Original Article

Antibiotic Resistance in Sepsis Patients: Evaluation and Recommendation of Antibiotic Use

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Abstract

Background: The appropriate selection of empirical antibiotics based on the pattern of local antibiotic resistance can reduce the mortality rate and increase the rational use of antibiotics. **Aims:** We analyze the pattern of antibiotic use and the sensitivity patterns of antibiotics to support the rational use of antibiotics in patients with sepsis. **Materials and Methods:** A retrospective observational study was conducted in adult sepsis patient at one of Indonesian hospital during January-December 2011. Data were collected from the hospital medical record department. Descriptive analysis was used in the processing and interpretation of data. **Results:** A total of 76 patients were included as research subjects. Lung infection was the highest source of infection. In the 66.3% of clinical specimens that were culture positive for microbes, *Klebsiella pneumoniae, Escherichia coli, Staphylococcus hominis* were detected with the highest frequency. The six most frequently used antibiotics, levofloxacin, ceftazidime, ciprofloxacin, cefotaxime, ceftriaxone, and erythromycin, showed an average resistance above 50%. **Conclusions:** The high use of antibiotic with a high level resistance requires a policy to support its rational use. Local microbial pattern based on site infection and pattern of antibiotics sensitivity test can be used as supporting data to optimize appropriateness of empirical antibiotics therapy in sepsis patients.

Keywords: Antibiotic resistance, Bacteremia, Sepsis, Systemic infection

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Introduction

Sepsis is a systemic infection that can lead to complications and death.[1] World-wide, 13 million people develop sepsis each year, and as many as 4 million people have died.[2] In 1996, there were 4.774 patients admitted to a teaching hospital in Surabaya, Indonesia, and 504 patients were diagnosed as having sepsis, with a mortality rate of 70.2%.[3] In a study at a teaching hospital in Yogyakarta, Indonesia, there were 631 cases of sepsis in 2007, with a 48.96% mortality rate.[4] A global effort is needed to improve the therapeutic management of sepsis because of its high prevalence and mortality rate.[2]

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The therapeutic management of sepsis, including septic shock, requires a comprehensive and systematic approach that includes a diagnostic method, the initiation of empirical antibiotic use and administration of supportive therapy.[5] Empirical antibiotic use is needed to eradicate the microbe that causes sepsis. Empirical antibiotic therapy must also consider the site of infection, the common pathogen that caused sepsis and antibiotic sensitivity based on local patterns of antibiotic resistance.[1] Failed to define the source of infection will potentially lead to wrong pathogen identified, and will also lead to inappropriate antibiotic selection.[1] The global escalation in both community- and hospital-acquired antimicrobial-resistant bacteria is increasingly compromising effective antimicrobial therapy, particularly when it comes to empiric antimicrobial selection.[6] The appropriate use of an empirical antibiotic is critical to decrease the mortality rate of sepsis[1] and should be started within 1-2 h after the diagnosis of severe sepsis.[7]

In this study, we analyzed the pattern of antibiotic use in septic patients and the pattern of microbial resistance based on the results of various cultures of microbial specimens from the sepsis patients. The information gained will be critical as a reference for pathogen identification, selection of empirical antibiotic therapy, and policies to control antibiotic resistance, especially in sepsis patients.

Materials and Methods

A retrospective observational study was conducted in a hospital in Bandung, Indonesia during May to August 2012. Adult patients aged 18-59 years, who were diagnosed with sepsis when admitted to the hospital from January 1st to December 31st, 2011, met the inclusion criteria for the study. The patients with incomplete information of antibiotic use were excluded. The data were collected from the medical records department of the hospital, including the patient identity, diagnosis, co-morbidities, source of infection, results of microbial culture, results of antimicrobial sensitivity testing, antibiotic use, length of stay and clinical outcome. The level of antibiotic resistance was obtained from the results of the microbial cultures and antibiotic sensitivity testing that were conducted at the time of hospitalization from the subject population. The data of antibiotic use were obtained from the medical records of the subject population.

