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The Relationship of Neutrophil Lymphocyte Ratio (NLR), Nutritional Status and Length of Hemodialysis to The Incidence of Inpatient Community Pneumonia in Regular Hemodialysis Patients

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ABSTRACT

Background: Pneumonia, a leading cause of death worldwide, is common in chronic kidney disease (CKD) patients undergoing hemodialysis due to pulmonary infections and poor nutritional status. Prolonged hemodialysis worsens nutritional disorders, increasing pneumonia risk. Biomarkers like the neutrophil-lymphocyte ratio (NLR) and low albumin can indicate infection and inflammation. This study explores the relationship between NLR, nutritional status, and hemodialysis duration with pneumonia in CKD patients. ***Methods:*** This study was an observational analytic study with a cross-sectional design. Using SPSS to univariate analysis in the form of tables with frequency, mean and media; bicariat analysis using chi square test and multivariate analysis with logistic regression. ***Results:*** 72 patients undergoing regular hemodialysis, ROC analysis obtained an NLR cut off value of 6.09. Chi Square test results showed a significant association between NLR and pneumonia (OR 2.04; $p < 0.05$; CI 95% 1.26-3.33) and Hemeodyalisis (HD) duration with pneumonia (OR 4.71 times; CI 95% 1.72-12.93; p 0.004), while there was no significant difference in nutritional status between community pneumonia and non-community pneumonia. Based on the results of multivariate analysis, it was found that NLR levels > 6.09, HD duration > 1 year, and the presence of comorbid heart failure were risk factors that significantly increased the incidence of community pneumonia in patients undergoing regular HD. ***Conclusion:*** There is a significant association between NLR >6.09 and HD duration and comorbid heart failure with community pneumonia in patients undergoing regular HD at Prof. I.G.N.G. Ngoerah Hospital.

Keywords: pneumonia; regular hemodialysis; neutrophil-lymphocyte ratio; nutritional status; duration of hemodialysis

INTRODUCTION

Pneumonia is an inflammation affecting the lung parenchyma, including the bronchioles, respiratory bronchioles, and alveoli, leading to lung tissue consolidation and localized gas exchange impairment. According to the Global Burden of Disease Study, pneumonia is the second leading cause of death globally, accounting for 3.85% of total deaths [1]. In Indonesia, the 2013 RISKESDAS data revealed a pneumonia prevalence of 4.5%. At RSUP Prof. DR. I. G. N. G. Ngoerah in 2021, pneumonia was among the top ten inpatient diseases with 354 cases. The Indonesian Society of Pulmonology (PDPI) in 2022 categorized pneumonia into Community-Acquired Pneumonia (CAP), Hospital-Acquired Pneumonia (HAP), and Ventilator-Associated Pneumonia (VAP) [2].

Community-Acquired Pneumonia is linked to various chronic diseases, including chronic kidney disease (CKD). In Taiwan, the prevalence of pneumonia in CKD patients is around 65% [3]. Research indicates an increased risk of pneumonia and mortality in CKD patients [4].

Studies have shown that patients with lower glomerular filtration rates (GFR) face higher risks of hospitalization and mortality from pneumonia. Additionally, a study found a 36% probability of pneumonia-related hospitalization within five years for CKD patients on hemodialysis [5].

CKD patients, especially those in stage 5 (end stage), require therapies like hemodialysis to replace kidney function and maintain quality of life. According to the Indonesian Nephrology Association (PERNEFRI) in 2018, there were 132,142 active hemodialysis patients and 66,433 new patients. Bali ranks second in the highest proportion of residents undergoing hemodialysis.

Common issues for hemodialysis patients include lung infections and nutritional problems. A retrospective cohort study in China found that 18.97% of regular hemodialysis patients were hospitalized with pneumonia. Out of 914 patients, 595 were diagnosed with CAP [6]. Malnutrition, caused by inadequate nutrition and chronic inflammation, affects up to 40% of patients starting hemodialysis. Malnutrition can be assessed using Body Mass Index (BMI). A study at Dr. M. Djamil Padang Hospital in 2014 reported a malnutrition rate of 33.9%-55.93% among long-term hemodialysis patients [7]. Poor nutritional status and hypoalbuminemia increase the risk of pneumonia, the most common infection in CKD patients [8,9].

Inflammatory biomarkers such as the neutrophil-to-lymphocyte ratio (NLR) can indicate infection in CKD patients [10]. Low albumin levels, reflecting poor nutritional status, also signal systemic inflammation in pneumonia cases [11]. NLR, derived from blood tests, reflects ongoing inflammatory processes and immune regulation. Increased NLR reveals the functional status of the immune system during inflammation. Given the high incidence of pneumonia, this study aims to explore the relationship between NLR, nutritional status, and the duration of hemodialysis with community-acquired pneumonia in CKD patients undergoing regular hemodialysis at RSUP Prof. DR. I. G. N. G. Ngoerah.

