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Neutrophil to lymphocyte ratio and platelet to lymphocyte ratio as diagnostic markers for pneumonia severity

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The severity of pneumonia should be determined in order to determine the most appropriate management. Most commonly, the pneumonia severity index scoring system has been used to decide whether pneumonia patients can be treated as outpatients or as inpatients.[1] The CURB score (evaluation of Confusion, Urea level, Respiratory rate and Blood pressure) is also a major tool used to anticipate the severity of pneumonia.[2] However, these scoring systems need some efforts to analyse several patient's data. Therefore, various laboratory biomarkers still have been developed to effectively discriminate. In this regard, c-reactive protein (CRP) is a blood marker of inflammation and the acute-phase response.[3] In pneumonia patients, admission CRP has a significant prognostic value in community-acquired pneumonia (CAP).[4] Serum CRP may be a useful adjunctive test in pneumonia as well as being a marker of treatment response.[5]

Recently, the concept of neutrophil to lymphocyte ratio (NLR) has been reported as being of potential value, with a significant correlation with inflammation, in several diseases.[6] NLR is a simple and useful laboratory marker to discriminate patients with pulmonary tuberculosis from patients with bacterial CAP.[7] Similarly, platelet-to-lymphocyte ratio (PLR) has been described as a novel inflammatory marker, which may be used in many diseases for predicting inflammation and mortality.[8] NLR and PLR can be easily obtained at low cost through an automatic haematology analyser However, these parameters were not evidence-based established as specific biomarkers in specific clinical fields. Therefore, further objective studies are warranted to understand the clinical value of these inflammation-related parameters. The aim of this study was to determine the usefulness of NLR or PLR in determining the severity of pneumonia compared to CRP level.

We recruited 227 pneumonia patients admitted to Osan Hankook General Hospital in Gyeonggi province of Korea from January 2013 to December 2014. Pneumonia was diagnosed by physicians based on patients' clinical symptoms, radiographic assessments and laboratory results. Patients were classified as being treated on a ward or in intensive care. Data from individuals attending for a health check-up were analysed as control group. All subjects' clinical data were protected and followed the World Medical Association Declaration of Helsinki. The NLR and PLR parameters were measured using an automated haematology analyser, Sysmex XE-2100D (Sysmex Corporation, Kobe, Japan). CRP was measured by Toshiba TBA-120 FR or TBA-40 FR (Toshiba LTD, Tokyo, Japan) chemistry autoanalyser with Auto CRP (Shinsung Pharm, Suwon, Korea) based on latex immunoturbidimetry. The CRP of the health check-up group was not measured, since a relatively low level of CRP was expected. All parameters were evaluated for distribution by Kolmogorov–Smirnov test. Mann–Whitney *U* test and Kruskal–Wallis tests were used in nonparametric comparison methods. Logistic regression analysis was performed to determine whether NLR or PLR is better at defining ICU admission than CRP. A *p*-value less than 0.05 was considered statistically significant. All analyses were performed using SPSS, version 12 (SPSS, Chicago, IL, USA).

Basic demographic parameters are summarised in Table 1. As most analysed parameters were not normally distributed we present median and interquartile ranges of each NLR, PLR and CRP level. NLR and PLR were highest in pneumonia patients in ICU, then in the ward patients, then in the control group (Table 1, Figure 1). CRP was higher in pneumonia patients in ICU than pneumonia patients on the ward. Length of stay was longer in ICU patients than in the ward patients. We performed a logistic regression which included age, sex ratio, NLR,

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Table 1. Laboratory and Demography of enrolled patients and health check-up controls and results of NLR and PLR.

	Health check-up (n = 45)	Ward (n = 134)	Intensive care unit (n = 93)
Mean age (year) (min–max)	71 (63–86)	74 (44–98)	76 (31–97)
Male to female ratio	0.8	1	0.9
Type of disease*	For health check-up	Pneumonia caused by unidentified sources	Pneumonia caused by unidentified sources
Length of stay (day) Median (interquartile range)	<1	7 (3.8–12)	10 (3–19)
NLR** ***	1.5 (1.2–2.2)	4.1 (2.4–7.0)	8.4 (4.4–17.5)
PLR** ***	105 (94–125)	163 (114–232)	219 (135–390)
CRP (mg/L)***	NA	7.62 (1.7–32.5)	18.44 (8.8–39.6)

ICU, intensive care unit; NLR, neutrophil to lymphocyte ratio; PLR, platelet to lymphocyte ratio; CRP, c-reactive protein; NA, not applicable.
*Most patients (>95%) were diagnosed pneumonia caused by unidentified sources by clinical symptoms, radiologic findings, and laboratory data.;
**Kruskal–Wallis and Mann–Whitney *U* tests between each group were performed. ***Mann–Whitney *U* test.