Culture and sensitivity test procedures were based on the principles of test that published by World Health Organization.[8] Sterile specimen such as blood and pleura fluid, processed by using two medium enrichment (tryptic soy broth and brain heart infusion), then incubated with BacT/ALERT® instrument. The specimens which non-steril, such as sputum, pus, and swab were not processed with enrichment medium and incubatation process by BacT/ALERT® instrument, but directly to the next step incubation. The next step was incubation process with two different medium (MacConkey agar and Blood agar) in the temperature 35-37°C for 18-24 h. Colonies from the each medium isolated and processed with the Vitek 2 Compact® automated instrument to identified microbe and susceptibility test to antibiotics. Manual method was using to anticipate the error of automatic method with modified Kirby Bauer method.[8] The determination of antibiotics types and sensitivity level of antibiotics in the susceptibility test were based on CLSI standard.[9] No growth in the inoculated blood culture media indicated a negative result. Determination of contaminants or pathogens from the microbial results was based on the clinician's decision by considering of infection source, clinical condition and microbial results that was not performed in this study.

This study was approved by Ethics Committee of Faculty of Medicine Universitas Padjadjaran, and also ethics committee of Hasan Sadikin Hospital, Indonesia. Descriptive analysis was used in the processing and interpretation of data.

Results

Characteristics of the subject population

A total of 192 patients, 103 males and 89 females, were diagnosed with sepsis during the study period, and 76 patients met the criteria for the study. The sepsis incidence rate was highest in the 55-59-year age range with 15 patients, followed by the 45-50-year age range with 14 patients. The incidence of sepsis was higher in females than males and the mortality rate from sepsis reached 53.95%. Comparing the mortality rate in males and females in the > 50 years age group, the study showed a higher mortality rate in males (40%) than in females (38.46%). In contrast, in the 15-50-year age group, the mortality rate in females (65.38%) was higher than in males (51.8%). There were 16 subject populations (21.05%) who got not recovered clinical outcomes. It's showed 15 subjects population had discharged against medical advice due to cost reasoning and 1 subject population transferred to other hospital.

Lungs infection, renal failure, malignancy, diabetes mellitus and intraabdominal infection is the highest co-morbidities in the subject population. In the lung infection groups, the major problem are hospital acquired pneumonia, community acquired pneumonia (CAP) and tuberculosis. The highest mortality showed in the subject population who got systemic lupus erythematous, hepatitis, meningitis, myocarditis, and human immunodeficiency virus infection. The characteristics of the subject population can be observed in Table 1.

Source of sepsis infection

There were 6 sites of infection that developed into sepsis. A total of 5 patients had sepsis with multiple infections. Lungs infection (49%) were the most common source of infection for sepsis in the subject population, followed intraabdominal (20%), skin and soft-tissue (11%), unknown resource (11%), urinary tract (8%), then central nervous system (1%).

Pattern of microbial culture and antimicrobial susceptibility test

Microbial cultures of blood, sputum, a wound swab, pus, abscess, feces, ascites fluid, and urine from each patient were performed. A total of 78 microbial cultures ($n = 78$) were conducted in the subject population, resulting in

Table 1: Characteristics of the subject population (*n*=76)

