Causative Microorganism of Pneumonia and Antibiotics Sensitivity Pattern on Teaching Hospital in Surakarta, Indonesia

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***Abstract*—Pneumonia still remains as a significant cause of mortality due to the virulence factors of the causative microorganism. The causative microorganism profile of pneumonia differs from one region to another. This study aimed to identify the etiology of pneumonia and bacterial sensitivity pattern to antibiotics. A cross-sectional study was conducted based on reports of bacteria isolates from the ward of Teaching Hospital, from May to October 2018. Microbiological isolates were collected from sputum patient. Identification of all causative microorganisms was performed by standard microbiologic methods. Susceptibility testing was performed using disk diffusion method. Among 47 patient, the subject was dominated by a male (51%) with mean age was 57±2.22. Streptococcus pneumoniae was the most common causative agent (28%) followed by Candida sp. (21%), Pseudomonas aeruginosa (8.8%), Klebsiella pneumoniae (8.8%) and Streptococcus viridans(8.8%). S pneumonia was sensitive to Levofloxacin (81.25%); Ceftriaxone (62.5%); and Ampicillin (75%). Cefoperazone was the only antibiotics showed high effectiveness against P. aeruginosa (83.3%) and K. pneumoniae (100%). Antibiotics susceptibility pattern surveillance should be done periodically.**

Keywords—antibiotics, causative microorganism, pneumonia, sensitivity pattern

I. INTRODUCTION

Pneumonia is an infection as a result of the invasion of an infective microorganism in the lower respiratory tract. World Health Organization (WHO) states that pneumonia was the third leading cause of death globally in 2016 and considers as one of the top causes of death in Indonesia [1,2]. In the US, about 50,000 adults die per 1 million cases hospitalized with pneumonia [3]. The number of pneumonia's prevalence in Indonesia was increased, from 2.1% (2007) to 2.7% (2013) [4].The prevalence of pneumonia had declined in 2017 to 1.6% but it had increased again in 2018 [2,5]. The CAP incidence was 988 cases per 100,000 discharges in Indonesia [6]. Globally, pneumonia still remains as a significant cause of mortality due to the virulence factors of the causative microorganism along with the increasing age of the population [7].

Pneumonia was caused by bacterial infection, mostly. The increasing number of multidrug-resistant bacteria, difficult-to-treat microorganisms, and the emergence of new pathogens are a major problem for clinicians when deciding antimicrobial therapy. The adequacy of initial antimicrobial therapy is a key factor for prognosis in pneumonia. The study by Martin et al [8] reported that 35% of cases CAP were caused by MDR pathogens. Streptococcus pneumoniae is the major bacterial pathogen causing Community-Acquired Pneumonia [9–11]. Streptococcus pneumoniae resistance varies by geographic location and previous antibiotic exposure history. The Tigecycline Evaluation and Surveillance Trial have found that there was an uplift of Streptococcus pneumoniae macrolide resistance in Asia to the current level of 70.1% in 2009. Almost all S. pneumoniae were recorded as resistant to erythromycin in Taiwan (98%) [12]. A study reported that 90.2% of Streptococcus pneumoniae has resistance to a macrolide. Meanwhile, the highest level of Streptococcus pneumoniae resistance was due to cephalosporin third generation [13].

The selection of antibiotics has to be based on the profile of the local bacterial etiology and antibiotic susceptibility. The causative microorganism profile of pneumonia differs from one region to another. Hence, having the causative microorganism profile of a pneumonia infection is important. This study aimed to identify the etiology of pneumonia and bacterial sensitivity pattern to antibiotics.

