Profile of Antibiotic Use and Germs Map in Pneumonia Patients in Pulmonary Room at RSUD dr. Iskak Tulungagung)

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Abstract—Pneumonia is an infection of lung tissue caused by bacteria, fungi, viruses or parasites. Antibiotics is a major therapy in pneumonia. The aim of this study was to determine the amount of antibiotic use in DDD / 100 patient-days and to know the profile of germs map in pneumonia patients in Pulmonary Room Dr. Iskak Hospital, Tulungagung during January-June 2017. The design of this research is observational research method with retrospective data retrieval from patient medical record data and antibiotic usage data from Pharmacy Installation and microbiology culture result data of patient, then analyzed descriptively. The results showed the total amount of antibiotic in 130 unspecified pneumonia patients non ICU inpatient in Pulmonary Room Dr. Iskak Hospital, Tulungagung during January-June 2017 was 51.28 DDD/100 patient-days. The most antibiotic types are levofloxacin iv 40.14 DDD /100 patient-days and ceftriaxone 8.71 DDD /100 patient-days. The profile of the pneumonia-causing germs map cannot be determined because there is no data on microbiological culture test results from the patient.

Keywords—antibiotic, ATC/DDD, infection, levofloxacin, pneumonia

1. INTRODUCTION
Pneumonia is a lung tissue infection caused by bacteria, fungi, viruses or parasites [1]. Pneumonia affects more than 450 million people per year and occurs in all parts of the world. Pneumonia is the main cause of death for all 4 million deaths (7% of the total world death) [2]. According to the 2013 Basic Health Research (Risksdas), it showed an increased in the prevalence of pneumonia in all ages from 2.1% in 2007 to 2.7% in 2013. Management of bacterial pneumonia with support and supportive treatment support [3].

The ability of antibiotics to overcome or prevent infectious diseases causes their use to increase extraordinary [4]. Excessive and irrational use of antibiotics raises various contradictions and is a global challenge for health supported by bacterial resistance to antibiotics [5][6]. Antibiotic resistance that improves antibiotic treatment becomes ineffective, increases patient morbidity and mortality and increases health care costs and prolongs the period of illness in the community thereby increasing the transmission of greater [7][8].

Indonesia is doing an effort to overcome the development of antibiotic-resistant bacteria, has been issued, among others, approving Permenkes No. 2406 of 2011 concerning General Guidelines for the Use of Antibiotics, formed the Infection Prevention and Control Program (PPI) team and connected the Minister of Health Regulation No. 8 of 2015 concerning the Antimicrobial Resistance Control Program (PPRA) in hospitals. Under this regulation every hospital in Indonesia must implement an Antimicrobial Resistance Control Program optimally. To appreciate the success of the Antimicrobial Resistance Program in hospitals, evaluation of antibiotic use is needed. One form of evaluation of antibiotic use in hospitals is by calculating the comparison of antibiotic use with the Daily Dose (DDD) / 100 patient-day method.

The choice of antibiotic type is ideally based on the results of the patient's microbiological examination or bacterial sensitivity test to antibiotics. From the results of receiving microbes through microbiological examination obtained germ map data or patterns of bacterial resistance to antibiotics. The presence of germ maps can be made as a reference for the use of antibiotics in hospitals so that antibiotic resistance can be controlled [5][9].

Most cases of infection in Dr. Hospital Iskak Tulungagung in the first semester of 2017 was pneumonia in the amount of 347 cases[10]. Increased use of antibiotics. Therefore, it is necessary to conduct research with the aim of studying the profile of antibiotic use and the profile of germs in pneumonia patients in the Lung Hospital Dr. Iskak Tulungagung.
2. Literature Review

Antibiotics have a significant contribution in limiting morbidity and mortality caused by infection with pathogenic bacteria. The ability of antibiotics to overcome or prevent infectious diseases by pathogenic bacteria causes their use to experience a tremendous increase [4][11]. Excessive and irrational use of antibiotics causes pathogenic bacteria to be able to develop themselves or gain the ability to withstand antibiotic attacks which results in a decrease in the effectiveness of antibiotics, increased morbidity and mortality and increased health care costs. The ability of bacteria to fight antibiotic attacks and gradual life is what is then called bacterial resistance to antibiotics [12][13].

