ABSTRACT

Gram-negative bacterial are known as common pathogen caused infection in Pediatric Intensive Care Unit (PICU). Microbial Pattern and Antibiotic Susceptibility are needed as clinical data for selected appropriate antibiotic therapy. In PICU Dr. Soetomo hospital until now still lacking of Microbial Pattern and Antibiotic Susceptibility data. This descriptive study is to recognized Microbial Pattern and Antibiotic Susceptibility in PICU patients from blood, urine, sputum, stool, cerebrospinal fluid, endotracheal tube, pus swab and pleural fluid culture specimens. Patients whose admitted into PICU without signs of infections were excluded from the study. The inclusion criteria are patients with sign infection as follows: fever < 36.5°C or > 37.5°C, leukocyte < 4000/mm³ or > 10000/mm³, marker infections CRP >10 mg/L or PCT >0,3 ng/mL, bradycardia or tachycardia, tachypnea, infiltrates on chest X-ray, turbid urine, dysuria, thrombophlebitis, abdominal pain or tenderness, and mucous or skin lesion. Medical record data from 2011 to 2016, revealed 1138 patients had positive microbial culture result, wherein positive result came from blood 44.46%, urine 19.15%, sputum 11.59%, stool 8.96%, cerebrospinal fluid 7.50%, endotracheal tube 4.04%, pus swab 2.89%, and pleural fluid 1.41%. The microorganisms found in PICU Dr. Soetomo was dominated with gram negative bacteria. Commonest bacterial that recognized from blood was B. cepacea, urine was E. coli, sputum was P. aeruginosa, stool was E. coli, cerebrospinal fluid was S. cohnii, endotracheal tube was K. pneumoniae ESBL, pus swab was S. aureus, and pleural fluid was S. maltophilia. Both gram-negative bacteria and gram-positive bacteria isolates revealed multiple drug resistance to commonly used antibiotic, but still had good susceptibility for antibiotic such as; amikacin, cefoperazone-sulbactam, linezolid, vancomycin and carbapenem group.

Keywords: PICU, Microbial Patern, Dr. Soetomo Hospital, Bacteria, Antibiotic.
pneumoniae ESBL pada ETT, S. aureus pada pus luka, S. maltophilia pada cairan pleura. Isolat bakteri gram negatif maupun gram positif yang telah didapatkan menunjukan adanya resistensi berberapa golongan antibiotik yang umumnya sering digunakan tetapi beberapa jenis antibiotik lain masih menunjukan kepekaan yang baik terhadap antibiotik seperti amikasin, cefoperazone-sulbactam, linezolid, vancomycin dan grup karbapenem.

Kata kunci: Rawat Intensif Anak, Pola Bakteri, Rumah Sakit Dr. Soetomo, Bakteri, Antibiotik.

INTRODUCTION

In this two decade nosocomial Infections are special health problem concerned in terms of morbidities, mortalities and economic consequences.1 Especially eventful in pediatric intensive care units (PICU) that have more eminent incidence rate than another ward in hospital.2 These outcome were correlated with prolonged hospital stay, severity of diseases in PICU patients, excessive use of antibiotic and patients often exposed to medical intervention tools such as; peripherals intravenous or central venous lines, urinary catheterization, mechanical ventilation, etc.2-3 Respiratory tract infections, and bloodstream infections are considerably occurring infection in PICU.3 Both gram-positive bacteria (GPB) and gram-negative bacteria (GNB) have been reported as commonly pathogen causing infection. Recently, GNB have been presented more often than GPB in this setting.4

Knowledge updated about prevalence of the causative agent’s infections and antimicrobial susceptibility patterns in PICU are important for proper management of nosocomial infections,4-5 There were lack quantity of published studies on microbial pattern and antibiotic susceptibility in PICU patients from Indonesia. This study was brought to determine it, especially from PICU patients in Dr. Soetomo Hospital Surabaya. This hospital provides tertiary health care as referral hospital from primary health care or secondary health care in East Java and East Indonesia region.

METHODS

This descriptive study was carried out in Dr. Soetomo General Hospital. The data were collected from medical record from January 2011 to January 2016. Ethical clearance issued by Medico-legal Committee Soetomo Hospital. Information collected include the demographic data, Primary diseases diagnosis, specimen, causative agent, and antibiotic sensitivity pattern. Patients admitted into PICU without signs of infections were excluded from the study. The inclusion criteria are patients with sign infection as follows: fever < 36.5°C or > 37.5°C, leucocyte < 4000/mm³ or > 10000/mm³, marker infections CRP >10 mg/L or PCT > 0.3 ng/mL, bradycardia or tachycardia, tachypnea, infiltrates on chest X-ray, turbid urine, dysuria, thrombophlebitis, abdominal pain or tenderness, mucous or skin lesion. SPSS 17 version was used to process descriptive statistics data.

RESULT

Over period of 5 years, 4144 patients admitted in the PICU were analyzed. There were 1138 (27.46%) patient with positive culture result (Table 1), girls (59.92%) are dominant than boys (40.07%) with mean age 4 ± 0.8 years.

