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

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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 baumanii (8.1%). The highest prevalence of gram-positive bacteria was Streptococcus mitis/oralis (30.7%), followed by Staphylococcus aureus (15.4%) 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. pneumonia as most common gram-negative bacteria followed by E. coli, P. aeruginosa and A. baumanii; 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.

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ABSTRAK

Latar Belakang: Pasien HIV dengan sistem imun yang lemah sangat rentan terhadap kejadian infeksi oportunistik, dapat memicu terjadinya aktivasi endoteli 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 menyebarakan infeksi opportunistik berserta 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 baumanii (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. pneumonia, bakteri gram-negatif terbanyak diikuti oleh E. coli, P. aeruginosa dan A. baumanii; 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.
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 lymphocytes, 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 (± 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/µL (23.4%) with an average of 155.9 cells/µL, a median value 38 cells/µL, the highest value 917 cells/µL and the lowest one cell/µL.

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 (Shah et al., 2020). Therapeutic options for *Acinetobacter baumannii* are Ampicillin-sulbactam and Imipenem (Morris and Cerceo, 2020). Therapeutic options for *Pseudomonas aeruginosa* are Amikacin, Ceftazidime 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

| 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)**

- *Streptococcus mitis/oralis*: 4 (30.7)
- *Staphylococcus aureus* (MRSA 1): 3 (23.1)
- *Staphylococcus epidermidis*: 2 (15.4)
- *Staphylococcus sciuri*: 1 (7.7)
- *Staphylococcus hominis*: 1 (7.7)
- *Cellulomonas turbata*: 1 (7.7)
- *Methicilin-resistant Staphylococcus aureus + Streptococcus mitis/oralis*: 1 (7.7)

**Gram-negative (n= 37)**

- *Klebsiella pneumoniae* (ESBL 6): 13 (35.1)
- *Escherichia coli* (ESBL 1): 4 (10.8)
- *Pseudomonas aeruginosa*: 3 (8.1)
- *Acinetobacter baumannii*: 3 (8.1)
- *Enterobacter cloacae*: 2 (5.4)
- *Proteus mirabilis*: 2 (5.4)
- *Klebsiella aerogenes*: 2 (5.4)
- *Salmonella spp.*: 2 (5.4)
- *Burkholderia cepo*: 1 (2.7)
- *Moraxella catarrhalis*: 1 (2.7)
- *Neisseria animaloris*: 1 (2.7)
- *Stenotrophomonas maltophilia*: 1 (2.7)
- *Klebsiella pneumoniae + Klebsiella aerogenes*: 1 (2.7)
- *Escherichia coli + Pseudomonas aeruginosa + Spingomonas paucimobilis*: 1 (2.7)

**Mixed (n= 2)**

- *Acinetobacter baumannii* (Gram-) + *Gemella morbillorum* (Gram+): 1 (½)
- *Pseudomonas pseudoalcaligenes* (Gram-) + *Staphylococcus hemolitycus* (Gram+): 1 (½)
| Specimen (n=83) | n  | (%)  |
|----------------|----|------|
| Positive culture | 52 | 62.7 |
| Negative culture | 31 | 37.3 |

**Bacteria**

| Specimen | n  | (%)  |
|-----------|----|------|
| **Blood** (n=27) | | |
| *Salmonella* spp. (Gram-) | 2 | 7.4 |
| *Staphylococcus epidermidis* (Gram+) | 2 | 7.4 |
| *Cellulomonas turbata* (Gram+) | 1 | 3.7 |
| *Methicillin-resistant Staphylococcus aureus* (Gram+) | 1 | 3.7 |
| *Neisseria animaloris* (Gram-) | 1 | 3.7 |
| *Staphylococcus hominis* (Gram+) | 1 | 3.7 |
| *Staphylococcus sciuri* (Gram+) | 1 | 3.7 |

