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ORIGINAL ARTICLE

Analysis of interleukin-8 (IL-8) level, blood urea nitrogen/albumin ratio, pneumonia severity index, and length of stay in patients undergoing pulmonary rehabilitation and shortwave diathermy

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ABSTRACT

Aim To analyse the effects of pulmonary rehabilitation (PR) and short-wave diathermy (SWD) on blood urea nitrogen (BUN)/albumin ratio, pneumonia severity index (PSI), IL-8 level, and length of stay (LOS) in hospitalized pneumonia patients.

Methods This randomized experimental study with a pre-post control group design included 24 pneumonia patients treated between 2022 and 2023. Patients were divided into three groups for five days: the control group (CO) that received standard pneumonia therapy only, PR group that received standard therapy combined with pulmonary rehabilitation, and PRSWD group that received standard therapy combined with pulmonary rehabilitation and short-wave diathermy. Blood samples were collected before and after the intervention to measure IL-8 levels and the BUN/albumin ratio. Delta (Δ) (change) values of each parameter were compared among the groups. Pneumonia severity was assessed using PSI and the CURB-65 score (confusion, urea, respiratory rate, blood pressure, and age ≥65 years).

Results IL-8 levels decreased in the PRSWD group (p=0.170). The BUN/albumin ratio was significantly reduced in the control group after intervention (p = 0.049). LOS in the PRSWD group was the shortest and showed a significant difference compared to other groups (p = 0.032). Significant negative correlations were observed between PSI and delta BUN/albumin ratio in the PRSWD group, and between CURB-65 and delta BUN/albumin ratio in the control group (p=0.045; p=0.030).

Conclusion This study reinforces the evidence that PRSWD can serve as an adjunctive therapy for patients with pneumonia.

Keywords: cytokines, inflammation mediators, rehabilitation centres, respiratory tract infections.

INTRODUCTION

Pneumonia is an acute disease caused by an infection of the lung parenchyma in and outside the hospital environment. This disease is one of the leading causes of morbidity and mortality in both immunocompetent and immunocompromised patients and has significant implications for global healthcare systems (1). The World Health Organization (WHO) data show that lower respiratory tract infections account for 6.1% of all global deaths (2). The incidence of pneumonia varies from 1 to 25 cases per 1,000 patients per year, with a higher prevalence in males, particularly those with comorbidities such as HIV and chronic obstructive pulmonary disease (COPD). Approximately 40% of patients with community-acquired pneumonia (CAP) require hospitalization, and 5% of them need intensive care unit (ICU) treatment (3).

In Indonesia, the prevalence of pneumonia reaches 2.21% across all ages, with the age group of 44-64 years recording 2.5%, 64-74 years 3.0%, and over 75 years 2.9% (4). JKN 2014-2018 data indicate that pneumonia is among the top ten most frequent inpatient cases (5). In Malang City, 2,161 patients (1.35%) were diagnosed with pneumonia. In contrast, at Dr. Saiful Anwar General Hospital in Malang, pneumonia accounted for 4.1% of inpatient cases and 5.7% of outpatient cases in the pulmonary department (4).

The pneumonia severity assessment often uses the pneumonia severity index (PSI) and the confusion–urea–respiratory rate–blood pressure–age ≥ 65 score (CURB-65), though both systems have limitations that may introduce bias in certain

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populations. Recent comparative studies show that while PSI may offer a more comprehensive risk stratification, CURB-65 is simpler and performs slightly better in early mortality prediction, with reported sensitivity up to 96.7% and specificity of 89.3% in some cohorts (6). However, both scoring systems may be less generalizable in low- and middle-income settings due to complexity or lack of validation (7).

In response to these limitations, recent studies emphasize the utility of the blood urea nitrogen (BUN)/albumin ratio as an alternative predictor of disease severity, demonstrating a sensitivity of 55.1% and specificity of 89.2% (8). Additionally, interleukin-8 (IL-8), particularly when measured in bronchoalveolar lavage fluid (BALF), has been identified as a prognostic factor for non-COVID-19 patients at risk of acute respiratory distress syndrome (ARDS), due to its role as a neutrophil chemotactic factor expressed by various immune and epithelial cells (9).