METHOD

This study is an observational analytical research with a cross-sectional design. Data on NLR, nutritional status, and duration of hemodialysis will be collected concurrently from patients with community-acquired pneumonia undergoing regular hemodialysis. The sampling technique used is consecutive sampling, gathering data from the medical records of CKD in patients undergoing regular hemodialysis at RSUP Prof. I.G.N.G. Ngoerah from January to December 2023.

Inclusion criteria include patients aged 18 years or older, who have undergone regular hemodialysis for at least 3 months, and who are hospitalized with or without community-acquired pneumonia. Exclusion criteria are: 1) Patients with COVID-19; 2) Pregnant patients; 3) Patients with other infections during hospitalization (e.g., tuberculosis, urinary tract infections, meningitis, encephalitis); 4) Patients with malignancies; 5) HIV-positive patients; 6) Use of immunosuppressive therapy; 7) Patients with fungal infections; 8) Patients with hepatic cirrhosis.

The collected data will be processed to provide the necessary information for the research. After obtaining secondary data, the next step is to enter the data into a computer program. The data will first be transformed into numerical categories (coding) to facilitate data analysis by the software. Data analysis will include descriptive statistics, prevalence comparison tests, and logistic regression tests.

RESULT

This study included 72 patients undergoing regular hemodialysis, with 41 patients having community-acquired pneumonia and 31 patients undergoing hemodialysis without pneumonia. The characteristics of the study subjects are presented in Table 1.

TABLE 1: Characteristics of Study Subjects.

Characteristics	Community Pneumonia	Community Non-Pneumonia	P
Age			
< 60th	26 (63.4%)	21 (67.7%)	
≥60 years old	15 (36.6%)	10 (32.3%)	
Average±Standard deviation	50.37±16,757	49.26±14,922	0.085
Median (min –max)	53 (15 – 80)	49 (16 – 74)	
Gender			
Man-man	28 (68.3%)	15 (48.4%)	0.098
Woman	13 (31.7%)	16 (51.6%)	
HD Frequency			
2x	31 (75.6%)	29 (93.5%)	0.089
3x	10 (24.4%)	2 (6.5%)	
HD Adequacy			
Adequate	14 (34.1%)	11 (35.5%)	
No adequate	27 (65.9%)	20 (64.5%)	1.00
DM			
Yes	18 (43.9%)	14 (45.2%)	
No	23 (56.1%)	17 (54.8%)	1.00

Characteristics	Community Pneumonia	Community Non-Pneumonia	P
HT			
Yes	33 (80.5%)	21 (67.7%)	
No	8 (19.5%)	10 (32.3%)	0.036
Heart failure			
Yes	23 (56.1%)	7 (22.6%)	
No	18 (43.9%)	24 (77.4%)	0.009
Total	**41 (100%)**	**31 (100%)**	

ROC analysis was performed to determine the cut-off value of NLR for distinguishing between community-acquired pneumonia and non-pneumonia cases.

The ROC analysis yielded an Area Under the Curve (AUC) of 0.664 (p = 0.018) and an NLR cut-off value of 6.09. Sensitivity was 70.7%, and specificity was 67.7% (Figure 1).

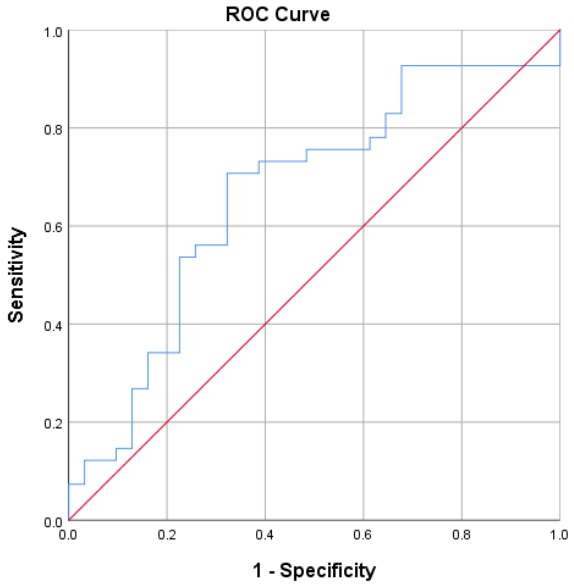

FIGURE 1: ROC Curve for NLR.

TABLE 2: Cross-Tabulation of NLR by Cut-Off with Community-Acquired Pneumonia.

