

The Effect of Pulmonary Rehabilitation on Length of Hospitalization, Alveolar-Arterial Oxygen Gradient, and Interleukin-8 Levels in Hospitalized Non-Severe Community-Acquired Pneumonia Patients at Prof. I.G.N.G Ngoerah General Hospital

I Wayan Angga Suamerta Putra¹, Ni Luh Putu Eka Arisanti^{1*}, Luh Kamiati², Ni Wayan Candrawati¹, Ida Ayu Jasminarti Dwi Kusumawardani¹, and I Desak Putu Agung Krisdanti¹

¹Department of Pulmonology and Respiratory Medicine, Prof. I.G.N.G Ngoerah General Hospital, Faculty of Medicine, Udayana University, 80114

²Department of Physical Medicine and Rehabilitation, Prof. I.G.N.G Ngoerah General Hospital, Faculty of Medicine, Udayana University, 80114

E-mail: anggasuamerta@gmail.com; eka.arisanti@unud.ac.id; luhkamiati@gmail.com; niwayancandrawati@gmail.com; jasminarti@unud.ac.id; desak.krisdanti21@gmail.com;

*Corresponding author details: Ni Luh Putu Eka Arisanti; eka.arisanti@unud.ac.id

ABSTRACT

Background: Community-acquired pneumonia is an acute infection of the lung parenchyma that can lead to inflammatory fluid exudation, thereby impairing oxygen diffusion. Pulmonary rehabilitation is a series of therapies aimed at enhancing respiratory efficiency, lung expansion, respiratory muscle strength, and clearing respiratory system secretions. Interleukin-8 (IL-8) is a pro-inflammatory cytokine that reflects epithelial injury in the respiratory system. The alveolar-arterial oxygen gradient (A-a O₂) measures the oxygen difference between alveoli and arteries, which is clinically important for assessing diffusion function and distinguishing between pulmonary and extra-pulmonary causes of hypoxemia. **Methods:** This study is a systematic, single-center randomized controlled trial (RCT) conducted at Prof. I.G.N.G. Ngoerah Hospital from July to September 2024. The study examined the effect of pulmonary rehabilitation on length of hospitalization, A-a O₂ gradient, and IL-8 levels. **Results:** The length of group P1 (pulmonary rehabilitation and conventional therapy) was significantly shorter by 1.16 days ($p = 0.013$). Pulmonary rehabilitation significantly reduced A-a O₂ and IL-8 levels, with a median decrease from day one to day five of 16.00 mmHg in group P1 and 7.50 mmHg in group P2 (conventional therapy) ($p = 0.000$). IL-8 levels also significantly decreased, with a median reduction of 41.81 pg/ml in group P1 and 18.35 pg/ml in group P2 ($p = 0.025$). **Conclusion:** The combination of pulmonary rehabilitation and antibiotic therapy effectively reduces the length of hospitalization, A-a O₂ levels, and IL-8 in hospitalized non-severe community-acquired pneumonia patients.

Keywords: non-severe pneumonia; pulmonary rehabilitation; length of hospitalization; IL-8, A-a O₂.

INTRODUCTION

Community-acquired pneumonia is an acute infection that affects the lung parenchyma and occurs in individuals outside of the hospital setting. According to the American Thoracic Society (2019), around one million adults in the United States seek medical care due to pneumonia each year, with a mortality rate of approximately 50,000 people. The risk of pneumonia increases with age and is among the top ten causes of hospital admissions in the United [1]. In Indonesia, pneumonia also ranks among the top ten causes of hospital admissions in various regions [2].

Pulmonary rehabilitation is a series of interventions aimed at improving respiratory efficiency, lung expansion, respiratory muscle strength, and facilitating the clearance of secretions from the respiratory system. This therapy is expected to alleviate symptoms such as cough and shortness of breath, expedite recovery during hospitalization, and improve patients' physical activity and quality of life. In patients with pneumonia, inflammatory fluid exudation disrupts oxygen diffusion from the alveoli to the arterial blood vessels [3,4].