Characteristics	Outcomes			Unknown (%)	Total (%)
	Recovered (%)	Died (%)	Not recovered (%)		
Gender					
Male	12 (32.43)	19 (51.35)	6 (16.22)	0 (0)	37 (48.68)
Female	6 (15.38)	22 (57.89)	10 (25.64)	1 (2.56)	39 (51.32)
Ages (years)					
15-50	13 (24.07)	30 (55.55)	10 (18.51)	1 (1.85)	54 (71.05)
>50	5 (22.72)	11 (20)	6 (27.27)	0 (0)	22 (28.95)
Co-mordibities					
Lung infection	6 (21.42)	15 (53.57)	6 (21.43)	1 (3.57)	28 (22.58)
Renal failure	3 (13.63)	12 (54.55)	6 (27.27)	1 (4.54)	22 (17.74)
Malignancy	3 (21.43)	6 (42.86)	5 (3.57)	0 (0)	14 (11.29)
Diabetes mellitus	4 (33.33)	6 (50)	2 (16.6)	0 (0)	12 (9.68)
Intrabdominal infection	2 (16.66)	6 (50)	4 (33.33)	0 (0)	12 (9.68)
Hypertension	4 (40)	1 (10)	5 (50)	0 (0)	10 (8.06)
Cardiovascular disesase (non-infection)	1 (25)	2 (50)	1 (25)	0 (0)	4 (3.23)
Systemic lupus erythematosus	0 (0)	3 (100)	0 (0)	0 (0)	3 (2.42)
Urinary tract infection	2 (66.66)	0 (0)	1 (33.33)	0 (0)	3 (2.42)
Hepatitis	0 (0)	3 (100)	0 (0)	0 (0)	3 (2.42
Asma	1 (50)	1 (50)	0 (0)	0 (0)	2 (1.61)
Meningitis	0 (0)	2 (100)	0 (0)	0 (0)	2 (1.61)
Malaria	2 (100)	0 (0)	0 (0)	0 (0)	2 (1.61)
Myocarditis	0 (0)	2 (100)	0 (0)	0 (0)	2 (1.61)
HIV	0 (0)	2 (100)	0 (0)	0 (0)	2 (1.61)
Cellulitis	0 (0)	1 (50)	1 (50)	0 (0)	2 (1.61)
Paroxysmal noctural hemoglobinuria	1 (100)	0 (0)	0 (0)	0 (0)	1 (0.81)

HIV: Human immunodeficiency virus

47 (66.3%) positive and 31 (33.7%) negative cultures. The results of the microbial cultures suggest that a patient could be infected by more than one microbe. There were 15 organisms detected by microbial culture from the various specimens. *Klebsiella pneumoniae, Escherichia coli, Staphylococcus hominis, Candida albicans* and *Candida non-albicans* were the organisms most frequently detected by microbial culture. The other culture results were limited to show gram stain features and features of an acid fast stain. The results showed two organisms that were acid-fast bacilli, 11 organisms that were gram-negative *cocci* and 12 organisms that were gram-positive *cocci*. The pattern of the organisms isolated from the various specimens can be observed in Table 2.

We conducted 342 susceptibility tests (n = 342) of 25 antibiotics. A total of 14 antibiotics showed a resistance level ≥ 50% and 9 antibiotics showed a resistance level of ≥ 50%. We did not conduct antibiotic susceptibility tests on all antibiotics. The antibiotic resistance pattern is shown in Table 3.

Pattern of antibiotic use

A total of 46 antibiotics were administered to the subject population with 255 episodes of use. The classes of antibiotics administered were penicillins, cephalosporins, carbapenems, quinolones, aminoglycosides, macrolides, glycopeptides, sulfonamides, polymyxins, antituberculosis agents, anthracyclines, antifungals, and others. The pattern of antibiotic use in the subject population can be observed in Figure 1.

Discussion

Characteristics of the subject population

Mortality rate in the sepsis patients affected by several factors, including early initiation and appropriateness of antimicrobial and non-antimicrobial therapy,[10] severity, age, gender, and co-morbidities.[11] In contras, the mortality rate of this study in the age group of 15-50 years were higher than the older (58.5% vs. 39.1%). Controlling factors that may affect mortality is important to understand the relationship between age and mortality. In this study, it is difficult to know this relationship, because several factors that affected in the mortality rate are uncontrolled. Furthermore, we also found 21.05% of the subject population had discharged against medical advise. Although in this study it is difficult to know the relationship between age and mortality, Carbajal-Guerrero *et al.*, have showed the co-morbidities in the elderly group (>65 years) is higher than the

