Characteristics of ESBL-Infected Intensive Observation Room Patients From 2019-2020 With Microbiology And Resistance Pattern Results

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Abstract

BACKGROUND Uncontrolled antibiotic use causes the rise of antibiotic-resistant bacteria, one of which is ESBL. ESBL is a resistance mechanism developed by several gram-negative bacteria which can render beta-lactam antibiotics ineffective against them. Infections caused by ESBL bacteria are on the rise in the whole world and can raise the cost of hospitalisation. Indonesia is one of countries with limited data regarding infections by antibiotic-resistant bacteria. Thus, a research regarding the characteristics of Intensive Observation Room patients with ESBL producing bacterial infection is urgent to be researched.

METHODS This research is a descriptive retrospective research with the whole ESBL-infected patients' data of RSUD Dr. Soetomo's Intensive Observation Room from 2019-2020 as its population. Sampling is done by total sampling for all data which fits the inclusion and exclusion criteria. The variables included in this research are patients' age, patients' sex, invasive devices installed, culture samples, bacteria species, and antibiotic resistance patterns.

RESULTS Based on available data which fits the inclusion and exclusion criteria, there are 81 patients with 10 patients cultured more than once which results in 91 culture data. From the patients' characteristics, patients' ages are dominated in the 18-60 y/o group with 51 patients (63%), male sex with 47 patients (58%), and appendicitis as the dominant diagnosis with 11 patients (13,6%). Ventilators and Nutrition Tubes are the most installed invasive devices with each being installed in 67 patients (82,7%). Microbiology data shows Escherichia coli is the dominant species with positive results showing from 51 cultures. Amikacin is the antibiotic with the least resistance of all samples.

Keywords: ESBL, Characteristics, Intensive Observation Room, Resistance Pattern

1. Introduction

The advent of antibiotics in the early 20th century was one of the major breakthroughs in the field of medicine. Its reckless usage however, has resulted in the emergence of antibiotic-resistant bacteria, one of which included ESBL in gram-negative bacteria[1]. Infection caused by ESBL-producing bacteria are on the rise and can impact hospitalisation length to 7 days and can increase the annual cost of healthcare to 40.000 dollars[2]. While Indonesia is one of the countries in Southeast Asia considered to have few data on infections by antibiotic-resistant bacteria[3], researches done in Pekanbaru and Lampung showed Eschierichia coli and Klebsiella pneumoniae as the dominant ESBL-producing bacteria[4,5]. Another research done in RSUD Dr. Soetomo in Surabaya also shows ESBL-producing bacteria as the cause of urinary tract infections in 167 patients[6]. In an intensive care setting, a study done in Banjarmasin shows K. pneumoniae as the dominant ESBL-producing bacteria[7].

Based on the evidence above, a study to determine informations regarding infections by ESBL-producing bacteria is needed. The purpose of this study is to know characteristics of patients of RSUD Dr. Soetomo's Intensive Observation Room, their microbiological culture results, and the bacteria's antibiotic resistances.

2. Methods

This research is a descriptive retrospective cross-sectional research. The data used are secondary data of patients' records taken from RSUD Dr. Soetomo's record database and culture results from RSUD Dr. Soetomo's Microbiology Department. The data was taken from patients of the Intensive Observation Room in RSUD Dr. Soetomo from January 2019-December 2020's afforementioned records. The sampling used are total sampling with the sampling inclusion criteria being a patient of RSUD Dr. Soetomo's Intensive Observation Room during the period of January 2019-December 2020 with an ESBL-positive culture result. Patients with multiple culture results are included if the culture differs in the culture period, culture result, and resistance pattern. The exclusion criteria are incomplete patient data and patients with multiple cultures whose culture sample, culture result, and resistance pattern don't have any differences. The variables in this research are patient's age, patient's sex, types of invasive devices installed on the patients, culture samples, culture bacteria's species, and resistance pattern. The data obtained are sorted and analysed using Microsoft Excel software. This research is performed from January 2021-April 2022 and has passed ethical clearance from RSUD Dr. Soetomo's Ethical Department.

3. Results and Discussion

3.1. *Patients'* Characteristics

There are 81 patients of RSUD Dr. Soetomo's Intensive Observation Room from January 2019-December 2020 with positive ESBL infection. 10 patients also had multiple cultures which brings the total number of cultures into 91 results. Of those 10 patients, 2 patients had their cultures taken in different dates, 5 patients had two samples taken from pus and tissue samples each, a patient had their sample taken from pus and urine, and two samples had their samples both taken from tissues but they all have differing resistance patterns. 2 patients had their samples resulted in different bacterial species, with K. pneumoniae and Klebsiella oxytoca and K. pneumoniae and E. coli as their results respectively. Resistance pattern of those 10 patients show a patient with the same resistance pattern from all their culture results and the other 7 patients showing different resistance patterns from all their culture results. This research is limited on the amount of data available and queueing period in RSUD Dr. Soetomo's Medical Records unit.