Pulmonary rehabilitation is expected to improve oxygen diffusion capacity through the clearance of exudative fluid in the alveoli, which can be measured using the alveolar-arterial oxygen gradient calculation. A 2022 study conducted in Malang demonstrated that pulmonary rehabilitation can shorten hospitalization, thereby reducing the risk of nosocomial infections and lowering patient costs [5]. Pulmonary rehabilitation has also been reported to reduce pro-inflammatory cytokines such as Interleukin-8 (IL-8). According to research by Szczegieliak et al. (2011), three weeks of pulmonary rehabilitation in patients with Chronic Obstructive Pulmonary Disease (COPD) significantly decreased IL-8 levels, which are known to reflect epithelial injury in the respiratory system [6]. High IL-8 levels also serve as an indicator in predicting the progression of infection to sepsis [7].

The alveolar-arterial oxygen gradient measures the difference in oxygen levels between the alveoli and arteries, which is clinically important in distinguishing the causes of hypoxemia, whether from pulmonary or extrapulmonary factors. In patients with pneumonia, inflammatory fluid exudation forms a barrier in the alveoli, impeding the process of oxygen diffusion to the capillary membrane. Although ventilation remains adequate, this reduced oxygen diffusion impacts arterial oxygen levels [8].

To date, no studies have specifically examined the impact of pulmonary rehabilitation on improving the alveolar-arterial oxygen gradient in pneumonia patients. Therefore, pulmonary rehabilitation is expected to reduce inflammatory fluid exudation in the alveoli, subsequently lowering IL-8 levels, reducing the alveolar-arterial oxygen gradient, and shortening the duration of hospitalization in patients with community-acquired pneumonia. Based on this background, the researcher aims to investigate the effect of pulmonary rehabilitation on length of hospitalization, alveolar-arterial oxygen gradient, and IL-8 levels in community-acquired pneumonia patients admitted to Prof. I.G.N.G Ngoerah Hospital.

METHOD

This study is a systematic, controlled, single-centered randomized controlled trial (RCT) conducted in the inpatient ward of Prof. I.G.N.G Ngoerah General Hospital, Denpasar, following approval from the hospital's Ethics Committee. The study focused on adult patients diagnosed with non-severe community-acquired pneumonia (CAP)

who met specific inclusion criteria and voluntarily agreed to participate by providing written informed consent. The primary aim was to investigate the effects of pulmonary rehabilitation combined with conventional therapy on the treatment outcomes of non-severe CAP patients.

Patients were systematically allocated on a 1:1 basis into two intervention groups using odd and even numbering. Those with odd numbers were assigned to Group P1, which received both pulmonary rehabilitation and conventional therapy, while patients with even numbers were assigned to Group P2, which received only conventional therapy (standard therapy such as fluoroquinolone or beta-lactam and macrolide antibiotics). Each procedure and intervention was clearly explained to the patients by the research team to ensure understanding and compliance.

The study took place at Prof. I.G.N.G Ngoerah Hospital over a period of three months, from July to September 2024. The target population consisted of hospitalized patients with non-severe CAP, while the accessible population included those admitted to the hospital with similar diagnoses during the study period. Sampling followed a systematic consecutive technique, ensuring that all inpatients with non-severe CAP who met the inclusion criteria and did not meet the exclusion criteria were included in the study.

The inclusion criteria specified patients aged 18-65 years with a first-time diagnosis of non-severe CAP and without contraindications to pulmonary rehabilitation. Exclusion criteria included individuals with contraindications to pulmonary rehabilitation, HIV/AIDS, acute or chronic cerebrovascular disease, active tuberculosis with hemoptysis or a history of hemoptysis within the last three months, resistance to empirical therapy as determined by aerobic sputum culture results, and patients referred from other hospitals or those who declined participation. Additionally, patients who passed away during hospitalization were classified as dropouts.

Based on the sample size calculation using the two-sample t-test formula, each group required a minimum of 14 subjects, totaling 32 participants to account for an anticipated 10% dropout rate. The study was designed with a statistical power of 95% and a significance level of $p < 0.001$ to detect meaningful differences between the control and intervention groups.

TABLE 1: Demographic Characteristics of Study Subjects.

