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Research Article

Antibiotic Susceptibility of Bacteria Isolated from Open Fracture Grade III Presenting to Dr. Soetomo General Hospital Surabaya

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ABSTRACT

Background: Open fracture is a typical case in the orthopedics field. Infection in the open fracture can cause osteomyelitis. Antibiotic susceptibility test of patient specimen bacteria with open fracture aims to obtain the suitable antibiotic agents to treat infectious diseases caused by these bacteria.
Methods: This research is a descriptive study to assess Antibiotic susceptibility in the case of open fracture grade III in Dr. Soetomo General Hospital Surabaya. A total sampling was performed from microbiological culture results of patients diagnosed with open fracture grade III after debridement from October 2018 to September 2019. The identification of the microbes was based on Gram-positive and Gram-negative categories and the classification based on susceptibility to antibiotics classified into sensitive, intermediate, and resistant.
Results: Data from microbiological culture results of patients with a diagnosis of open fracture grade III after debridement in October 2018 to September 2019 in Dr. Soetomo General Hospital Surabaya showed 56 research subjects who met the criteria. *Acinetobacter baumannii* is the most common bacterial species found in the microbiological examination of patients with open fractures, 15.84%. Cefazoline and ceftriaxone showed low susceptibility. Meanwhile, levofloxacin showed a relatively good value of susceptibility in both Gram-positive and negative bacterial groups.
Conclusion: The antibiotic susceptibility pattern of bacteria from specimens in open fracture grade III patients in Dr. Soetomo General Hospital Surabaya varies between each species of bacteria isolate.

Keywords: Open fracture; Grade III; Antibiotics; Susceptibility

INTRODUCTION

Osteomyelitis is challenging to eradicate and requires a long treatment period and will significantly impact function, quality of life, financial, and psychosocial.[1] The number of post-debridement bacterial colonies significantly affects the risk of infection in an open fracture.[2] Therefore, it is necessary to reduce the number of bacterial colonies in open fractures. One of the therapies to achieve this is by debriding and providing effective antibiotic therapy.[3]

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The hospital must have a bacterial susceptibility pattern as a reference for effective antibiotics and prevent irrational antibiotic therapy.[4] This study aims to obtain data on the bacterial susceptibility pattern in open fracture cases at Dr. Soetomo General Hospital Surabaya, so it is hoped that it can become a reference for providing rational and adequate antibiotic therapy in open fracture cases.

MATERIAL AND METHODS

This study was approved by Dr. Soetomo General Hospital Surabaya Ethical Committee. This research is a descriptive study regarding bacterial susceptibility patterns in open fracture III degrees at Dr. Soetomo General Hospital Surabaya. This study's sampling technique was a total sampling of bacterial data from microbiological cultures of patients diagnosed with post debridement grade III open fracture in the period from October 2018 to September 2019 at Dr. Soetomo General Hospital Surabaya.

The inclusion criteria of this research are 1. Patients who were diagnosed with grade III open fracture includes humerus, radius, ulna, femur, tibia, fibula, clavicle, scapula, spine, pelvis, carpal, patella, metacarpal, phalanx, talus, calcaneus, tarsal, and metatarsal; 2) Patients underwent debridement; 3) The specimen from the patient underwent microbiological culture. Exclusion criteria were: 1) Patients diagnosed with grade III open fracture include the skull, ribs, vertebrae; 2) Patients underwent debridement surgery in a hospital outside Dr. Soetomo General Hospital Surabaya.

The microbiological cultures are classified into Gram-positive and Gram-negative bacteria.[5] The antibiotic susceptibility determines the response of bacterial to an antibiotic at a concentration level that can inhibit/kill bacterial. The results are divided into sensitive, intermediate, and resistant.[6] After classifying bacterial based on Gram-positive and Gram-negative categories followed by bacterial classification based on susceptibility to antibiotics. The analysis is carried out to obtain a profile of bacterial susceptibility in patients with open fracture degree III at Dr. Soetomo General Hospital Surabaya.

