

## Evaluation of Current Practice of Antibiotic Use and Clinical Outcomes of Community-Acquired Pneumonia Patients with Type 2 Diabetes Mellitus at Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia

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### ABSTRACT

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Impaired immunity in diabetes mellitus (DM) causes reduced lung function, which increases the incidence of various types of infections, including community-acquired pneumonia (CAP). The main principle of CAP therapy is the administration of antibiotics. This study aims to assess the appropriate use of antibiotics according to existing clinical practice guidelines using the Gyssen algorithm, and to determine its effect on clinical outcomes in hospitalized patients. It is an observational study with a retrospective cohort design and a total sampling technique. The research was conducted at Dr. Cipto Mangunkusumo Hospital Jakarta, with the research subjects being 98 hospitalized CAP patients with type 2 DM (T2DM) over the period January 2018 - December 2019. The collection of data on patient characteristics and clinical outcomes was made through patient medical records. 28.6% of the subjects were in the severe category of CAP. The results of the evaluation using the Gyssens algorithm showed that 59.2% of the subjects receive the appropriate antibiotics, while 40.8% receive non-appropriate antibiotics. The clinical outcomes in the group receiving appropriate antibiotics (70.7%) were significantly higher than the non-appropriate group (42.5%). The results of the multivariate analysis show that the group receiving appropriate antibiotics experienced 2.7 times greater clinical outcomes (RR 2.683, 95% CI: 1.102-6.592) after controlling for the degree of CAP and the onset of antibiotic administration. The use of appropriate antibiotics in CAP patients with T2DM significantly enhanced clinical outcomes.

**Keywords:** Antibiotics; Clinical outcomes; Community Acquired Pneumonia; Type 2 Diabetes Mellitus

### INTRODUCTION

Diabetes mellitus (DM) is a serious public health problem because of its high prevalence, and it continues to increase worldwide and it is estimated will increase to 700 million by 2045. (IDF, 2019). Hyperglycemic conditions can increase the virulence of pathogens, reduce interleukin production, reduce chemotaxis and phagocytosis ability, and interfere with the mobilization of polymorphonuclear leukocytes (Casqueiro *et al.*, 2012).

CAP in DM patients has more serious symptoms, a longer length of hospitalization, more frequent complications, and a higher mortality rate

(Ljubic *et al.*, 2005). Poor glycemic control and long duration of DM increase the risk of mortality in CAP patients (Errlich *et al.*, 2010). The risk of death at 30 and 90 days increases by 1.2 times in such patients with DM (Kornum *et al.*, 2007).

The pathogens that cause CAP in patients with DM can be different from those of non-DM patients. *Klebsiella pneumoniae*, *E. coli*, *Pseudomonas aeruginosa*, and *Acinetobacter* have been more frequently found in the sputum of patients with DM (Saibal *et al.*, 2012). Infections caused by *Acinetobacter* are more difficult to treat because of the high level of resistance, which leads to the death of 60% of patients (Edis *et al.*, 2010).

Guidelines used in various hospitals for the management of community pneumonia is a guide according to the Infectious Disease Society of America/American Thoracic Society (IDSA/ATS) 2007, British Thoracic Society 2009 which includes the procedures for using antibiotics, monitoring and evaluation to assess treatment response. Since The pathogens that cause CAP in patients with DM can be different from those of non-DM, patients with DM are more difficult to treat because of the high level of resistance, which leads to the death of 60% of patients (Edis *et al.*, 2010). Therefore, the appropriate selection of antibiotics as curative therapy in CAP patients with DM is very important to improve therapeutic outcomes and prevent resistance.

In 1992, Gyssens *et al* developed a flow chart adapted from the criteria original Kunin *et al* to evaluate the use of antibiotics. In the diagram, various evaluations are evaluated matters relating to the administration of antibiotics, namely regarding the indications, are there other choices of antibiotics which is more effective, whether there are other antibiotic options less toxic and cheaper, and with a spectrum narrower one. Further evaluation is also carried out regarding drug dose, duration of treatment, interval and route and timing of administration (Gyssens, 1992). This study aims to assess the appropriateness use of antibiotics for 5 days of the medication and their effect on clinical improvement in CAP patients with T2DM.

## MATERIALS AND METHODS

### Study design

This is an observational study with a retrospective cohort design. The research was conducted at Dr. Cipto Mangunkusumo hospital, Jakarta, Indonesia, which is the national referral center for government hospital in Indonesia, and is also a teaching hospital. The research period was January 2018 – December 2019.