NLR	Community Pneumonia	Community Non-Pneumonia	Total	PR	P
≥6.09	29 (74.4%)	10 (25.6%)	39 (100%)	2.04 (1.26-3.33)	0.003
< 6.09	12 (36.4%)	21 (63.6%)	33 (100%)		

**Uji Chi-Square.*

Cross-tabulation (Table 2) shows that out of 39 patients with NLR ≥ 6.09, 74.4% had community-acquired pneumonia, while 63.6% of 33 patients with NLR < 6.09 had non-pneumonia community-acquired pneumonia. This data indicates a higher proportion of patients with NLR ≥ 6.09 having community-acquired pneumonia compared to those with non-pneumonia. The Chi-Square test revealed a significant association between NLR and pneumonia (p < 0.05), with NLR ≥ 6.09 being 2.04 times more likely to be associated with community-acquired pneumonia (95% CI 1.26-3.33).

TABLE 3: Relationship Between Body Mass Index and Community-Acquired Pneumonia in Patients Undergoing Regular Hemodialysis.

Nutritional status	Community Pneumonia	Community Non-Pneumonia	Total	p value
Abnormal	15 (36.6%)	11 (35.5%)	26(36.1%)	1.00
Normal	26 (63.4%)	20 (64.5%)	46 (63.9%)	
Total	**41 (100%)**	**31 (100%)**	**72 (100%)**	

**Chi-Square Test.*

Chi-Square analysis of Body Mass Index with community-acquired pneumonia in patients undergoing regular hemodialysis (Table 3) shows that both pneumonia and non-pneumonia cases are predominantly in patients with normal nutritional status. The Chi-Square test indicated no significant difference in nutritional status between community-acquired pneumonia and non-community-acquired pneumonia ($p > 0.05$).

TABLE 4: Relationship Between Duration of Hemodialysis and Community-Acquired Pneumonia in Patients Undergoing Regular Hemodialysis.

Status			PR	P
Old HD	Pneumonia	Non-Pneumonia		
> 1 year	27 (75.0%)	9 (25.0%)	4.71 (CI 95% 1.72-12.93)	0.004
≤ 1 year	14 (38.9%)	22 (61.1%)		

**Chi-Square Test.*

Analysis of the duration of hemodialysis with community-acquired pneumonia (Table 4) shows that the majority of patients with a hemodialysis duration > 1 year (75.0%) had community-acquired pneumonia, while the majority with a hemodialysis duration ≤ 1 year (61.1%) did not have pneumonia. The Chi-Square test revealed a significant association between hemodialysis duration and pneumonia ($p < 0.05$), with a duration > 1 year being 4.71 times more likely to be associated with community-acquired pneumonia (95% CI 1.72-12.93; $p = 0.004$).

To control for confounding factors, multivariate analysis using logistic regression was conducted, including factors such as age, sex, adequacy of hemodialysis, diabetes mellitus (DM), hypertension (HT), and heart failure. Multivariate analysis revealed that NLR ≥ 6.09, hemodialysis duration > 1 year, and the presence of heart failure were significant risk factors for community-acquired pneumonia in regular hemodialysis patients. Conversely, nutritional status did not significantly affect the incidence of community-acquired pneumonia.

TABLE 5: Multivariate Analysis of Factors Associated with Community-Acquired Pneumonia in Regular Hemodialysis Patients.

Step 1				
Factor	**b**	**P**	**Adjusted PR**	**CI 95%**
NLR≥6.09	2.46	0.001	11.71	2.65-51.75
Duration of HD >1 year	1.42	0.042	4,145	1.05-16.34
Abnormal nutritional status	0.254	0.70	1.29	0.35-4.71
Age≥60 years old	-0.209	0.75	0.81	0.22-2.96
Male gender	0.805	0.216	2.24	0.63-8.0
HD adequacy (inadequate)	0.533	0.434	1,704	0.45-6.47
DM	0.057	0.938	1,058	0.26-4.39
HT	-0.02	0.977	0.98	0.22-4.42
Constant	-3,386	0.005		
Step 7				
Factor	**b**	**P**	***Adjusted* PR**	**CI 95%**
NLR≥6.09	2,353	0.001	10.51	2.52-43.72
Duration of HD >1 year	1,358	0.025	3.89	1.18-12.8
Heart failure	2,301	0.002	9.98	2.25-44.18
Constant	-2,438	0.001		

*Stepwise logistic regression.

The multivariate analysis indicates that NLR ≥ 6.09 is the strongest factor associated with an increased incidence of community-acquired pneumonia in regular hemodialysis patients, with patients having NLR ≥ 6.09 being 10.51 times more likely to experience community-acquired pneumonia. The analysis also shows that a hemodialysis duration > 1 year and the presence of heart failure increase the risk of community-acquired pneumonia by 3.89 times and 9.98 times, respectively, in regular hemodialysis patients.

DISCUSSION

Old age increases the risk of morbidity and mortality from pneumonia in CKD patients. Aging is associated with changes in inflammatory regulation. There is an increase in chronically circulating inflammatory markers such as IL-6 and TNF-α [12]. Between the ages of 40 and 60, there is a reduction of approximately 10% in the number of functional nephrons due to nephrosclerosis and glomerulosclerosis [13].

