# Clinical and Non-Clinical Predictors of Length of Stay in Indonesian hospitalized COPD (Chronic Obstructive Pulmonary Disease) Patients

## (Prediktor Klinik dan Non-Klinik Lama Rawat Inap Pasien PPOK (Penyakit Paru Obstruktif Kronis) di Rumah Sakit)

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## ABSTRACT

**Background:** COPD (chronic obstructive pulmonary disease) is a chronic disease characterized by persistent airflow limitation and is a major cause of morbidity and mortality. **Objectives:** This study aimed to analyze potential predictors of the length of hospitalization (length of stay/LOS) of COPD patients in the Anutapura Hospital, Central Sulawesi Province, Indonesia. **Material and Methods:** This study is an analytical cross-sectional design. The data were collected from medical records of COPD patients at Anutapura Hospital, Central Sulawesi Province, during 2018-2021. Information about demographic data (age, sex, weight), clinical data (comorbidities, type of antibiotics therapy, route of antibiotic administration, class of antibiotics, oxygen therapy, history of hospital admission due to pneumonia, with/without exacerbations), and non-clinical data (type of insurance and treatment class) were extracted. Multivariate linear regression was used to identify the predictors of LOS. **Results:** A total of 210 COPD patients were identified. The results of univariate analysis showed that there were several potential predictors of LOS in COPD patients ($p < 0.25$), namely: age (B: 0.03, 95% CI: 0.01-0.05), treatment class (B: 1.16, 95% CI: 0.01-2.33), exacerbation (B: 0.55, 95% CI: -0.24-1.35), comorbidities (B: 0.68, 95% CI: 0.25-1.12), and type of antibiotics therapy (single/combination antibiotics) (B: 1.43, 95% CI: 0.33-2.54). The results of the multivariate analysis indicated that the older (B: 0.03, 95% CI: 0.01-0.06, $p = 0.02$) COPD patients and the more comorbidities (B: 0.54, 95% CI: 0.07-1.00, $p = 0.02$) that they had, the longer the LOS that they experienced. **Conclusions:** In this study, age and patient comorbidities are independent predictors of LOS in COPD patients in the Anutapura Hospital, Central Sulawesi Province, Indonesia.

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## ABSTRAK

Latar Belakang: PPOK (Penyakit Paru Obstruktif Kronik) adalah penyakit kronis yang ditandai dengan keterbatasan aliran udara yang persisten dan merupakan penyebab utama morbiditas dan mortalitas. Tujuan: Penelitian ini bertujuan untuk menganalisis potensi prediktor lama rawat inap (length of stay/LOS) pasien PPOK di Rumah Sakit Anutapura Provinsi Sulawesi Tengah, Indonesia. Bahan dan Metode: Penelitian ini merupakan penelitian analitik dengan desain penelitian *cross sectional*, dimana data diambil dari rekam medis pasien PPOK di RSUD Anutapura Provinsi Sulawesi Tengah selama tahun 2018-2021. Informasi tentang data demografi (usia, jenis kelamin, berat badan), data klinis (penyerta, antibiotik tunggal/kombinasi, rute pemberian antibiotik, jenis antibiotik, terapi oksigen, riwayat masuk rumah sakit karena pneumonia, dengan/tanpa eksaserbasi) dan non- data klinis (jenis asuransi dan kelas pengobatan) dikumpulkan. Regresi linier multivariat digunakan untuk mengidentifikasi prediktor LOS. Hasil: Sebanyak 210 pasien PPOK teridentifikasi. Hasil analisis univariat menunjukkan bahwa terdapat beberapa potensi prediktor LOS pada pasien PPOK (p < 0,25), yaitu: umur (B: 0,03, CI 95%: 0,01-0,05), kelas pengobatan (B: 1,16, CI 95% : 0,01-2,33), eksaserbasi (B: 0,55, 95% CI: -0,24-1,35), penyakit penyerta (B: 0,68, 95% CI: 0,25-1,12), dan antibiotik tunggal/kombinasi (B: 1,43, 95% CI : 0.33- 2.54). Hasil analisis multivariat menunjukkan bahwa semakin tua usia pasien PPOK (B: 0,03, 95% CI: 0,01-0,06, p = 0,02) dan semakin banyak penyakit penyerta yang dimiliki (B: 0,54, 95% CI: 0,07-1,00, p = 0,02) maka semakin lama rawat inap yang dijalani oleh pasien tersebut. Kesimpulan: Dalam penelitian ini, usia dan penyakit penyerta pasien merupakan prediktor lama rawat inap yang paling berpengaruh pada pasien PPOK di Rumah Sakit Anutapura Provinsi Sulawesi Tengah, Indonesia.

