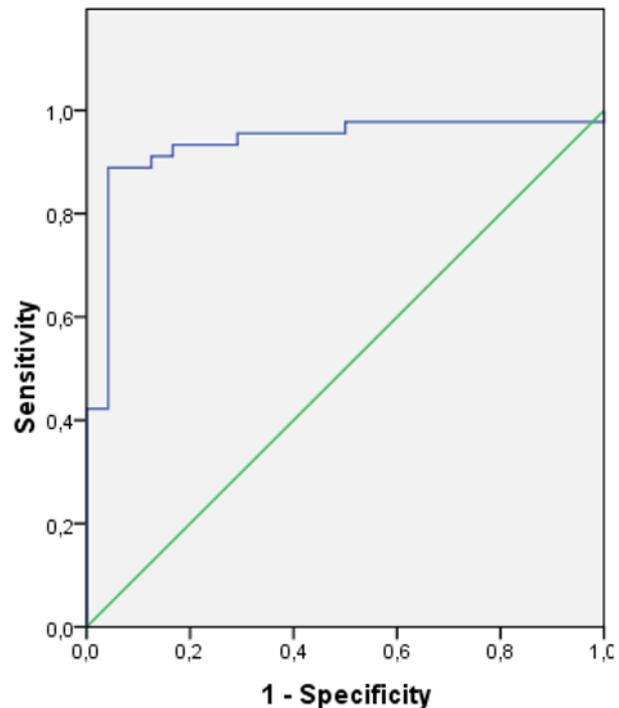
*coli* (15), *Streptococcus pneumoniae* (4), *Haemophilus parainfluenzae* (1) and *Staphylococcus hominis* (1). In three patients, the etiology of IMD was confirmed using a polymerase chain reaction (PCR) analysis of the blood or cerebrospinal fluid. Three patients with pneumonia had an etiologic diagnosis that was established by a significant increase in specific IgG antibodies against *Chlamydomphila pneumoniae* (2) and *Legionella pneumophila* (1). The cohort of patients with viral infection included 24 patients (8 females, 16 males) with a mean age of 41.5 yrs spanning 19–69 yrs. In these patients, the following diagnoses were established: tick-borne encephalitis (15), enteroviral meningitis (4), viral hepatitis A (2), chicken pox (2) and parvovirus (1). In the control group, 18 healthy adult persons were enrolled (5 females and 13 males) with a mean age 43 yrs spanning 23–69 yrs. The details describing the inclusion and exclusion criteria and clinical diagnostics have been reported elsewhere [5].

Neutrophil and lymphocyte counts were determined using a Coulter STKS clinical analyzer (Coulter Electronics Inc., Miami, USA). NLCR was expressed as the absolute number of neutrophils divided by the absolute number of lymphocytes [6]. Statistical analyses were performed by a certified statistician. The data were expressed as the medians (interquartile ranges). Receiver operating characteristic (ROC) curves were drawn for NLCR as a measure of discriminating power between bacterial and viral infections and as a measure of capability to detect bacterial infections. The ROC curve demonstrated the false positive rate (x axis) and the sensitivity of the test (y axis). The areas under the curves (AUC) were also evaluated.

### 3. Results

The medians of NLCR were 11.73 (7.73–21.87) in patients with bacterial infections, 2.86 (1.95–4.15) in patients with viral infections and 1.86 (1.44–2.73) in healthy adults. The optimal cutoff value for NLCR was determined as 6.2, which exhibited a sensitivity value of 0.91 and a specificity value of 0.96. The AUC was 0.971 for predicting bacterial infection in all 87 enrolled subjects and 0.956 for differentiating between bacterial and viral infections. The ROC curve is presented in Figure 1.

ROC Curve



**Figure 1.** ROC curve of NLCR values demonstrating the high diagnostic value for discrimination between bacterial and viral infections.

### 4. Discussion

Diagnostic markers that are currently used for discrimination of bacterial etiology are not sufficiently reliable. Moreover, the markers that have been recently introduced into clinical practice are associated with high costs that serve as major limitations. These markers include PCT, which is considered a fast and specific marker for infection in critically ill patients and is currently implemented in routine diagnostic panels [9,10]. Conversely, the NLCR is a low-cost and easily obtainable parameter that does not require any special equipment for NLCR measurements. Similar to PCT, the changes of WBC populations have rapid kinetics, reflecting the role of neutrophils in the early stage of the inflammatory response. Neutrophilia is usually accompanied with lymphocytopenia, which has also been suggested as a good predictor of bacteremia [11]. Lymphocytopenia probably develops because of the need to suppress the adaptive immune response in favor of innate immunity. This notion is supported by data showing that CD4+ T cells are the most altered lymphocyte subset during severe bacterial infections and sepsis [12]. The AUC for the NLCR that was observed in our study was similar

to that of PCT and significantly higher than the AUC of neutrophilia and lymphocytopenia (data not shown). This finding is in accordance with a previous study documenting the importance of the NLCR in the prediction of bacteremia in emergency settings (7).

There are some conditions when the diagnostic value of NLCR is reduced. These conditions include bacterial infections in neutropenic patients or neutropenic enterocolitis resulting from *Clostridium species*, *Escherichia coli* and *Pseudomonas aeruginosa* and diseases that are constitutively associated with lymphocytopenia, including acquired immunodeficiency syndrome, measles, tuberculosis, high plasma corticosteroids levels, obstructed lymphatic circulation, severe systemic illness, systemic lupus erythematosus, sarcoidosis, cytotoxic or immunosuppressive therapy and severe right-sided congestive heart failure [13-18]. Finally, increased numbers of circulating lymphocytes are observed in Pertussis, which is a potentially re-emerging infection in industrialized countries [19].

## 5. Conclusion

In conclusion, the NLCR may serve as a simple marker for discrimination between severe bacterial and viral infections. Direct availability, low cost, and high reliability of the NLCR support its incorporation into routine diagnostic panels.

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### Statement

This study was conducted after obtaining approval from the Ethics Committee of the University Hospital Bulovka (IRB00002721 – Fakultni nemocnice Na Bulovce IRB #1 – Biomedical) and all patients gave written informed consent prior to their inclusion in the study.

This publication has been approved by all co-authors, has not been published before and it is not under consideration for publication anywhere else.

All authors declare that they have no conflict of interest.

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