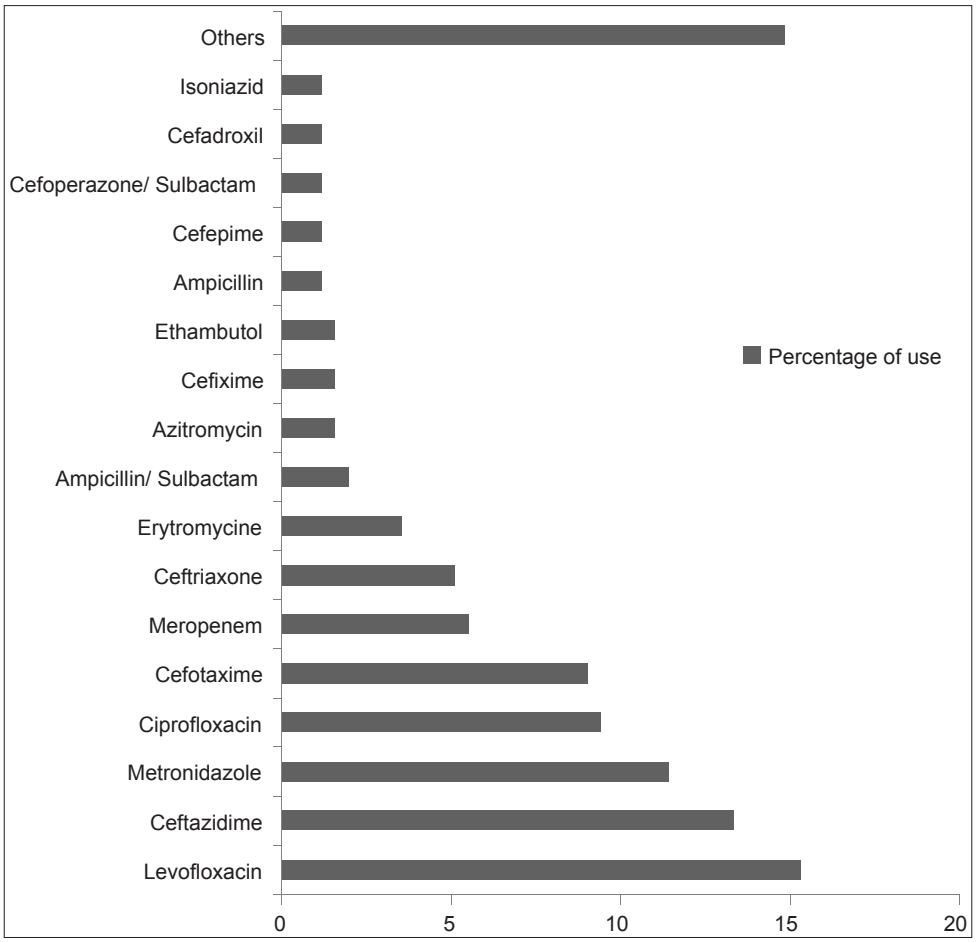

Figure 1: Pattern of antibiotic use at an Indonesian hospital (n = 255), *Other antibiotics include amikacin, cotrimoxazole, fosfomycin, gentamycin, ketoconazole, pyrazinamide, rifampicin, teicoplanin, vancomycin at 0.78%, lamivudine, alostil, amoxicillin, amoxicillin/clavulanate, benzyl penicillin, bleomycin, cefazoline, cefpirome, clarithromycin, clindamycine, colistin, doripenem, doxorubicin, fluconazole, ganciclovir, imipenem-cilastatin, nystatin, streptomycin, sulbactam, and tenofovir at 0.39%

younger groups and their co-morbidities associated to the mortality rate.[12]

The influence of gender on the development of sepsis is still under debate. Studies show a higher incidence of sepsis in men[13] than in women. Other studies have evaluated the influence of gender on survival in patients with sepsis[13,14] with conflicting results.[15] Various studies show that, in surgical units, survival was better in women,[15] better in men[16] or similar in men and women.[14] Although still in debate, a study by Adrie *et al*. concluded that in a group of severe sepsis patients of 50 years of age, women have a lower mortality risk than men.[15]

The difference between men and women in the risk of septicemia is due to differences in the immune response. Women have more estrogen production than men, which influences greater activity of the immune system.[17] Increasing age and body mass index in women can affect the production of estrogen by increasing aromatase activity in adipose tissue, increasing estrogen, which provides better protection through the action of the immune system.[17] Women also showed higher secretion of cytokines by peripheral blood mononuclear cells.[17] Other factors that influenced the immune system are non-hormonal factors such as the production of interleukin-6 and lipopolysaccharide-stimulated tumor necrosis, social factors, economic factors, levels of physical activity, the source of infection, and hormonal modification factors.[15,17,18]