### Study subject

The study sample comprised inpatients with a diagnosis of CAP and with a history of T2DM at Dr. Cipto Mangunkusumo Jakarta during the period 2018 - 2019, who met the inclusion and exclusion criteria. To be included, patients needed to be aged  $\geq 18$  years and to have been receiving antibiotic therapy for at least five days. Patients with other infection and those with malignant diseases were excluded.

The data were collected using the total sampling technique. The minimum sample size was 38 patients per group. The sample size was determined using the formula for the difference in the proportions of the two populations (Lameshow, 1991) with a significance degree of 5% dan a test power of 80%. The value of the proportion (P) referring to previous studies by Rumende, *et al* (2019) which is 0,33 (P1) and 0,49 (P2). P for the total proportion, P1 for the proportion of clinical outcomes that have not improved in the appropriate antibiotic group, P2 for the proportion of clinical outcomes that have not improved in the appropriate antibiotic group. Sample size is calculated by the following formula:

$$n = \frac{\{Z_{1-\alpha} \sqrt{2P(1-P)} + Z_{1-\beta} \sqrt{p_1(1-p_1) + p_2(1-p_2)}\}^2}{(p_1 - p_2)^2}$$

A total of 98 patients were included in this study, 58 of whom were receiving appropriate antibiotics, and 40 who were not receiving appropriate antibiotics in accordance with the applicable guidelines.

### Study approval

The research was approved by the Ethics Committee of the University of Indonesia-RSUPN Dr. Cipto Mangunkusumo, Jakarta, as stated on the certificate of passing the ethical review number 97/UN2.F1/ETIK/PPM.00.02/2020. Informed consent was not applied because it was a retrospective study with data collection made using patients' medical records.

### Data collection and analysis

The data collection included details of demographics; socioeconomic status (occupation, education); previous medical history; smoking status; comorbidity, symptoms, and vital signs while being treated; laboratory data on leukocytes (neutrophils, random blood glucose, HbA1c, kidney function, liver function); examination support (chest x-rays, culture data); duration of T2DM; antibiotic therapy; T2DM therapy used while the patient was being treated (type, dose, route, duration); and data on the progress of the patient's clinical condition during treatment (body temperature, heart rate, respiratory rate, blood pressure, oxygen saturation, mental status).

The independent variable in the study was the appropriateness of antibiotic use, as evaluated using the Gyssens algorithm. Evaluation of the use of antibiotics was carried out by a team consisting of 2 pharmacists and 1 doctor from the internal

medicine department. The evaluation following a series of questions, including: 1. indication of antibiotics (there are indications); 2. antibiotic choice (most effective, inexpensive, lowest toxicity, narrowest spectrum); 3. duration of antibiotic use (right duration); 4. antibiotic dosage (right dose, interval dan route); 5. time of administration of antibiotics (right time), which were then classified into one of the categories in the algorithm. The use of antibiotics is considered appropriate if it meets each category and is considered non-appropriate if it does not meet one or more categories. Evaluation of the use of antibiotics is carried out by referring to the following applicable guidelines, namely PPAB (Guidelines for the Use of Antibiotics) RSCM 2017, supported by IDSA/ATS (Infectious Disease Society of America/American Thoracic Society) Consensus Guidelines 2007; Guidelines for Diagnosis and Management of Pneumonia Community (Indonesian Lung Doctors Association, 2014); Drug Information Handbook; and Lexicomp. Several guidelines are used to support all aspects of assessing the appropriateness of antibiotic use according to the patient's clinical condition.

The dependent variable was whether the patient's clinical improvement was assessed after five days of antibiotic use. The clinical improvement criteria included temperature  $\leq 37.5^{\circ}\text{C}$ , heart rate  $\leq 100$  beats/minute, respiratory rate  $\leq 24$  beats/min, systolic blood pressure  $\geq 90$  mmHg, oxygen saturation  $\geq 90\%$ , the ability to receive oral food intake, and conditions of normal mental status (Indonesian Lung Doctors Association, 2014). Patients were considered to have experienced clinical improvement if they met at least three of the improvement criteria.