Pulmonary rehabilitation has become an essential non-pharmacological management strategy, highly effective in improving exercise capacity and symptom control in patients with chronic lung diseases, including COPD (10). Pneumonia patients should also undergo pulmonary rehabilitation to alleviate dyspnoea and enhance cough ability (5). Research indicates that pulmonary rehabilitation can improve the lung function of severely ill pneumonia patients undergoing mechanical ventilation (11).While pneumonia severity indices such as PSI and CURB-65 are commonly used in clinical practice, they have notable limitations, including potential bias in the elderly or patients with comorbidities, and limited utility in monitoring a treatment response (5,12). Additionally, not all healthcare facilities in Indonesia, especially in remote areas, have adequate equipment like blood gas analysers and radiology. Recent studies (6) suggest that biomarkers such as the blood urea nitrogen (BUN)/albumin ratio may provide additional prognostic value in pneumonia. Moreover, although pulmonary rehabilitation (PR) and shortwave diathermy (SWD) have shown benefits in chronic respiratory diseases, their roles in acute pneumonia, particularly when used together, remain underexplored. Investigating their effect on clinical and inflammatory parameters may offer insights into adjunctive strategies for improving pneumonia outcomes.

The aim of this study was to analyse IL-8 level, the BUN/albumin ratio, disease severity indices (PSI and CURB-65), and the duration of hospitalization in pneumonia patients undergoing pulmonary rehabilitation.

PATIENTS AND METHODS

Patients and study design

This study employed an experimental design with a pre-test-posttest control group approach and observational analysis. The data used were obtained from primary and secondary sources involving non-intensive care hospitalized pneumonia patients. A total of 24 eligible patients were randomly allocated into three groups, each receiving conventional pneumonia therapy. The groups were as follows: control group (CO), receiving conventional therapy only; pulmonary rehabilitation group (PR), receiving conventional therapy plus pulmonary rehabilitation, and PR and shortwave diathermy group (PR-SWD), receiving conventional therapy combined with both pulmonary rehabilitation and shortwave diathermy (SWD).

The study involved pneumonia patients hospitalized at Dr. Saiful Anwar General Hospital Malang and Lawang Hospital during the study period from March to November 2023. Inclusion criteria were patients (males and females) aged 18-65 diagnosed with pneumonia, hospitalized at Dr. Saiful Anwar General Hospital Malang or Lawang Hospital, and willing to participate in the study by signing an informed consent form. Exclusion criteria included patients with acute cerebrovascular disease, active pulmonary tuberculosis, acute exacerbation of asthma, asthma COPD overlap (ACO), active haemoptysis or a history of haemoptysis in the last three months, malignancies in the thoracic cavity, acute coronary syndrome, severe angina pectoris, use of a pacemaker, severe pulmonary hypertension, and psychiatric disorders or dementia.

Data on baseline patient characteristics, including age, gender, smoking status, pollution exposure, comorbidities, radiological findings, antibiotic regimen, risk class, and length of stay, were collected from clinical records and structured observation forms. The data were analysed as follows (Table 1): age, gender, smoking status, pollution exposure history, comorbidities, chest X-ray findings, antibiotic therapy (intravenous administration of cephalosporine, respiration quinolones and macrolides), pneumonia severity index (PSI) risk class (I–V) (5), and length of stay (LOS).

Risk class (RC) was determined using PSI scoring (5) for determining indication of hospitalization and risk of mortality, which stratifies patients into five categories: Class I (very low risk), Class II (low risk), Class III (moderate risk), Class IV (high risk), and Class V (very high risk).

Antibiotic therapy was administered following hospital protocol, with regimens adjusted based on clinical severity and microbiological considerations. Frequently used antibiotics included intravenous levofloxacin 750 mg once daily, intravenous ceftriaxone 1 g twice daily, and oral azithromycin 500 mg daily. In more severe cases, anti-MRSA agents such as vancomycin or linezolid, and antipseudomonal agents such as piperacillin–tazobactam, meropenem, or cefepime were administered intravenously.

The duration of intravenous antibiotic use before switching to oral therapy was also recorded and categorized by day (1–7) for descriptive analysis.

