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Research Report

MICROBIAL PATTERN AND ANTIBIOTIC SUSCEPTIBILITY IN PEDIATRIC INTENSIVE CARE UNIT DR. SOETOMO HOSPITAL, SURABAYA

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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/mm^3 or > 10000/mm^3, 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 Paterrn, Dr. Soetomo Hospital, Bacteria, Antibiotic.*

ABSTRAK

Bakteri gram negatif merupakan patogen tersering penyebab infeksi di ruang rawat intensif anak. Pola bakteri dan kepekaan antibiotik diperlukan sebagai data klinis dalam pemilihan terapi antibiotik yang sesuai. Di ruang rawat intensif anak RS.Dr. Soetomo hingga saat ini masih sangat kekurangan data mengenai pola bakteri dan kepekaan antibiotik. Penelitian deskriptif ini bertujuan untuk membuat pola bakteri dan kepekaan antibiotika pada pasien yang dirawat di ruang rawat intensif anak dari spesimen darah, urin, sputum, feces, cairan serebrospinal,tabung endotrakeal (ETT), pus luka dan cairan pleura. Pasien yang masuk ke PICU yang tidak menunjukkan tanda dan gejala infeksi di eklusi dari penelitian. Kriteria inklusi pada penelitian ini adalah ditemukannya tanda dan gejala infeksi, antara lain ;demam < 36,5°C or > 37.5°C, kadar leukosit darah < 4000/mm3 or > 10000/mm3, marker infeksi CRP >10 mg/L or PCT >0,3 ng/mL, bradikardi atau takikardi, takipneu, gambaran infiltrate pada radiologi paru,urine yang keruh, nyeri berkemih, tromboplebitis, nyeri perut, dan lesi pada mukosa atau kulit. Dari data rekam medis dari tahun 2011 sampai 2016 didapatkan 1138 pasien dengan hasil kultur mikrobiologi positif, dimana 44.46% dari spesimen darah, 19.15% dari urin, 11.59% dari sputum,8.96% dari feces,7.50% dari cairan cerebrospinal, 4.04% dari ETT, 2.89% dari pus luka, dan 1.41% dari cairan pleura. Mikroorganisme terbanyak yang ditemukan di rawat intensif anak adalah bakteri gram negatif. Bakteri tersering dari spesimen darah adalah B. cepacea, E. coli pada urine, P. aeruginosa pada sputum,E. coli pada feces,S. cohnii pada cairan serebrospinal, K.

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 antibiotic 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, leukocyte < 4000/mm^3 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

Table 3. GNB species finding in blood culture

Bacteria Species	(n=334)	(%)
B. cepacea	57	17.06
K. pneumoniae (ESBL+)	56	16.76
A. baumannii	44	13.17
K. pneumoniae	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. pneumoniae (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. rettgeri	1	0.63
P. mirabilis	1	0.63
Aeromonas spp.	1	0.63

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.

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	23	52.27
MRSA	8	18.18
S. capitis	6	13.64
S. haemolyticus	6	13.64
S. pneumonia	1	2.27

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.

Endotracheal tube (ETT) aspirate culture specimen was dominated with GNB (6 species) followed GPB (4 species). The commonest GNB species were *K. pneumonia (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

Table 9. GNB species in stool culture

Bacteria Species	(n=65)	(%)
E. coli	34	52.30
E. cloacae	21	32.32
E. coli (ESBL+)	2	3.07
E. aerogenes	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
MRSA	3	8.11
S. paratyphi	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. faecium	7	12.50
E. faecalis	7	12.50
A. viridans	4	7.15
MRSA	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. diminuta	2	6.67
P. stutzeri	1	3.33
B. cepacea	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. cepacea	1	2.70

commonest GPB were *S. aureus* (Table 15) and GNB were *P. aeruginosa* (Table 16). Over 32 wound positive culture isolate in our study were undertaken from 37 pediatric patients with history surgical site infection.

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. cephacea* in blood, nitrofurantoin (97.53%) for *E. coli* in urine, cefo-sulbactam (88.09%) for *P. aeruginosa* in sputum, both of amikacin

Tabel.19. Antibiotics sensitivity pattern of gram negative bacteria isolate from different samples

Antibiotics	The most gram negative bacteria (GNB) species in isolate samples								
	Blood	Urine	Sputum	Stool	CSF Fluid	ETT	Pus/Wound	Pleural Fluid	
	B. cepachea n=57	E. coli n=81	P. aeruginosa n=42	E. coli n=34	A. baumanii n=10	K. pneumonia n=16	P.aeruginosa n=5	S.maltophilia n=4	GNB Sensitivity
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%
Astreonam	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%
Ceftazidime	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 (11.11%)	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%

Tabel.20. Antibiotics sensitivity pattern of gram positive bacteria isolate from different samples

Antibiotics	The most gram positive bacteria (GPB) species in isolate samples								GPB Sensitivity
	Blood	Urine	Sputum	Stool	CSF Fluid	ETT	Pus/Wound	Pleural Fluid	
	S. B-haemolyticus n = 55	S. B-haemolyticus n = 11	S. coagulase negatif N = 23	E. cloacae n = 19	S. cohnii n = 11	S. B-haemolyticus N = 6	S. aureus n = 9	S. haemolyticus n = 4	
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 (26.08%)	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 (1.11%)	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 (63.63%)	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. malthopnilia* 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. cohnii* 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 tracts 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.[5] Other study in PICU Mohammad Hoesin Palembang stated that commonest respiratory tract infection diagnosis was broncho-pneumonia (33.3%).[6]

In our present study, the frequency Gram-Negative Bacteria (GNB) isolates was slightly higher than that 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.[3,7] For approximately the past 2 decades, GNB have been the pathogens most frequently associated with respiratory system diseases and Urinary tracts infections(UTIs).[4,7]

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, Haeusler et.al, and Kirsty et.al,* showed GNB as predominant pathogen for blood stream infection.[7,8,9] 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.[7,8,10] *Antony et.al.* stated that the intensive care unit bloodstream infections in tertiary hospital often caused by *B. cepacea* infections.[10]

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[11,12] 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.[13]

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.[14] *P. aeruginosa* 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.[3,15] It was also reported that *P. aeruginosa* is one of the most common nosocomial pathogen and a leading cause of nosocomial respiratory tract infection.[5,15]

Stool culture is obtain positivity rate was 17.52% majority caused by GNB (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.[16] Some country reported different bacteria as the leading entero-pathogen, such a *Salmonella spp* in South Korea,[17] *and Aeromonas spp*. in Singapore. [18] 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 (ESBL+)* (43.24%). 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.[19] *Kalanuria et.al* are stated that Pseudomonas *spp* was common isolate from ETT tips.[20] This differences result 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.[21] While it appears that colonization of the ETT may begin from as early as 12 hours, it is most abundant at 96 hours.[20,21]

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.[22] *Chawla et.al* are stated that S. *maltophilia* often cause pneumonia infection.[23] 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.[23,24] 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%). *Negi 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, chloram- phenicol, 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 heath 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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