The data obtained were analyzed using the SPSS program (Statistical Program for Social Science) version 22.0, with a test power of 80% and a significance level of 5%. Data analysis included univariate, bivariate, and multivariate analyzes, and the categorical variables were expressed as a percentage. In this study, the patient's age was categorized into 18-65 years and over 65 years because age over 65 years, diabetes, immunocompromised conditions and the presence of comorbidities were risk factors for CAP. Bivariate analysis was performed using the chi-square method to determine the relationship between the appropriateness of antibiotic use and the outcome of therapy, namely clinical improvement. In addition, multivariate logistic

regression analysis was performed to assess the effect of the independent variables (age, gender, degree of CAP, initial of random blood glucose, duration of T2DM, comorbidity and antibiotic onset) on the outcome of therapy. The onset in this study was the period of first antibiotic administration after the diagnosis of CAP was established, which consisted of subjects who received antibiotic therapy within the first 8 hours (onset 8 hours) and subjects who received the first antibiotic more than 8 hours (onset  $> 8$  hours) referring by previous study by Bader, *et al* (2016). Covariates were analyzed using the chi-square test, and variables with  $p < 0.25$  were included in the multivariate analysis using logistic regression; a  $p$ -value of  $< 0.05$  was considered statistically significant.

## RESULTS AND DISCUSSION

Out of the total 98 patients who were research subjects, 61 (62.2%) were female, and 37 (37.8%) were male. Based on age, it was found that the proportion was almost the same for those aged over 65 years (51%) and those under 65 years (49%), with a mean age of  $63.36 (\pm 12.16)$  years. The majority of patients had suffered from T2DM for less than five years (53.1%), and 59.2% had comorbidities other than T2DM (Table I).

The clinical characteristics of the study subjects when being treated were shortness of breath (80.6%), coughing with phlegm (58.2%), fever (34.7%), and decreased consciousness (21.4%). Assessment of the degree of CAP based on the CURB-65 system (confusion, respiratory rate  $\geq 30$  breaths  $\text{min}^{-1}$ , low blood pressure systolic value  $< 90$  mmHg or diastolic value  $\leq 60$  mmHg and age  $\geq 65$  years) showed 69.4% of patients with moderate severity and 30.6% with severe symptoms. Score system on CURB-65 more ideal for identifying patients with high mortality rates, each risk factor is assigned a value of one, severity was assessed based on the CURB-65 score was a score of 0-1 (mild), 2 (moderate), 3 (high), and severe with 4-5 score (Association Indonesian Lung Doctor, 2014). The complications experienced by patients in the study were pleural effusion (12.2%), sepsis (12.2%), and 8.2% with ADRS (Acute Distress Respiratory Syndrome), which caused the patient to die. 23 subjects were subjected to culture examination using sputum and blood samples and 33 isolates were found, the most common being gram-negative bacteria (78.8%), and *Klebsiella pneumoniae* (27.3%) (Table II).

Table I. Basic and Clinical characteristics of the patient

Patient characteristics		Number (n)	Percentage (%)
Age group	1. 18-65 years	50	51
	2. > 65 years	48	49
Mean (SD)		63.36(±12.16)	
Gender	1. Male	37	37.8
	2. Female	61	62.2
Duration of T2DM	1. ≤5 years	52	53.1
	2. >5 years	46	46.9
Random blood glucose	1. <200 mg/dL(controlled)	34	34.7
	2. >200 mg/dL (uncontrolled)	64	65.3
DM therapy while being treated	1. Insulin	72	73.5
	2. Combination insulin and oral antidiabetic	2	2.0
	3. Oral antidiabetic	24	24.5
Comorbidity	1. Not present	40	40.8
	2. Present	58	59.2
Type of comorbidity	1. Hypertension	26	26.5
	2. Kidney dysfunctions	29	29.6
	3. Liver dysfunctions	2	2.04
	4. Congestive heart failure	21	21.4
Length of hospitalization	1. < 7 days	19	19.4
	2. 7-14 days	41	41.8
	3. > 14 days	38	38.8

Description: SD: Standard deviation; DM: Diabetes mellitus;