II. METHODS

A. Patient Setting

A cross-sectional study was conducted based on reports of bacteria isolates from the ward of Teaching Hospital, from May to October 2018. It is a secondary care and teaching hospital with 105 beds, which was located in Surakarta Central Java, Indonesia. Adult patients were admitted to hospitalized due to pneumonia or suspect pneumonia were eligible. Clinical criteria of the patient were tachypnea (RR>20x/min), tachycardia(HR>100x/min), hypoxemia (PaO2 <80 mmHg), radiological pulmonary infiltrate examination. The severity level of pneumonia patient was assessed using Pneumonia Severity Index (PSI). Microbiological isolates were collected from sputum patient. Identification of all causative microorganisms was performed by standard microbiologic methods. Susceptibility testing was performed using disk diffusion method.

The study was approved by Health Research Ethics Committee dr. Moewardi General Hospital, School of Medicine Universitas Sebelas Maret No. 442/IV/HREC/2018. Informed written consent was obtained from all participants at time of recruitment.

III. RESULT

A. Patient Characteristic

During the study period, a total of 47 consecutive samples were identified. Among 47 patient, the mean age was 57±2.22 years with a range from 19 until 91 years. It was almost close to elderly. Based on table 1, patient was dominated by a male (51%). It was related to environmental factors, such as smoking exposure which was more common in men in Indonesia. Previously study reported that male and elderly was a risk factor of pneumonia, mortality also increases by age [14,15].

Most of the subjects were moderate risk of pneumonia. Severity level was due to the mortality risk of patient. Moreover, presence of comorbidities also associated with mortality[15]. The risk factor of pneumonia was elevated in patient of chronic disease. Pneumonia may exist concomitantly with another pulmonary disease such as COPD, TB, and Asthma. In this study, TB was the most underlying disease. Cohort study showed that pulmonary tuberculosis patient has a higher risk (HR:2.14;95%CI: 1.96–2.32) of developing pneumonia[16].

TABLE I. CHARACTERISTIC OF RESEARCH SUBJECT

Age (years)	
< 65	66%
≥ 65	34%
Sex (%) :	
Female	49
Male	51
Severity level based on PSI score	
Low risk	30.6
Moderate	52.7
High risk	16.7
Comorbidities (%)	
pulmonary tuberculosis (TB)	19.1
COPD	12.8
Asthma	6.4
Hypertension	4.2
Diabetes Mellitus	4.2
Chronic Kidney Disease	2.1

B. Causative Organism

TABLE II. MICROBIAL ETIOLOGY OF PNEUMONIA DETECTED FROM SPUTUM SPECIMEN

Microorganism (N=57)	**Species**	**Frequency (%)**
Gram positive	*Streptococcus pneumoniae*	16 (28)
	Enterococcus sp.	2 (3.5)
	Staphylococcus aureus	1 (1.8)
	Streptococcus pyogene	1 (1.8)
	Staphylococcus epidermidis	1 (1.8)
	Kocuria kristinae	1 (1.8)
	Streptococcus viridans	5 (1.8)
Gram Negative	*Klebsiella pneumoniae*	5 (8.8)
	Enterobacter aerogenes	3 (5.3)
	Acinetobacter sp.	1 (1.8)
	Citrobacter sp.	2 (3.5)
	Pseudomonas aeruginosa	5 (8.8)
	Escherichia coli	2 (3.5)
Yeast	*Candida sp.*	12 (21)

Table 2 shows the causative organism of pneumonia cases. The number of microorganisms was different from the number of the subject because there were some patients were infected by two organisms, seen on table 3. In this study, most cases were caused by a bacterial infection (79%). As we know that S.pneumoniae was identified as the most common CAP-causing pathogen worldwide, this study also reported that most of the isolates were S.pneumoniae (28%). In Asia country, S.pneumoniae was the most prevalent bacteria in CAP patient [17]. Study in Europe and the United State showed that about 30-35% of cases were caused by S pneumoniae [18].

Besides S.pneumoniae, this study also found other Gram-positive bacteria (Streptococcus viridans) as a causative agent. Viridans usually omit as etiology of pneumonia because normally, it is found in the upper respiratory tract. Antibiotics overuse may cause transformation of non-pathogenic agent increase their virulence [19].