Pneumonia is an infection in the bronchial end and alveoli which can be caused by various pathogens such as bacteria, fungi, viruses and parasites so that the lung becomes inflamed [14]. Bacterial resistance to antibiotics in pneumonia patients in a report on the results of a prospective cohort study in Barcelona (Spain) and Edinburgh (UK) shows that the prevalence of Multi Drug Resistance (MDR) pathogens in pneumonia patients admitted to hospital is 7.6% in Barcelona and 3.3% in Edinburgh [15].

Research on the use of antibiotics in pneumonia patients has been carried out before, but as far as the search has been carried out researchers have not there is research similar to the research that researchers do. The similar research is Kamal (2015) about Evaluation The Use Of Antibiotics in Patients Sukoharjo Hospital With Pneumonia in 2014. In this study did not analyze the amount of antibiotic use in DDD / 100 patient-days. This research is different from previous studies, the difference can be seen in the subjects, places and methods studied about pneumonia disease [16].

The other research showed by Zhukova et al (2017) about Analysis of the efficiency of antimicrobial treatment for community-acquired pneumonia in clinical practice. The difference with this research can be seen in subjects, places and results, in this study did not analyze the germ map [17].

3. Research Method

This design of the research was an observational descriptive study with retrospective data collection on pneumonia patients who received antibiotics and were hospitalized in the Pulmonary Room of Dr. Hospital. Iskak Tulungagung from January to June 2017. The data used are patient medical record data and records of antibiotic use from the Pharmacy Installation as well as data on the results of testing of microbiological cultures of patients. Respondents in this study were non ICU hospitalized pneumonia patients who received antibiotics in the Pulmonary Room of Dr. Hospital. Iskak Tulungagung on January-June 2017 that meets the inclusion criteria is adult patients, patients with or without germ culture tests, patients with or without comorbidities. The exclusion criteria were patients admitted to the ICU, patients forcibly returning and patients with incomplete medical record records. For sample profiles of germs that cause pneumonia follow the number of populations undergoing culture examination. The sample size in this study is all samples that meet the criteria. Analysis of data taken in the form of the characteristics of pneumonia patients based on funding, gender, age of the patient, route of administration and diagnosis of comorbidities. Measurement of the number of antibiotics used by patients with ATC / DDD standards which is a standard measurement of the quantity of antibiotics recommended by WHO. The calculation formula based on DDD / 100 patient-days is as follows [9]:

$$\text{DDD/100 patient days} = \frac{\text{Amount gram AB sold in a month}}{\text{Standart DDD WHO (g)}} \times \frac{100}{(\text{Population} \times 30)}$$

How to calculate antibiotic use for one month:

a. The amount of antibiotics (AB) sold is the amount of antibiotics sold in one month in the smallest units (tablets / vials / ampules / bottles).

b. WHO DDD according to ATC / DDD

c. Number 100 for 100 days of hospitalization.

d. Population: number of Hospital Bed Occupation Rate (BOR) beds in the same month.

e. Number of 30 days in one month.

In the profile of the germ data taken from the results of the culture include the type of bacteria and its sensitivity to antibiotics. All research data are analyzed descriptively presented in the form of tables and graphs.
4. Result and Discussion

Patients suffering from pneumonia in the Pulmonary Room at Dr. Hospital Iskak Tulungagung from January to June 2017 was diagnosed as 171 unspecified pneumonia patients. Based on the inclusion and exclusion criteria there were 130 patients who were subjected to the study. Management of therapy refers to non-ICU inpatient community pneumonia because the patient enters hospitalization diagnosed with pneumonia or suspect pneumonia, not pneumonia obtained at the hospital.