Primary diseases admitted patients in PICU with culture positive result were dominated with respiratory tracts infection and followed by nervous system diseases (Table 2). Microbial culture also undertaken in patients such as; Congenital Heart Diseases (CHD), Acute Leukemic Lymphoblastic (ALL), Dengue Hemorrhagic Fever (DHF), Acute diarrhea, and others, because while being treated show clinical signs or symptom suggested of infections.

Blood culture result were dominated with gram-negative bacteria (GNB) (14 species bacteria), followed 16 species gram-positive bacteria (GPB). The commonest GNB were B. cepacea (Table 3) and GPB were S. haemolyticus (Table 4).

Table 1. Positive culture result from various specimen in PICU patients

| Specimen       | Total Sample | Positive Result (%) |
|----------------|--------------|---------------------|
| Blood          | 1345         | 506 (37.62)         |
| Urine          | 824          | 218 (26.45)         |
| Sputum         | 643          | 132 (20.52)         |
| Stool          | 582          | 102 (17.52)         |
| Cerebrospinal fluid | 348    | 86 (24.71)         |
| Endotracheal tube | 213    | 46 (21.59)         |
| Pus            | 102          | 32 (31.37)          |
| Pleural        | 87           | 16 (18.39)          |

Table 2. Primary diseases distribution of positive culture result in PICU Patient.

| Primary Diseases         | (f) | (%)  |
|--------------------------|-----|------|
| Pneumonia                | 341 | 29.96|
| Encephalitis             | 248 | 21.79|
| s. Meningoencephalitis   | 149 | 13.09|
| Bronchopneumonia         | 124 | 10.89|
| Congenital Heart Diseases| 97  | 8.52 |
| Oncologic Diseases       | 49  | 4.30 |
| Renal Diseases           | 44  | 3.86 |
| Post-surgery procedure   | 38  | 3.33 |
| Diarrhea                 | 32  | 2.81 |
| Dengue Hemorrhagic Fever | 25  | 2.19 |
| Diabetic ketoacidosis    | 17  | 1.49 |
| Biliary atresia          | 5   | 0.43 |
Urine culture specimen were dominated with GNB (10 species) followed GPB (8 species). The commonest GNB were *E. coli* (Table 5) and GPB were *S. haemolyticus* (Table 6).

Sputum culture specimen were dominated with GNB (8 species) followed GPB (9 species). The most common GNB were *P. aeruginosa* (Table 7) and GPB were *S. epidermidis* (Table 8). Higher rate of *S. epidermidis* in this study might be caused by contaminant at recruitment sampling process.

Stool culture specimen were also dominated with GNB (8 species) followed GPB (6 species). The commonest GNB were *E. coli* (Table 9) and GPB were *Enterococcus* spp. (Table 10).

Cerebrospinal fluid (CSF) culture was dominated with GPB (8 species) followed GNB (7 species). The commonest GPB species were *S. cohnii* (Table 11) and GNB were *A. baumannii* (Table 12). CSF culture with *S. cohnii* and *A. baumannii* in the study result, might be considered as contaminant bacteria while recruitment process because 52 patients with surgery history with device insertion. It is connected the intracerebral area with outer enviroment from External Ventriculo Drainage (EVD) device while sampling process.

Endotracheal tube (ETT) aspirate culture specimen was dominated with GNB (6 species) followed GPB (4 species). The commonest GNB were *K. pneumoniae* (ESBL+) (Table 13) and GPB were *S. haemolyticus* (Table 14).

Pus/ wound swab culture specimen were dominated with GPB (8 species) followed GNB (5 species). The GNB were *P. aeruginosa* (Table 7) and GPB were *S. epidermidis* (Table 8). Higher rate of *S. epidermidis* in this study might be caused by contaminant at recruitment sampling process.

Stool culture specimen were also dominated with GNB (8 species) followed GPB (6 species). The commonest GNB species were *E. coli* (Table 9) and GPB were *Enterococcus* spp. (Table 10).

Cerebrospinal fluid (CSF) culture was dominated with GPB (8 species) followed GNB (7 species). The commonest GPB species were *S. cohnii* (Table 11) and GNB were *A. baumannii* (Table 12). CSF culture with *S. cohnii* and *A. baumannii* in the study result, might be considered as contaminant bacteria while recruitment process because 52 patients with surgery history with device insertion. It is connected the intracerebral area with outer enviroment from External Ventriculo Drainage (EVD) device while sampling process.