Early detection of sepsis is needed for early treatment to minimize mortality incidence. One of the marker that can be used to detect sepsis is procalcitonin, as shown by Azevedo *et al.* in adult subjects and also by Nnanna *et al.* in infant populations.[19,20] Azevedo *et al.* showed a higher level of procalcitonin in sepsis and severe sepsis in adult patients were related to increase risk mortality.[19] In the neonatus population, the level of procalcitonin can be used as a marker for early detection of sepsis in the intensive care unit.[21,20] As a sepsis marker in the neonatus, procalcitonin is better than

C-Reactive Protein (CRP);[21] however, CRP can be used as a marker for bacterial co-infection in the viral-induced bronchiolitis infant populations.[22]

Table 2: Organisms isolated from various specimens (*n*=78)

Organism	%	Specimen
Klebsiella pneumonia	8.14	Blood, sputum, wound swab
Escherichia coli	4.65	Pus
Staphylococcus hominis	4.65	Blood
Candida albicans	3.49	Sputum
Candida non-albican	2.33	Sputum, blood
Acinetobacter baumanii	1.16	Blood
Aeromonas hydrophila	1.16	Sputum
Enterococcus faecalis	1.16	Blood
Enterobacter aerogenes	1.16	Urine
Escherichia coli (non-pathogenic)	1.16	Feces
Serratia marcescens	1.16	Sputum
Staphylococcus haemolyticus	1.16	Blood
Staphylococcus aureus	1.16	Abscess
Staphylococcus epidermidis	1.16	Blood
Streptococcus viridians	1.16	Sputum
Acid-fast *bacilli*	2.33	Sputum
Gram-negative *cocci*	13.95	Sputum, pus
Gram-positive *cocci*	15.12	Sputum, pus
Negative	33.72	Blood, sputum, pus, urine, ascites

Pattern of infection source

The most commonly found a source of infection for sepsis in this study was the lungs. This finding concurs with previous studies that reported that lung infections were the highest source of infection for sepsis development.[23] The common causes of lung infection that developed into sepsis are hospital-acquired pneumonia and CAP.[24] Wang *et al*. suggested that as a source of infection, lung infections may contribute to 15.6-69% of the incidence of sepsis.[25] A separate study showed that from 1963 to 1998, the predominant site of infection that develops to sepsis changed from intra-abdominal infections to lung infections.[26-28] Knowledge of the common pathogens that develop into sepsis based on the site of infection will help us determine a rational empirical antibiotic to use.[29] The common pathogens that cause sepsis based on the site of infection are shown in Table 4.

Pattern of microbial culture

Based on the results of the bacterial cultures, *K. pneumoniae* was the microbe most commonly detected in the specimens (sputum, blood, throat swab). *K. pneumoniae* is the common pathogen in lung infections and intra-abdominal infections that develop into sepsis.[7,30] Another microbe detected in cultures was *E. coli*, which can develop into sepsis from many initial sites of infection.[2,7,30] In this study, *E. coli* pathogens were found in pus specimens from 4 septic patients who had

Table 3: The level of antibiotic resistance based on susceptibility testing of the subject population

Antibiotics	*N*	*S*	*I*	*R*	Resistance (%)	Efficacy (%)
Amoxicillin	5	-	-	5	100	0
Ampicillin	5	-	-	5	100	0
Cefuroxime	3	-	-	3	100	0
Cefadroxil	6	1		5	83.3	16.7
Cefoperazone	15	2	1	12	80	20
Cefotaxime	22	4	2	16	72.7	27.3
Ceftriaxone	19	4	2	13	68.4	31.6
Ceftazidime	22	4	3	15	68.2	31.8
Cefepime	24	6	2	16	66.7	33.3
Cotimoxazole	20	6	1	13	65	35
Levofloxacin	19	7	-	12	63.2	36.8
Ciprofloxacin	23	9	-	14	60.9	39.1
Erythromycin	10	3	1	6	60	40
Cefoxitin	6	2	1	3	50	50
Cefoperazone/sulbactam	10	5	1	4	40	60
Piperacillin/tazobactam	21	12	2	7	33.3	66.7
Ampicillin/sulbactam	10	4	3	3	30	70
Meropenem	26	17	2	7	26.92	73.08
Amoxicillin/clavulanate	22	10	8	4	18.2	81.8
Tigecycline	20	16	2	2	10	90
Vancomycin	9	8	1	-	0	100
Linezolid	9	8	1	-	0	100
Amikacin	16	15	1	-	0	100