The majority of subjects received combination antibiotic therapy (67.3%), with 32.7% receiving a single antibiotic. The combination of ceftriaxone and azithromycin was the most widely used (Table III). After evaluating the appropriateness use of antibiotics using the Gyssen algorithm, it was found that 59.2% of subjects received ones according to the guidelines, while 40.8% did not. The non-appropriate use of antibiotics was spread across several categories (Table IV): 19.4% in category IVa (the antibiotic choice was not effective); 8.1% in category IIIa (duration of antibiotic use too long), where there is no evaluation of antibiotics after 3 days of use, while based on the guidelines clinical evaluation should be done within the first 72 hours of using antibiotics to see the clinical response of the patient, if there is clinical improvement then therapy can be continued and if there is no response or worsening then therapy can be changed based on culture results or based on empiric therapy guidelines. On In this study a number of 7 subjects used antibiotics for too long because it is possible that evaluation and consideration of antibiotic replacement have not been carried out based on the patient's clinical response. Based on records of the development of

the patient's clinical condition listed in the subject's medical record did not give a good clinical response to antibiotics and 1 subject experience worsening condition, namely experiencing acute respiratory failure. Meanwhile 1 subject who have received empiric antibiotic therapy have not improved conditions and based on the results of culture (3rd day) found *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*, but the changes in antibiotic therapy were not carried out until the 7th day. According to PPAB RSCM recommendations for antibiotic therapy for the pathogen *Pseudomonas aeruginosa* is a broad spectrum beta-lactam and a macrolide or fluoroquinolone (PPRA RSCM, 2017); 1% in category IIIb (duration of antibiotic use too short) where antibiotics are changed on the second day without any consideration of clinical conditions that require antibiotics to be changed; 8.1% in category IIa (incorrect dose) where dose adjustment has not been carried out for patients with renal failure who use antibiotics whose main elimination (80%) is in the kidney; and 4.1% in category IIb (inappropriate interval between doses) where there are patients who receive beta-lactam antibiotics which are antibiotics with time dependent activity.

Table II. Clinical aspects of CAP patients on admission

Subject characteristics		Number (n)	Percentage (%)
Symptoms during admitted to the hospital	1. Breathlessness	79	80.6
	2. Cough with phlegm	57	58.2
	3. Fever (temperature $\geq 37.5$ °C)	34	34.7
	4. Loss of consciousness	21	21.4
Complications	1. Not present	66	67.3
	2. Present	32	32.7
Types of complications	1. Pleural effusion	12	12.2
	2. Sepsis	12	12.2
	3. ARDS (Acute Respiratory Distress Syndrome)	8	8.2
Degree of severity	1. Mild (score 0-1)	0	0
	2. Moderate (score 2)	68	69.4
	3. Severe (score $\geq 3$ )	30	30.6
	4. Causative bacteria (n=23)	0	0
Gram-positive :		7	21.2
1. <i>S. epidermidis</i>		3	10
2. <i>S. saproticus</i>		2	6.1
3. <i>S. aureus</i>		2	6.1
Gram-negative :		26	78.8
1. <i>A. baumannii</i>		4	12.1
2. <i>Acinetobacter iwoffii</i>		2	6.1
3. <i>E. Coli</i>		5	15.1
4. <i>Enterobacter</i>		1	3.0
5. <i>Klebsiella oxytoca</i>		1	3.0
6. <i>K. pneumoniae</i>		9	27.3
7. <i>P. aeruginosa</i>		4	12.1

Table III. Overview of the 5 days of antibiotic use

Antibiotic	Recommended dose	Dosing interval	route	Use of antibiotics	
				Amount (n)	Percentage (%)
<b>Single</b>				<b>32</b>	<b>32.7</b>
Ceftriaxone	2 g	Every 24 h	iv	8	8.2
Ampicillin sulbactam	1.5 g	Every 6 h	iv	9	9.2
Levofloxacin	750 mg	Every 48 h	iv	6	6.1
Meropenem	1 g/ 500 mg	Every 8 h	iv	5	5.1
Cefepime	2 g	Every 24 h	iv	4	5.1
<b>Combination</b>				<b>66</b>	<b>67.3</b>
Ceftriaxone/ Azithromycin	2 g/ 500 mg	Every 24 h	iv/p.o	32	32.6
Ceftriaxone/ Levofloxacin	2 g/ 750 gr	Every 24 h	iv/iv	18	18.36
Ampicillin sulbactam/Azithromycin	1.5 g/ 500 mg	Every 6 h/ every 24 h	iv/p.o	7	7.14
Ampicillin sulbactam+Levofloxacin	1 g/ 500 mg	Every 6 h/ every 24 h	iv/iv	1	1.0
Cefepime +Azithromycin				1	1.02
Meropenem + Levofloxacin				2	2.04
Cefepime + Levofloxacin				4	4.1
Cefoperazone + Levofloxacin				1	1.02
Amount				98	100