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Pus/ wound swab culture specimen were dominated with GPB (8 species) followed GNB (5 species). The

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**Table 3.** GNB species finding in blood culture

| Bacteria Species | (n=334) | (%)   |
|------------------|---------|-------|
| B. cepacea       | 57      | 17.06 |
| K. pneumonia (ESBL+) | 56     | 16.76 |
| A. baumannii     | 44      | 13.17 |
| K. pneumonia      | 37      | 11.14 |
| P. aeruginosa     | 33      | 9.88  |
| E. coli          | 29      | 8.68  |
| E. cloacae       | 21      | 6.28  |
| S. marcescens    | 15      | 4.49  |
| M. catarrhalis   | 12      | 3.59  |
| S. typhi         | 9       | 2.69  |
| E. coli (ESBL+)  | 9       | 2.69  |
| P. alcalifaciens | 7       | 2.09  |
| Pasteurella spp. | 3       | 0.89  |
| S. paratyphi     | 2       | 0.59  |

**Table 4.** GPB species finding in blood culture

| Bacteria Species | (n=172) | (%)   |
|------------------|---------|-------|
| S. haemolyticus  | 55      | 31.97 |
| S. hominis       | 35      | 20.35 |
| S. epidermidis   | 16      | 9.30  |
| S. saprophyticus | 14      | 8.13  |
| S. aureus        | 13      | 7.55  |
| MRSA             | 12      | 6.97  |
| S. intermedius   | 5       | 2.90  |
| S. cohnii        | 4       | 2.32  |
| E. faecalis      | 3       | 1.75  |
| Corynebacterium spp. | 3 | 1.75 |
| M. lylae         | 3       | 1.75  |
| S. gallinarum    | 2       | 1.17  |
| S. kloosii       | 2       | 1.17  |
| S. warneri       | 2       | 1.17  |
| S. ureolyticus   | 2       | 1.17  |
| S. parasanguinis | 1       | 0.58  |

**Table 5.** GNB species finding in urine culture

| Bacteria Species | (n=159) | (%)   |
|------------------|---------|-------|
| E. coli          | 81      | 50.94 |
| E. coli (ESBL+)  | 33      | 20.75 |
| K. pneumonia (ESBL+) | 13  | 8.18  |
| E. cloacae       | 11      | 6.92  |
| B. cepacea       | 5       | 3.14  |
| P. aeruginosa     | 5       | 3.14  |
| A. baumannii     | 3       | 1.89  |
| E. aerogenes     | 3       | 1.89  |
| S. marcescens    | 2       | 1.26  |
| P. retgeri       | 1       | 0.63  |
| P. mirabilis     | 1       | 0.63  |
| Aeromonas spp.   | 1       | 0.63  |

**Table 6.** GPB species finding in urine culture

| Bacteria Species | (n=59) | (%)   |
|------------------|--------|-------|
| Gram Positive Bacteria : | | |
| S. haemolyticus  | 11     | 18.64 |
| S. epidermidis   | 10     | 16.94 |
| S. cohnii        | 9      | 15.26 |
| E. faecalis      | 9      | 15.26 |
| MRSA             | 8      | 13.56 |
| E. faecium       | 5      | 8.47  |
| S. warneri       | 3      | 5.09  |
| S. ureolyticus   | 2      | 3.39  |
| S. parasanguinis | 2      | 3.39  |

**Table 7.** GNB species in sputum culture.

| Bacteria Species | (n=88) | (%) |
|------------------|--------|-----|
| P. aeruginosa    | 42     | 47.72 |
| K. pneumonia     | 22     | 25.00 |
| E. coli (ESBL+)  | 9      | 10.22 |
| A. baumannii     | 6      | 6.82  |
| S. maltophilia   | 3      | 3.42  |
| E. cloacae       | 3      | 3.42  |
| S. marcescens    | 2      | 2.27  |
| S. fonticola     | 1      | 1.13  |

**Table 8.** GPB species in sputum culture.

| Bacteria Species | (n=44) | (%) |
|------------------|--------|-----|
| S. epidermidis   | 25     | 52.27 |
| MRSA             | 8      | 18.18 |
| S. capitis       | 6      | 13.64 |
| S. haemolyticus  | 6      | 13.64 |
| S. pneumonia     | 1      | 2.27  |
Putra, et al.: Microbial Pattern and Antibiotic Susceptibility

Pleural fluid culture specimen was dominated with GNB (5 species bacteria) followed GPB (4 species bacteria). The commonest GNB were *S. maltophilia* (Table 17) and GPB were *S. epidermidis* (Table 18). Over 32 wound positive culture isolate in our study were undertaken from 37 pediatric patients with history surgical site infection.

### Table 9. GNB species in stool culture

| Bacteria Species | n=65 | (%) |
|------------------|------|-----|
| *E. coli*        | 34   | 52.30 |
| *E. coli* (ESBL+) | 2   | 3.07 |
| *E. coli* (ESBL+) | 2   | 3.07 |
| *K. pneumoniae* (ESBL+) | 2   | 3.07 |
| *C. youngae*     | 2    | 3.07 |
| *C. jejuni*      | 1    | 1.55 |
| *C. testosteroni*| 1    | 1.55 |

### Table 10. GPB species in stool culture

| Bacteria Species | n=37 | (%) |
|------------------|------|-----|
| *E. cloacae*     | 19   | 51.35 |
| *S. aureus*      | 10   | 27.03 |
| *S. epidermidis* | 3    | 8.11 |
| *M. testosteroni*| 1    | 2.70 |
| *C. difficile*   | 1    | 2.70 |