*N: Number of susceptibility test; S: Sensitive; I: Intermediate; R: Resistant; Efficacy (%)=(S+I)/*N*×100%; Resistance (%)=R/N×100%[3]

Table 4: Common pathogens that can develop into sepsis based on the source of infection[2,7,29-35]

Source of infection	Pathogen
Lungs	*Klebsiella pneumoniae*; *Escherichia coli*; *Streptococcus pneumoniae*; *Haemophillus influenza*; *Moraxella catarrhalis*; *Mycoplasma pneumoniae*; *Chlamydia pneumoniae*; *Legionella* sp.; *Legionella pneumophila*; *Enterobacter*; *Klebsiella* sp.; *Staphylococcus aureus*; *Pseudomonas aeruginosa*; *Pseudomonas* spp.; *Mycobacterium tuberculosis*; *Acinetobacter* sp.; MRSA; *Pseudomonas aeruginosa*; *Enterobacter* sp.
Intra-abdominal	Gram-negative enteric bacilli; *Enterobacter* sp.; *Escherichia coli*; *Klebsiella pneumoniae*; *Pseudomonas aeruginosa*; *Proteus* sp.; MRSA
Skin and soft tissue	Group A *Streptococcus*; *Clostridium perfringens*; *Neisseria meningitidis*; *Rickettsia rickettsia*; *Streptococcus pneumoniae*; *Haemophilus influenzae*; *Staphylococcus aureus*; *Streptococcus pyogenes*
Urinary tract	*Escherichia coli*; *Pseudomonas aeruginosa*; *Pseudomonas* spp.; *Enterococcus* spp.; *Klebsiella pneumoniae*; *Proteus mirabillis*
Unknown source	*Staphylococcus aureus*; MRSA; *Streptococcus pneumoniae*; *Escherichia coli*; *Klebsiella* sp.; Gram negative *bacteria*; *Proteus* sp.

MRSA: Methicillin-Resistant *Staphylococcus aureus*

diabetes mellitus. *E. coli* and *S. aureus* were the most common agents isolated from the diabetic patients.[36] *E. coli* is also the causative pathogen in infections in immunosuppressed patients, patients with severe burns, cancer patients and patients using catheters, antibiotics or corticosteroids.[37]

S. hominis was found in blood specimens in this study. *S. hominis* is a coagulase-negative *staphylococcal* strain (CoNS). CoNS are common organisms in nosocomial bacteremia due to the increases in medical device use including intravenous catheters, vascular grafts, prosthetic heart valves, and devices used in the treatment of joint disease. CoNS microorganisms are most frequently isolated from blood cultures. The presence of CoNS in blood cultures cannot directly determine that the species is pathogenic, because in 85% isolate CoNs found as a contaminant.[38]

The most commonly used antibiotics varied among institutions, but were typically composed of drugs that have levels of high resistance from some bacteria, such as *Pseudomonas*, *E. coli*, *K. pneumoniae*, *Acinetobacter* sp. and *S. aureus*. Making a microbiological diagnosis is mandatory.[30] A multicenter randomized trial showed lower mortality using a microbiological-based approach (after adequate empirical treatment) compared to a clinical only approach (Hazard Ratio: 1.54, Confidence Interval: 1.1-2.16, $P = 0.01$).[35]

Negative result and contaminant result from the microbial cultures requires an evaluation to increase quality of microbiology diagnosis. Internal evaluations are needed to maintain the quality of microbiology diagnosis. Nwose have showed the difference results of culture and susceptibility test in some clinical laboratories; therefore, the program of quality assurance and quality control should be made available through the availability of Standard Operational Procedures and improving the competency and skills of personnel's.[39]