Parameter	Group P1 (Rehabilitation + conventional therapy) N=31 (%)	Group P2 (Conventional therapy) N=31 (%)	P value
Age (Median min-max)	60 (20 – 65)	53 (22 – 65)	0,330
Sex			
Male	18 (58,1)	16 (51,6)	0,610
Female	13 (41,9)	15 (48,4)	
Occupation			
Unemployed	0 (0)	1 (3,2)	0,384
Farmer	6 (19,4)	1 (3,2)	
Housewife	8 (25,8)	10 (32,3)	
Private Sector Worker	8 (25,8)	11 (35,5)	
Craftsman	1 (3,2)	1 (3,2)	
Civil servant	3 (9,7)	1 (3,2)	
Others	5 (16,1)	6 (19,4)	
Smoking status			
Yes	13 (41,9)	10 (32,3)	0,430
No	18 (58,1)	21 (67,7)	
Brinkman Index			
Mild	1 (7,7)	1 (7,7)	0,858
Moderate	8 (61,5)	5 (50,0)	
Severe	4 (30,8)	4 (40,0)	

In this study, the independent variable was pulmonary rehabilitation in hospitalized patients with non-severe CAP. The primary dependent variables included the length of hospitalization, alveolar-arterial oxygen gradient (A-a O₂) values, and IL-8 levels, all chosen to assess the effectiveness of the interventions on clinical outcomes. Additionally, several confounding variables were identified and included in the analysis, such as age, gender, occupation, smoking history, Brinkman index, comorbidities, leukocyte count, type of cough, and respiratory rate.

RESULT

The bivariate analysis was conducted following normality tests on the data. For numerical variables, mean comparisons were performed using the independent t-test for normally distributed data or the Mann-Whitney test for non-normally distributed data. Categorical variables were analyzed using chi-square tests, employing a 2x2 cross-tabulation format. Statistical significance was defined as a p-value of less than 0.05.

Between July and September 2024, a total of 68 subjects with non-severe community-acquired pneumonia were recruited for this study at Prof. I.G.N.G Ngoerah General Hospital. Of these, 5 subjects were excluded: 2 subjects did not meet the inclusion criteria, and 3 declined to participate. Sampling was conducted systematically using odd-even numbering, resulting in two intervention groups: Group P1 (receiving pulmonary rehabilitation plus conventional therapy) and Group P2 (conventional therapy).

In Group P2, 1 subject dropped out, reducing the final sample size to 31 subjects in each group for analysis.

Based on the demographics shown in Table 1, among the 62 study subjects, the median age in Group P1 was 60 years (ranging from 20 to 65 years), whereas in Group P2, the median age was 53 years (ranging from 22 to 65 years). The Kolmogorov-Smirnov test confirmed that the age data were not normally distributed; thus, a Mann-Whitney test was conducted, yielding a p-value of 0.330, indicating no statistically significant age difference between the groups.

Regarding gender distribution, there were 34 male subjects in total, with 18 subjects (58.1%) in Group P1 and 16 subjects (51.6%) in Group P2. The remaining 28 subjects were female, with 13 (41.9%) in Group P1 and 15 (48.4%) in Group P2, indicating a relatively balanced gender distribution between groups.

In terms of smoking status, 27 subjects were classified as smokers, while 41 subjects were non-smokers. Within Group P1, 16 subjects (47.1%) reported being smokers, while in Group P2, there were 11 smokers (32.4%). Analysis of the Brinkman index distribution showed that in the moderate category, 13 subjects were included (8 subjects (61.5%) in Group P1 and 5 subjects (50%) in Group P2). In the severe category, there were 8 subjects (4 subjects (40%) in Group P1 and 4 subjects (50%) in Group P2), while the mild category had 2 subjects (1 subject (7.7%) in each group).

Table 2 summarizes the clinical characteristics of the subjects, including leukocyte count, cough type, respiratory rate, and comorbidities. The median leukocyte level in Group P1 was 11.11 (ranging from 4.63 to 51.18), while in Group P2, the median leukocyte count was 14.40 (ranging from 4.66 to 38.12). Cough type was classified as either

productive or non-productive; in Group P1, 18 subjects (58.1%) had productive coughs, while 13 subjects (41.9%) had non-productive coughs. In Group P2, 23 subjects (74.2%) experienced productive coughs, while 8 subjects (25.8%) had non-productive coughs, indicating a higher proportion of productive coughs in Group P2.