| Specimen | n  | (%)  |
|-----------|----|------|
| **Sputum** (n=43) | | |
| *Klebsiella pneumoniae* (Gram-) | 12 | 27.9 |
| *Streptococcus mitis/oralis* (Gram+) | 4 | 9.3 |
| *Pseudomonas aeruginosa* (Gram-) | 3 | 7 |
| *Acinetobacter baumannii* (Gram-) | 2 | 4.7 |
| *Enterobacter cloacae* (Gram-) | 2 | 4.7 |
| *Staphylococcus aureus* (Gram+) | 2 | 4.7 |
| *Burkholderia cepo* (Gram-) | 1 | 2.3 |
| *Klebsiella aerogenes* (Gram-) | 1 | 2.3 |
| *Moraxella catarrhalis* (Gram-) | 1 | 2.3 |
| *Stenotrophomonas maltophilia* (Gram-) | 1 | 2.3 |
| *Acinetobacter baumannii* (Gram-)+ *Gemella morbillorum* (Gram+) | 1 | 2.3 |
| *Methicillin-resistant Staphylococcus aureus* (Gram+)+ *Streptococcus mitis/oralis* (Gram+) | 1 | 2.3 |
| *Pseudomonas pseudoalcaligenes* (Gram-)+ *Staphylococcus hemolyticus* (Gram+) | 1 | 2.3 |
| *Escherichia coli* (Gram-)+ *Pseudomonas aeruginosa* (Gram-)+ *Spingomonas paucimobilis* (Gram-) | 1 | 2.3 |

| Specimen | n  | (%)  |
|-----------|----|------|
| **Urine** (n=9) | | |
| *Escherichia coli* (Gram-) | 2 | 22.2 |
| *Proteus mirabilis* (Gram-) | 2 | 22.2 |
| *Acinetobacter baumannii* (Gram-) | 1 | 11.1 |
| *Klebsiella aerogenes* (Gram-) | 1 | 11.1 |

| Specimen | n  | (%)  |
|-----------|----|------|
| **Fecal/Pus** (n=4) | | |
| *Escherichia coli* (Gram-) | 2 | 1/2 |
| *Klebsiella pneumoniae* ESBL (Gram-) | 1 | 1/4 |
| *Klebsiella pneumoniae* (Gram-)+ *Klebsiella aerogenes* (Gram-) | 1 | 1/4 |

**Note:** (-) = Antibiotic not tested
**Antibiotic sensitivity in HIV patient**

Table 4. Antibiotic sensitivity in gram-positive bacteria

| Antibiotik                        | *Streptococcus mitis/oralis* (5) | *Staphylococcus aureus* (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%)                 |
| Erithromycin                      | 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

| Antibiotic                    | Klebsiella pneumonia (n=14) | Escherichia coli (n=5) | Acinetobacter baumannii (n=4) | Pseudomonas aeruginosa (n=4) | Klebsiella aerogenes (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%)                  |
| Astreomam                     | 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%)               |
| Cephalozin                    | 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%)               |
| Levofoxacin                   | 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 Aiyiulu (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/µL 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. pneumonia* followed by *E. coli*, *P. aeruginosa* and *A. baumanii*, 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. pneumonia* 52.08% and *E. coli* 47.92% and studies with pediatric patients at the same location obtained *K. pneumonia* 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. pneumonia and K. aerogenes, some isolates are still sensitive, and in A. Baumanii, 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. pneumonia, P. aeruginosa, E. coli and Acinetobacter spp. (Rooku et al., 2019). A study in Tanzania shows a very high resistance from Cotrimoxazole against K. pneumoniae (100%) 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 (± 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 (± 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 (± 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).

CONCLUSION

This study showed bacteria pattern that caused opportunistic infection in RSUD Dr. Soetomo, Surabaya, Indonesia is K. pneumonia as most common gram-negative bacteria followed by E. coli, P. aeruginosa and A. baumanii; 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.

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REFERENCES

BPS, 2019. Indikator Pendidikan 1994-2020. Jakarta.