Patterns of antibiotic use and sensitivity

Forty-seven antibiotics were used. In our study, the most frequently used (74.5%) were levofloxacin, ceftazidime, metronidazole, ciprofloxacin, cefotaxime, meropenem, ceftriaxone, erythromycin, and ampicillin/sulbactam. In our study, Six of these nine antibiotics, levofloxacin, ceftazidime, ciprofloxacin, cefotaxime, ceftriaxone, and erythromycin, showed resistance rates above 50%. Based on the results of the microbial cultures, antibiotic susceptibility tests and patterns of antibiotic use, 61.35% of the antibiotics used showed resistance rates of more than 50%. A total of 10 antibiotics with resistance rates below 50% were cefoxitin, cefoperazone/sulbactam, gentamicin, piperacillin/tazobactam, ampicillin/sulbactam, meropenem, amoxicillin/clavulanate, vancomycin, linezolide and amikacin. The high sensitivity of these antibiotics contributes to their use as an option in empirical antibiotic therapy, but the selection of which antibiotic to use should consider the location of the infection source and factors specific to the patient. The pattern of antibiotic use with high resistance rates can be observed in Figure 2.

The high frequency of use of antibiotics with high levels of resistance required special attention.[40] Inappropriateness of empirical antibiotic therapy can contribute to high level of mortality.[10] Patients who received appropriate initial antimicrobial treatment have lower mortality than those of who didn't.[29] The early administration of appropriate antibiotic therapy for serious infection is associated with lower mortality, shorter duration of hospitalization, and lower health care cost.[17,18] In other hand, wrong or inappropriate use of antibiotic will contributed to the development of antibiotic resistance and multi drug resistance (MDR). The high incidence of MDR can reduce the opportunities of patients to get the appropriate antimicrobial that can affect to increase the risk of death.[13] Raymond in his study have suggested a high mortality cases founded in the patients with MDR and the study also showed that

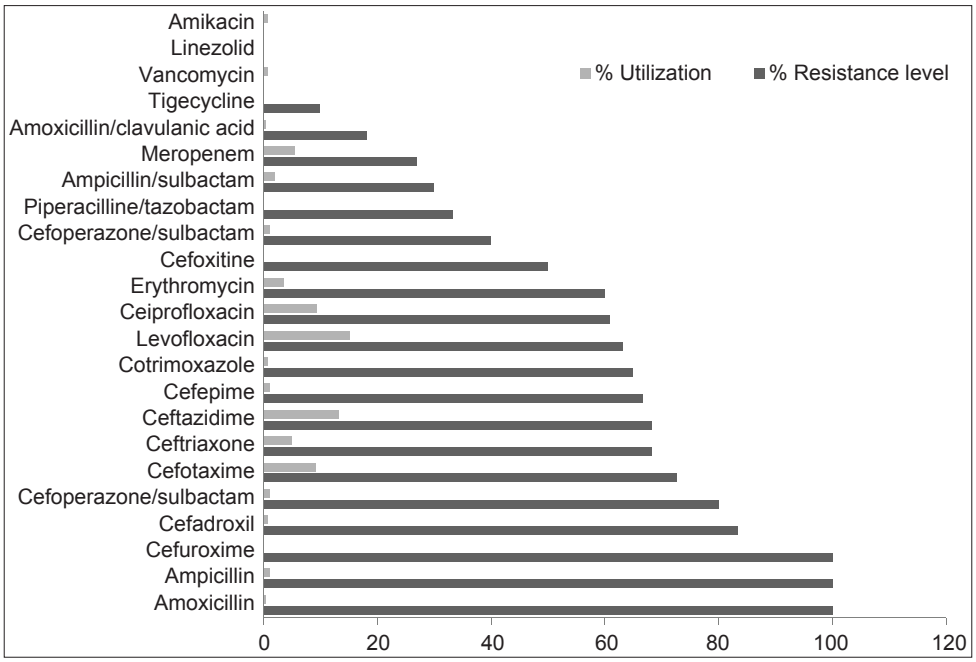

Figure 2: Pattern of antibiotic use with their resistance level at an Indonesian hospital

the patients get inappropriate empirical antibiotic and severity of co-morbid.[41]