Table 1 shows patients' age grouped in groups of <18 years old, 18-60 years old, and >60 years old, and patients' sexes. Patients are mostly from the 18-60 age group with 51 patients (63%) and of male sex with 47 patients (58%). A study performed in Denpasar showed similar results from the same age groups [8]. Immunological factors are in play as different age groups have different immunological makeups [9]. Meanwhile, another study in Saudi Arabia showed sex has no relations with infections by ESBL-producing bacteria [10]

Table 1 Patients' age and sex table

Characteristics	**Total(N=81)**	**%**
Age		
<18 y/o	17	21.0
18-60 y/o	51	63.0
>60 y/o	13	16.0
Sex		
Male	47	58.0
Female	34	42.0

Table 2 shows patients'diagnosis during their stay in RSUD Dr. Soetomo's Intensive Observation Room. 10 patients who had multiple culture results have 5 patients diagnosed with Appendicitis, 2 patients with Peritonitis, and a patient each diagnosed with Intestinal Perforation, Intestinal Obstruction, and Intracerebral Haemorrhage respectively. Appendicitis is the most prevalent condition in all patients' data with 11 patients (13,6%).

Table 2 Patients' diagnosis table

Diagnosis	**n**	**(%)**
Appendicitis	11	13.6
Wound Disruption	10	12.3
Peritonitis	6	7.4
Combustion	4	4.9
Intracerebral Haemorrhage	4	4.9
Intestinal Perforation	4	4.9
Abscess	3	3.7
Malignant Neoplasm	3	3.7
Bile Duct Obstruction	3	3.7
Diabetes Mellitus	2	2.5
Hydrocephalus	2	2.5
Pneumonia	2	2.5
Tuberculosis	2	2.5
Benign Neoplasm	1	1.2
Focal Brain Injury	1	1.2
Burst Abdomen	1	1.2
Abdominal Wall Contusion	1	1.2
Diffuse Brain Injury	1	1.2
Epidural Haemorrhage	1	1.2
Intestinal Fistule	1	1.2
Fracture	1	1.2
Cervical HNP	1	1.2
Hydronephrosis	1	1.2
Infected Wound	1	1.2
Nerve Injury	1	1.2
Internal Bleeding	1	1.2
Intracranial Haemorrhage	1	1.2
Intracranial Injury	1	1.2
Intussuception	1	1.2
Meningoencephalitis	1	1.2
Observation	1	1.2
Partus	1	1.2
Placenta Previa	1	1.2

Pleural Effusion	1	1.2
Preeclampsia	1	1.2
Rupture of Bladder	1	1.2
Volvulus	1	1.2
Abortus	1	1.2
Total	81	100.0

Table 3 Installed invasive devices' table

Invasive Devices	**N (%)**	
Ventilator	67	82.7
Gastric Tubes	67	82.7
Urinary Catheter	45	55.6
Central Venous Catheter	39	48.1

Table 3 shows invasive devices common in an intensive care setting that are installed in patients. This research does not divide gastric tubes as nasogastric and orogatric ones, thus the combined category. Based on the data shown, ventilator and gastric tubes are the most installed invasive devices in patients of RSUD Dr. Soetomo's Invasive Observation Room with 67 patients each (82,7%) had it installed. Invasive devices are known to increase the likelihood of infections by ESBL-producing bacteria [3].

3.2. Microbiology data

Table 4 Patients' samples and species of bacteria table

Culture Sample	**Species of bacteria**					**N(91)**
	E. coli	**E. vulneris**	**K. pneumoniae**	**K. oxytoca**	**K. ozaenae**	
Pus	18	0	5	0	0	23
Sputum	6	0	11	0	2	19
Urine	9	0	7	0	0	16
Tissue	11	0	2	1	0	14
Blood	5	1	7	0	0	13
Others	2	0	3	1	0	6
Total	51	1	35	2	2	91

These are several samples from patients of RSUD Dr. Soetomo's Intensive Observation Room from January 2019-December 2020 with positive ESBL infection. The sample with the most culture results in

general are pus samples with 23 patients had their samples taken. On the contrary, other sources are the least sampled from patients.

However, samples categorised by each bacteria species vary in comparison. E. coli samples are most collected from pus and least collected from other samples, *E. vulneris'* lone sample was taken from blood, K. pneumoniae samples are most taken from sputum and least taken from tissue samples, Klebsiella. oxytoca samples are each taken from a tissue and another source, and Klebsiella. ozaenae samples are both taken from sputum. A study in Bali in comparison shows similar results for K. pneumoniae but shows E. coli samples mostly taken from sputum [12].