### Table 11. GPB species in CSF culture

| Bacteria Species | n=56 | (%) |
|------------------|------|-----|
| *S. cohnii*      | 11   | 19.64 |
| *S. epidermidis* | 9    | 16.07 |
| *S. haemolyticus*| 8    | 14.28 |
| *S. aureus*      | 7    | 12.50 |
| *E. faecalis*    | 7    | 12.50 |
| *A. viridans*    | 4    | 7.15 |
| *M. testosteroni*| 3    | 5.36 |

### Table 12. GNB species in CSF culture

| Bacteria Species | n=30 | (%) |
|------------------|------|-----|
| *A. baumannii*   | 10   | 33.33 |
| *E. cloacae*     | 7    | 23.34 |
| *P. aeruginosa*  | 6    | 20.00 |
| *E. coli* (ESBL+) | 3  | 10.00 |
| *B. liminata*    | 2    | 6.67 |
| *P. stutzeri*    | 1    | 3.33 |
| *B. cepacia*     | 1    | 3.33 |

### Table 13. GNB species in ETT aspirate

| Bacteria Species | n=37 | (%) |
|------------------|------|-----|
| *K. pneumonia* (ESBL+) | 16  | 43.24 |
| *P. aeruginosa*     | 11   | 29.72 |
| *A. baumannii*   | 6    | 16.22 |
| *E. coli* (ESBL+) | 2    | 5.42 |
| *S. marcescens*  | 1    | 2.70 |
| *B. cepacia*      | 1    | 2.70 |

### Table 14. GPB species in ETT aspirate

| Bacteria Species | n=9 | (%) |
|------------------|-----|-----|
| *S. haemolyticus* | 6   | 66.67 |
| *MRSA*           | 1   | 11.11 |
| *S. epidermidis*  | 1   | 11.11 |
| *S. capitis*     | 1   | 11.11 |

### Table 15. GPB species in pus wound swab

| Bacteria Species | n=23 | (%) |
|------------------|------|-----|
| *S. aureus*      | 9    | 39.13 |
| *S. epidermidis* | 7    | 30.43 |
| *S. haemolyticus* | 2  | 8.69 |
| *S. constellatus* | 1   | 4.35 |
| *S. acidominus*  | 1    | 4.35 |
| *E. faecalis*    | 1    | 4.35 |
| *MRSA*           | 1    | 4.35 |
| *S. capitis*     | 1    | 4.35 |

### Table 16. GNB species in pus wound swab

| Bacteria Species | n=9 | (%) |
|------------------|-----|-----|
| *P. aeruginosa*  | 5    | 55.56 |
| *K. pneumonia (ESBL+)* | 1  | 11.11 |
| *P. mirabilis*   | 1    | 11.11 |
| *C. testosteroni* | 1  | 11.11 |
| *C. striatum*    | 1    | 11.11 |

### Table 17. GNB species in pleural fluid.

| Bacteria Species | n=10 | (%) |
|------------------|------|-----|
| *S. maltophilia* | 4    | 40.00 |
| *P. putida*      | 3    | 30.00 |
| *L. adecarboxylata* | 1 | 10.00 |
| *C. farmeri*     | 1    | 10.00 |
| *K. pneumonia (ESBL+)* | 1  | 10.00 |

### Table 18. GPB species in pleural fluid.

| Bacteria Species | n=6 | (%) |
|------------------|-----|-----|
| *S. epidermidis* | 3    | 50.00 |
| *S. haemolyticus* | 1  | 16.66 |
| *S. capitis*     | 1    | 16.66 |
| *MRSA*           | 1    | 16.66 |

Pleural fluid culture specimen was dominated with GNB (5 species bacteria) followed GPB (4 species bacteria). The commonest GNB were *S. maltophilia* (Table 17) and GPB were *S. epidermidis* (Table 18). Antibiotic sensitivity pattern of GNB (Table 19) are showed that almost all of the isolate are resistant to; penicillin cephalosporin, tetracycline, chloram- phenicol, sulfa and quinolones groups.

