

Microbial patterns of hospitalized HIV Positive patients admitted in Dr Soetomo General Hospital, Surabaya Indonesia

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Submission date: 28-Dec-2022 11:33AM (UTC+0800)

Submission ID: 1987014180

File name: admitted_in_Dr_Soetomo_General_Hospital,_Surabaya_Indonesia.pdf (380.52K)

Word count: 5879

Character count: 31064



MICROBIAL PATTERNS OF HOSPITALIZED HIV POSITIVE PATIENTS ADMITTED IN DR. SOETOMO GENERAL HOSPITAL, SURABAYA INDONESIA

POLA MIKROBA PADA PASIEN RAWAT INAP HIV POSITIF DI RSUD DR.SOETOMO SURABAYA INDONESIA

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Research Report
Penelitian

ABSTRACT

Background: HIV patients with a weak immune system are very vulnerable to opportunistic infections, can trigger systemic endothelial activation and end up as a condition of sepsis. In Indonesia currently, there is no bacterial epidemiological mapping of the etiology of opportunistic infections in HIV patients. **Purpose:** To determine the pattern of bacteria that cause opportunistic infections and their antibiotic sensitivity in HIV patients. **Method:** Prospective observational study design. Data were obtained from medical records of hospitalized patients at RSUD Dr. Soetomo Surabaya from August 2019 - February 2020. **Result:** Out of 64 patients, 83 specimens were found with the most types of gram-negative bacteria 44.6%, while gram-positive bacteria were 15.7% and a mix of 2.4% and 37.3% negative culture. The highest prevalence of gram-negative bacteria was *Klebsiella pneumoniae* (35.15), followed by *Escherichia coli* (10.8%), *Pseudomonas aeruginosa* (8.1%), and *Acinetobacter baumannii* (8.1%). The highest prevalence of gram-positive bacteria was *Streptococcus mitis/oralis* (30.7%), followed by *Staphylococcus aureus* (23.1%) and *Staphylococcus epidermidis* (15.4%). Among gram-negative bacteria antibiotic, Cefoperazone-sulbactam showed the greatest sensitivity, following by Amikacin, Gentamycin and Piperacillin-tazobactam; while among gram-positive bacteria are Chloramphenicol, Linezolid and Vancomycin. Almost all isolates showed resistance to Ampicillin. **Conclusion:** Bacteria pattern that caused opportunistic infection in RSUD Dr. Soetomo is *K. pneumoniae* as most common gram-negative bacteria followed by *E. coli*, *P. aeruginosa* and *A. baumannii*; while the most gram-positive bacteria found are *S. mitis/oralis* and *S. aureus*. Among antibiotic used, Ampicillin showed the lowest sensitivity to almost all bacteria isolates.

ABSTRAK

Latar Belakang: Pasien HIV dengan sistem imun yang lemah sangat rentan terhadap kejadian infeksi oportunistik, dapat memicu terjadinya aktivasi endotel sistemik dan berakhir menjadi kondisi sepsis. Di Indonesia saat ini belum ada pemetaan epidemiologi bakteri yang sering menjadi sumber infeksi oportunistik pada pasien HIV. **Tujuan:** Untuk mengetahui pola bakteri yang menyebabkan infeksi oportunistik beserta sensitivitas antibiotiknya pada pasien HIV. **Metode:** Penelitian deskriptif dengan rancangan studi prospektif observasional. Data didapatkan dari rekam medik pasien rawat inap di RSUD Dr. Soetomo Surabaya periode Agustus 2019 – Februari 2020. **Hasil:** Dari 64 pasien didapatkan 83 spesimen dengan jenis bakteri terbanyak bakteri gram negatif 44.6% sedangkan bakteri gram positif 15.7% serta campuran 2.4% dan kultur negatif 37.3%. Prevalensi bakteri gram negatif terbanyak *Klebsiella pneumoniae* (35.15) diikuti *Escherichia coli* (10.8%), *Pseudomonas aeruginosa* (8.1%) dan *Acinetobacter baumannii* (8.1%). Prevalensi bakteri gram positif terbanyak *Streptococcus mitis/oralis* (30.7%), diikuti *Staphylococcus aureus* (23.1%) dan *Staphylococcus epidermidis* (15.4%). Di antara antibiotik bakteri gram negatif, Cefoperazone-sulbactam menunjukkan sensitivitas terbesar, diikuti oleh Amikacin, Gentamycin dan Piperacillin-tazobactam; sedangkan bakteri gram positif adalah Kloramfenikol, Linezolid dan Vankomisin. Hampir semua isolat menunjukkan resistensi terhadap Ampisilin. **Kesimpulan:** Pola bakteri penyebab infeksi oportunistik di RSUD Dr. Soetomo adalah *K. pneumoniae*, bakteri gram-negatif terbanyak diikuti oleh *E. coli*, *P. aeruginosa* dan *A. baumannii*; sedangkan bakteri gram-positif yang paling banyak ditemukan adalah *S. mitis/oralis* dan *S. aureus*. Di antara antibiotik yang digunakan, Ampisilin menunjukkan sensitivitas paling rendah terhadap hampir semua isolat bakteri.