RESULTS

Fifty-six subjects met the inclusion criteria and did not meet the exclusion criteria. Based on Table 1, most open fracture sufferers are aged 11-30 years (46.40%). The male gender group had a higher number than female, namely 39 subjects or 69.7%. The most common open fractures location was in the lower leg region in 22 cases, or 39.29%. Meanwhile, the number of open fracture cases in the forearm and foot regions had a similar value, namely 8 cases or 14.29%.

In Table 2, the distribution of bacteria shows that *Acinetobacter baumannii* is the most common species of bacteria found on the microbiological examination of open fracture

sufferers, which is 15.84%. In comparison, *E. Coli* ESBL is the pathogen with the second largest number of 11.88%. Meanwhile, other pathogens found from isolated cultures can be seen in the table below. An overview of the pattern of bacterial susceptibility to various kinds of antibiotics can be seen in more detail in the table below, shown in Table 3 and 4. This test results show that the susceptibility value varies based on the bacteria species and the kinds of antibiotics used.

Table 1. Subject Characteristics

	Total (n = 56)	Percentage (%)
Age		
11-30 years	26	46.40
31-50 years	20	35.70
> 50 years	10	17.90
Gender		
Male	39	69.7
Women	17	30.3
Fracture Location		
Forearm	8	14.29
Thigh	18	32.14
Lower leg	22	39.29
Foot	8	14.29

DISCUSSION

Open fracture type IIIB is associated with extensive injury or soft tissue loss, accompanied by periosteal stripping and bone exposure, massive contamination, and a severe degree of comminution.[7] Based on the results of the characteristics of the research subjects, it appears that the majority of open fracture sufferers are between 11-30 years old (46.40%). Several studies reported by Arti *et al*. (2012) and Court-brown *et al*. (2012) expressed mean age at 23±1.5 years and 29.5 years, respectively. It is because this age group have activities or activities that are more prone to serious injury than other age groups.[8,9]

Table 2. Distribution of Bacteria based on Microbiological Examination

	Total (n = 101)	Percentage (%)
Bacteria		
Acinetobacter baumannii	16	15.84
E. coli ESBL	12	11.88
Pseudomonas aeruginosa	10	9.90
Proteus mirabilis	9	8.91
Enterobacter cloacae	7	6.93
Providencia stuartii	6	5.94
MRSA	5	4.95
Staphylococcus aureus	5	4.95
Morganella morganii	3	2.97
Globicatella sanguinis	2	1.98
Enterococcus faecalis	2	1.98
Bacillus cereus	2	1.98
Corynebacterium striatum	2	1.98
Staphylococcus epidermidis	2	1.98
Enterobacter aerogenes	2	1.98
Streptococcus gordonii	2	1.98
Gemella haemolysans	1	0.99
Pantoea agglomerans	1	0.99
Candida Parapsilosis this is fungi, not bacteria	1	0.99
Enterococcus faecalis	1	0.99
Klebsiella pneumoniae ESBL	1	0.99
Staphylococcus schleiferi	1	0.99
E. coli	1	0.99
Aeromonas hydrophila	1	0.99
Providencia rettgeri	1	0.99
Amycolatum striatum	1	0.99
Kluyvera ascorbata	1	0.99
Stenotrophomonas maltophilia	1	0.99
Streptococcus anginosus	1	0.99
Ralstonia pickettii	1	0.99