Kata kunci: Lama rawat inap; PPOK.

## INTRODUCTION

COPD (chronic obstructive pulmonary disease) is a significant cause of morbidity and mortality worldwide. In Indonesia, the prevalence of COPD is 8.7%, with Central Sulawesi as among the provinces with the highest case (Ministry of Health of the Republic of Indonesia, 2019). Length of stay (LOS) in a hospital is a vital indicator in health services that evaluate the success of treatment, management of service quality, and outcome therapy (Alemu *et al.,* 2019). LOS represents the duration of hospital stay, starting from admission to discharge from the hospital. LOS is calculated by subtracting the discharge dates (alive or dead) from the hospital admission date (Tedja, 2011). Previous studies have found several predictors of LOS in COPD patients in the hospital, such as socio-demographic data, clinical variables, comorbidities, as well as number and type of drugs used (Díaz-Peromingo *et al.,* 2004; Harries *et al.,* 2015; Wang *et al.,* 2014; Wong *et al.,* 2008). However, no similar studies have been found in Indonesia, so there is no information about the prognostic factors which might influence LOS in COPD patients in Indonesia. Clinical and non-clinical predictors of LOS in COPD patients in Indonesia can be utilized to develop statistical models that can be used to predict the LOS of COPD patients in hospitals. The ability to predict the LOS of COPD patients can contribute to a better planning and implementation process for COPD patient care to shorten LOS and save hospitalization costs.

## METHODS

### Study design, data source, and patient population

This study is a retrospective study with a cross-sectional design at Anutapura Hospital, Central Sulawesi Province, Indonesia. Patient data were collected from the medical records. The study population

consisted of patients diagnosed with COPD (J44) according to the International Statistical Classification of Disease and Related Health Problems (ICD-10) criteria in the study period between 2018 and 2021. We excluded data from patients hospitalized due to non-COPD primary diagnosis, discharged from the hospital for non-medical reasons, who died, and who had illegible medical records.

### Sampling method and sample calculation

This study used a total sampling method by including all eligible patients during the study period. The minimum sample size needed for this study (13 potential predictors) according to the formula (50 + 8m in which "m" is the number of potential predictors) proposed by Tabachnick and Fidell (2013) are 154 patients. (Tabachnick and Fidel, 2007).

### Outcome measurement

LOS is calculated by subtracting the dates of hospital discharge from the date of hospital admission (Tedja, 2011).

### Potential predictors

We collected the following information for each patient: demographic data (age, weight, sex), type of insurance (national health insurance or private insurance), type of hospital ward (3rd class: six beds in one room, 2nd class: four beds in one room and 1st class: two beds in one room),  blood pressure (normal: <120/<80 mm/Hg, prehypertension: 120-139/80-89 mmHg, hypertension grade 1: 140-159/90-99 mmHg, hypertension grade 2 : ≥160/≥100 mmHg), respiratory rate (normal: 12-20 breaths per minute, abnormal: under 12 or over 25 breaths per minute), class of antibiotics, route of antibiotic administration (oral or intravenous), duration of antibiotic therapy, type of antibiotics therapy (single or combination), oxygen therapy, comorbidities, exacerbation status, and history of hospital admission due to pneumonia.

### Statistical Analysis

Descriptive statistics were used to give an overview of the characteristics of each research variable. The normally distributed data (ratio) were expressed as a mean value ($\pm$ SD). Meanwhile, the skewed data were presented as a median value (Interquartile Range/IQR). Categorical data were expressed in numbers and percentages (%). Multicollinearity was checked among the potential predictors (Variance Inflation Factor/VIF should be less than 10) (Tabachnik and Fidell, 2007). The 'complete case analysis' method was used in this study. Univariate linear regression was applied to check the relationship between each potential predictor with LOS (normally distributed). A potential predictor with a p-value $< 0.25$ was included in the multivariate analysis. Multivariate linear regression was performed to determine the independent predictors of LOS ($p < 0.05$). The coefficient B and 95% Confidence Interval

(CI) values were presented to show the strength of the association between potential predictors and LOS. The statistical analysis was run using Statistical Package for Social Sciences (SPSS) version 25.