ARTICLE INFO

Received 11 May 2020

Revised 22 July 2020

Accepted 05 April 2021

Online 31 July 2021

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Keywords:

AIDS, Antibiotic sensitivity, Bacterial infection, HIV, Turnaround time

Kata kunci:

AIDS, HIV, Infeksi Bakteri, Sensitivitas Antibiotik, Turnaround time



INTRODUCTION

HIV or Human Immunodeficiency Virus is a virus that attacks and infects white blood cells that cause the decrease of the human immune system. This virus infection is persistent because our body cannot eliminate the virus, even with renewable therapy (CDC, 2019a). The replication of HIV will continuously attack the body's immune system, especially CD4 lymphocyte cells, which play a role in protecting the body from various kinds of infections. If not appropriately treated, HIV will progressively decrease CD4 lymphocyte cells so the body will be susceptible to opportunistic infections. When CD4 lymphocyte cell counts <200 cells/microliters and the body no longer have the ability to fight various infections and diseases, this is called the AIDS (Acquired Immuno Deficiency Syndrome) phase (WHO, 2018).

According to the World Health Organization, since this virus became an epidemic, more than 70 million people were infected, and around 35 million people were reported dead. At present, there are 36.9 million people with HIV, and around 0.8% (0.6-0.9%) in the 15-49 year age group (WHO, 2017). In Indonesia, based on reports of the development of HIV-AIDS by the Ministry of Health, until December 2017, the number of people infected with HIV was reported as many as 280.623. The number of HIV cases found and reported is still far from the estimated ODHA (people with HIV-AIDS) in 2016, which amounted to 640.443. The case of HIV/AIDS becomes an essential problem because the highest percentage of infections is in the productive age group of 20-49 years and not all receive ARV therapy, so they are vulnerable to falling into the AIDS phase (Kemenkes, 2018).

Opportunistic infections are defined as infections that often occur in people with decreased body immune systems and tend to be more severe than people with normal immune condition. This becomes a severe problem because it increases morbidity and mortality rates in HIV patients (CDC, 2019b).

This study aims to analyze bacterial patterns in opportunistic infections in HIV patients and their antibiotic sensitivity. Several international journals indicate differences in microbial patterns in HIV patients by geographic region, and at present, there is no routine monitoring of the etiology of opportunistic infections in HIV patients (Chandra *et al.*, 2013; Huson *et al.*, 2014; Iribarren *et al.*, 2016; Japiassu *et al.*, 2010; Melindah *et al.*, 2016).

MATERIAL AND METHOD

This is a descriptive research study with a prospective observational study design that uses medical records of HIV patients who are hospitalized in Dr. Soetomo General Hospital, Surabaya, Indonesia, in the period August 2019 - February 2020. Inclusion criteria were HIV-positive patients who were hospitalized and had a microbiological culture examination.