Budayanti, N.S., Suryawan, K., Iswari, I.S., Sukrama, D.M., 2019. The Quality of Sputum Specimens as A Predictor of Isolated Bacteria from Patients with Lower Respiratory Tract Infections at A Tertiary Referral Hospital, Denpasar, Bali, Indonesia. Front. Med. 5, 64.

CDC, 2019a. About HIV/AIDS | HIV Basics | HIV/AIDS | CDC [WWW Document]. Cent. Dis. Control Prev. URL https://www.cdc.gov/hiv/basics/whatishiv.html (accessed 5.7.19).

CDC, 2019b. Opportunistic Infections | Living with HIV | HIV Basics | HIV/AIDS | CDC [WWW Document]. Cent. Dis. Control Prev. URL https://www.cdc.gov/hiv/basics/livingwithhiv/opportunisticinfections.html (accessed 5.7.19).
Chandra, A., Firth, J., Sheikh, A., Patel, P., 2013. Emergencies Related to HIV Infection and Treatment (Part 1) (Part 2). African J. Emerg. Med. 3, 142–149.

Chandwani, J., Vyas, N., Hooja, S., 2017. Antibiotic Susceptibility Pattern of Bacteria Causing Lower Respiratory Tract Infections in HIV/AIDS Patients with Correlation to CD4+ T Cell Counts. Int. J. Med. Res. Prof. 3, 228–233.

Chaula, T., Seni, J., Ng’walida, N., Kajura, A., 2017. Urinary Tract Infections among HIV-Positive Pregnant Women in Mwanza City, Tanzania, Are High and Predicted by Low CD4+ Count. Int. J. Microbiol. 1, 1–7.

Davenport, M., Mach, K.E., Shortliffe, L.M.D., Banaei, N., Wang, T.-H., Liao, J.C., 2017. New and Developing Diagnostic Technologies for Urinary Tract Infections. Nat. Rev. Urol. 14, 296–310.

Enany, S., Zakeer, S., Sayed, A.A., Magdeldin, S., 2020. Shotgun Proteomic Analysis of ESBL-producing and Non-ESBL-producing Klebsiella Pneumoniae Clinical Isolates. Microbiol. Res. 234, 126423.

Huson, M.A., Grobusch, M.P., Van der Poll, T., 2014. The Effect of HIV Infection on the Host Response to Bacterial Sepsis. Lancet Infect. Dis. 15, 95–108.

Irawan, D., Hamidah, Purwati, E.A., 2012. Profil Penderita Sepsis Akibat Bakteri Penghasil ESBL. J. Kependud. Indones. 3, 75–95.

Iribarren, J.A., Rubio, R., Aguirrebengoa, K., Arribas, J.R., Barea-Etxaburu, J., Gutierrez, F., Bernaldo de Quiros, J.C.L., Lasa, J.E., Miro, J.M., Moreno, S., Molina, J.P., Podzamczer, D., Pulido, F., Riera, M., Rivero, A., Moreno, J.S., Amador, C., Antela, A., Arazo, P., Arribabagala, J., Bachiller, P., Barros, C., Berenguer, J., Cayla, J., Domingo, P., Estrada, V., Knobel, H., Locutura, J., Aldeguer, J.L., Llibre, J.M., Lozano, F., Mallolas, J., Malmierca, E., Miralles, C., Miralles, P., Munoz, A., Ocampo, A., Olalla, J., Perez, I., Elias, M.J.P., Arellano, J.L.P., Portilla, J., Ribera, E., Rodriguez, F., Santin, M., Sanz, J.S., Tellez, M.J., Torralba, M., Valencia, E., Von Wichmann, M.A., Committee, G.W., 2016. Executive Summary: Prevention and Treatment of Opportunistic Infections and other Coinfections in HIV-Infected Patients: May 2015. Enfermedades Infecc. Microbiol. Clin. 34, 517–523.

Japiassu, A.M., Amancio, R.T., Mesquita, E.C., Medeiros, D.M., Bernal, H.B., Nunes, E.P., Luz, P.M., Grinztejn, B., Bozza, F.A., 2010. Sepsis is A Major Determinant of Outcome in Critically Ill HIV/AIDS Patients. Crit. Care 14, 1–8.