## RESULTS AND DISCUSSION

Among 317 COPD patients during the period 2018-2021, there were 210 eligible patients (Figure 1).
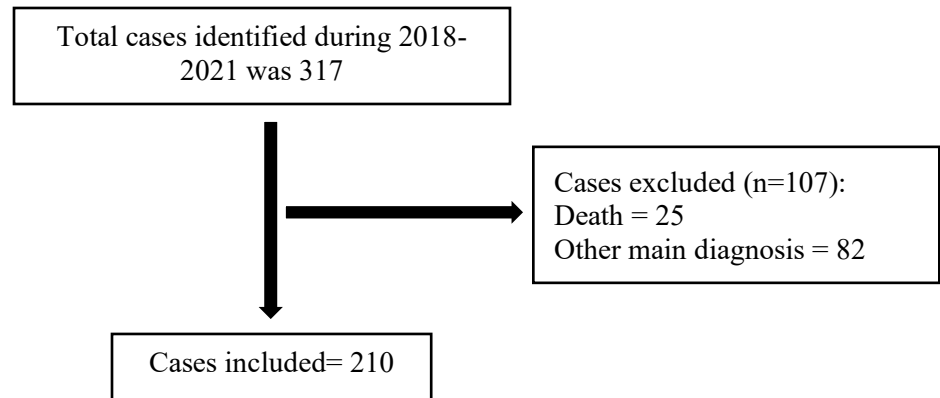


Figure 1. Case selection process.

Table 1 presents the baseline characteristics of the patients. The median age of our study population was 65 (IQR=14), and most were male patients (77.6%). These results are in line with the previous studies in which the prevalence of males in COPD patients is higher than female patients (Arto Yuwono Soeroto, 2014). Another study also reported (Tandon *et al.,* 2016) comparable results where the number of male COPD patients was 94.3%. According to the Basic health research 2016, the age group above 60 has a higher risk of developing COPD than the younger age group (Ministry of Health of the Republic of Indonesia, 2017).

An abnormal (faster) respiratory rate was the most common symptom experienced by COPD patients. The quicker the respiratory rate, the more effort is required to breathe (Arto Yuwono Soeroto, 2014). In our cohort, 190 patients (90.5%) had an abnormal respiratory rate.

Table 1. Characteristic Of COPD Patient (n = 210)

| Variables | | N = 210 |
|---|---|---|
| Age, Median (IQR) | | 65 (14) |
| Sex | Male (*n*, %) | 163 (77.6) |
| | Female (*n*, %) | 47 (22.4) |
| Weight, Median (IQR) | | 62 (6) |
| Respiration Rate | Normal (*n*, %) | 20 (9.5) |
| | Abnormal (*n*, %) | 190 (90.5) |
| Comorbidities | Heart disease (n, %) | 22 (10.5) |
| | Lung disease (n, %) | 119 (56.7) |
| | Stomach disease (n, %) | 17 (8.1) |
| | Kidney disease (n, %) | 13 (6.2) |

| | | |
|---|---|---|
| Hypertension (n, %) | | 4 (1.9) |
| Prostate disease (n, %) | | 4 (1.9) |
| Hyperthyroid disease (n, %) | | 2 (1.0) |
| Diabetes (n, %) | | 3 (1.4) |
| Anemia (n, %) | | 1 (0.5) |
| No-Comorbidities (n, %) | | 25 (11.9) |
| Number of Comorbidities, Median (IQR) | | 1 (1) |
| Exacerbation status | Yes (n, %) | 143 (68.1) |
| | No (n, %) | 67 (31.9) |
| Oxygen Therapy | Yes (n, %) | 192 (91.4) |
| | No (n, %) | 18 (8.6) |
| Type of Insurance | BPJS (n, %) | 208 (99) |
| | Private Insurance (n, %) | 2 (1) |
| Treatment class | Class 1 or VIP (n, %) | 25 (11.9) |
| | Class 2 (n, %) | 34 (16.2) |
| | Class 3 (n, %) | 151 (71.9) |
| Type of Antibiotic therapy | Monotherapy (*n*, %) | 183 (87.1) |
| | Combination therapy (*n*, %) | 27 (12.9) |
| Route of Antibiotics administration | | |
| | IV (*n*, %) | 181 (86.2) |
| | oral (*n*, %) | 20 (9.5) |
| | IV+ oral (*n*, %) | 9 (4.3) |
| Class of Antibiotics | | |
| | cephalosporins (*n*, %) | 170 (81) |
| | macrolides (*n*, %) | 8 (3.8) |
| | fluoroquinolones (*n*, %) | 7 (3.3) |
| | cephalosporins + macrolides (*n*, %) | 6 (2.9) |
| | sulfonamide + nitroimidazole (*n*, %) | 1 (0.5) |
| | cephalosporins + fluoroquinolones (*n*, %) | 6 (2.9) |
| | beta-lactam + fluoroquinolones (*n*, %) | 10 (4.8) |
| | nitroimidazole (*n*, %) | 2 (1.0) |
| Previous hospitalization due to pneumonia | Yes (*n*, %) | 60 (28.6) |
| | No (*n*, %) | 150 (71.4) |