RESULT

Most patients in the age group 30-39 years (43.8%) with an average age of 37.6 (\pm 11.1) years, median value 35.5, the youngest patient aged 19 years, and the oldest patient aged 82 years. Patients are predominantly male (78.1%). The highest education status that has been taken by patients is Senior High School Graduate (67.2%). Patient's occupations most frequently found in this study were Private Employees (48.4%) and Housewives (12.5%). The religion most widely adopted by patients in this study was Muslim (93.8%). The CD4 cell count range of the most common HIV patients found in this study was <100 cells/ μ L (23.4%) with an average of 155.9 cells/ μ L, a median value 38 cells/ μ L, the highest value 917 cells/ μ L and the lowest one cell/ μ L.

From the 64 patients was found, 83 specimens with the most bacterial types are gram-negative bacteria 44.6%. The most common bacteria found are gram-negative *Klebsiella pneumoniae*. In the group of gram-positive bacteria, the most common was *Streptococcus mitis/oralis* 30.7%, followed by *Staphylococcus aureus* (23.1%). One of them was found with MRSA/Methicillin-resistant *Staphylococcus aureus*. In the group of gram-negative bacteria, the most common was *K. pneumoniae* (35.1%). Six of them were ESBL/extended-spectrum beta-lactamases.

In blood specimens, the most common bacteria were *Salmonella spp.* (7.4%) and *Staphylococcus epidermidis* (7.4%). The most common bacterial in sputum specimens were gram-negative *K. pneumoniae* (27.9%). Five of them were ESBL/extended-spectrum beta-lactamases (11.6%). In urine specimens, only found gram-negative bacteria, *Proteus mirabilis* (22.2%) and *Escherichia coli* (22.2%), one of them with ESBL/extended-spectrum beta-lactamases (11.1%). In the fecal/pus specimens, the most common bacterial found was gram-negative *E. coli* (50%).

As an opportunistic bacterium, the therapeutic choice of *Streptococcus mitis/oralis* is Ampicillin or macrolide (Erythromycin) (Budayanti *et al.*, 2019). Therapeutic options for *Methicillin Susceptible Staphylococcus aureus* (MSSA) are oxacillin, clindamycin, erythromycin. Therapeutic options for MRSA are Teicoplanin or Vancomycin (Shah *et al.*, 2020). The therapeutic choice for *K. pneumoniae* is Aminoglycoside (Gentamycin or Amikacin) (Piperaki *et al.*, 2017). *E. coli* therapeutic options are Imipenem and Gentamycin (Rooku *et al.*, 2019). Therapeutic options for *Acinetobacter baumannii* are Ampicillin-sulbactam and Imipenem (Morris and Cerceo, 2020). Therapeutic options for *Pseudomonas aeruginosa* are Amikacin, Cefazidime and Piperacillin-Tazobactam (Melindah *et al.*, 2016). Treatment options for *Klebsiella aerogenes* are Amikacin and Gentamycin (Malek *et al.*, 2019).

The examination time was calculated from the time the specimen was received at Clinical Microbiology until the release of the culture results and their antibiotic sensitivity.

• Sociodemographic characteristics and CD4 counts

Table 1. Sociodemographic characteristics and CD4 counts in HIV patient

Variable	n	%
Age		
< 20 years old	1	1.6
20 – 29 years old	13	20.3
30 – 39 years old	28	43.8
40 – 49 years old	13	20.3
50 – 59 years old	7	10.9
> 60 years old	2	3.1
Sex		
Male	50	78.1
Female	14	21.9
Education		
Not complete Primary School	3	4.7
Graduated Primary School	4	6.3
Graduated JHS	7	10.9
Graduated SHS	43	67.2
Graduated D3	1	1.6
Graduated S1	5	7.8
Graduated S2	1	1.6
Occupation		
Private employees	31	48.4
Housewife	8	12.5
Student	6	9.4
Government employees	5	7.8
Entrepreneur	5	7.8
TNI/POLRI	1	1.6
Teacher	1	1.6
Others	4	6.3
No work	3	4.7
Religion		
Muslim	60	93.8
Catholic	2	3.1
Christian	1	1.6
Buddhist	1	1.6
CD4 (cells/μL)		
> 500	2	3.1
200 - 499	4	6.3
100 - 199	5	7.8
< 100	15	23.4