Jaspan, H.B., Haung, L.C., Cotton, M.F., Whetlalaw, A., Myer, L., 2008. Bacterial Disease and Antimicrobial Susceptibility Patterns in HIV-Infected, Hospitalized Children: A Retrospective Cohort Study. PLoS One.

Kambu, Y., Waluyo, A., Kuntarti, K., 2016. Umur Orang dengan HIV AIDS (ODHA) Berhubungan dengan Tindakan Pencegahan Penularan HIV. J. Keperawatan Indones. 19, 200–207.

Kemenkes, 2018. Laporan Situasi Perkembangan HIV/AIDS dan PIMS di Indonesia Januari-Desember 2017. Jakarta.

Laah, J., Ayiwulu, E., 2010. Socio-Demographic Characteristics of Patients Diagnosed with HIV/AIDS in Nasara West, Nigeria. Asian J. Med. Sci. 114–120.

Malek, A., McGlyn, K., Taffner, S., Fine, L., Tesini, B., Wang, J., Mostafa, H., Petry, S., Perkins, A., Graman, P., Hardy, D., Pecora, N., 2019. Next Generation-Sequencing-Based Hospital Outbreak Investigation Yields Insight into Klebsiella Aerogenes Population Structure and Determinants of Carbapenem Resistance and Pathogenicity. Antimicrob. Agents Chemother. 63, 1–16.

McCarter, Y.S., Burd, M.B., Hall, G.S., Zervos, M., 2009. Laboratory Diagnosis of Urinary Tract Infections. Cumittec 2C. Amer Society for Microbiology, Washington DC.

Melhuish, A., Lewthwaite, P., 2018. A Natural History of HIV and AIDS. Medicine (Baltimore). 46, 356–361.

Melindah, Santos, P., Supriatna, Y.A., Turbawati, D.K., 2016. Korelasi Jumlah Cluster of Differentiation 4 dengan Jenis Bakteri Penyebab Infeksi Paru pada Kultur Bilasan Bronkoalveolar pada Pasien Human Immunodeficiency Virus. Maj. Kedokt. Bandung 48, 32–38.

Morris, S., Cerceo, E., 2020. Trends, Epidemiology and Management of Multi-Drug Resistant Gram-Negative Bacterial Infections in the Hospitalized Setting. Antibiotics 9, 1–20.

Mortensen, J.E., Ventrola, C., Hannda, S., Walter, A., 2015. Comparison of Time-motion Analysis of Conventional Stool Culture and The BD MAXTM Enteric Bacterial Panel (EBP). BMC Clin. Pathol. 15, 1–6.

Muhajar, A., Purwono, P.B., Handayani, S., 2016. Gambaran Terapi dan Luaran Infeksi Saluran Kemih oleh Bakteri Penghasil Extended Spectrum Beta Lactamase pada Anak di RSUD Dr. Soetomo Surabaya. Sari Pediatri. 18, 111–116.

Pan, S.W., Tang, W., Cao, B., Ross, R., Tucker, J.D., 2017. Buddhism and Coping With HIV in China. J. Assoc. Nurses AIDS Care Janac 28, 666–667.

Piperaki, E., Syrogiannopoulos, G.A., Tzouvelekis, L.S., Daikos, G.L., 2017. Klebsiella Pneumoniae: Virulence, Biofilm and Antimicrobial Resistance. Pediatr. Infect. Dis. J. 36, 1002–1005.

Preau, M., Bouhnik, A.D., Roussiau, N., Lert, F., Spire, B., 2008. Disclosure and Religion among People Living with HIV/AIDS in France. AIDS Care 20, 521–526.

Purwaningsih, S.S., Widajatun, N., 2008. Perkembangan HIV dan AIDS di Indonesia: Tinjauan Sosio Demografis. J. Kependud. Indonesia. 3, 75–95.