By gender, more men are diagnosed with community-acquired pneumonia (CAP) in hemodialysis (HD) patients, whereas in non-community-acquired pneumonia (non-CAP) patients with HD, the gender distribution is more even. Biological differences, including hormonal cycles, immune responses, socio-economic factors, and the tendency for men to smoke more than women, increase the risk of lung infections [14].

In this study, it was found that most patients with both CAP and non-CAP underwent HD twice a week, and the majority of both CAP and non-CAP patients experienced inadequate HD. CAP patients had an average Kt/V of 1.335 ± 0.380, while non-CAP patients had an average Kt/V of 1.347 ± 0.242 with a P-value of 0.820. Both groups showed HD inadequacy. This study also noted that the use of central venous catheters (CVC) as vascular access and shorter dialysis times were associated with an increased risk of pneumonia [15].

Research on 40,696 pneumonia patients showed that 16.3% had comorbid diabetes mellitus (DM), 12% had chronic obstructive pulmonary disease (COPD), and 11.4% had kidney disease, while 4.8% had heart disease [16]. In this study, 43.9% of CAP patients had DM, and 80.5% had hypertension (HT). CAP patients also tended to have heart disease (56.1%). Jiang's study indicated that patients on regular hemodialysis with an average age of 55.0 ± 9.9 years, mostly male, and with a dialysis duration of 23.4 ± 11.5 months, often had inadequate dialysis status and suffered from comorbid hypertension (98.5%), accompanied by clinical symptoms such as fever, cough, and shortness of breath [17].

This study found a significant difference in the Neutrophil-to-Lymphocyte Ratio (NLR) with a cut-off of 6.09 from the ROC curve concerning the incidence of community-acquired pneumonia in patients undergoing regular hemodialysis. A case-control study stated that an NLR cut-off of 7.41 (0.69-0.78) with a P-value < 0.001 could predict the occurrence of pneumonia in patients with regular HD. The study concluded that an increased NLR ≥ 7.41 better predicts lung infection in hemodialysis patients. NLR can reflect the balance between innate immune response (neutrophils) and adaptive immune response (lymphocytes) [10].

Previous research indicated that elevated NLR reflects a state of micro-inflammation in patients undergoing regular hemodialysis. In a study of 100 regular hemodialysis patients, divided into pneumonia and non-pneumonia groups, NLR values were 3.2 (2.7-4.1) for the non-pneumonia group and 6.6 (4.2-11.6) for the pneumonia group, with a P-value < 0.001. The study concluded that an NLR > 5.52 (95% CI 0.74-0.897) is associated with lung infection. Univariate logistic regression analysis showed that NLR, hemoglobin, red blood cells, white blood cells, neutrophils, lymphocytes, and albumin are factors influencing lung infection in hemodialysis patients. Multivariate analysis indicated that each 1-unit increase in NLR raises the risk of lung infection by 46% (OR: 1.46, 95% CI = 1.14-1.86). NLR negatively correlates with red blood cells, hemoglobin, and albumin, leading to impaired immune function and increased risk of lung infections in dialysis patients [18].

Pneumonia is a common disease in dialysis patients and is a risk factor for cardiovascular disorders (CVD) and mortality. Patients with end-stage renal disease (ESRD) undergoing hemodialysis are usually older, immunocompromised, and often have multiple comorbidities. Therefore, dialysis patients are at high risk of infections. Studies show that up to 90% of dialysis patients require hospitalization due to pneumonia, imposing a significant economic burden [4].

The Neutrophil-to-Lymphocyte Ratio (NLR) combines neutrophils and lymphocytes. Neutrophils are the first inflammatory cells to arrive during an infection, part of the innate immune response characterized by non-specific inflammation. Lymphocytes are crucial in the adaptive immune response. During an infection, inflammation drives the activity of neutrophils, lymphocytes, and endothelial cells, promoting the aggregation of various adhesion molecules and chemokines to the infection site. The increase in white blood cells in CKD patients is largely due to increased neutrophils. Kartal et al. explained that the rise in neutrophils results from neutrophil demargination, delayed apoptosis, and stem cell stimulation by growth factors. Other studies suggest that increased NLR is likely due to elevated neutrophils and decreased lymphocytes. Chung et al. noted that the decrease in lymphocyte count compensates for the increase in neutrophils to maintain leukocyte homeostasis.

NLR has been used as a predictive biomarker in many infectious diseases. It is a cost-effective and easily accessible inflammatory biomarker compared to others like CRP, procalcitonin, IL-6, TNF, and erythrocyte sedimentation rate (ESR). Serum NLR is significantly higher in CKD patients with pneumonia compared to those without. Kartal et al. found that NLR significantly increased in community-acquired pneumonia (CAP) and can be used as a predictor for CAP [15].