• The bacterial pattern in HIV patient

Table 2. The bacterial pattern based on gram-staining

Specimen (n= 83)	n	(%)
Gram-positive	13	15.7
Gram-negative	37	44.6
Mixed	2	2.4
Normal flora/ negative	31	37.3
Gram-positive (n= 13)		
<i>Streptococcus mitis/oralis</i>	4	30.7
<i>Staphylococcus aureus</i> (MRSA 1)	3	23.1
<i>Staphylococcus epidermidis</i>	2	15.4
<i>Staphylococcus sciuri</i>	1	7.7
<i>Staphylococcus hominis</i>	1	7.7
<i>Cellulomonas turbata</i>	1	7.7
<i>Methicilin-resistant Staphylococcus aureus + Streptococcus mitis/oralis</i>	1	7.7
Gram-negative (n= 37)		
<i>Klebsiella pneumoniae</i> (ESBL 6)	13	35.1
<i>Escherichia coli</i> (ESBL 1)	4	10.8
<i>Pseudomonas aeruginosa</i>	3	8.1
<i>Acinetobacter baumannii</i>	3	8.1
<i>Enterobacter cloacae</i>	2	5.4
<i>Proteus mirabilis</i>	2	5.4
<i>Klebsiella aerogenes</i>	2	5.4
<i>Salmonella spp.</i>	2	5.4
<i>Burkholderia cepo</i>	1	2.7
<i>Moraxella catarrhalis</i>	1	2.7
<i>Neisseria animaloris</i>	1	2.7
<i>Stenotrophomonas maltophira</i>	1	2.7
<i>Klebsiella pneumoniae + Klebsiella aerogenes</i>	1	2.7
<i>Escherichia coli + Pseudomonas aeruginosa + Spingomonas paucimobilis</i>	1	2.7
Mixed (n= 2)		
<i>Acinetobacter baumannii</i> (Gram-) + <i>Gemella morbillorum</i> (Gram+)	1	½
<i>Pseudomonas pseudoalcaligenes</i> (Gram-) + <i>Staphylococcus hemolyticus</i> (Gram+)	1	½

Table 3. Bacterial pattern based on specimen types

	Specimen (n=83)	n	(%)
Positive culture		52	62.7
Negative culture		31	37.3
Bacteria		58	-
Blood (n=27)			
	<i>Salmonella spp.</i> (Gram-)	2	7.4
	<i>Staphylococcus epidermidis</i> (Gram+)	2	7.4
	<i>Cellulomonas turbata</i> (Gram+)	1	3.7
	Methicilin-resistant <i>Staphylococcus aureus</i> (Gram+)	1	3.7
	<i>Neisseria animaloris</i> (Gram-)	1	3.7
	<i>Staphylococcus hominis</i> (Gram+)	1	3.7
	<i>Staphylococcus sciuri</i> (Gram+)	1	3.7
Sputum (n=43)			
	<i>Klebsiella pneumoniae</i> (Gram-)	12	27.9
	<i>Streptococcus mitis/oralis</i> (Gram+)	4	9.3
	<i>Pseudomonas aeruginosa</i> (Gram-)	3	7
	<i>Acinetobacter baumannii</i> (Gram-)	2	4.7
	<i>Enterobacter cloacae</i> (Gram-)	2	4.7
	<i>Staphylococcus aureus</i> (Gram+)	2	4.7
	<i>Burkholderia cepo</i> (Gram-)	1	2.3
	<i>Klebsiella aerogenes</i> (Gram-)	1	2.3
	<i>Moraxella catarrhalis</i> (Gram-)	1	2.3
	<i>Stenotrophomonas maltophira</i> (Gram-)	1	2.3
	<i>Acinetobacter baumannii</i> (Gram-)+ <i>Gemella morbillorum</i> (Gram+)	1	2.3
	Methicilin-resistant <i>Staphylococcus aureus</i> (Gram+)+ <i>Streptococcus mitis/oralis</i> (Gram+)	1	2.3
	<i>Pseudomonas pseudoalcaligenes</i> (Gram-)+ <i>Staphylococcus hemolyticus</i> (Gram+)	1	2.3
	<i>Escherichia coli</i> (Gram-)+ <i>Pseudomonas aeruginosa</i> (Gram-)+ <i>Spingomonas paucimobilis</i> (Gram-)	1	2.3
Urine (n=9)			
	<i>Escherichia coli</i> (Gram-)	2	22.2
	<i>Proteus mirabilis</i> (Gram-)	2	22.2
	<i>Acinetobacter baumannii</i> (Gram-)	1	11.1
	<i>Klebsiella aerogenes</i> (Gram-)	1	11.1
Fecal/Pus (n=4)			
	<i>Escherichia coli</i> (Gram-)	2	1/2
	<i>Klebseilla pneumoniae</i> ESBL(Gram-)	1	1/4
	<i>Klebseilla pneumoniae</i> (Gram-)+ <i>Klebseilla aerogenes</i> (Gram-)	1	1/4