Regarding comorbidities, although certain conditions, such as active tuberculosis, malignancy, and severe cardiovascular or psychiatric disorders, were excluded, other common comorbidities, including controlled COPD, diabetes mellitus, and hypertension, were permitted and recorded for descriptive analysis.

Ethical approval was obtained from the Health Research Ethics Commission, General Hospital, Dr. Saiful Anwar (No: 400/033/K.3/102.7/2023).

Methods

Consecutive sampling on pneumonia patients hospitalized in non-intensive care at Dr. Saiful Anwar General Hospital Malang and Lawang Hospital, adhering to the established inclusion and exclusion criteria was done. The research began with blood sampling for IL-8 level measurement, which was conducted using the ELISA method (Elabscience®, Houston, TX, USA).

IL-8 levels and the blood urea nitrogen (BUN)/albumin ratio were analysed in all three study groups (control, PR, and PR-SWD) to compare pre- and post-intervention values. The change in each parameter (delta) was used to assess treatment effects. Subsequently, the relationships between IL-8 levels, BUN/albu-

min ratio, and length of stay (LOS) with pneumonia severity indices - pneumonia severity index (PSI) and CURB-65 scores—were evaluated to explore their prognostic associations.
Subsequently, therapeutic procedures were carried out, including breathing exercises, clapping vibration, effective cough techniques, postural drainage, and short wave diathermy (SWD) therapy.

Statistical analysis

The data were presented as mean ± standard deviation (SD). Normality of data distribution was assessed using the Shapiro–Wilk test. Homogeneity of variance was evaluated using Levene's test. To compare pre- and post-intervention values within each group, paired t-tests were used for normally distributed data, and Wilcoxon signed-rank tests were used for non-normally distributed data. The differences between pre- and post-intervention values were calculated and defined as "delta" (Δ), representing the magnitude of change due to the intervention. Mean delta values were used to summarize group-level effects. Intergroup comparisons of delta IL-8 levels, delta blood urea nitrogen (BUN)/albumin ratios, and length of stay (LOS) across the three study groups (control, PR, and PRSWD) were conducted using one-way ANOVA for normally distributed data, or Kruskal–Wallis tests otherwise.
The relationships between IL-8 levels, BUN/albumin ratio, and LOS with pneumonia severity indices—pneumonia severity index (PSI) and CURB-65—were analysed using Pearson correlation for parametric data and Spearman correlation for non-parametric data. Post hoc analyses and linear regression models were performed where appropriate.
Statistical significance was defined as $p<0.05$, with a confidence level of 95% and statistical power of 80%.

RESULTS

The study involved 24 patients divided into three groups: a control group receiving standard pneumonia therapy, a treatment group with standard therapy and pulmonary rehabilitation (PR), and a treatment group with standard therapy, PR, and modality therapy.
The average age was 57.58±8.34 years, with most being active smokers (58.3%) and exposed to outdoor pollution (50%). Common comorbidities included COPD (50%), diabetes (25%), and heart failure (25%). Chest X-ray results showed that 75% had pneumonia. Standard therapy included antibiotics, with most patients receiving levofloxacin and ceftriaxone (Table 1).
This study compared three treatment groups (CO, PR, and PRSWD) based on four primary variables: interleukin-8 (IL-8) levels, BUN/albumin ratio, length of stay (LOS), and pneumonia severity index. The PRSWD group showed the most significant reduction in IL-8 levels (–4.66±8.61 pg/mL), whereas the CO and PR groups showed increasing trends (25.36±76.32 pg/mL and 29.26±72.79 pg/mL, respectively). The PRSWD group also had the shortest average length of stay (LOS) (3.88 days). The CO group showed the most significant reduction in the BUN/albumin ratio (–1.02±1.70 mg/g) (Table 2a, 2b, 2c). The PRSWD group found a significant negative relationship between PSI and the Delta BUN/albumin ratio ($p=0.045$; $r=-0.719$), indicating that higher PSI scores were associated with greater reductions in the BUN/albumin ratio. However, no significant correlations were found between PSI and delta IL-8 or delta BUN/albumin ratio in the CO and PR groups ($p > 0.05$), with weak correlation coefficients ($r= –0.206$ and $r= –0.315$, respectively) (Table 3).
A significant relationship was found in the PR group between CURB-65 and Delta BUN/albumin ratio ($p=0.030$; $r=-0.756$), with higher CURB-65 correlating with a lower Delta BUN/albumin ratio. However, any significant relationship between