Pseudomonas aeruginosa and Klebsiella pneumoniae were associated with the severe clinical manifestation of CAP. It was commonly found in CAP patient that admitted to Intensive Care Unit (ICU). Study in another hospital in Indonesia stated that P aeruginosa and K. pneumoniae was two of the most frequently isolated bacteria in ICU [20]. P aeruginosa commonly found in a patient with lung disease comorbidities or used antibiotics frequently[21]. Although rare, P aeruginosa was also found in previously healthy individuals that rapidly progress to fatal cases [22]. Difficulty to treat was due to its resistance to antibiotics used [23].

Beside pathogen organism, some normal microbial flora such as Staphylococcus epidermidis, also reported as an isolate in sputum culture. Staphylococcus epidermidis was known as epithelial microflora in human skin that doesn't produce aggressive virulent. However, it can developed as an opportunistic pathogen that causes most of the nosocomial infection [24].

Despite of mono-infection, some cases were also caused by polymicrobial infection. Table 3 shows a combination of the causative agent in pneumonia. Most of the cases were

caused by Candida sp. It was normal microbial flora of human that often found in respiratory secret of mechanically ventilated patient. However, it didn't have clinical effect significantly because it just represents colonization instead of infection [25].

TABLE III. MIX INFECTION AGENT IN PNEUMONIA

Microorganism 1	Microorganism 2	Frequency (%)
Candida sp	*Pseudomonas aeruginosa*	1 (1.8)
	Streptococcus pyogene	1 (1.8)
	Streptococcus pneumoniae	1 (1.8)
	Enterococcus sp.	1 (1.8)
	Kocuria kristinae	1 (1.8)
	Streptococcus viridan	1 (1.8)
	Citrobacter sp.	1 (1.8)
Klabsiella pneumoniae	*Streptococcus pneumoniae*	2 (3.5)
Enterobacter aerogenes	*Streptococcus pneumoniae*	1 (1.8)

The two of the subject [47] were infected by Gram-negative bacteria (Klebsiella pneumonia) and Gram-positive bacteria (Streptococcus pneumoniae) concomitantly. Klebsiella pneumonia was found as bacterial etiology in many cases of community-acquired pneumonia in some Asian country and associated with a high mortality rate [17]. It was associated with multidrug resistance [20].

C. ANTIBIOTICS SENSITIVITY PATTERN

Commonly, empirical antibiotics were given to the initial treatment of pneumonia patient. Therefor, surveillance of sensitivity pattern was important to do periodically. It was beneficial to guide the clinician to choose antibiotics appropriately. The proper antibiotics not only important to ensuring outcome but also to avoid multidrug resistance cases.

Sensitivity pattern of S.pneumoniae to some antibiotics was shown in figure 1. The highest sensitivity level of antibiotics was Levofloxacin (81.25%) followed by Ampicillin (75%) and Ceftriaxone (62.5%). S pneumoniae were reported to be moderate to high resistance against Penicillin in another Asian country [21,26]. However, in this study, it still has good sensitivity level, in spite of infrequently uses.

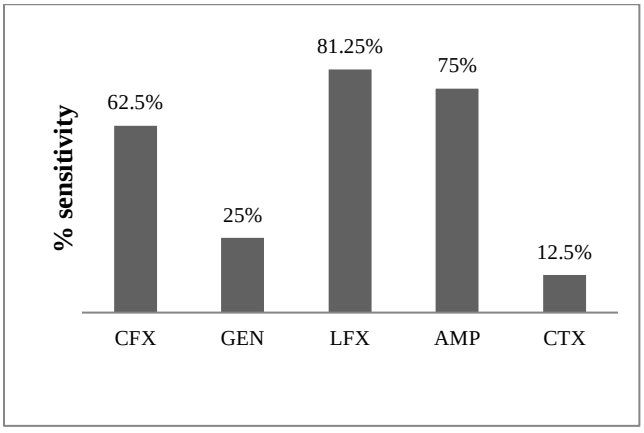

Figure 1. Sensitivity pattern of *Streptococcus pneumoniae (n=16)* (CFX: ceftriaxone,GEN:gentamicin; LFX: levofloxacin; Co-AMOX: Co Amoxiclave; AMP: Ampicilin; CTX: Cotrimoxazol)