n= number of samples

Most COPD patients had comorbidities, with the highest number being lung-related diseases (56.7%), such as COPD, asthma, pneumonia, tuberculosis, bronchopneumonia, bronchitis, and pulmonary edema. These results were consistent with the previous reports that COPD patients mostly have another pulmonary disease (Huang *et al.,* 2006) (Cavaillès *et al.,* 2013).

Only about 29% of the patients had previous hospitalizations due to pneumonia, and about 32% had exacerbations. Most patients (91%) needed oxygen support since they had a high respiratory rate and shortness of breath, as characteristic of COPD patients. Administration of oxygen therapy is crucial to maintain cellular oxygenation and prevent cellular damage in muscle and other organs (Indonesian Lung Doctors Association, 2016).

All patients were insured, and most (99%) used national health insurance (BPJS Kesehatan). About 72% of the patients were enrolled in the third-class hospital ward (six beds per room), and only a fraction (about 12%) could afford first-class and VIP hospital wards. Comfortable treatment classes affect the length of patient care in the hospital. Management of patients in the ward can affect the delay in the patient's discharge. The higher class of care, the better service, so it impacts the length of stay of patients in the hospital.

Cephalosporins were mainly chosen for treating the patients (81%), followed by the macrolides group (3.8%), fluoroquinolone group (3.3%), and nitroimidazole (1.0%). Some patients (13%) were given a combination of antibiotics such as a combination of cephalosporins and macrolides (2.9%), a combination of sulfonamide and nitroimidazole group (0.5%), a combination of cephalosporins and fluoroquinolone (2.9%), and a combination of beta-lactam and fluoroquinolone (4.8%). The use of antibiotics in COPD patients at Anutapura Hospital Palu is in accordance with COPD therapy management (University of Nebraska Medical Center, 2016). Moreover, the results align with previous studies where the antibiotics used most in COPD patients are macrolides, fluoroquinolones, cephalosporins, and penicillins (Varol *et al.,* 2020). The selection of antibiotics is adjusted to the local bacterial pattern and the latest antibiotic composition. Most COPD patients' exacerbations have a Gram-negative pattern (with poor risk prognosis), so it is recommended to use intravenous antibiotics of the 2nd and 3rd generation cephalosporins and fluoroquinolones (Indonesian Lung Doctors Association, 2016). Some patients use a combination of antibiotics because of the presence of other bacteria, so it is necessary to give them a combination of antibiotics to eliminate the pathogens.

Table 2. Univariate Linear Regression for potential predictors of LOS in COPD patients (n=210).

| No | Variables | B | *p*-value | 95% CI Min. | 95% CI Max. |
|----|-----------|------|-----------|------|------|
| 1. | Gender | -0.34 | 0.45 | -1.24 | 0.55 |
| 2. | Weight | -0.03 | 0.39 | -0.10 | 0.04 |
| 3. | Age | 0.03 | 0.04$^*$ | 0.01 | 0.05 |
| 4. | Respiration Rate | 0.29 | 0.65 | -0.98 | 1.57 |
| 5. | Oxygen Therapy | -0.14 | 0.82 | -1.49 | 1.19 |
| 6. | Type of Insurance | 1.60 | 0.41 | -2.26 | 5.46 |

| | | B | p-value | Min | Max |
|---|---|---|---|---|---|
| 7. | Type of hospital ward[¥] | | | | |
| | Class 1+VIP | 1.16 | 0.04[*] | 0.01 | 2.33 |
| | Class 2 | -0.22 | 0.66 | -1.24 | 0.80 |
| 8. | Previous hospitalization due to Pneumonia | -0.21 | 0.61 | -1.04 | 0.61 |
| 9. | Exacerbation status | 0.55 | 0.17[*] | -0.24 | 1.35 |
| 10. | Comorbidities | 0.68 | 0.002[*] | 0.25 | 1.12 |
| 11. | Type of Antibiotic therapy | 1.43 | 0.01[*] | 0.33 | 2.54 |
| 12. | Route of Antibiotics Administration[€] | | | | |
| | Intravena | -0.14 | 0.82 | -1.42 | 1.14 |
| | Intravena+oral | 0.83 | 0.45 | -1.35 | 3.01 |

n= number; B: *Beta Coefficient*; CI: *Confidence Interval*; Min: *Minimum*; Max: *Maximum.*
*:p-value <0.25*; *Reference group*: [¥]Class 3; [€]Oral**.**