E. coli are the most abundant result of patients' cultures with 51 cultures, followed by K. pneumoniae with 35, K. oxytoca and K. ozaenae with 2 each,and Escherichia vulneris with only a sample.

Table 5 E. coli's resistance pattern

CLSI Classification	**Antibiotic Classes**	**Antibiotics and Samples Tested**	**Resistance Pattern**		
			R(%)	**I(%)**	**S(%)**
A	Penicilin	Ampicilin (41)	100	0	0
	Aminoglycoside	Gentamicin (51)	49	0	51
B	Aminoglycoside	Amikacin (50)	8	0	92
	Beta Lactam + Beta Lactamase Inhibitor	Amoxicilin-Clavulanic Acid (51)	39.2	15.7	45.1
		Ampicilin-Sulbactam (51)	47.1	25.5	27.5
		Piperacilin-Tazobactam (51)	13.7	7.8	78.4
	Cephalosporin	Cefepime (50)	88	4	8
		Cefoxitin (1)	100	0	0
		Cefotaxime (50)	96	0	4
		Ceftriaxone (49)	93.9	0	6.1
	Floroquinolon	Ciprofloxacin (46)	91.3	0	8.7
		Levofloxacin (45)	88.9	2.2	8.9
	Carbapenem	Imipenem (51)	19.6	5.9	74.5
		Meropenem (51)	13.7	2	84.3
	Sulfonamid	Trimetoprim-Sulphametoxazole (41)	68.3	0	31.7
C	Cephalosporin	Ceftazidime (49)	95.9	0	4.1
	Chloramphenicol	Chloramphenicol (40)	52.5	5	42.5
	Tetracycline	Tetracycline (40)	72.5	2.5	25
U	Phosphonic Acid	Fosfomycine (22)	13.6	0	86.4
	Nitrofurantoin	Nitrofurantoin (2)	50	0	50

Table 6 E.vulneris's resistance pattern

CLSI Classification	Antibiotic Classes	Antibiotics and Samples Tested	Resistance Pattern		
			R(%)	I(%)	S(%)
A	Penicilin	Ampicilin	100	0	0
	Cephalosporin	Cefazolin	0	0	0
	Aminoglycoside	Gentamycin	0	0	100
B	Aminoglycoside	Amikacin	0	0	100
	Beta Lactam + Beta Lactamase Inhibitor	Amoxicilin-Clavulanic Acid	0	100	0
		Ampicilin-Sulbactam	100	0	0
		Piperacilin-Tazobactam	0	100	0
	Cephalosporin	Cefepime	100	0	0
		Cefoxitin	100	0	0
		Cefotaxime	100	0	0
		Ceftriaxone	100	0	0
	Floroquinolon	Ciprofloxacin	0	100	0
		Levofloxacin	0	0	100
	Carbapenem	Imipenem	0	0	100
		Meropenem	0	0	100
	Sulfonamid	Trimetoprim-Sulphametoxazole	100	0	0
C	Cephalosporin	Ceftazidime	0	100	0
	Chloramphenicol	Chloramphenicol	100	0	0
	Tetracycline	Tetracycline	100	0	0
U	Phosphonic Acid	Fosfomycine	0	0	0
	Nitrofurantoin	Nitrofurantoin	0	0	0

Table 7 K. pneumoniae's resistance pattern

CLSI Classification	Antibiotic Classes	Antibiotics and Samples Tested	Resistance Pattern		
			R(%)	I(%)	S(%)
A	Penicilin	Ampicilin (30)	100	0	0
	Cephalosporin	Cefazolin (3)	100	0	0
	Aminoglycoside	Gentamycin (34)	32.4	0	67.6
B	Aminoglycoside	Amikacin (34)	8.8	0	91.2
	Beta Lactam + Beta Lactamase Inhibitor	Amoxicilin-Clavulanic Acid (35)	42.9	14.3	42.9
		Ampicilin-Sulbactam (35)	60	28.6	11.4
		Piperacilin-Tazobactam (35)	25.7	14.3	60
	Cephalosporin	Cefepime (34)	91.2	5.9	2.9
		Cefoxitin (5)	40	0	60
		Cefotaxime (35)	97.1	2.9	0
		Ceftriaxone (34)	94.1	0	5.9
	Floroquinolon	Ciprofloxacin (31)	61.3	9.7	29
		Levofloxacin (27)	55.6	0	44.4
	Carbapenem	Imipenem (34)	17.6	8.8	73.5
		Meropenem (35)	17.1	5.7	77.1
	Sulfonamid	Trimetoprim-Sulphametoxazole (33)	66.7	0	33.3
C	Cephalosporin	Ceftazidime (35)	97.1	0	2.9
	Chloramphenicol	Chloramphenicol (27)	48.1	3.7	48.1
	Tetracycline	Tetracycline (31)	54.8	0	45.2
U	Phosphonic Acid	Fosfomycine (16)	37.5	6.3	56.3
	Nitrofurantoin	Nitrofurantoin (4)	100	0	0