A. Characteristics of Pneumonia Patients

1) Based on Funding Sources

Based on observations of 130 pneumonia patients who received antibiotics, they were distinguished by funding from the Social Security Organizing Agency (BPJS) and the public (Table 1). Funding by BPJS consists of BPJS PBI (Contributing Aid Recipients) of 39 people (30%) and BPJS Mandiri (Non PBI) as many as 51 people (39%), so the total funding by BPJS is 69%. Patients with self-financing or general as many as 40 people (31%). These results indicate the number of patients using independent BPJS is higher than other funding sources. This has been in line with the government program regarding the implementation of national health insurance (JKN) through the health BPJS. With the BPJS program it is hoped that it will alleviate public health costs when needed [18].

Table 1. Characteristics of Pneumonia Patients in Pulmonary Room (January-June 2017) Based on Financing

| Months   | BPJS PBI | Non PBI | General | Other Assurance |
|----------|----------|---------|---------|-----------------|
| January  | 4        | 7       | 6       | 0               |
| February | 5        | 12      | 11      | 0               |
| March    | 6        | 7       | 5       | 0               |
| April    | 6        | 8       | 3       | 0               |
| May      | 10       | 12      | 8       | 0               |
| June     | 8        | 7       | 5       | 0               |
| Total    | 39       | 51      | 40      | 0               |
| Percentage | 30%   | 39%     | 31%     | 0%              |

2) Based on Gender

Based on the sex of 130 patients consisting of male patients as many as 78 people (60%) and female patients 52 people (40%) as in Table 2. Pneumonia patients are more commonly found in men than women because men are more often activities outside the home, smoking habits and lifestyle factors and environmental influences. Smoking habits change the shape of the airway tissue and the function of the cilia as a filter is damaged, the channel swells and narrows [19]. Another study with the same results was carried out in the Russian Nizhny Novogorod Hospital by Zhukova et al. of 117 CAP pneumonia patients consisting of 60% male patients and 40% female patients [17].

Table 2. Characteristics of Pneumonia Patients in Pulmonary Room (January-June 2017) Based on Gender

| Gender | Total (person) | Percentage |
|--------|----------------|------------|
| Female | 52             | 40%        |
| Male   | 78             | 60%        |
| Total  | 130            | 100%       |

3) Based on Age

Based on the analysis of the patient's age the highest results were obtained in the elderly age group/geriatric (≥ 65 years) as many as 51% of 130 patients (Table 3). These results are consistent with the statement from Dhar R (2012) that the prevalence of pneumonia sufferers increases 2-4 times in people over 60 years of age [20]. This is due to a decrease in the immune system along with increasing age, starting at the age of 50 years so it is easy to catch an infectious disease. Decreased pulmonary function with increasing age, decreased respiratory system flexibility due to increased chest wall stiffness facilitates lower airway infections including pneumonia [21].
Table 3. Characteristics of Pneumonia Patients based on Age

| Ages (Years) | Total (Persons) | Percentage |
|--------------|-----------------|------------|
| 20-39 (young)| 6               | 5%         |
| 40-54 (mature)| 20             | 18%        |
| 55-64 (adult)| 38              | 26%        |
| ≥ 65 (geriatric) | 66             | 51%        |
| Total        | 130             | 100%       |

Note: Age limits according to Statistics Indonesia

4) Based on Giving Routes

The antibiotic route is given to patients parentally and orally. All patients received 100% parenteral antibiotics. There were 4 patients receiving oral antibiotics of 3.08% in addition to getting parenteral antibiotics. Antibiotics are dominated by parenteral dosage forms influenced by the condition of patients who must immediately get treatment for eradication or inhibition of growth of germs that cause infection. In addition to providing a rapid effect the form of parenteral dosage form, it can be given to unconscious patients, patients in a deteriorating clinical situation / emergency, or cannot be given orally. This is in accordance with the results of the study of Cyric JM and James E (2014) which reported that the majority of hospitalized patients with infections will start from parenteral treatment for 2-3 days and will be followed by oral treatment for the remainder of the treatment [22]. In patients with pneumonia in the Pulmonary Room generally changes / switches to parenteral drugs orally are carried out on day’s 3-5 hospitalizations or when patients are discharged from the hospital (KRS). The faster the transition from parenteral to oral is, the lower the swamp day in the hospital, reducing the cost of treatment and minimizing the side effects of injection action in patients [23].