TABLE 2: Clinical Characteristics of Study Subjects.

Parameter	Group P1 (Rehabilitation+conventional therapy) N=31 (%)	Group P2 (Conventional therapy) N=31 (%)	P value
Leukocyte(10 ³ /ml)	11,11 (4,63 – 51,18)	14,40 (4,66 – 38,12)	0,186
Type of Cough			
Productive	18 (58,1)	23 (74,2)	0,180
Non-Productive	13 (41,9)	8 (25,8)	
Respiratory Rate			
>20x/minute	26 (83,9)	26 (83,9)	1,000
≤ 20x/minute	5 (16,1)	5 (16,1)	
Comorbidities			
COPD			
Yes	3 (9,7)	1 (3,2)	0,301
No	28 (90,3)	30 (96,8)	
Malignancy			
Yes	7 (22,6)	4 (12,9)	0,319
No	24 (77,4)	27 (87,1)	
DM			
Yes	10 (32,3)	11 (35,5)	0,788
No	21 (67,7)	20 (64,5)	
Heart Failure			
Yes	10 (32,3)	6 (19,4)	0,246
No	21 (67,7)	25 (80,6)	
Asthma			
Yes	1 (3,2)	1 (3,2)	1,000
No	30 (96,8)	30 (96,8)	

TABLE 3: Data Analysis of Pulmonary Rehabilitation on Length of Hospitalization.

Length of Hospitalization	Group P1 (Rehabilitation + conventional therapy)	Group P2 (Conventional therapy)
Mean (±SD)	4,84 ± 0,69 days	6,00 ± 1,90 days
Median	5 days	5 days
Mann-Whitney Test Result	p = 0,013	

The majority of patients in both groups had a respiratory rate of >20 breaths per minute. In Group P1, 26 subjects (83.9%) had a respiratory rate >20 breaths/min, while 5 subjects (16.1%) had a respiratory rate of ≤20 breaths/min. Similarly, in Group P2, 26 subjects (83.9%) also had a respiratory rate >20 breaths/min, and 5 subjects (16.1%) had a rate ≤20 breaths/min, indicating a consistent distribution across both groups.

Comorbid conditions observed among the study subjects included chronic obstructive pulmonary

disease (COPD) in 4 subjects, malignancy in 11 subjects, diabetes mellitus in 21 subjects, heart failure in 16 subjects, and asthma in 2 subjects. Table 5.2 provides detailed demographic data for both study groups, with all comparisons showing non-significant p-values, indicating no significant demographic differences between Groups P1 and P2.

Table 3 presents an analysis of the length of hospitalization. The length of hospitalization was calculated from the time patients were first diagnosed with non-severe pneumonia until discharge.

The mean length of hospitalization in Group P1 (pulmonary rehabilitation and conventional therapy) was shorter at 4.84 ± 0.69 days, compared to 6.00 ± 1.90 days in Group P2 (conventional therapy only). The Mann-Whitney test revealed a significant difference between the two groups with a p-value of 0.013 and a mean difference of 1.16 days. The median length of hospitalization for both groups was 5 days.

Based on Table 4, the A-a O2 value in Group P1 on the first day before pulmonary rehabilitation was 32.97 ± 14.13 mmHg, whereas Group P2, which received only conventional therapy, had a mean of 37.32 ± 13.66 mmHg. The Mann-Whitney test indicated a significant difference between the two groups ($p = 0.000$).

On the fifth day, the A-a O2 value in Group P1 decreased to 14.70 mmHg, while Group P2 showed a median of 22.10 mmHg. The Mann-Whitney test on the fifth day also revealed a significant difference ($p = 0.000$).

The analysis of the difference between the first and fifth days showed that Group P1 experienced a median reduction of 16.00 mmHg, while Group P2 had a median reduction of 7.50 mmHg, with a significant difference between the two groups ($p = 0.008$).