Among GNB isolate, Cefo-sulbactam has the highest susceptibility rate (87.71%) for *B. cepacea* in blood, nitrofurantoin (97.53%) for *E. coli* in urine, cefo-sulbactam (88.09%) for *P. aeruginosa* in sputum, both of amikacin
| Antibiotics          | Blood                  | Urine                  | Sputum                | Stool                  | CSF Fluid               | ETT                   | Pus/Wound             | Pleural Fluid         | GNB Sensitivity |
|----------------------|------------------------|------------------------|-----------------------|------------------------|-------------------------|------------------------|----------------------|-----------------------|---------------------|
|                      | B. cepachea n=57       | E. coli n=81           | P. aeruginosa n=42    | E. coli n=34           | A. baumanii pneumonia n=10 | K. pneumonia n=16      | P.aeruginosa n=5     | S.maltophilia n=4    |                     |
| Amikacin             | 50 (87.71%)            | 79 (97.53%)            | 33 (78.57%)           | 33 (97.05%)            | 7 (70.00%)              | 15 (93.75%)            | 4 (80.00%)            | 3 (75.00%)            | 84.95%              |
| Tobramycin           | 39 (68.42%)            | 49 (60.49%)            | 23 (54.76%)           | 22 (64.70%)            | 5 (50.00%)              | 11 (68.75%)            | 2 (40.00%)            | 2 (50.00%)            | 57.14%              |
| Gentamycin           | 37 (64.91%)            | 47 (58.02%)            | 32 (76.19%)           | 20 (58.82%)            | 5 (50.00%)              | 13 (81.25%)            | 3 (60.00%)            | 3 (75.00%)            | 65.52%              |
| Astreconam           | 20 (35.08%)            | 32 (39.50%)            | 27 (64.28%)           | 14 (41.17%)            | 0 (0%)                  | 8 (50.00%)             | 3 (60.00%)            | 2 (50.00%)            | 42.50%              |
| Amoxicillin - Clavulanic | 18 (31.57%)          | 38 (46.91%)            | 0 (0%)                | 15 (44.11%)            | 0 (0%)                  | 8 (50.00%)             | 0 (0%)               | 0 (0%)                | 21.57%              |
| Ampicillin           | 4 (7.17%)              | 13 (16.04%)            | 0 (0%)                | 5 (14.70%)             | 0 (0%)                  | 0 (0%)                 | 0 (0%)               | 0 (0%)                | 4.74%               |
| Ampicillin- Sulbactam | 25 (43.85%)           | 32 (39.50%)            | 5 (11.90%)            | 13 (38.23%)            | 7 (7.00%)               | 7 (43.75%)             | 1 (20.00%)            | 1 (25.00%)            | 28.65%              |
| Pippe - Tazobactam   | 35 (61.40%)            | 59 (72.83%)            | 27 (64.28%)           | 25 (73.52%)            | 4 (40.00%)              | 10 (62.50%)            | 3 (60.00%)            | 3 (75.00%)            | 63.69%              |
| Cefazolin            | 13 (22.80%)            | 23 (28.39%)            | 0 (0%)                | 10 (29.41%)            | 0 (0%)                  | 8 (50.00%)             | 0 (0%)               | 0 (0%)                | 16.33%              |
| Cefazidime           | 21 (36.84%)            | 38 (46.91%)            | 36 (85.71%)           | 16 (47.05%)            | 4 (40.00%)              | 9 (56.25%)             | 4 (80.00%)            | 4 (100%)              | 61.60%              |
| Cefotaxime           | 22 (38.59%)            | 34 (41.97%)            | 0 (0%)                | 14 (41.17%)            | 4 (40.00%)              | 7 (43.75%)             | 0 (0%)               | 0 (0%)                | 25.69%              |
| Ceftriaxone          | 11 (19.29%)            | 9 (11.12%)             | 12 (28.57%)           | 4 (11.76%)             | 2 (20.00%)              | 2 (12.50%)             | 1 (20.00%)            | 1 (25.00%)            | 18.53%              |
| Cefo – Sulbactam     | 54 (94.73%)            | 76 (93.82%)            | 37 (88.09%)           | 32 (94.11%)            | 8 (86%)                 | 15 (93.75%)            | 4 (80.00%)            | 4 (100%)              | 91.31%              |
| Cefepime             | 27 (47.36%)            | 35 (43.20%)            | 26 (61.90%)           | 15 (44.11%)            | 4 (40.00%)              | 7 (43.75%)             | 3 (60.00%)            | 3 (75.00%)            | 51.92%              |
| Cotrimoxazole        | 32 (56.14%)            | 29 (35.80%)            | 7 (16.66%)            | 12 (35.29%)            | 8 (80.00%)              | 12 (75.00%)            | 1 (20.00%)            | 1 (25.00%)            | 42.99%              |
| Tetracycline         | 21 (36.84%)            | 22 (27.16%)            | 0 (0%)                | 10 (29.41%)            | 4 (40.00%)              | 8 (50.00%)             | 0 (0%)               | 0 (0%)                | 22.93%              |