Table 1. Baseline characteristics of hospitalized pneumonia patients (n = 24)

Characteristics of research subjects	
Age	
mean±SD	57.58±8.34
Min-max	27-65
	No (%) of patients
Gender	
Male	17 (70.8)
Female	7 (29.2)
Status of smoking	
No	4 (16.7)
Passive	6 (25)
Active	14 (58.3)
History of pollution exposure	
No exposure	3 (12.5)
Indoor	8 (33.3)
Outdoor	12 (50)
Indoor and outdoor	1 (4.2)
Comorbidity	
Chronic obstructive pulmonary disease (COPD)	12 (50)
Pleural effusion	4 (16.7)
Diabetes mellitus	6 (25)
Heart failure	6 (25)
Hypertension	4 (16.7)
Cerebrovascular accident	1 (4.2)
Chronic kidney disease	3 (12.5)
Chest X-ray	
Pneumonia	18 (75)
Cardiomegaly	9 (37.5)
Emphysematous lung	4 (16.7)
Pleural effusion	4 (16.7)
Pleuropneumonia	3 (12.5)
Antibiotic therapy	
Levofloxacin 1x750mg (i.v)	11 (45.8)
Moxifloxacin 1x400mg (i.v)	1 (4.2)
Ceftriaxone 2x1 gr (i.v)	11 (45.8)
Azithromycin 1x500mg (oral)	9 (37.5)
Switch to oral antibiotic (days)	
1	1 (4.2)
4	8 (33.3)
5	9 (37.5)
6	5 (20.8)
7	1 (4.2)
Risk class (RC)	
II	9 (37.5)
III	9 (37.5)
IV	5 (20.8)
V	1 (4.2)
Length of stay (LOS) (days)	
2	2 (8.3)
3	5 (20.8)
4	7 (29.2)
5	6 (25)
6	3 (12.5)
7	1 (4.2)

Table 2a. IL-8 level, BUN/albumin ratio pre-post intervention, length of stay (LOS), and pneumonia severity index in three groups of patients

Patients group	Il-8 before (pg/mL) Mean ± SD	Il-8 after (pg/mL) Mean ± SD	p	Δ IL-8 (pg/ml) Mean ± SD	Δ BUN/albumin (pg/ml) Mean ± SD
CO	83.45±89.84	108.71±97.16	0.380	25.36±76.32	–1.02±1.70
PR	17.78±22.44	47.03±65.36	0.889	29.26±72.79	–0.39 ±0.84
PRSWD	12.55±8.43	7.89± 3.79	0.170	4.66±8.61	–0.49±0.85

*Δ, post-intervention minus pre-intervention value; IL-8, interleukin-8; BUN, blood urea nitrogen; PSI, pneumonia severity index; CURB-65, confusion, urea, respiratory rate, blood pressure, age ≥ 65; CO, control; PR, pulmonary rehabilitation; PRSWD, pulmonary rehabilitation and shortwave diathermy;

Table 2b. Mean length of stay (LOS) in each treatment group

Patient Group	LOS (days)
CO	5.125
PR	4.5
PRSWD	3.875

LOS, length of stay; CO, control; PR, pulmonary rehabilitation; PRSWD, pulmonary rehabilitation and shortwave diathermy;

Table 2c. Pneumonia severity index (PSI) and CURB-65 (confusion, urea, respiratory rate, blood pressure, age ≥ 65) scores by group

Patient group	PSI score	CURB-65 score
CO	97.75	1.125
PR	68.5	0.5
PRSWD	72	1.25

CO, control; PR, pulmonary rehabilitation; PRSWD, pulmonary rehabilitation and shortw ave diathermy;

Table 3. Correlation test results between pneumonia severity index (PSI) and changes in IL-8 and BUN/albumin ratio (delta/Δ) in each treatment group

Correlation between PSI with	Group of patients					
	CO		PR		PRSWD	
	r	p	r	p	r	p
Delta IL-8	0.190	0.651	**-0.695**	**0.056**	0.192	0.649
Delta ratio BUN/albumin	-0.476	0.233	-0.180	0.670	-0.719	0.045