Rahardjo, W., Rutagule, I.I., 2016. Harga Diri Sekual, Kompsulivitas Sekual dan Perlaku Seks Berisiko pada Orang dengan HIV/AIDS. J. Psikol. 43, 52–65.
Rangkuti, A.Y., 2013. Karakteristik Penderita AIDS dan Infeksi Opurtunistik di Rumah Sakit Umum Pusat (RSUP) Hh. Adam Malik Medan Tahun 2012. J. Univ. Sumatera Utara 2, 1–16.

Riley, J.A., Heiter, B.J., Bourbeau, RP., 2003. Comparison of Recovery of Blood Culture Isolates from Two Bact/ALERT FAN Aerobic Blood Culture Bottles with Recovery from One FAN Aerobic Bottle and One FAN Anaerobic Bottle. J. Clin. Microbiology 41, 213–217.

Rooku, K.C., Adhikari, S., Bastola, A., Devkota, L., Bhandari, P., Prabina, G., Adhikari, B., Raj Rijal, K., Raj Banjara, M., Prakash, G., 2019. Opportunistic Respiratory Infections in HIV Patients Attending Sukraraj Tropical and Infectious Diseases Hospital in Kathmandu, Nepal. HIV/AIDS - Res. Palliat. Care 11.

Shah, S., Golden, M., E., T.J., McManus, D., 2020. Intravenous (IV) Cefazolin with Oral Probenecid: A Novel Daily Regimen for The Management of Methicillin-Sensitive Staphylococcus Aureus (MSSA) Bacteremia in A Patient with Renal Dysfunction. IDCases 19, 1–3.

Sobczyk, J., Jain, S., Sun, X., Karris, M., Wooten, D., Stagnaro, J., Reed, S., 2020. Comparison of Multiplex Gastrointestinal Pathogen Panel and Conventional Stool Testing for Evaluation of Patients with HIV Infection. Oxford Univ. Press behalf Infect. Dis. Soc. Am. 7, 1–6.

Tabak, Y.P., Vankeepuram, L., Ye, G., Jeffers, K., Gupta, V., Murray, P.R., 2018. Blood Culture Turnaround Time in U.S. Acute Care Hospital and Implications for Laboratory Process Optimization. J. Clin. Microbiology 56, 1–8.

Taylor, J., Ossei, P.P., Agyeman-Duah, E., Baah, E., Fenteng, E.A., Ayilbor, W., 2018. Sociodemographic Characteristics of People Living with HIV/AIDS at The Komfo Anokye Teaching Hospital, Ghana: A Five-Year Retrospective Study. Acta Sci. Medial Sci. 2, 42–47.

Terry, D.J., Burton, G., T., P., 2016. Clinical Manifestations and Assessment Of Respiratory Disease, 7th ed. Elsevier.

Velayati, A.-A., Bakayev, V., Bahadori, M., Tabatabaei, S.-J., Alaei, A., Farahbood, A., Masjedi, M.-R., 2007. Religious and Cultural Traits in HIV/AIDS Epidemics in Sub-Saharan Africa. Iran. Med. 10, 486–497.

WHO, 2014. Guidelines On Post-Exposure Prophylaxis For HIV And The Use Of Co-Trimoxazole Prophylaxis For HIV-Related Infections Among Adults, Adolescents, And Children. Switzerland.

WHO, 2017. HIV/AIDS [WWW Document]. URL https://www.who.int/hiv/data/en/ (accessed 5.7.19).

WHO, 2018. HIV/AIDS [WWW Document]. URL https://www.who.int/en/news-room/fact-sheets/detail/hiv-aids (accessed 5.7.19).

Yelfi, A., Nugroho, S.A., Tantri, N.D., 2018. Karakteristik Sosiodemografi, Klinis dan Pola Terapi Antiretroviral Pasien HIV/AIDS di RSPI Prof. Dr. Sulianti Saroso Periode Januari - Juni 2016. J. Pharm. Indones. 15, 72–89.