| Chloramphenicol      | 30 (52.63%)            | 58 (71.60%)            | 12 (28.57%)           | 25 (73.52%)            | 0 (0%)                  | 12 (75.00%)            | 1 (20.00%)            | 1 (25.00%)            | 43.29%              |
| Ciprofloxacin        | 31 (54.38%)            | 32 (39.50%)            | 27 (64.28%)           | 14 (41.17%)            | 5 (50.00%)              | 9 (56.25%)             | 3 (60.00%)            | 2 (50.00%)            | 51.95%              |
| Levofloxacin         | 33 (57.89%)            | 35 (43.20%)            | 30 (71.42%)           | 15 (44.11%)            | 6 (60.00%)              | 9 (56.25%)             | 3 (60.00%)            | 3 (75.00%)            | 58.48%              |
| Fosfomycin           | 37 (64.91%)            | 79 (97.53%)            | 20 (47.61%)           | 32 (94.11%)            | 1 (10.00%)              | 7 (43.75%)             | 2 (40.00%)            | 2 (50.00%)            | 55.99%              |
| Nitrofurantoin       | -                      | 80 (98.76%)            | 0 (0%)                | 33 (97.05%)            | 0 (0%)                  | 12 (75.00%)            | 0 (0%)               | 0 (0%)                | 38.69%              |
| Imipenem             | 46 (80.70%)            | 69 (85.18%)            | 32 (76.19%)           | 29 (85.29%)            | 7 (70.00%)              | 15 (93.75%)            | 4 (80.00%)            | 3 (75.00%)            | 80.76%              |
| Meropenem            | 45 (78.94%)            | 73 (90.12%)            | 32 (76.19%)           | 31 (91.17%)            | 7 (70.00%)              | 14 (87.50%)            | 4 (80.00%)            | 3 (75.00%)            | 81.12%              |
| Antibiotics         | Blood | Urine | Stool | CSF Fluid | ETT | Pus/Wound | Pleural Fluid | GPB Sensitivity |
|---------------------|-------|-------|-------|-----------|-----|-----------|---------------|-----------------|
| Gentamicin          | 16 (29.09%) | 2 (18.18%) | 12 (52.17%) | 8 (42.10%) | 6 (54.54%) | 2 (33.33%) | 8 (88.89%) | 3 (75.00%) (49.16%) |
| Ampicillin          | 1 (1.81%) | 1 (5.56%) | 8 (34.78%) | 4 (21.05%) | 1 (5.56%) | 0 (0%) | 1 (1.11%) | 1 (25.00%) (11.86%) |
| Ampicillin-sulbactam | 9 (16.36%) | 2 (18.18%) | 6 (26.68%) | 3 (15.78%) | 1 (5.56%) | 1 (16.66%) | 7 (77.78%) | 2 (50.00%) (28.30%) |
| Penicillin          | 2 (3.36%) | 1 (5.56%) | 4 (17.39%) | 4 (21.05%) | 2 (18.18%) | 1 (16.66%) | 1 (11.11%) | 1 (25.00%) (13.54%) |
| Oxacillin           | 12 (21.81%) | 3 (27.27%) | 10 (43.47%) | 8 (42.10%) | 6 (54.54%) | 1 (16.66%) | 6 (66.67%) | 3 (75.00%) (43.44%) |
| Cotrimoxazole       | 4 (7.72%) | 2 (18.18%) | 11 (47.82%) | 8 (42.10%) | 5 (45.45%) | 1 (16.66%) | 8 (88.89%) | 1 (25.00%) (36.48%) |
| Tetracycline        | 29 (52.72%) | 6 (54.54%) | 6 (20.08%) | 7 (36.84%) | 3 (27.27%) | 0 (0%) | 0 (0.00%) | 1 (25.00%) (27.06%) |
| Chloramphenicol     | 25 (45.45%) | 5 (45.45%) | 8 (34.78%) | 9 (47.36%) | 3 (27.27%) | 3 (50.00%) | 6 (66.67%) | 2 (50.00%) (45.87%) |
| Erythromycin        | 18 (32.72%) | 3 (27.27%) | 13 (56.52%) | 11 (57.89%) | 6 (54.54%) | 3 (50.00%) | 6 (66.67%) | 2 (50.00%) (49.45%) |
| Clindamycin         | 21 (38.18%) | 5 (45.45%) | 16 (69.56%) | 12 (63.15%) | 4 (36.36%) | 2 (33.33%) | 6 (66.67%) | 2 (50.00%) (50.34%) |
| Ciprofloxacin       | 38 (69.09%) | 7 (36.36%) | 0 (0.00%) | 12 (63.15%) | 6 (54.54%) | 3 (50.00%) | 0 (0.00%) | 2 (50.00%) (43.80%) |
| Levofloxacin        | 31 (56.36%) | 9 (81.81%) | 14 (60.86%) | 13 (68.42%) | 7 (63.63%) | 4 (66.67%) | 3 (33.33%) | 2 (50.00%) (60.14%) |
| Moxifloxacin        | 49 (89.09%) | 9 (81.81%) | 16 (69.56%) | 12 (63.15%) | 6 (54.54%) | 4 (66.67%) | 3 (33.33%) | 3 (75.00%) (66.64%) |
| Fosfomycin          | 48 (87.27%) | 10 (90.90%) | 19 (82.60%) | 11 (57.89%) | 9 (81.81%) | 3 (50.00%) | 8 (88.89%) | 3 (75.00%) (76.80%) |
| Nitrofurantoin      | 46 (83.63%) | 9 (81.81%) | 20 (96.95%) | 14 (73.68%) | 6 (54.54%) | 3 (50.00%) | 8 (88.89%) | 3 (75.00%) (75.56%) |
| Meropenem           | 8 (14.54%) | 2 (18.18%) | 18 (78.26%) | 10 (52.63%) | 5 (45.45%) | 2 (18.18%) | 8 (88.89%) | 2 (50.00%) (45.77%) |
| Vancomycin          | 52 (94.54%) | 11 (100.00%) | 22 (95.65%) | 16 (84.21%) | 9 (81.81%) | 5 (83.33%) | 9 (100.00%) | 4 (100.00%) (92.44%) |
| Linezolid           | 53 (96.36%) | 11 (100.00%) | 20 (86.95%) | 17 (89.47%) | 11 (100.00%) | 5 (83.33%) | 8 (88.89%) | 4 (100.00%) (93.13%) |
| Daptomycin          | 52 (94.54%) | 10 (90.91%) | 21 (91.30%) | 16 (84.21%) | 9 (81.81%) | 4 (66.67%) | 8 (88.89%) | 4 (100.00%) (87.29%) |
and nitrofurantoin (97.05%) for *E. coli* in stool isolate. Amikacin, Cefo-sulbactam and imipenem (93.75%) had highest sensitivity for *K. pneumonia* in ETT isolate and at the last cefo-sulbactam (100%) also had highest sensitive for *S. maltophilia* in pleural isolates.