Chi-square tests on body mass index (BMI) with the incidence of community-acquired pneumonia in regular hemodialysis patients showed no significant nutritional status difference between CAP and non-CAP patients (p > 0.05). Previous literature identified two types of malnutrition related to hemodialysis: type 1, where inadequate intake due to anorexia, nausea, and vomiting improves with dialysis and proper nutrition; and type 2, mediated by chronic inflammation and not always improved with adequate dialysis and nutrition [19].

Research conducted in Houston also found that among 317 pneumonia patients, the majority (107) had normal body weight, 36 were underweight, and 70 were overweight. Multivariate analysis revealed that BMI did not have a significant correlation with

pneumonia incidence and mortality. Malnutrition generally occurs in individuals over 60 years old, rarely in younger adults, due to decreased growth hormone and insulin-like growth factor-1, free radical accumulation, reduced immunity, and chronic inflammation contributing to malnutrition in the elderly ($p > 0.05$) [20] . This may be due to a non-uniform population and variations in nutritional status at the time of initial hemodialysis, affecting the distribution of results. One study noted that patients undergoing hemodialysis for over a year found no significant relationship between the duration of dialysis and nutritional status, with most patients having normal nutritional status. It was stated that adequate hemodialysis plays a role in maintaining nutritional status, but nutritional status is also influenced by dietary intake. When regular hemodialysis patients consume balanced caloric and protein intake, their nutritional status is maintained [21].

In this study, BMI (Body Mass Index) was used to measure nutritional status in patients. BMI is a simple and inexpensive standard measurement for assessing nutritional status. However, every measurement method has its limitations. BMI has limitations in its predictability for assessing body fat mass at an individual level due to variability in body composition across different age groups, genders, and ethnicities [22]. One study that assessed the relationship between nutritional status and the incidence of pneumonia analyzed nutritional status using the NRS-2002 (Nutritional Risk Screening 2002) scale, developed in 2002 by a group of experts from the European Society for Clinical Nutrition and Metabolism (ESPEN). This questionnaire is based on randomized clinical trial results and includes several stages of assessment: nutritional risk, disease severity, initial and final screening. Nutritional risk is assessed based on current nutritional status and the anticipated risk of worsening due to increased needs during the course of illness and surgical interventions. A total score of ≥ 3 indicates a risk of nutritional deficiency [23].

In one study evaluating nutritional status in dialysis patients, it was found that BMI has low specificity in assessing body fat mass, so this parameter should not be used in isolation for nutritional assessment, especially in CKD (chronic kidney disease) patients. The study used another measure, LMI (Lean Mass Index). LMI is calculated by determining Lean Body Mass (LBM) using the formula Total Body Weight minus Fat Weight, where Fat Weight is Total Body Weight divided by body fat percentage divided by 100. LMI is then calculated using the formula LBM divided by height squared. The study found that patients with low LMI are associated with poor prognosis in dialysis patients. LMI is classified as follows: Low LMI: < 17 kg/m^2, Normal: 17-19 kg/m^2, Excessive: 19-21 kg/m^2, Very Excessive: > 21 kg/m^2. Dialysis patients had a low average LMI of 13.3 kg/m^2 [24].

A significant relationship was found between the duration of dialysis and pneumonia ($p < 0.05$), with dialysis lasting > 1 year associated with a 3.89 times increased risk of community-acquired pneumonia requiring hospitalization (95% CI 1.18-12.8; p 0.025).

Patients undergoing hemodialysis for more than a year generally experience increased creatinine and urea levels. In uremia, there is an imbalance between pro-inflammatory and anti-inflammatory factors, leading to disruptions in innate and adaptive immune systems. Impaired PMN (polymorphonuclear) function in bacterial phagocytosis and decreased response to T lymphocytes occur. A weakened immune defense facilitates infection. Bacterial infections lead to the release of inflammatory mediators and an excessive response to these mediators (TNF-α and IL-6), causing increased oxidative stress correlated with the severity of CKD. CKD patients undergoing hemodialysis are vulnerable to infections due to impaired phagocytic function caused by uremic toxins, anemia, and bioincompatibility of dialyzers [25].

Another effect of uremic toxin accumulation is uremic arteriolopathy, which is a dysfunction of the autonomic nervous system that can present symptoms similar to uremic gastropathy. These symptoms can stimulate gastric acid production, resembling gastritis, such as epigastric pain, nausea, vomiting, abdominal bloating, and reduced appetite. Chronic hyperuricemia also causes chronic proteolysis (hypercatabolism of protein). Uremic gastritis and hypercatabolism contribute to nutritional disorders, making infections more likely [9].