Table 3. Antibiotic Susceptibility to Gram-positive Bacteria

	MRSA	*Staphylococcus aureus*	*Globicatella sanguinis*	*Enterococcus faecalis*	*Bacillus cereus*	*Corynebacterium striatum*	*Gemella haemolysans*	*Streptococcus Gordonii*	*Staphylococcus schleiferi*	*Amycolatum striatum*	*Streptococcus angionosus*	*Staphylococcus epidermidis*
	The number of bacteria tested(percentage)											
Amikacin	-	5(100)	0	0	-	0	-	-	1(100)	1(100)	-	-
Gentamicin	0	4(80)	0	0	2(100)	-	0	-	1(100)	1(100)	0	1(100)
Aztreonam	-	-	-	-	-	-	-	-	-	-	-	-
Amoxicillin-Clavulanic Acid	0	4(80)	2(100)	2(100)	-	0	-	-	0	-	-	1(100)
Ampicillin	0	0	-	1(50)	0	-	-	0	0	-	1(100)	0
Ampicillin-sulbactam	-	-	-	-	0	-	-	-	-	-	-	-
Piperacillin	-	-	-	-	-	-	-	-	-	-	-	-
Tazobactam	-	-	-	2(100)	2(100)	0	-	-	-	1(100)	1(100)	1(100)
Oxacillin	0	4(80)	-	0	0	-	-	-	0	0	-	1(100)
Cefazolin	-	-	-	-	-	-	-	-	-	-	-	-
Ceftazidime	-	-	-	-	-	-	-	-	-	-	-	-
Cefotaxime	0	-	-	0	-	0	0	0	-	-	0	-
Ceftriaxone	-	-	-	0	-	0	0	2(100)	-	-	1(100)	-
Cefepime	-	-	-	-	-	-	-	-	-	-	-	-
Trimethoprim-Sulfamethoxazole	2(40)	5(100)	0	0	0	0	0	0	1(100)	0	1(100)	1(100)
Tetracyclin	1(20)	0	-	-	-	-	-	-	0	-	0	1(100)
Tigecycline	-	-	-	-	-	-	-	2(100)	-	-	-	1(100)
Chloramphenicol	2(40)	60	0	2(100)	1(50)	1(50)	0	2(100)	-	1(100)	0	1(100)
Erythromycin	2(40)	4(80)	1(50)	0	1(50)	0	0	2(100)	0	0	0	1(100)
Clindamycine	3(60)	4(80)	0	0	0	0	0	2(100)	0	0	0	0
Quinopristin-dalfopristin	5(100)	5(100)	-	0	-	-	-	-	-	-	-	-
Ciprofloxacin	0	4(80)	-	-	-	-	-	-	100	-	-	1(100)
Levofloxacin	0	75	1(50)	2(100)	2(100)	0	-	2(100)	-	0	1(100)	1(100)
Moxifloxacin	2(40)	75	-	-	-	-	-	2(100)	-	-	-	1(100)
Fosfomycin	5(100)	4(80)	-	2(100)	2(100)	1(50)	-	-	-	0	0	1(100)
Nalidixic Acid	-	-	-	-	-	-	-	-	-	-	-	-
Imipenem	-	-	-	-	-	-	-	-	-	-	-	-
Meropenem	-	-	-	-	-	-	-	-	-	-	-	-
Vancomycin	5(100)	5(100)	1(50)	2(100)	0	2(100)	1(100)	2(100)	0	-	1(100)	1(100)
Linezolid	5(100)	5(100)	1(50)	2(100)	2(100)	2(100)	1(100)	2(100)	0	-	1(100)	1(100)
Fosfomycin	0	5(100)	0	0	-	-	-	-	-	1(100)	-	1(100)

The male gender group had a greater number than women, namely 39 subjects or 69.7%. It is explained that men are generally more prone to injury due to exposure to risky activities both at work and in their leisure time.[10] The most common location of open fractures was in the lower leg region in 22 cases, or 39.29%. Several studies reported the same thing, Kale *et al*. (2017) stated 40.62% and Arti *et al.* (2012). 62% incidence of open fractures in the lower leg region.[8,11] Meanwhile, the number of open fracture cases in the forearm and foot regions had a similar value, namely 8 cases or 14.29%.