Figure II showed sensitivity pattern of antibiotics to P aeruginosa and K.pneumoniae. Some Cephalosporine third generation such as Ceftazidime, Cefotaxime, and Ceftriaxone was less sensitive to P.aeruginosa.While the sensitivity of bacteria to Cefoperazone was high relatively (83.3%). Not only to Cephalosporin, but P. aeruginosa also showed less active to other antibiotics such as levofloxacin, gentamycin, ampicillin, co-amoxiclav and cotrimoxazole. This result confirms the other previous study [27–29]. P aeruginosa has some kind of drug resistance mechanism such as increased expression of an active efflux pump system, biofilm formation, suppression of enzyme production and decreased expression of outer membrane proteins. A study revealed that a high intensity of use antibiotics related to resistance rate[28]. In Indonesia, Cephalosporins third generation widely used [30].

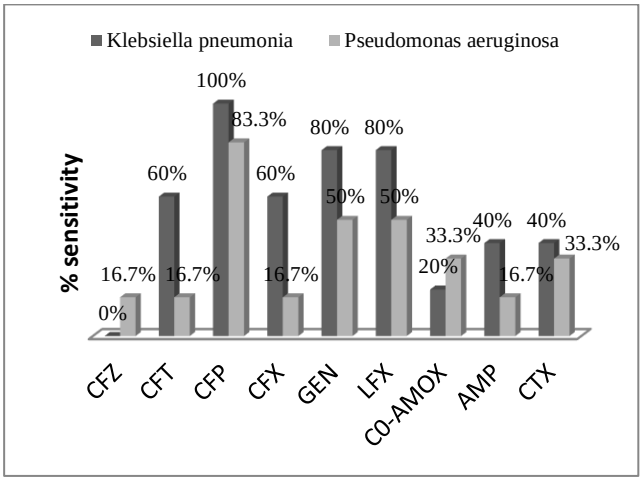

Figure II. Sensitivity patern of *Klabsiella pneumoniae* (n=5) *and Pseudomonas aeruginosa* (n=5) (CFZ:ceftazidim;CFT cefotaxim; CFP:cefoperazone, CFX: ceftriaxone,GEN:gentamicin; LFX: levofloxacin; Co-AMOX: Co Amoxiclave; AMP: Ampicilin; CTX: Cotrimoxazol)

Based on figure II, Cefotaxime, Cefoperazone, Ceftriaxone, Gentamycin, and Levofloxacin showed high sensitivity level to against K pneumonia. Cefoperazone was the most effective antibiotics against K.pneumonia. This result different from a study in ICU of another hospital in Indonesia that found K. pneumoniae showed a high rate of resistance to third-generation cephalosporins (20). It caused by the profile of bacterial sensitivity to antibiotics differs from one region to another. So that, periodically study on microorganism profile and its sensitivity pattern was noteworthy.

This study has some limitation such as a limited number of the subject involved due to the time period of data collection, the type of antibiotics tested for sensitivity has not yet represented all antibiotic classes and has not yet evaluated the effectiveness of antibiotics on patients. Future study is expected to involve more sample and add an evaluation of antibiotics effectiveness.

IV. CONCLUSION

Streptococcus pneumoniae was the most common causative agent (28%) followed by Candida sp. (21%), Pseudomonas aeruginosa (8.8%), Klebsiella pneumoniae (8.8%) and Streptococcus viridans (8.8%). S pneumonia was sensitive to Levofloxacin (81.25%); Ceftriaxone (62.5%); and

Ampicillin (75%). Cefoperazone was the only antibiotics showed high effectiveness against P aeruginosa (83.3%) and K.pneumoniae (100%).

CONFLICT OF INTEREST

The authors declare that no conflict of interest.

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