note: (-) = Antibiotic not tested

• Antibiotic sensitivity in HIV patient

Table 4. Antibiotic sensitivity in gram-positive bacteria

Antibiotik	<i>Streptococcus mitis/oralis</i> (5)	<i>Staphylococcus aureus</i> (4)
Amoxicillin-Clavulanic acid	-	2/4 (50 %)
Ampicillin	2/5 (40%)	0/4 (0%)
Cefixime	1/1 (100%)	-
Cefotaxime	4/4 (100%)	-
Cefoxitin	-	0/1 (100%)
Ceftriaxone	5/5 (100%)	-
Chloramphenicol	4/5 (80%)	2/3 (66.7%)
Ciprofloxacin	-	2/4 (50%)
Clindamycin	4/5 (80%)	1/4 (25%)
Cotrimoxazole	1/1 (100%)	4/4 (100%)
Erythromycin	2/5 (40%)	1/4 (25%)
Gentamycin	1/3 (33.3%)	3/4 (75%)
Levofloxacin	1/5 (20%)	1/2 (50%)
Linezolid	4/4 (100%)	3/3 (100%)
Moxifloxacin	2/5 (40%)	2/2 (100%)
Mupirocin High Level	-	1/1 (100%)
Oxacillin	-	2/3 (66.7%)
Penicillin G	2/5 (40%)	0/4 (0%)
Quinupristin-dalfopristin	-	3/3 (100%)
Rifampin	-	3/3 (100%)
Teicoplanin	-	4/4 (100%)
Tetracycline	2/5 (40%)	3/4 (75%)
Tigecycline	5/5 (100%)	-
Vancomycin	4/4 (100%)	3/3 (100%)