Description: iv: intravenous; p.o: per oral

Table IV. Evaluation of 5 days of antibiotic use based on Gyssen's algorithm

Category	Parameter	Evaluation	
		Yes	No
VI	Complete data	98	0
V	Antibiotics are indicated	98	0
IV a	The choice of antibiotic has been effective	77	19
IV b	The alternative is less toxic	77	0
IV c	Cheaper alternative	77	0
IV d	The spectrum is narrower	77	0
IIIa	The duration of administration is too long	8	72
IIIb	The duration of administration is too short	1	71
II a	The dosage is right	62	8
II b	The interval is right	58	4
II c	The route is right	58	0
I	Right time	58	0
0	In accordance/correct	58	0

Table V. Relationship of 5 days antibiotic use and clinical outcomes

Appropriateness of antibiotic use	Clinical outcomes		P	RR	95% CI
	Improved	Not yet improved			
Appropriate	41 (70.7%)	17 (29.3%)	0.010	1.663	1.119-2.473
Non-appropriate	17 (42.5 %)	23 (57.5 %)			

Note: Results are expressed in n (%) with a significance of p <0.05; RR: relative risk

Table VI. Effect of antibiotic appropriateness and confounding variables on patient clinical outcomes

Variable	Category	RR	95% CI	P
<b>Model 1</b>				
Antibiotic appropriateness	Appropriate	1.663	1.119-2.473	0.010
	Non-appropriate			
<b>Model 2</b>				
Antibiotic appropriateness	Appropriate	2.683	1.102-6.592	0.030
	Non-appropriate			
Degree of CAP	Moderate	2.989	1.138-7.846	0.026
	Severe			
Antibiotic onset	≤ 8 h	2.728	1.069-6.961	0.036
	>8 h			

Note: Significant with a p-value of <0.05. RR: relative risk

There are 2 patients with septic who received meropenem at 12 hour interval, according to PPAB recommendation the administration of meropenem for septic patient is every 8 hours (PPRA RSCM, 2017). Two other patients received ampicillin sulbactam at 12 hour intervals. Determination of this interval is not effective because ampicillin sulbactam has a half-life about 1 hour and will completely eliminated in about 5 hours in an unchanged form through urine. Based on pharmacokinetic profile ampicillin

sulbactam should be given at 6-8 hour intervals. According to PDPI guideline, the recommended interval of ampicillin sulbactam for CAP patient is 4 times a day.

The proportion of subjects who experienced clinical improvement was 70.7% in the group of patients who received appropriate antibiotics and 42.5% in the group who did not receive them according to the guidelines. The results of this study indicate that the appropriateness of antibiotic use according to the guidelines

significantly enhanced clinical outcomes in the CAP patients with T2DM, by 1.7 times, with  $p = 0.01$  (Table V).

After analysis using the Chi-square method, the results show that gender, degree of CAP, duration of T2DM, and antibiotic onset had a significance value of  $p < 0.25$  (Table VI). All these independent variables were analyzed in a multivariate using logistic regression methods, and the results show that the use of appropriate antibiotics significantly improved the clinical condition of CAP patients with T2DM by 2.7 times (RR 2.683, 95% CI: 1.102-6.592,  $P = 0.030$ ) after controlling for the variables of the degree of pneumonia, and antibiotic onset (Table VI).

In this study, most of the subjects (62.2%) were female. This is in line with a study conducted in Turkey, which found that 57.4% of CAP patients with T2DM were female, compared to 42.6% men (Polat *et al.*, 2017). Epidemiological studies in the United States have also shown that the prevalence of CAP patients with DM is more common in women (52%) than men (48%) (Liu *et al.*, 2019). However, these findings are contrary to research in India, in which the number of male subjects (60%) was greater than that of female ones (40%) (Bhambar *et al.*, 2017), with almost the same proportion of subjects aged over 65 years (51%) and under 65 (49%). This is different to a study conducted in Spain, which found that 71.5% of community-acquired pneumonia patients with T2DM were over 65 years of age (Yacovo *et al.*, 2013).