The routes of antibiotics administration were predominantly intravenous (86.2%) and followed by oral administration (9.5%). For the patients with antibiotics combination, some of them (4.3%) used antibiotics by intravenous and oral administration. Intravenous antibiotics are injected directly into the vein so that the intended drug level in the blood can be obtained with fast and precise estimation. Moreover, the blood concentration of the antibiotics could be adapted directly according to the patient's needs. Since intravenous administration can avoid first-pass metabolism by the liver, this route gives an immediate effect and good control over drug levels in the blood circulation (Nuryati, 2017). Administration of antibiotics in the hospital, preferably by drip or intravenous (Indonesian Lung Doctors Association, 2016).

The results of univariate linear regression analysis showed that several variables such as age, type of hospital ward, comorbidities, exacerbation status, and type of antibiotic therapy could be potential predictors of LOS in hospitalized COPD patients (table 2). Those variables were then processed into the multivariate linear regression analysis. The results indicated that age and comorbidity were independent predictors of LOS in the hospitalized COPD patients in this study (table 3). Older patients with more comorbidities were more likely to stay in the hospital longer.

Table 3. Multivariate Linear Regression for LOS Predictors in Hospitalized COPD Patients (n=210)

| No. | Variables | LOS | | | |
|---|---|---|---|---|---|
| | | B | 95% Cl | | p-value |
| | | | Min. | Max. | |
| 1. | Age | 0.03 | 0.01 | 0.06 | 0.02* |
| 2. | Type of hospital ward¥ | | | | |
| | Class 1+VIP | 0.72 | -0.43 | 1.89 | 0.21 |
| | Class 2 | -0.10 | -1.12 | 0.90 | 0.83 |
| 3. | Exacerbation status | 0.41 | -0.44 | 1.28 | 0.34 |
| 4. | Comorbidities | 0.54 | 0.07 | 1.00 | 0.02* |
| 5. | Type of Antibiotic therapy | 0.80 | -0.42 | 2.02 | 0.19 |

n= number; B: *Beta Coefficient*; CI: *Confidence Interval*; Min: *Minimum*; Max: *Maximum.*
*: p-value <0.05; Reference: ¥Class 3.

Our results were in line with the previous findings. Inabnit et al. (2018) reported that COPD patients with at least one comorbidity had a 13% longer hospital stay than patients with no comorbidities. The study showed that the number of comorbidities positively correlated with the LOS of COPD patients. Certain comorbid conditions significantly predict prolonged hospitalization (Inabnit *et al.,* 2018).

As patients get older, they are more prone to a progressive decline in lung functions. Older COPD patients generally have a higher risk of acute exacerbations, leading to increased LOS. The prevalence of COPD in older patients has a negative impact on the length of stay (Li *et al.,* 2021). The results of research conducted by Agboado et al. (2012) found a significant increase in the LOS of patients aged 80 years and over compared to patients aged 40-59 years. Patients aged 80 years and older were 41% less likely to be discharged early and patients aged 70 years and older were 31% less likely to be discharged early from the hospital (Agboado *et al.,* 2012).

The results of this study are in line with the results of previous report where the number of comorbidities is one of the factors that affect the length of stay of COPD patients in the hospital (Wang *et al.,* 2014). Another study also stated that age is one of the factors that can affect the length of stay of COPD patients in the hospital (Harries *et al.,* 2015)

It is worth mentioning that there are several limitations to this study. First, we found only two predictors of LOS, possibly due to the limited number of patients (210 patients) and the limited number of predictors in this study. Several potential predictors that have been reported in previous studies could not be obtained in this study due to limited data availability, such as laboratory data, for example, FEV (forced expiratory volume) data. Second, since this study is a retrospective study, it relied on secondary data. Therefore, we cannot do a follow-up on patients' clinical conditions who were being treated. For further research, factors that are indirectly related to health should also be included.

## CONCLUSION

Age and comorbid variables are independent predictors of LOS in COPD patients in the Anutapura Hospital, Central Sulawesi, Indonesia.

## ACKNOWLEDGEMENT

## CONFLICT OF INTEREST

We declare no conflict of interest.

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