note: (-) = Antibiotic not tested

Table 5. Antibiotic sensitivity in gram-negative bacteria

Antibiotik	<i>Klebsiella pneumoniae</i> (n= 14)	<i>Escherichia coli</i> (n= 5)	<i>Acinetobacter baumannii</i> (n= 4)	<i>Pseudomonas aeruginosa</i> (n= 4)	<i>Klebsiella aerogenes</i> (n= 3)
Amikacin	14/14 (100%)	5/5 (100%)	3/4 (75%)	3/4 (75%)	3/3 (100%)
Amoxicillin-Clavulanic acid	12/14 (85.7%)	2/5(40%)	0/4 (0%)	0/4 (0%)	0/3 (0%)
Ampicillin	0/14 (0%)	0/5 (0%)	0/4 (0%)	0/4 (0%)	0/3 (0%)
Ampicillin-sulbactam	9/13 (69.2%)	1/5 (20%)	4/4 (100%)	0/4 (0%)	0/3 (0%)
Astreonom	7/14 (50%)	5/5 (100%)	0/4 (0%)	3/4 (75%)	2/3 (66.7%)
Cefepime	5/11 (45.5%)	4/5(80%)	2/4 (50%)	3/4 (75%)	1/3 (33.3%)
Cefoperazone-Sulbactam	13/13 (100%)	5/5 (100%)	4/4 (100%)	3/4 (75%)	3/3 (100%)
Cefotaxime	8/14 (57.1%)	4/5 (80%)	2/4 (50%)	0/4 (0%)	1/3 (33.3%)
Ceftazidime	8/14 (57.1%)	4/5 (80%)	3/3 (100%)	4/4 (100%)	2/3 (66.7%)
Ceftriaxone	8/12 (66.7%)	4/5 (80%)	0/4 (0%)	0/4 (0%)	1/3 (33.3%)
Cephazolin	7/14 (50%)	4/5 (80%)	0/4 (0%)	0/4 (0%)	0/3 (0%)
Chloramphenicol	7/14 (50%)	2/5 (40%)	0/4 (0%)	0/4 (0%)	0/3 (0%)
Ciprofloxacin	12/14 (85.7%)	2/5 (40%)	3/4 (75%)	3/4 (75%)	1/3 (33.3%)
Cotrimoxazole	7/14 (50%)	0/5 (0%)	3/4 (75%)	0/4 (0%)	1/3 (33.3%)
Ertapenem	-	1/1 (100%)	-	-	1/1 (100%)
Fosfomycin	3/3 (100%)	-	-	1/1 (100%)	
Gentamycin	14/14 (100%)	4/5 (80%)	3/4 (75%)	4/4 (100%)	2/3 (66.7%)
Imipenem	13/14 (92.8%)	4/4 (100%)	2/3 (66.7%)	3/4 (75%)	1/3 (33.3%)
Levofloxacin	12/13 (92.3%)	2/5 (40%)	3/4 (75%)	3/4 (75%)	2/3 (66.7%)
Meropenem	14/14 (100%)	5/5 (100%)	2/3 (66.7%)	3/4 (75%)	2/2 (100%)
Moxifloxacin	12/14 (85.7%)	2/4 (50%)	-	-	0/3 (0%)
Piperacillin	6/14 (42.9%)	1/4 (25%)	2/4 (50%)	3/4 (75%)	0/2 (0%)
Piperacillin-tazobactam	13/13 (100%)	5/5 (100%)	3/4 (75%)	4/4 (100%)	2/3 (66.7%)
Tetracycline	8/14 (57.1%)	0/4 (0%)	1/1 (100%)	0/4 (0%)	1/3 (33.3%)
Teicoplanin	-	-	0/1 (0%)	0/1 (0%)	-
Tigecycline	7/12 (58.3%)	2/5 (40%)	3/3 (100%)	0/3 (0%)	1/2 (50%)

note: (-) = Antibiotic not tested

Table 6. Turnaround Time (TAT)

Specimen	n	Examination Time (days)
Blood	27	4.63 (± 0.8)
Sputum	43	3.02 (± 1.1)
Urine	9	2.89 (± 0.8)
Feses/Pus	4	3.75 (± 0.9)

DISCUSSION

• Sociodemographic and CD4 counts

In this study, most HIV/AIDS patients found were in the age group 30-39 years according to HIV/AIDS reports in Indonesia and the world (Kemenkes, 2018; WHO, 2018). This is due to the current structure of the Indonesian population at a young age (Purwaningsih and Widyatun, 2008), active sexual behavior that engages in unprotected sexual behavior, and the use of syringes mainly occurs in young age groups (Kambu *et al.*, 2016). The high prevalence of HIV/AIDS cases due to risky sexual behavior is more vulnerable in men (Kambu *et al.*, 2016) and psychology journals show that men have higher sexual compulsiveness than women (Rahardjo and Hutagalung, 2016).

The level of education of HIV patients found tends to be the same as other studies, i.e., senior high school graduates. According to Yelfi *et al.* (2018), education in Indonesia is not difficult because there is a compulsory education program from the government, data from the Central Statistics Agency in the last ten years Senior High School is the latest education that has been the most completed by the Indonesian population (BPS, 2019). Other studies have shown that there is no significant relationship between education level and HIV transmission prevention measures because there has been a paradigm shift where the level of education is no longer directly proportional to the awareness of HIV infection (Kambu *et al.*, 2016; Taylor *et al.*, 2018).