GPB antibiotic sensitivity pattern (Table 20), are showed that almost all of isolate resistant for aminoglycoside, penicillin, macrolide, tetracycline, and carbapenem antibiotic groups. In GPB isolate, Linezolid (100%) has highest susceptibility rate for *S. colnii* in CSF fluid and vancomycin (100%) high sensitive for *P. aeruginosa* in pus/wound swab isolated.

**DISCUSSION**

In this study totally 4144 PICU patients were followed the study and only 27.46% had positive culture result, female higher than male in distribution gender, with mean age 4 ± 0.8 years. Primary diseases distribution was dominated with respiratory tract infection. Previous study by Camilla et al., positive culture result in PICU patient dominant respiratory tract infection as primary diseases (33.26%), female more often than male, with higher age incidence at less than five years. Other study in PICU Mohammad Hoesin Palembang stated that commonest respiratory tract infection diagnosis was broncho-pneumonia (33.3%).

In our present study, the frequency Gram-Negative Bacteria (GNB) isolates was slightly higher than than Gran-Positive Bacteria (GPB) isolates. GNB constituted the majority of bacterial pathogens associated with the 6 major specimen, blood (66.01%), urine (72.69%), sputum (66.67%), stool (63.73%), ETT aspirate (80.43%) and pleural fluid (62.50%). The predominance of GNB is a relevant reminder that these pathogens were once the most common human pathogens. For approximately the past 2 decades, GNB have been the pathogens most frequently associated with respiratory system diseases and Urinary tracts infections (UTIs).

Blood culture result of our study demonstrated GNB (66.01%) were the most common organisms causing blood stream infection, various literatures from the world are showed these phenomena such as; Gupta et al., Haeuseler et al., and Kirsty et al., showed GNB as predominant pathogen for blood stream infection.

Our study is gained commonest GNB species was *B. cepacea* (11.26%). *B. cepacea* has emerged as a serious human pathogen in the last two decades, causing fatal necrotizing pneumonia and bacteremia. *B. cepacea* has been associated with out breaks involving infections of the bloodstream, respiratory tract, and urinary tract in intensive care unit setting. Antony et al. stated that the intensive care unit bloodstream infections in tertiary hospital often caused by *B. cepacea* infections.

Urine culture demonstrated positivity rate for 26.45%, clinically with urinary tract infection cases. Several study are showed vary positivity of the urine culture e.g. Salar et al. 17%. Kaur et al. 15.7% are showed an occurrence of urinary tract infection among PICU patients. This difference could possibly due to various antibiotic prescribing practices, variations in sample collection, culture technique and susceptibility testing practices in our hospital than others. Our study was also shown that GNB, *E. coli* (50.94%) was the most common organisms in urinary tract infection. This finding similar with microbial pattern in adult patients in same hospital, that *E. coli* is the most common cause UTIs.

Sputum culture revealed positivity rate 20.52% of respiratory tract infection cases. Its majority caused by GNB with dominant *P. aeruginosa* (47.72%). Piyush et al. is stated 34.23% patient had *P. aeruginosa* etiology from sputum sample in respiratory tract infection. *Aeromonas* is a gram-negative aerobic rod. It became considered as most challenging pathogen bacteria globally because of its high rate of resistance to antimicrobial agent. It was also reported that *P. aeruginosa* is one of the most common nosocomial pathogen and a leading cause of nosocomial respiratory tract infection.

Stool culture is obtain positivity rate was 17.52% majority caused by *E. coli* (63.73%) were dominant *E. coli* (52.30%). *E. coli* has been reported as the most frequently identified pathogen in other study throughout the world like China. Some country reported different bacteria as the leading entero-pathogen, such a *Salmonella spp* in South Korea, and *Aeromonas spp* in Singapore. Some of these regional differences may be related to study population or stool culture techniques.