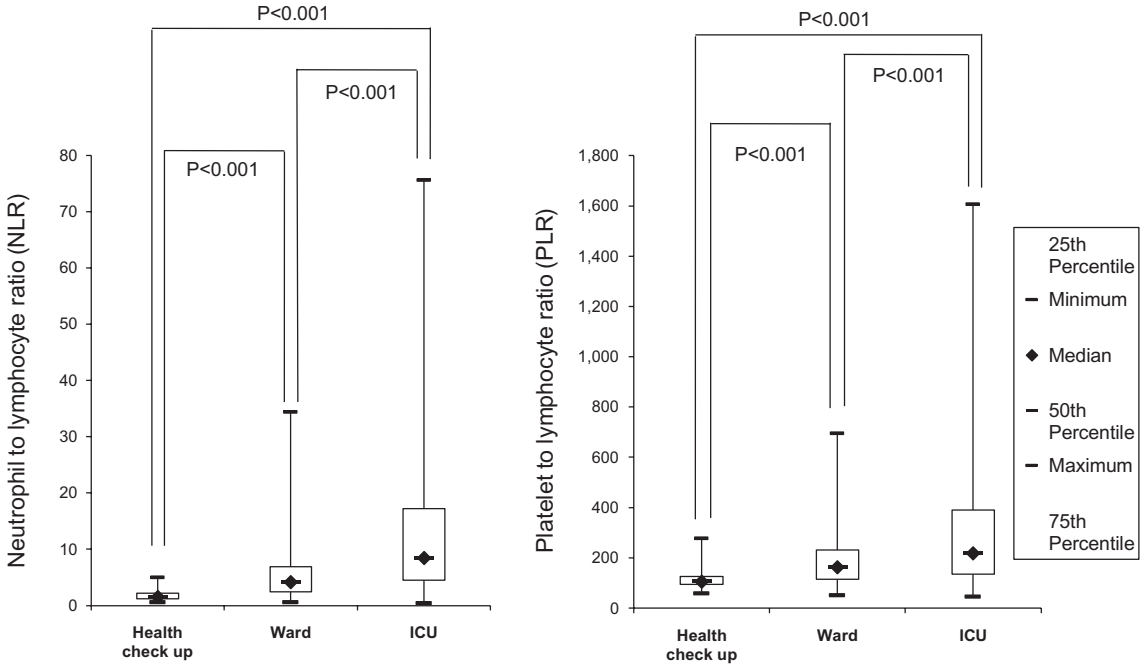

Figure 1. Comparison of the level of NLR and PLR in pneumonia patients and in normal health control. Abbreviations: NLR, neutrophil to lymphocyte ratio; PLR, platelet to lymphocyte ratio; ICU, intensive care unit.

PLR and CRP, hypothesising that ICU admission patients had more severe risks than ward admission patients. A higher NLR level brought a hazard ratio of an ICU admission of 1.099 (95% confidence interval: 1.036 – 1.167) (p = 0.002). Other parameters such as age, sex ratio, PLR and CRP did not show statistical significance in logistic regression (p > 0.05).

Recently, cost-effective full blood count parameters such as NLR, PLR or delta neutrophil index (DNI) have been investigated for their clinical impacts on various diseases' diagnosis or prognosis. Kim et al. [9] reported that DNI showed significantly better diagnostic power in the lower grade CAP group than in the upper respiratory infection and control groups. In the present study, we compared the levels of NLR and PLR in pneumonia patients in general ward and in ICU in addition to the CRP level. NLR and PLR were present in higher levels in ICU patients than in general ward patients as compared to CRP. NLR or PLR might have diagnostic utilities such as CRP in evaluation of severity of pneumonia patients. Especially, higher NLR increased the risk of ICU treatment of pneumonia patients through logistic regression analysis. CRP has been reported to have significant prognostic value and a useful adjunctive test as well as being a marker of treatment response in pneumonia.[4, 5] Therefore, NLR might be a useful marker compared to CRP level for determination of pneumonia severity. The present biomarkers in this study should be considered for their differences of half-life. The plasma half-life of CRP is 19 h [10] and physiological half-life of the neutrophil in the circulation is only 6 h.[11] The recirculating lymphocyte pool was found to reproduce itself every 16.5 ± 3.0 days. [12] Platelet lifespan was known as long as 8–9 days.[13] The peak level of these parameters might be related with their half-life time. Although the half-lives of CRP, NLR and PLR were different, they showed increased levels in more severe status of pneumonia. Actually, NLR has proven to be a useful measure of systemic inflammation. [14] NLR was reported as a possible surrogate marker of inflammation in pneumonia patients.[15, 16] In addition, numerous cancer survival studies also suggest that NLR is a significant predictor of overall and disease-specific

survival in patients.[17, 18] Also, NLR at the emergency department predicts severity and outcome of CAP with a higher prognostic accuracy as compared with traditional infection markers.[15] PLR has not been widely reported in the evaluation of the severity of pneumonia patients. This study has limitations in that it was a limited retrospective case control study, patients' health conditions such as smoking, alcohol, hypertension, diabetes or any other underlying disease history were not fully assessed. Also, the severity of pneumonia was only classified as ward or ICU admission without considering other underlying diseases and not categorised as specific types or causes of pneumonia or CURB criteria. Except for CRP, other suggestive inflammatory biomarkers such as procalcitonin, interlukin-6 were not evaluated. However, this study suggested a possibility to consider NLR and PLR as useful surrogate inflammatory markers like CRP which could represent pneumonia severity. We found the level of NLR and PLR increased in pneumonia patients in ICU than in ward care as compared to CRP level. In particular, a higher NLR level increased ICU admission risk 1.099 times as compared to those of general ward patients. Further, well-organised large-scale prospective studies are warranted to understand the exact role of NLR and PLR parameters.

This report represents an advance in biomedical science because NLR and PLR may be useful parameters in determining the severity of pneumonia.

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No potential conflict of interest was reported by the authors.

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