Regarding the levels of IL-8, the median in Group P1 before therapy was 48.48 pg/ml, while in Group P2 it was 36.76 pg/ml. The Mann-Whitney test indicated no significant difference on the first day ($p = 0.195$).

After rehabilitation, the IL-8 levels in Group P1 decreased to 36.76 pg/ml, and on the fifth day, it reached 18.41 pg/ml. Group P2 also experienced a significant reduction with a p-value of 0.000.

The analysis of the difference in IL-8 levels showed a median reduction of 41.81 pg/ml in Group P1 and 18.35 pg/ml in Group P2, with a significant difference ($p = 0.025$). Table 5 presents the analysis of the IL-8 level data.

TABLE 4: Analysis of Pulmonary Rehabilitation Data on A-a O2 Values.

A-a O2 Value	Group P1 (Rehabilitation+conventional therapy)	Group P2 (conventional therapy)
First Day Median (min-max)	$32,97 \pm 14,13$ mmHg	$37,32 \pm 13,66$ mmHg
Mann-Whitney Test Result (First Day)	$p = 0,000$	
Fifth Day Median (min-max)	14,70 (5,50-27,90) mmHg	22,10 (16,00-41,00) mmHg
Mann-Whitney Test Result (Fifth Day)	$p = 0,000$	
Δ Fifth Day - First Day	16,00 (1,70-45,50) mmHg	7,50 (0,20-56,20) mmHg
Mann-Whitney Test Result Δ (h5-h1)	$p = 0,008$	

DISCUSSION

The median age of Group P1 was 60 years (ranging from 20 to 65 years), while Group P2 had a median age of 53 years (ranging from 22 to 65 years). A study by Khipiyah et al. reported a mean age of 56.5 ± 10.55 years in the treatment group and 57.5 ± 10.75 years in the control group, which aligns with the current findings where subjects were predominantly between 50 and 60 years old. Similarly, research by Liu et al. found a mean age of 56.7 ± 13.6 years in the treatment group and 52.3 ± 9.6 years in the control group, further supporting the results observed in this study [9].

Among the subjects, 34 were male, with 18 subjects (58.1%) in Group P1 and 16 subjects (51.6%) in Group P2. Additionally, there were 28 female subjects, comprising 13 (41.9%) in Group P1 and 15 (48.4%) in Group P2. These findings are consistent with Khipiyah et al., who also found a predominance of male subjects. In contrast, a study by Marques et

al. reported a higher percentage of female subjects (58.76%) compared to males (41.24%) [10].

Regarding smoking status, 27 subjects were identified as smokers, all of whom were male, with 16 in Group P1 and 11 in Group P2. The distribution of the Brinkman index in Group P1 revealed 8 subjects (61.5%) in the moderate category, 4 subjects (40%) in the heavy category, and 1 subject (7.7%) in the light category. In Group P2, 5 subjects (50%) were in the moderate category, 4 subjects (50%) in the heavy category, and 1 subject (7.7%) in the light category. Khipiyah et al. reported that 25 subjects (62.5%) were male smokers, with a higher prevalence of moderate and heavy categories compared to the present study [5]. This difference suggests that the history of smoking in this study was lower, resulting in an insignificant impact on the independent variable.

Overall, these demographic findings highlight the characteristics of the study population and provide a context for understanding the effects of pulmonary

rehabilitation in patients with non-severe community-acquired pneumonia.

TABLE 5: Analysis of Pulmonary Rehabilitation Data on IL-8 Levels.

IL-8 Levels	Group P1 (Rehabilitation+conventional therapy)	Group P2 (conventional therapy)
First Day Median (min-max)	48,48 (3,75-302,76) pg/ml	36,76 (2,03-512,50) pg/ml
Mann-Whitney Test Result (First Day)	$p = 0,195$	
Fifth Day Median (min-max)	8,71 (0,81-44,12) pg/ml	18,41 (1,41-56,53) pg/ml
Mann-Whitney Test Result (Fifth Day)	$p = 0,000$	
Δ Fifth Day - First Day	41,81 (0,91-296,51) pg/ml	18,35 (28,99 – 489,38) pg/ml
Mann-Whitney Test Result Δ (h5-h1)	$p = 0,025$	