Clinical manifestations of CAP can vary based on the patients' condition, the causative pathogen, and the severity of the disease. In this study, 80.6% of the participants experienced symptoms of shortness of breath, and 58.2% experienced ones of coughing with phlegm. Other symptoms that may be experienced by CAP patients include increased body temperature and pulse, shortness of breath, coughing with phlegm or no phlegm, and chest pains, while 20% of patients experience gastrointestinal-related symptoms such as nausea, vomiting, and diarrhea. In elderly patients (age > 65 years), the symptoms that arise can be different, namely in the form of decreased consciousness, gastrointestinal discomfort, and no fever, so that the diagnosis of pneumonia in elderly patients is often detected slowly (Mandell *et al.*, 2007).

CAP in patients with T2DM is more likely to cause complications than in non-DM patients (Ljubic *et al.*, 2005). Complications experienced by

those in this study were pleural effusion (12.2%), sepsis (12.2%), and ADRS (Acute Distress Respiratory Syndrome) (8.2%), which caused the patient to die. A study in Spain involving 516 community-acquired pneumonia patients with DM found that 12.8% had pleural effusions, and 9.3% had sepsis (Yacovo *et al.*, 2013). In addition, a study in India found that the mortality rate in pneumonia patients with DM (24%) was higher than in those without DM (10%), and that the prevalence of complications was also higher in patients with DM (36%) than those without (20%) (Bhambar *et al.*, 2017).

In this study, the most common isolates found were gram-negative bacteria (78.8%) and *Klebsiella pneumoniae* (27.3%), which are the most common gram-negative bacteria found. *Klebsiella pneumoniae* is the most common pathogen found in the sputum of community pneumonia patients with T2DM (Saibal *et al.*, 2012). CAP is caused by gram-negative bacteria, which is more difficult to treat because their structure, which has an outer membrane, making it difficult for antibiotics to reach them (Exner *et al.*, 2017).

The results of this study indicate that the appropriateness of administering 5 days of antibiotics based on the evaluation using the Gyssen algorithm significantly increased the clinical improvement of CAP patients with T2DM by 1.7 times ( $p = 0.01$ ). This result is different from the research conducted by Rumende *et al.*, who found that the use of appropriate antibiotics based on evaluation using the Gyssen algorithm did not have a significant effect on the clinical improvement of CAP patients (Rumende *et al.*, 2019). The occurrence of improvement is one parameter of the success of CAP therapy. Most of the patients showed clinical improvement within the first 72 hours after antibiotic administration, whereas 6-15% showed no response. Some of the factors that can cause the failure of therapy are misdiagnosis, patient factors such as errors in determining the severity or degree of the pneumonia, drug factors, and pathogenic factors (PDPI, 2014).

In this study, the appropriate use of antibiotics within 5 days based on the evaluation using Gyssen's algorithm significantly enhanced the clinical condition improvement of CAP subjects with T2DM by 2.7 times after controlling for the variables of the degree of community-acquired pneumonia and antibiotic onset. Research in Croatia found that the severity and any delay in the first antibiotic administration of more than 8 hours increased the

length of hospitalization of patients (Bader *et al.*, 2016). A study in England also found that administering the first antibiotic within 4 hours reduced the incidence of mortality (Daniel *et al.*, 2015).

The authors realizes that there are still many limitations in this research including the relatively small number of samples and data collection carried out systematically retrospectively sourced from secondary data through patients medical record. So the completeness of this research data is very dependent on recording medical records carried out by health workers involved in current care CAP patients with type 2 DM were hospitalized. Value data HbA1C which better describes glycemic control cannot be obtained directly complete, as well as data from culture results to determine pathogens mreason. Another data that is difficult for authors to obtain is data on side effects antibiotics. These data can be obtained more fully by conducting a prospective study. In this study, there is a possibility of bias due to deviations in the relationship between appropriateness of antibiotics and clinical outcomes by other factors (confounders) namely age, gender, severity of CAP, duration of DM, comorbidities and antibiotic onset. These confounders were controlled by stratification and performed multivariate analysis using logistic regression.

The results of this study cannot represent the condition of CAP patients with DM in Indonesia because it is only carried out in one hospital. The same study in different hospitals can be carried out so that in the end conclusions can be drawn that describe the condition of CAP patients with DM and the effect of appropriate use of antibiotics on clinical improvement of CAP patients with type 2 DM.

## CONCLUSIONS

Based on the results of the study it can be concluded that the use of appropriate antibiotics according to clinical practice guidelines in community-acquired pneumonia patients with Type 2 DM significantly enhanced clinical outcomes. The severity of CAP, and the time of the first antibiotic administration, were other independent variables that influenced patients' clinical outcomes.

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## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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