5) Based on the Diagnosis of Co-Diseases

Of the 130 patients studied there were 45 patients (34.62%) diagnosed with pneumonia without comorbidities and 85 patients (65.38%) diagnosed with pneumonia with comorbidities (Table 4). Other studies conducted by Kamal AM (2014) in Sukoharjo Hospital with a sample of 28 pneumonia patients, 28.14% of patients diagnosed with pneumonia without comorbidities and 67.85% diagnosed with pneumonia with comorbidities. The presence of comorbid factors or comorbidities can complicate therapy with antibiotics so that the duration of therapy becomes longer [16].

Table 4. Characteristics of Pneumonia Patients Based on Diagnosis of Concomitant Diseases

| Diagnosis | Concomitant Disease | Patients Total (Persons) | Percentage (%) |
|-----------|---------------------|--------------------------|----------------|
| Pneumonia | Without Concomitant Diseases | 45 | 34.62 |
| Pneumonia | With Concomitant Diseases | 85 | 65.38 |
| Total     | ADHF/HF             | 26 | 20.00 |
|           | Diabetes mellitus   | 20 | 15.38 |
|           | chronic obstructive pulmonary disease | 12 | 5.38 |
|           | Asthma              | 6  | 4.62 |
|           | pleural effusion    | 5  | 3.85 |
|           | CVA infark          | 3  | 2.31 |
|           | Lung Tumor          | 3  | 2.31 |
|           | Pulmonary tuberculosis | 3  | 2.31 |
|           | Dyspepsia           | 2  | 1.54 |
|           | Atrial Fibrilation  | 2  | 1.54 |
|           | Urinary Tract Infection (UTI) | 1 | 0.77 |
|           | Ca Mamae            | 1  | 0.77 |
|           | Allergic dermatitis | 1  | 0.77 |
B. Quantity of Use of Antibiotics

For the calculation of quantity of antibiotic use in pneumonia patients in the Pulmonary Room of Dr. Hospital Iskak Tulungagung during January-June 2017 the results of total antibiotic use were 51.28 DDD / 100 patient-days (Table 5). There are 4 classes of antibiotics consisting of 8 types of antibiotics. The largest group of antibiotics used was quinolones of 41.19 DDD / 100 patient-days. For the type of antibiotics dominated by levofloxacin IV of 40.14 DDD / 100 patient-days and ceftriaxone at 8.71 DDD / 100 patient-days. The highest use of quinolone antibiotics, this is in accordance with the working mechanism and indications of quinolones. The mechanism of action of the quinolone group is to inhibit bactericidal DNA-gyrate. The indications include urinary bladder infections, gastrointestinal infections, respiratory tract infections, bone and joint infections and skin and soft tissue infections. Good pharmacokinetic profiles, especially high bioavailability and long elimination half-lives. The oral form is well absorbed and some of its derivatives are also available in parenteral form so that it can be used to treat severe infections. For new types of fluoroquinolones (moxifloxacin, gemifloxacin and levofloxacin) have broader spectrum activity against gram-positive and gram-negative germs and atypical germs causing lower respiratory tract infections including pneumonia [1] [24].

The high use of levofloxacin for therapy in pneumonia patients is in accordance with therapeutic guidelines and guidelines. Management of therapy refers to community pneumonia because the patient enters hospitalization diagnosed with pneumonia or suspect pneumonia. Based on the Clinical Practice Guide of Dr. Iskak hospital SM Paru 2014, Guidelines for Diagnosis and Management in Indonesia from PDPI for community pneumonia (PDPI, 2014) and Infectious Diseases Society of America / American Thoracic Society Consensus Guidelines on Management of Community-Acquired Pneumonia in Adults (IDSA / ATS, 2007 ), management of patients with non-ICU inpatient pneumonia, fluoroquinolone respiration, levofloxacin (level 1 evidence) or combination betalactam with macrolides (level 1 evidence) [25].