The clinical characteristics of the subjects in this study included data on leukocytes, type of cough, respiratory rate, and comorbidities. The average leukocyte count in group P1 was $11.11 \times 10^3/\mu\text{L}$ (minimum $4.63 \times 10^3/\mu\text{L}$, maximum $51.18 \times 10^3/\mu\text{L}$), while in group P2 it was $14.40 \times 10^3/\mu\text{L}$ (minimum $4.66 \times 10^3/\mu\text{L}$, maximum $38.12 \times 10^3/\mu\text{L}$). A study by Khipiyah et al. also found an increase in leukocyte count on the first day, where 24 subjects experienced an increase (Khipiyah et al., 2020). The types of cough were categorized as productive and non-productive. In group P1, 18 subjects (58.1%) had a productive cough, while in group P2, 23 subjects (74.2%) had a productive cough. Khipiyah et al. also showed a higher proportion of subjects with productive cough [5].

The majority of patients in both groups had a respiratory rate > 20 breaths/minute, with 26 subjects (83.9%) in P1 and the same proportion in P2. Khipiyah et al. noted that most subjects also had a respiratory rate > 20 breaths/minute on the first day [5].

Based on the results of this study, the average duration of hospitalization for non-severe pneumonia patients from diagnosis to discharge was calculated. Group P1, which received pulmonary rehabilitation and conventional therapy, had a shorter average length of hospitalization of 4.84 ± 0.69 days, compared to group P2, which only received conventional therapy, with an average of 6.00 ± 1.90 days.

The Mann-Whitney test showed a significant difference between the two groups with a p-value of 0.01, as well as a statistically significant average difference of 1.16 days ($p = 0.025$). These results are in line with research by Santony et al., which showed that the duration of hospitalization for community pneumonia patients receiving standard therapy plus pulmonary rehabilitation was 5.35 days, while those

receiving only standard therapy had 7.6 days, resulting in a 2.25-day shorter in the pulmonary rehabilitation group [11].

Khipiyah et al. also found that the administration of pulmonary rehabilitation along with conventional therapy could shorten the time to switch antibiotics, with an average of 5.05 days in the treatment group compared to 7.26 days in the group without treatment, showing a difference of 2.21 days [5].

Castro et al. reported that the duration of ICU care was shorter in the group that received 24-hour pulmonary physiotherapy, averaging 10 days, compared to 15 days for the group that only received pulmonary physiotherapy for 6 hours per day. These results support this study, reinforcing that pulmonary physiotherapy, part of pulmonary rehabilitation, can shorten the length of hospital hospitalization for pneumonia patients [12].

The results of this study indicate that the A-a O₂ value in group P1 before pulmonary rehabilitation and conventional therapy was 32.97 ± 14.13 mmHg, while group P2, which only received conventional therapy, recorded a value of 37.32 ± 13.66 mmHg. The Mann-Whitney test showed a significant difference between the two groups on the first day with a p-value of 0.000. On the fifth day, group P1 showed an A-a O₂ value of 14.70 mmHg, and group P2 recorded 22.10 mmHg, with a significant difference as well ($p = 0.000$).

The median decrease in A-a O₂ value in group P1 was 16.00 mmHg (1.70 – 45.50 mmHg), while in group P2 it was 7.50 mmHg (0.20 – 56.20 mmHg). The Mann-Whitney test showed a significant difference between the two groups with a p-value of 0.008, indicating that pulmonary rehabilitation and conventional therapy were more effective in lowering A-a O₂ compared to conventional therapy alone, with a difference of 8.5 mmHg.

Factors affecting the A-a O₂ gradient, according to Fick's law, include membrane thickness, partial pressure differences of gases, gas diffusion constants, and membrane surface area. In community pneumonia, alveoli filled with fluid or pus can reduce the surface area of the membrane, increasing the distance that oxygen must travel and reducing the efficiency of oxygen diffusion from the alveoli to the pulmonary vasculature [13]. Additionally, cytokine secretion can limit oxygen diffusion in the capillaries, even while ventilation continues well, leading to decreased oxygen levels in the capillaries and increased A-a O₂ gradient [14].