Research on the duration of hemodialysis and the incidence of pneumonia is still limited. A study conducted in China involving 24,363 dialysis patients found that 6,065 patients died. Of these, 17.9% aged ≥ 65 years had pneumonia, and 38.3% had undergone hemodialysis for > 1 year. Increased mortality among those over 75 years old with regular hemodialysis reached 73.6%, caused by pneumonia [26].

One study indicated that patients undergoing hemodialysis for more than a year experienced weight loss and more frequent malnutrition, associated with a 1.34 times increased risk of infection and mortality [27]. This finding aligns with Iseki's research involving 1,243 pneumonia patients undergoing HD with an average duration of 5.2 years (range 1 month to 19.4 years), showing that mortality and infection risks increased with dialysis duration, particularly in diabetic patients [28].

In a retrospective study of 100 patients undergoing hemodialysis (50 with newly diagnosed pneumonia and 50 without pneumonia), data from medical records from 2017 to 2019 showed that the main complication in dialysis patients is infection, with pneumonia occurring 15 times more frequently. One-fifth of patients experienced community-acquired pneumonia after 1 year of hemodialysis.

Factors associated with infection risk include age, comorbidities (DM, heart failure, pre-existing lung disease), low serum albumin levels, and chronic micro-inflammation [18].

A study by Sumida found that 59% of HD patients had undergone hemodialysis for ≥ 5 years, including long-term patients with ≥ 15 years, representing 15% of the total. Longer hemodialysis duration was associated with a higher incidence of infection [29].

Multivariate analysis found that an NLR ≥ 6.09 was most strongly associated with prolonged HD (> 1 year) and comorbid heart failure, increasing the risk of community-acquired pneumonia in regular HD patients. Previous studies showed that elderly patients with pneumonia, poor nutritional status, high inflammatory markers, poor cardiac function, and higher fluid volume burdens had increased pneumonia risk. Multivariate analysis emphasized that thoracic fluid volume and higher NLR are independent predictors of pneumonia development. Approximately 40% of regular hemodialysis patients have heart problems, with heart function and fluid volume correlating with pneumonia and overall mortality in regular HD patients. Indicators of heart function and fluid volume show that NT-proBNP is an independent risk factor for pneumonia in regular HD patients. Pulmonary edema can lead to pneumonia through mechanisms that alter the microalveolar environment, including increased bacterial colonization and infectivity and decreased host bactericidal capacity. Chronic kidney disease patients receiving regular HD experience chronic inflammation and fluid overload, strongly correlating with chronic inflammation, which facilitates infection. Fluid overload (pulmonary edema) indicates a high risk of infection, particularly pneumonia, necessitating increased ultrafiltration to reduce excess fluid volume in the thoracic cavity [30].

A study involving 289,210 dialysis patients from the Renal Beneficiary Utilization System identification and death notification files and the Centers for Medicare & Medicaid Services (CMS) Institutional Inpatient Standard Analytic Files found that comorbid heart failure was significantly associated with pneumonia ($p<0.001$) with an Adjusted Hazard Ratio of 1.15 (1.13-1.17). Other cardiovascular disorders such as atherosclerotic heart disease and arrhythmias were not significantly associated ($p=0.9$ and $p=0.8$) [31].

An observational study conducted in Spain from 1995-2010 also found that comorbid heart failure was significantly associated with pneumonia incidence ($p<0.001$), with 46.8% of chronic kidney disease patients having this comorbidity. This study highlighted that chronic kidney disease patients are often associated with conditions like kidney failure and diabetes mellitus, which can increase the risk of pneumococcal infections such as S. pneumoniae [32].

This study has several strengths. It provides important contributions to the medical literature by focusing on factors such as Neutrophil-Lymphocyte Ratio (NLR), nutritional status, duration of hemodialysis, and heart failure related to pneumonia incidence in regular hemodialysis patients. This is significant because pneumonia is a common complication in dialysis patients. Additionally, measuring these factors provides deep insights into pneumonia risk in dialysis patients, potentially forming the basis for more effective prevention strategies. The findings have significant clinical implications by offering valuable information for managing hemodialysis patients to reduce pneumonia risk.

However, this study also has some limitations. Some variables were not available at the time patients were selected as samples, so data from the nearest variables were used. As an observational study, it is difficult to establish causality between the studied variables, limiting the ability to draw conclusions about predictors of pneumonia incidence in dialysis patients. The study also used retrospective data from medical records, which may introduce bias. BMI as a nutritional status measure has limitations in assessing body fat amount or distribution, which may affect result significance. Other measurements like NRS 2002 and LMI can be used to assess nutritional status. Finally, difficulties in controlling other factors influencing pneumonia incidence also pose a weakness in this study.

CONCLUSSION

Based on the research above, the following conclusions can be drawn:

1. An increase in NLR (Neutrophil-Lymphocyte Ratio) is associated with a higher incidence of community-acquired pneumonia in patients undergoing regular hemodialysis.