Table 8 K. oxytoca's resistance pattern

CLSI Classification	Antibiotic Classes	Antibiotics and Samples Tested	Resistance Pattern		
			R(%)	I(%)	S(%)
A	Penicilin	Ampicilin	100	0	0
	Aminoglycoside	Gentamycin	0	0	100
B	Aminoglycoside	Amikacin	0	0	100
	Beta Lactam + Beta Lactamase Inhibitor	Amoxicilin-Clavulanic Acid	50	0	50
		Ampicilin-Sulbactam	50	0	50
		Piperacilin-Tazobactam	0	0	100
	Cephalosporin	Cefepime	100	0	0
		Cefotaxime	100	0	0
		Ceftriaxone	100	0	0
	Floroquinolon	Ciprofloxacin	50	0	50
		Levofloxacin	50	0	50
	Carbapenem	Imipenem	50	0	50
		Meropenem	50	50	0
	Sulfonamid	Trimetoprim-Sulphametoxazole	50	0	50
C	Cephalosporin	Ceftazidime	100	0	0
	Chloramphenicol	Chloramphenicol	100	0	0
	Tetracycline	Tetracycline	100	0	0

Table 9 K. ozaenae's resistance pattern

CLSI Classification	Antibiotic Classes	Antibiotics and Samples Tested	Resistance Pattern		
			R(%)	I(%)	S(%)
A	Penicilin	Ampicilin	100	0	0
	Cephalosporin	Cefazolin	0	0	0
	Aminoglycoside	Gentamycin	0	0	100
B	Aminoglycoside	Amikacin	0	0	100
	Beta Lactam + Beta Lactamase Inhibitor	Amoxicilin-Clavulanic Acid	100	0	0
		Ampicilin-Sulbactam	100	0	0
		Piperacilin-Tazobactam	0	0	100
	Cephalosporin	Cefepime	100	0	0
		Cefoxitin	0	0	0
		Cefotaxime	100	0	0
		Ceftriaxone	100	0	0
	Floroquinolon	Ciprofloxacin	100	0	0
		Levofloxacin	50	0	50
	Carbapenem	Imipenem	100	0	0
		Meropenem	50	50	0
	Sulfonamid	Trimetoprim-Sulphametoxazole	100	0	0
	Cephalosporin	Ceftazidime	100	0	0
C	Chloramphenicol	Chloramphenicol	100	0	0
	Tetracycline	Tetracycline	50	50	0

Antibiotics tested are categorised in accordance with CLSI's manual, 2020 edition as the last of the samples are from the year 2020 and shown in percentages because not every antibiotic is tested in each sample. The test results are graded accordingly to determine their usefulness in a clinical setting. A sensitivity result of over 60% is recommended, between 30% to 60% can be discussed, and under 30% are not to be used [12]. Resistance to beta-lactam antibiotics in each bacteria sampes has nearly reached 90 percents or above. While resistance to beta-lactam and beta-lactamase inhibitors in E.coli and K. pneumoniae are the highest in Ampicilin-Sulbactam with 47,1% and 60% each and the lowest in Piperacilin-Tazobactam with 13,7% and 25,7% respectively. E. vulneris' lone sample and all of K. ozaenae's samples has become resistant to Ampicilin-Sulbactam while K. *oxytoca'*s sample are split with resistant and sensitive. Resistance to non-beta-

lactam antibiotics are the highest in Ciprofloxacin for E.coli samples and Nitrofurantoin for K. pneumoniae samples. Lastly, Amikacin is the antibiotic with the least resistance in each bacteria samples. According to the afforementioned recommendations, therefore antibiotics Amikacin, Piperacilin-Tazobactam, Imipenem, Meropenem, and Fosfomycin are recommended for use in E.coli. Gentamycin, Amikacin, Levofloxacin, Imipenem, and Meropenem are recommended for E. vulneris. Gentamycin, Amikacin, Imipenem, and Meropenem are recommended for K. pneumoniae. While the next bacteria species have much less samples than two of thGentamycin and Amikacin are recommended for K. oxytoca, and lastly Gentamycin, Amikacin, and Piperacilin-Tazobactam are recommended for K. ozaenae. A Balinese study in comparison recommended Piperacilin-Tazobactam, Cefepime, Ceftazidime, Gentamycin, Meropenem, and Nitrofurantoin for E. coli while only recommending Meropenem for K. pneumoniae.

4. Conclusion

From the data shown, Aminoglycosides Gentamycin and Amikacin and Carbapenems Imipenem and Merpenem are recommended to treat patients with infections from ESBL-producing bacteria. Further researches can be performed with live cultures taken from patients and their invasive devices instead of secondary data to attain a more updated results and resistance patterns.

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