Research by Avci et al. showed that the A-a O₂ gradient better predicts 30-day mortality in pneumonia compared to CURB-65 and PSI scores [15]. This study found a significant difference in median A-a O₂ between groups P1 and P2, with the decrease in A-a O₂ related to a reduction in inflammatory cytokine secretion. Pulmonary rehabilitation accelerates mucus clearance, so the combination of pulmonary rehabilitation and conventional therapy is more effective in reducing A-a O₂ in hospitalized non-severe pneumonia patients.

IL-8 levels in group P1 before pulmonary rehabilitation were 48.48 pg/ml (min 3.75 – 302.76 pg/ml) and in group P2 were 36.76 pg/ml (min 2.03 – 512.50 pg/ml). After pulmonary rehabilitation, IL-8 levels in group P1 dropped to 36.76 pg/ml (min 2.03 – 512.50 pg/ml) and on the fifth day to 18.41 pg/ml (min 1.41 – 56.53 pg/ml). In the Mann-Whitney test, the IL-8 levels on the fifth day between the two groups were significantly different ($p = 0.000$).

The median decrease in IL-8 levels in group P1 was 41.81 pg/ml, while in group P2 it was 18.35 pg/ml, with a significant difference ($p = 0.025$), indicating that pulmonary rehabilitation was more effective in lowering IL-8 levels with a difference of 23.46 pg/ml. No previous studies have linked IL-8 levels with pulmonary rehabilitation in pneumonia. A study by Szczegieliak et al. showed a decrease in IL-8 levels in COPD patients after pulmonary physiotherapy (average from 18.91 pg/ml to 9.69 pg/ml, $p = 0.025$). IL-8 plays a role in attracting neutrophils to the lungs and is regulated by NF κ B, which also induces MMP-9 and causes mucus hypersecretion [16].

Research by Bohnet et al. found a correlation between IL-8 and microbial load in the alveoli and neutrophil influx, as well as higher IL-8 levels in patients with pathogen counts $> 10^4$ CFU, indicating the potential of IL-8 as a prognostic factor for the risk of ARDS [17].

CONCLUSIONS

Pulmonary rehabilitation combined with conventional therapy has a significant impact on shortening the duration of hospitalization for non-severe community-acquired pneumonia patients admitted to the hospital. Additionally, pulmonary rehabilitation along with conventional therapy also affects the reduction of the alveolar-arterial oxygen

gradient in patients with the same condition. Furthermore, the combination of pulmonary rehabilitation and conventional therapy has proven effective in lowering IL-8 levels in hospitalized patients with non-severe community-acquired pneumonia.

Acknowledgments

All patients, all authors, and all support in research.

DECLARATIONS

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by

Udayana University with the number

1421/UN14.2.2.VII.14/LT/2024.

REFERENCES

- [1] Metlay, J. P., Waterer, G. W., Long, A. C., Anzueto, A., Brozek, J., Crothers, K., Cooley, L. A., Dean, N. C., Fine, M. J., & Flanders, S. A. (2019). Diagnosis and treatment of adults with community-acquired pneumonia. An official clinical practice guideline of the American Thoracic Society and Infectious Diseases Society of America. *American Journal of Respiratory and Critical Care Medicine*, 200(7), e45–e67.
- [2] Perhimpunan Dokter Paru Indonesia. (2022). *Pneumonia Komunitas: Pedoman Diagnosis dan Penatalaksanaan di Indonesia*. Jakarta: Perhimpunan Dokter Paru Indonesia, 1-2.
- [3] Hasanudin, H., Sukartini, T., Makhfudli, M., Rosyid, A. N., Revita, N. C. T., & Aini, H. N. (2022). The Effectiveness of Pulmonary Rehabilitation on Pulmonary Function among Adults Patients of COVID-19 Survivors: A Systematic Review. *Jurnal Respirasi*, 8(1), 15. <https://doi.org/10.20473/jr.v8-i.1.2022.15-25>
- [4] Noor Chozin, I., Rahayu Sartono, T., & Al Rasyid, H. (2022). Impact of Pulmonary Rehabilitation on Hospitalization Duration, IL-6 Levels, and Respiratory Muscle Power in Hospitalized Community-Acquired Pneumonia Patients. In *J Respir Indo* (Vol. 42, Issue 1).
- [5] Khipiyah, M., Chozin, I. N., Pratiwi, S. D., Rahmad, R., & Al Rasyid, H. (2020). The Effect of Pulmonary Rehabilitation on The Duration of Antibiotic Switches, IL-10 Levels and PEFr Values in Hospitalized Community Pneumonia Patients. *Jurnal Respirologi Indonesia*, 40(4), 198-209.
- [6] Feldman, C., & Anderson, R. (2018). Pneumonia as a systemic illness. *Current Opinion in Pulmonary Medicine*, 24(3), 237–243.
- [7] Peneva, P., Nikolova, S. P., & Bocheva, Y. (2022). Predictive Value of Delta Neutrophil Index, Interleukin 8 and C-Reactive Protein for Septic Patients.