2. Nutritional status is not related to the incidence of community-acquired pneumonia requiring hospitalization in patients undergoing regular hemodialysis.

3. The duration of hemodialysis is associated with an increased incidence of community-acquired pneumonia requiring hospitalization in patients undergoing regular hemodialysis.

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Declarations

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REFERENCES

[1] Wang B, Lin W, Qian C, Zhang Y, Zhao G, Wang W, et al. Disease Burden of Meningitis Caused by Streptococcus pneumoniae Among Under-Fives in China: A Systematic Review and Meta-analysis. Infect Dis Ther 2023;12:2567–80. https://doi.org/10.1007/s40121-023-00878-y.

[2] Perhimpunan Dokter Paru Indonesia. Pedoman Diagnosis dan Penatalaksanaan Pneumonia Komunitas di Indonesia. Jakarta: Balai Penerbit FKUI 2022.

[3] Chou C-Y, Wang S-M, Liang C-C, Chang C-T, Liu J-H, Wang I-K, et al. Risk of Pneumonia Among Patients with Chronic Kidney Disease in Outpatient and Inpatient Settings. Medicine 2014;93:e174. https://doi.org/10.1097/MD.0000000000000174.

[4] Pant A, Prasai A, Rauniyar AK, Adhikary L, Basnet K, Khadka T. Pneumonia in Patients with Chronic Kidney Disease Admitted to Nephrology Department of a Tertiary Care Center: A Descriptive Cross-sectional Study. JNMA J Nepal Med Assoc 2021;59:1000–3. https://doi.org/10.31729/jnma.7074.

[5] Slinin Y, Foley RN, Collins AJ. Clinical epidemiology of pneumonia in hemodialysis patients: the USRDS waves 1, 3, and 4 study. Kidney Int 2006;70:1135–41. https://doi.org/10.1038/sj.ki.5001714.

[6] Lee JH, Moon JC. Clinical characteristics of patients with hemodialysis-associated pneumonia compared to patients with non-hemodialysis community-onset pneumonia. Respir Med 2016;111:84–90. https://doi.org/10.1016/j.rmed.2015.12.009.

[7] Fataya E, Fadrian, Mustafa Noer, Dwitya Elvira, Yuliarni Syafrita, Netti Suharti. Characteristics of Adult Sepsis Patients Admitted to Department of Internal Medicine, Dr. M. Djamil General Hospital, Padang, Indonesia. Bioscientia Medicina : Journal of Biomedicine and Translational Research 2023;7:3191–8. https://doi.org/10.37275/bsm.v7i3.791.

[8] Zhu X, Li G, Li S, Gong Z, Liu J, Song S. Neutrophil-to-lymphocyte ratio and red blood cell distribution width-to-platelet ratio predict cardiovascular events in hemodialysis patients. Exp Ther Med 2020;20:1105–14. https://doi.org/10.3892/etm.2020.8756.

[9] Zhu L, Li X-L, Shi R, Wang D-G. Dialysis vintage is associated with a high prevalence and severity of unpleasant symptoms in patients on hemodialysis. Ren Fail 2023;45. https://doi.org/10.1080/0886022X.2023.2201361.

[10] Beberashvili I, Omar MA, Nizri E, Stav K, Efrati S. Combined use of CRP with neutrophil-to-lymphocyte ratio in differentiating between infectious and noninfectious inflammation in hemodialysis patients. Sci Rep 2023;13:5463. https://doi.org/10.1038/s41598-023-32270-8.

[11] Soeters PB, Wolfe RR, Shenkin A. Hypoalbuminemia: Pathogenesis and Clinical Significance. Journal of Parenteral and Enteral Nutrition 2019;43:181–93. https://doi.org/10.1002/jpen.1451.

[12] Chebib N, Cuvelier C, Malézieux-Picard A, Parent T, Roux X, Fassier T, et al. Pneumonia prevention in the elderly patients: the other sides. Aging Clin Exp Res 2021;33:1091–100. https://doi.org/10.1007/s40520-019-01437-7.

[13] Hommos MS, Glassock RJ, Rule AD. Structural and Functional Changes in Human Kidneys with Healthy Aging. Journal of the American Society of Nephrology 2017;28:2838–44. https://doi.org/10.1681/ASN.2017040421.

[14] Barbagelata E, Cillóniz C, Dominedò C, Torres A, Nicolini A, Solidoro P. Gender differences in community-acquired pneumonia. Minerva Med 2020;111. https://doi.org/10.23736/S0026-4806.20.06448-4.

[15] Kartal O, Kartal AT. Value of neutrophil to lymphocyte and platelet to lymphocyte ratios in pneumonia. Bratislava Medical Journal 2017;118:513–6. https://doi.org/10.4149/BLL_2017_099.