Note: Significant p<0.05
Δ, post-intervention minus pre-intervention value; r , correlation coefficient; IL-8, Interleukin-8; BUN, blood urea nitrogen; CO, control group; PR, pulmonary rehabilitation; PRSWD, pulmonary rehabilitation and shortwave diathermy

Table 4. Correlation between CURB65 score and Δ IL8 and Δ BUN/albumin ratio in each treatment group

Correlation between CURB-65 with	Group of patients					
	CO		PR		PRSWD	
	r	p	r	p	r	p
Δ IL-8	0.164	0.696	0.344	0.405	-0.039	0.927
Δ BUN/albumin	**-0.756**	**0.030**	-0.536	0.171	-0.091	0.830

Note: Significant p<0.05
Δ, post-intervention minus pre-intervention value; r, correlation coefficient; PSI, pneumonia severity index; IL-8, interleukin-8; BUN, blood urea nitrogen; CO, control group; PR, pulmonary rehabilitation; PRSWD, pulmonary rehabilitation and shortwave diathermy

Table 5. Correlation of Δ IL-8, Δ BUN/albumin ratio, and length of stay (LOS) between treatment groups*

Correlation between groups (CO, PR, PRSWD) with	r	p
Delta IL-8	0.000	1.0
Ratio Delta BUN/albumin	0.118	0.583
LOS	-0.518	0.009

Δ, post-intervention minus pre-intervention value; r, correlation coefficient; PSI, pneumonia severity index; IL-8, interleukin-8; BUN, blood urea nitrogen; CO, control group; PR, pulmonary rehabilitation; PRSWD, pulmonary rehabilitation and shortwave diathermy

CURB-65 and Delta IL-8 in the CO group was found (p>0.05). In the PRSWD group, no significant relationship was found for either variable (Table 4).
The PRSWD group showed the shortest LOS (p=0.009; r = -0.518). However, there was no significant relationship between the groups (CO, PR, PRSWD) and Delta IL-8 (p=1.0) or Delta BUN/albumin ratio (p=0.583) (Table 5).

DISCUSSION

The average age of pneumonia patients was 57.58±8.34 years, which is consistent with national data and international studies (10,11). Most patients were male (70.8%), with high rates of smoking (58.3%) and pollution exposure (50.0%), factors previously associated with increased pneumonia risk (11–14). Comorbidities such as COPD, diabetes mellitus, and heart failure were common and likely influenced disease severity and inflammatory responses (11,13). Radiological findings, including cardiomegaly in 37.5% of patients, were in line with earlier studies (10,14).
IL-8 level increased in the CO and PR groups, possibly due to residual inflammation and antibiotic variability, whereas a decrease was observed in the PRSWD group. This is consistent with findings on IL-8 behaviour during infection and rehabilitation (15–20). Physical activity in the PR group may have contributed to IL-8 elevation, while SWD may have exerted an anti-inflammatory effect (21). Prior studies support the role of ultra short wave diathermy (USWD) in reducing systemic inflammation and improving pulmonary function (21,22).
Length of stay (LOS) was shortest in the PRSWD group, followed by the PR and CO groups, indicating better recovery outcomes with combined therapy. This aligns with evidence supporting PRSWD in reducing the length of stay (LOS) and improving patient function (23–26). Higher CURB-65 and PSI scores were associated with more extended hospitalization and elevated IL-8 levels (27–29), reinforcing their prognostic value. The correlation between severity indices and inflammatory markers also affected by differences in initial severity between the groups, as the CO and PRSWD groups had higher PSI scores than the PR group. The absence of microbiological

confirmation may also have influenced the expression of inflammatory markers (30).

Limitations of the study include the small sample size, short observation period, and variability in patient characteristics and therapy adherence. Further studies with larger cohorts and etiological stratification are warranted.

In conclusion, the addition of shortwave diathermy to pulmonary rehabilitation may offer clinical benefits in hospitalized pneumonia patients by reducing inflammatory responses and shortening hospital stays. These findings support the integration of pulmonary rehabilitation and adjunctive physical modalities as part of comprehensive pneumonia management, particularly in patients with moderate to severe disease.

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TRANSPARENCY DECLARATION

Conflicts of interest: None to declare

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