- [8] Secco, G., Salinaro, F., Bellazzi, C., La Salvia, M., Delorenzo, M., Zattera, C., Barcella, B., Resta, F., Vezzoni, G., Bonzano, M., Cappa, G., Bruno, R., Casagranda, I., & Perlini, S. (2021). Can alveolar-arterial difference and lung ultrasound help the clinical decision making in patients with COVID-19? *Diagnostics*, 11(5), 1–12. <https://doi.org/10.3390/diagnostics11050761>.
- [9] Liu, W., Mu, X., Wang, X., Zhang, P., Zhao, L., & Li, Q. (2018). Effects of comprehensive pulmonary rehabilitation therapy on pulmonary functions and blood gas indexes of patients with severe pneumonia. *Experimental and Therapeutic Medicine*, 16(3), 1953 – 1957.
- [10] Marques, A., Pinho, C., De Francesco, S., Martins, P., Neves, J., & Oliveira, A. (2020). A randomized controlled trial of respiratory physiotherapy in lower respiratory tract infections. *Respiratory Medicine*, 162(October 2019). <https://doi.org/10.1016/j.rmed.2019.105861>.
- [11] Santony, S., Chozin, I. N., Sartono, T. R., Rahmad, R., & Al Rasyid, H. (2022). Impact of Pulmonary Rehabilitation on Hospitalization Duration, IL-6 Levels, and Respiratory Muscle Power in Hospitalized Community-Acquired Pneumonia Patients. *Jurnal Respiriologi Indonesia*, 42(1), 34-42.
- [12] Castro, A. A. M., Calil, S. R., Freitas, S. A., Oliveira, A. B., & Porto, E. F. (2013). Chest physiotherapy effectiveness to reduce hospitalization and mechanical ventilation length of stay, pulmonary infection rate and mortality in ICU patients. *Respiratory Medicine*, 107(1), 68–74.
- [13] Wibowo, C. P., Wisudarti, C. F. R., & Jufan, A. Y. (2020). The Relationship Between "Lung Ultrasound Score (LUS)" and P/F Ratio in Pneumonia Patients Admitted to the ICU at Dr. Sardjito General Hospital. *Jurnal Komplikasi Anestesi*, 7(2), 21–29.
- [14] Bhutta, B. S., Alghoula, F., & Berim, I. (2022). Hypoxia. In *StatPearls* [Internet]. StatPearls Publishing.
- [15] Avci, S., & Perincek, G. (2020). The alveolar-arterial gradient, pneumonia severity scores and inflammatory markers to predict 30-day mortality in pneumonia. *The American Journal of Emergency Medicine*, 38(9), 1796–1801.
- [16] Kasumadewi, L., Suradi, S., & Setijadi, A. R. (2020). The Effect of Thymoquinone on Interleukin-8 Levels,% FEV1 and CAT Scores in Chronic Obstructive Pulmonary Disease. *Jurnal Respiriologi Indonesia*, 40(4), 210–218.
- [17] Bohnet, S., Kötschau, U., Braun, J., & Dalhoff, K. (1997). Role of interleukin-8 in community-acquired pneumonia: Relation to microbial load and pulmonary function. *Infection*, 25(2), 95–100. <https://doi.org/10.1007/BF02113584>.