[16] Hespanhol V, Bárbara C. Pneumonia mortality, comorbidities matter? Pulmonology 2020;26:123–9. https://doi.org/10.1016/j.pulmoe.2019.10.003.

[17] Jiang Z, Pan Y, Zhu J, Wang Y. Risk Prediction of Pneumonia in Maintenance Hemodialysis Patients with COVID-19: A Single-center Retrospective Study in China. Reserach Square 2023:1–15.

[18] Li L-L, Yang Y-Q, Qiu M, Wang L, Yuan H-L, Zou R-C. The clinical significance of neutrophil-lymphocyte ratio in patients treated with hemodialysis complicated with lung infection. Medicine 2021;100:e26591. https://doi.org/10.1097/MD.0000000000026591.

[19] Bramania P, Ruggajo P, Bramania R, Mahmoud M, Furia F. Nutritional Status of Patients on Maintenance Hemodialysis at Muhimbili National Hospital in Dar es Salaam, Tanzania: A Cross-Sectional Study. J Nutr Metab 2021;2021:1–7. https://doi.org/10.1155/2021/6672185.

[20] Kiesswetter E, Colombo MG, Meisinger C, Peters A, Thorand B, Holle R, et al. Malnutrition and related risk factors in older adults from different health-care settings: an enable study. Public Health Nutr 2020;23:446–56. https://doi.org/10.1017/S1368980019002271.

[21] Maulida NR, Rahayu LS, Andengganan Y, Al Bina S. Kecukupan Asupan Gizi Dalam Peningkatan Status Gizi Pasien Hemodialisis Berdasarkan Dialysis Malnutrition Scores. ARGIPA 2019;4:28–36.

[22] Chetboun M, Raverdy V, Labreuche J, Simonnet A, Wallet F, Caussy C, et al. BMI and pneumonia outcomes in critically ill COVID-19 patients: An international multicenter study. Obesity 2021;29:1477–86. https://doi.org/10.1002/oby.23223.

[23] Ścisło L, Walewska E, Bodys-Cupak I, Gniadek A, Kózka M. Nutritional Status Disorders and Selected Risk Factors of Ventilator-Associated Pneumonia (VAP) in Patients Treated in the Intensive Care Ward—A Retrospective Study. Int J Environ Res Public Health 2022;19:602. https://doi.org/10.3390/ijerph19010602.

[24] Yuste C, Abad S, Vega A, Barraca D, Bucalo L, Pérez-de José A, et al. Assessment of nutritional status in haemodialysis patients. Nefrologia 2013;33:243–9. https://doi.org/10.3265/Nefrologia.pre2013.Jan.11670.

[25] Reindl-Schwaighofer R, Kainz A, Kammer M, Dumfarth A, Oberbauer R. Survival analysis of conservative vs. dialysis treatment of elderly patients with CKD stage 5. PLoS One 2017;12:1–10. https://doi.org/10.1371/journal.pone.0181345.

[26] Liu J, Zhang H, Diao Z, Guo W, Huang H, Zuo L, et al. Epidemiological analysis of death among patients on maintenance hemodialysis: results from the beijing blood purification quality Control and Improvement Center. BMC Nephrol 2023;24:236. https://doi.org/10.1186/s12882-023-03271-6.

[27] Podewils LJ, Holtz T, Riekstina V, Skripconoka V, Zarovska E, Kirvelaite G, et al. Impact of malnutrition on clinical presentation, clinical course, and mortality in MDR-TB patients. Epidemiol Infect 2011;139:113–20.

[28] Iseki K, Tozawa M, Takishita S. Effect of the duration of dialysis on survival in a cohort of chronic haemodialysis patients. Nephrology Dialysis Transplantation 2003;18:782–7. https://doi.org/10.1093/ndt/gfg145.

[29] Sumida K, Yamagata K, Iseki K, Tsubakihara Y. Different impact of hemodialysis vintage on cause-specific mortality in long-term hemodialysis patients. Nephrology Dialysis Transplantation 2015:gfv402. https://doi.org/10.1093/ndt/gfv402.

[30] Yan L, Qiu Y, Liu J, Wu J, Yang J, He W. Increased thoracic fluid content is associated with higher risk for pneumonia in patients undergoing maintenance hemodialysis. Ren Fail 2023;45. https://doi.org/10.1080/0886022X.2023.2207666.

[31] Guo H, Liu J, Collins AJ, Foley RN. Pneumonia in incident dialysis patients--the United States Renal Data System. Nephrology Dialysis Transplantation 2007;23:680–6. https://doi.org/10.1093/ndt/gfm474.

[32] Viasus D, Garcia-Vidal C, Cruzado JM, Adamuz J, Verdaguer R, Manresa F, et al. Epidemiology, clinical features and outcomes of pneumonia in patients with chronic kidney disease. Nephrology Dialysis Transplantation 2011;26:2899–906. https://doi.org/10.1093/ndt/gfq798.