The endotracheal tube aspirated is performed 21.59% positivity rate which were dominated with GNB dominantly *K. pneumonia* (63.73%) were most common isolate. In contrast to our study Rehman et al. are reported 93.65% culture positive in ETT tips, they also revealed that *K. pneumoniae* (41.93%) was the most common isolate. Kalanuria et al. are stated that *Pseudomonas spp* was common isolate from ETT tips. This differences rate may be most of these microorganism acquired from environment and their concentrations varying depend on hospital geographical distribution and their ability to survive in particular conditions. The lumen of ETT in patients using mechanical ventilation usually became colonized with GNB which commonly appeared to survive within a biofilm. While it appears that colonization of the ETT may begin from as early as 12 hours, it is most abundant at 96 hours. Pleural fluid culture is attained positivity rate for 18.39% and were dominated with GNB (62.50%) with majority species *S. maltophilia* (40.00%). Jones et al. in their study are got positivity culture of pleural fluid rate was 11.50% with *S. maltophilia* (59.16%) are commonest bacterial. Chawla et al. are stated that *S. maltophilia* often cause pneumonia infection. In our study these microbes may affect pleural fluid after infected lower respiratory tract such as pneumonia by organ lesion caused diseases progression. At present, the incidence of nosocomial infections cause by *S. maltophilia* is increasing; in
particular, intensive care units are leading areas with high risk of these infections. These organisms also resistance to many broad-spectrum antibiotics including carbapenem causes an increase in the mortality and morbidity rates in the intensive care units.22,24

Cerebrospinal fluid culture had gram positive bacteria (65.12%) as the common microorganism with majority species S. cohnii (52.30%). Previous study conducted by Jiang et.al. are showed (50.8%) acute bacterial meningitis in pediatric caused GPB infections.25 Zhu et.al. are found GPB predominant pathogen in pediatric patients caused purulent meningitis were E. coli and Staphylococcus spp.26 In our finding has similar perform with the other literature, its suggest that the development of nosocomial staphylococcal meningitis may subsequent to central nervous system conditions and neurosurgery interventions, which include ventriculo-peritoneal shunts, or other embedded devices. In this study over 52 patients also known had surgery history for inserting neurosurgery device. Generally, as is common in other surgical practice, the risk factor of inserting device infection, the venue of procedure and the surgical technique are know by surgeon’s experience.27

Wound culture were dominated with GPB (71.87%), with isolate was S. aureus (39.13%) and followed GNB P. aeruginosa (55.56%). Negin et.al are found 96.4% surgical site infection yielding bacteria growth with S. aureus (54.4%), P. aeruginosa (21.7%) and E. coli.28 These infections are usually caused by exogenous or endogenous microorganisms that enter the operative wound during the course of the surgery.29 In our study over 32 of 37 patients with history surgical site infection had positive result culture. These wound infections may have occurred at hospital and recognized to be associated with an infection before-after or during surgery, extended length of hospital stays and prolonged or permanent disability.

Antibiotics susceptibility pattern of GNB isolates (blood, urine, sputum, stool, ETT and pleural fluid) in our study finding were resistant to three or more groups antimicrobial agents and therefore consider multidrug resistant (MDR), almost all of the isolate are resistant to; penicillin, cephalosporin, tetracycline, chloramphenicol, sulfa and quinolones groups. The development of antibiotic resistant in our hospital might be caused by unnecessary, inappropriate, or suboptimal prescribed antibiotic therapy from community before, previous health care and our hospital itself. Previous study similar that, find very high level of resistance penicillin derivate, approximately one half isolate in infants and young children.30 Other study in Africa 75% isolate are MDR to ampicillin, chloramphenicol and cotrimoxazole.31 WHO in 2014 report that five out of the six WHO regions had more than 50% resistant to third generation of cephalosporin and fluoroquinolones in hospital setting.32 In GPB isolates (CSF and Wound swab) also found multidrug resistance, over two third of antibiotic testing had resistance. Only vancomycin, linezolid and daptomycin had highest susceptibility for all GPB isolates. Sarangi et.al and Singh et.al. were also found that vancomycin and linezolid had highest antibiotic susceptibility NICU setting.33,34 Highest prevalence isolates with multiple drug resistance that observed in our study may cause our hospital is a tertiary care center with large range health service not only in east java but also in east region Indonesia. Patient adjoining provinces are admitted for treatment that before attending the hospital, most of the patient get different antibiotic from low level health care centers or due to over the counter sell of antibiotics often in improper dose. Limited population in some specimen and obtain of some pathogen or contaminant bacteria were all limitation in our study, multicenter prospective studies are needed to validated our finding.

CONCLUSION

Our study revealed GNB isolates as the predominant pathogen in all PICU isolates sampling, with most microorganism found were B. cepacea in blood, P. aeruginosa in sputum, E. coli in urine and stool, S. cohnii in CSF fluid, K. pneumoniae ESBL in ETT aspirate, S. aureus in pus, and S. maltophilia in pleural fluid culture. Both GNB and GPB isolates showed multiple drug resistance to commonly used antibiotic but still had good susceptibility for amikacin, cefoperazone-sulbactam, linezolid, vancomycin and carbapenem group.

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