In this study, most HIV patients had jobs, and only a small proportion did not. The most common jobs found are private employees and housewives following data from the Directorate General of P2PL Ministry of Health in 2017. Yelfi *et al.* (2018) said that the same thing, according to him, increasing one's education would make it easier to find work. Other studies in India say housewives are very vulnerable to HIV infection because it is transmitted by their partners

In this study predominantly Muslim religion this finding is different from research in other countries, such as in France showing the majority of HIV patients are Catholic (Preau *et al.*, 2008), research in sub-Saharan Africa found the majority of Islamic patients (Velayati *et al.*, 2007), research in China found that the majority of non-religious patients (Pan *et al.*, 2017). This difference, according to Laah and Ayiwulu (2010), depends on the characteristics of religious adherents in the country where the study was conducted.

The average CD4 count of patients found in this study was meager at <200 cells/ μ L with the clinical condition found to be accompanied by various comorbid diseases according to other studies conducted at H. Adam Malik General Hospital Medan and RSPI Sulianti Saroso (Rangkuti, 2013; Yelfi *et al.*, 2018) this is because most patients will seek treatment if only they feel sick, a low CD4 cell count will increase the risk of various diseases, especially opportunistic infections and malignancies (Yelfi *et al.*, 2018; Melhuish and Lewthwaite, 2018).

• Opportunistic bacterial infection in HIV patient

In this study, it was found that gram-negative bacteria infected more HIV patients than gram-positive bacteria (44.6%:15.7%). The most common gram-negative bacteria found are *K. pneumoniae* followed by *E. coli*, *P. aeruginosa* and *A. baumannii*, while the most gram-positive bacteria found are *S. mitis/oralis* and *S. aureus*. The results of this study were also found by studies in Bandung (Melindah *et al.*, 2016), in Nepal (Rooku *et al.*, 2019) and Brazil (Japiassu *et al.*, 2010).

Other studies have shown some differences in bacterial patterns in HIV patients. As a whole, NTS/Non-Typhoidal *Salmonella*, *S. pneumoniae* and *S. aureus* were the most frequently found, but the frequency depends on the region. In Europe, America and Africa, *S. pneumoniae* has the most bacteria, 22.8-58.5%, but in Asia, there are 47.1% NTS, *S. aureus* 14.1%, and *E. coli* 9.2% (Huson *et al.*, 2014). In addition to the geographical problem, *S. pneumoniae* is rarely found because these microorganisms are difficult to culture because they need nutrition and a good environment to grow (Melindah *et al.*, 2016).

In this study, many interesting things were also found, which is the presence of bacteria with ESBL/extended-spectrum beta-lactamases in *Klebsiella pneumoniae* (46.2%) and *E. coli* (20%). ESBL is a group of enzymes that have the hydrolysis and inactivation capabilities of beta-lactam antibiotics, including third-generation cephalosporin, penicillin and aztreonam (Enany *et al.*, 2020). Previous research studies supported the type of ESBL-producing bacteria found in this study also carried out at Dr. Soetomo General Hospital Surabaya by Irawan *et al.* (2012) which got *K. pneumoniae* 52.08% and *E. coli* 47.92% and studies with pediatric patients at the same location obtained *K. pneumoniae* with ESBL 60.7% and *E. coli* with ESBL 37.5% (Muhajir *et al.*, 2016). The ESBL bacteria problem is not only experienced in Indonesia, but research in Nepal also shows the same results *K. pneumoniae* 44%, *P. aeruginosa* 29%, *E. coli* 20% (Rooku *et al.*, 2019).

• Effective antibiotic treatment in HIV patient

In this study, a lot of antibiotics resistance was found. In gram-negative bacteria antibiotic, Cefoperazone-sulbactam showed the greatest sensitivity where only one *P. aeruginosa* resistant isolate was found while in other bacteria, it still showed 100% sensitivity. Other antibiotics that can be considered are Amikacin, Gentamycin and piperacillin-tazobactam, which still show good sensitivity where no more than one isolate in one type of bacteria is resistant. In gram-positive bacteria, antibiotics that show good sensitivity are Chloramphenicol, Linezolid and Vancomycin, but Chloramphenicol shows low sensitivity to gram-negative bacteria.