The results of the Langtry HD and Lamb HM (1999) study show that levofloxacin is a broad-spectrum antibiotic, well distributed and reaches high levels in many tissues such as the lungs, skin and prostate. High oral bioavailability allows switching from intravenous to oral without dose adjustment. In patients with intravenous and / or oral levofloxacin administration pneumonia is superior to intravenous ceftriaxone and / or oral cefuroxime. The use of levofloxacin in respiratory tract infections by Streptococcus pneumonia is more active than ciprofloxacin or ofloxacin [24].

Another study regarding the quantity of antibiotic use in community pneumonia patients was carried out by Alifia N (2015) at Dr. Mintoharjo, Jakarta showed the results of using the most antibiotics were levofloxacin for 122 DDD / 100 patient-days [26]. Another study conducted in Nizhny Novgorod Hospital, Russia with a sample of 117 CAP pneumonia patients resulted in the highest use of ceftriaxone by 43.43 DDD / bed-days [17].

### Table 5. Quantity of Antibiotic Use of Pneumonia Patients in Pulmonary Room DDD / 100 patient-days (January-June 2017)

| Groups                  | ATC Code   | Antibiotic Name | DDD/100 patient-days | Total DDD/100 patient-days |
|-------------------------|------------|-----------------|-----------------------|----------------------------|
| Quinolones              | J01MA12    | Levofloxacin IV | 40,14                 |                            |
|                         | J01MA02    | Ciprofloxacin IV| 1,05                  |                            |
| Generation 3 cephalosporins | J01DD04    | Ceftriaxone 1g Inj | 8,71            | 9,71                        |
|                         | J01DD01    | Cefotaxime 1g Inj| 0,91                  |                            |
|                         | J01MA02    | Cefadroxil 500mg | 0,06                  |                            |
|                         | J01DE01    | Cefixime 100 mg  | 0,03                  |                            |
| Betalactam + betalactamase inhibitor | J01CR01    | Cinam Inj       | 0,32                  | 0,32                        |
| Carbapenem              | J01DH02    | Meropenem 1g Inj | 0,06                  | 0,06                        |
|                         |            |                 |                       | Total 51,28                 |
C. Profile of Germ Map Causes of Pneumonia
This study has not been able to determine the profile of the germ map that causes pneumonia because there are no data on the results of microbiological testing of patients with pneumonia. Both from the patient's medical record data and search results from the Microbiology Laboratory, there were no culture data for pneumonia patients who were the subjects of the study found during the period of January-June 2017. Based on information from the Microbiology Laboratory at Dr. Hospital. Iskak Tulungagung is only around July intensively conducting a culture test.

5. Conclusion
Amount of antibiotic use in 130 unspecified pneumonia patients non ICU inpatient in Pulmonary Room of Dr. Iskak Tulungagung Hospital for the January-June 2017 period is 51.28 DDD / 100 patient-days. The largest group of antibiotics used was quinolones of 41.19 DDD / 100 patient-days. The most types of antibiotics used were levofloxacin iv of 40.14 DDD / 100 patient-days and ceftriaxone of 8.71 DDD / 100 patient-days.

Profile of germs causing pneumonia in the Pulmonary Room of Dr. Iskak Tulungagung Hospital for the period of January-June 2017 cannot be determined because there are no data on the results of microbiological culture testing from patients.

6. Suggestions
Based on the research results obtained, suggestions that can be given are:
Sputum culture testing is needed in patients with pneumonia to determine the bacteria that causes infection and antibiotic sensitivity so that using of antibiotics is more optimal and rational and can know the profile of germs that cause infection.
Need further research to evaluate antibiotic prescribing by considering germ map and bacterial sensitivity to antibiotics.

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