The emergence of microbial resistances were not by the availability of novel antimicrobial agents, which is marked by only four new classes of antibacterials have been discovered in the last 11 years.[42] The strategies for limiting or modifying antibiotic use are needed to control resistance growth and to improve the rational use of antibiotics.[43] The seven strategies to prevent antibiotic resistance that were suggested by Kollef in 2005[44] are as follows: (1) Establishment of a formal protocol and guidelines, (2) Hospital formulary restrictions, (3) Use of narrow spectrum antibiotics when supported by clinical situation and culture data, (4) Combination antibiotic therapy, (5) Shorter courses of antibiotic treatment, (6) Antibiotic heterogeneity, and (7) Optimization of pharmacokinetic/pharmacodynamic principles. There are three option that can be used in antibiotic heterogeneity strategies, namely antibiotic cycling/rotation, scheduled antibiotic changes, and antibiotic mixing.[44] Antibiotic cycling/rotation can be used with a fixed temporal pattern for predominant use of antibiotic class or classes, followed by their repeated and reintroduction over time. In contrast with scheduled antibiotic changes, it has a predetermined and scheduled change in the predominant antimicrobial agent employed. The changes of antibiotic classes are often based on changing patterns of antimicrobial sensitivities and not simply time based. The others antibiotics heterogeneity strategy is antibiotic mixing, a strategy whereby all or most available antimicrobial classes are employed to minimize undue pressure for the emergence of resistance from having single or limited number of antibiotic classes available.[45]

Broad spectrum antibiotics can be used in the critical ill patients to avoid inappropriateness of antibiotics which can be fatality.[44] The modification broad spectrum for initial therapy is needed based on clinical condition of patient, microbial culture, and antibiotics susceptibility test. Modification of the initial antibiotics regimen should include decreasing the number and or spectrum antibiotics. Shortening the duration of therapy in patients with uncomplicated infections who are demonstrating signs of clinical improvement or discontinuing antibiotics altogether in patients who have a non-infectious etiology identified for the patient's signs and symptoms.[46] The long duration of broad spectrum antibiotic used will lead to the development of antibiotics resistance; therefore, it is very important to know the local pattern of pathogen based on the infection site and microbial sensitivity to minimize use of broad spectrum antibiotic and inappropriateness of empirical antibiotic use.

Carbapenem is a broad spectrum antibiotic, which came in to use in 1985, since then, due to their good intrinsic bacterial activity and stability to most of the prevalent beta lactamase, they have been a drug of choice for extended spectrum beta lactamase-producing organism.[47] Restricted use of specific antibiotics has generally been applied to those drugs with a broad spectrum of action (e.g., carbapenems), rapid emergence of antibiotic resistance (e.g., cephalosporins), and drugs with readily identified toxicity (e.g., aminoglycosides).[44] In the hospital setting, restrictions on the use of antibiotics

are administered through the hospital formulary and treatment guidelines and policies. An evaluation of an antibiotic used and its susceptibility should be monitored periodically to control the alteration of susceptibility. The most successful strategies to combat antibiotic resistance will be multidisciplinary, involving cooperation from the pharmacy, infection control, nursing staff, treating physicians, microbiology laboratory personnel, and infectious disease consultants. Such programs should also focus on promoting infection control practices and employing rational antibiotic utilization aimed at minimizing future emergence of resistance.[43]

Conclusions

Lung infection is the most common infection that is found in sepsis patient. *K. pneumoniae, E. coli* and *S. hominis* is the most widely isolated organisms that were detected in septic patients. The high use of antibiotics with high levels of resistance such as levofloxacin, ceftazidime, ciprofloxacin, cefotaxime, ceftriaxone, and erythromycin requires a policy to control the use of antibiotics. Microbial culture and resistance pattern were obtained from the local sepsis patients can be used as data to choose appropriatness of empirical antibiotic therapy for reducing mortality and morbidity in the sepsis patients.

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