Ampicillin in this study showed the greatest resistance where almost all isolates were resistant. This result is supported by research conducted in India where the antibiotic Ampicillin showed high resistance to the

bacteria *Acinetobacter spp.*, *E. coli*, *Klebsiella spp.* and other gram-negative bacteria (Chandwani *et al.*, 2017). The same goes for studies in South Africa where *E. coli* and *K. pneumoniae* show high resistance to ampicillin (Jaspan *et al.*, 2008).

In this study, Cotrimoxazole, the WHO (2014) antibiotic recommendation for prophylaxis of opportunistic infections, has been resistant in many HIV patients. In gram-positive bacteria, this antibiotic still shows good results. However, this is not the case in gram-negative bacteria where *E. coli* and *P. aeruginosa* bacteria were found all isolates resistant. In *K. pneumoniae* and *K. aerogenes*, some isolates are still sensitive, and in *A. baumannii*, it is still 75% sensitive. These results are not much different from studies in Nepal where the Cotrimoxazole resistance is found in more than 80% to the bacteria *K. pneumoniae*, *P. aeruginosa*, *E. coli* and *Acinetobacter spp.* (Rooku *et al.*, 2019). A study in Tanzania shows a very high resistance from Cotrimoxazole (100%) against *K. pneumoniae* and 93.3% against *E. coli* (Chaula *et al.*, 2017) as well as in research at Hasan Sadikin Hospital Bandung where Cotrimoxazole 37% is resistant to *K. pneumoniae* and 100% against *P. aeruginosa* (Melindah *et al.*, 2016).

• Specimen examination time

In blood culture, it takes 4.63 (\pm 0.8) days. This time is longer when compared to the study of Tabak *et al.* (2018) where the average time taken from the specimen is taken until the release of organism identification results is only two days and three days when it comes to antibiotic sensitivity tests, while other studies mention that three days is sufficient to find up 97% of clinically significant microorganisms (Riley *et al.*, 2003).

In sputum culture, it takes 3.02 (\pm 1.1) days. This amount of time, when compared to one of the hospitals in the U.K. Oxford University Hospital (2018), recorded better results where they needed an average of 5 days. In the book "Clinical Manifestations & Assessment of Respiratory Disease," the time needed for bacterial identification and antibiotic sensitivity testing in sputum culture is 2-3 days (Terry *et al.*, 2016).

In urine culture, it takes 2.89 (\pm 0.8) days. This amount of time is quite appropriate when compared with research by Davenport *et al.* (2017), which says the time taken from urine collection to identification of pathogens is around 0.75-1.25 days and an additional 1-2 days for antibiotic sensitivity tests. Other studies say the recommended minimum incubation time is 16 hours (0.67 days), and a urine culture can be reported negative after 18 hours (0.75 days) incubation (McCarter *et al.*, 2009).

In fecal and pus cultures, it takes 3.75 (\pm 0.9) days. This time is longer when compared to the study of Mortensen *et al.* (2015) where the culture results only require 1.7-2.25 days. In another study in California, it was mentioned that the time needed for fecal culture was 2.97 days (Sobczyk *et al.*, 2020).

CONCLUSION

This study showed bacteria pattern that caused opportunistic infection in RSUD Dr. Soetomo, Surabaya, Indonesia is *K. pneumoniae* as most common gram-negative bacteria followed by *E. coli*, *P. aeruginosa* and *A. baumannii*; while the most gram-positive bacteria found are *S. mitis/oralis* and *S. aureus*. Ampicillin in this study showed the lowest sensitivity to almost all bacteria isolates.

ACKNOWLEDGMENTS

Researchers would like to thank the Intermediate Care Unit and Infectious Diseases Unit (UPIPI) Department/SMF Internal Medicine and Clinical Microbiology Installation Faculty of Medicine, Universitas Airlangga/Dr. Soetomo General Hospital Surabaya, Indonesia. The author states that there is no conflict of interest in this study.

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