Table 4. Antibiotic Susceptibility to Gram-negative Bacteria

	Acinetobacter baumanni	*E.Coli ESBL*	*Pseudomonas aeurigenosa*	*Proteus mirabilis*	*Enterobacter cloaca*	*Providencia stuartii*	*Morganella morgagnii*	*Enterobacter aerogenes*	*Pantoea agglomerans*	*Klebsella pneumonia*	*E.Coli*	*Providencia rettgeri*	*Amycolatum striatum*	*Kluyvera ascorbata*	*Stenotrophomonas maltophila*	*Ralstonia pickettii*
	The number of bacteria tested(percentage)															
Amikacin	0	9(100)	6(60)	9(100)	7(100)	4(67)	3(100)	2(100)	0	0	1(100)	1(100)	1(100)	1(100)	0	1(100)
Gentamicin	0	-	6(60)	5(55)	2(29)	0	2(67)	50	0	1(100)	-	0	1(100)	1(100)	0	0
Aztreonam	0	3(33)	3(30)	8(88)	1(14)	0	2(67)	50	0	-	1(100)	0	-	0	0	0
Amoxicillin/Clavulanic Acid	0	-	0	5(55)	0	0	0	0	0	-	0	0	-	0	0	0
Ampicillin	0	0	0	1(11)	0	0	0	0	0	1(100)	0	0	-	0	0	0
Ampicillin-sulbactam	0	2(22)	0	5(55)	0	1(17)	0	0	0	-	0	0	-	0	0	0
Piperacillin	0	0	8(80)	5(55)	1(14)	0	-	2(100)	0	-	0	0	-	0	0	0
Tazobactam	0	8	8(80)	7(77)	3(43)	5(83)	3(100)	2(100)	0	-	1(100)	0	1(100)	0	0	1(100)
Oxacillin	-	-	-	-	-	-	-	-	-	0	-	-	0	-	-	-
Cefazolin	0	0	0	6(67)	0	0	0	0	0	-	0	0	-	0	0	0
Ceftazidime	0	8(88)	8(80)	9(100)	1(14)	0	3(100)	1(50)	0	-	1(100)	0	-	0	0	0
Cefotaxime	0	-	1(10)	5(55)	1(14)	0	1(33)	1(50)	0	-	1(100)	0	-	0	0	0
Ceftriaxone	0	-	2(20)	7(77)	1(14)	0	1(33)	1(50)	0	-	1(100)	0	-	0	0	1(100)
Cefepime	0	0	4(40)	7(77)	4(57)	0	1(33)	2(100)	0	-	1(100)	0	-	1(100)	-	0
Trimethoprim/Sulfamethoxazole	2(13)	-	0	1(11)	3(43)	0	1(33)	1(50)	0	0	1(100)	1(100)	0	1(100)	1(100)	0
Tetracyclin	0	0	0	0	5(71)	0	0	2(100)	0	-	0	0	-	1(100)	0	-
Tigecycline	4(25)	0	0	4(44)	4(57)	6(100)	0	-	0	-	1(100)	0	-	-	1(100)	-
Chloramphenicol	0	0	0	1(11)	2(29)	0	0	1(50)	0	-	-	0	1(100)	1(100)	0	0
Erythromycin	-	-	-	-	-	-	-	-	-	0	1(100)	-	0	-	-	-
Clindamycin	-	9(100)	-	-	-	-	-	-	-	0	-	-	0	-	-	-
Quinopristin-dalfopristin	-	-	10(100)	-	-	-	-	-	-	1(100)	-	-	-	-	-	-
Ciprofloxacin	0	0	3(30)	4(44)	1(14)	5(83)	2(67)	2(100)	0	-	1(100)	0	-	1(100)	-	0
Levofloxacin	0	2(22)	6(60)	4(44)	4(57)	3(50)	1(33)	1(50)	0	1(100)	1(100)	0	0	1(100)	0	0
Moxifloxacin	-	-	-	3(33)	2(29)	2(33)	1(33)	2(100)	0	-	1(100)	0	-	1(100)	-	-
Fosfomycin	0	3(33)	3(30)	5(55)	4(57)	0	0	0	-	-	1(100)	0	0	1(100)	0	0
Nalidixic Acid	-	5(55)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Imipenem	0	5(55)	6(60)	-	6(86)	-	-	0	0	-	1(100)	0	-	1(100)	0	0
Meropenem	0	-	7(70)	9(100)	7(100)	5(83)	3(100)	2(100)	0	-	1(100)	0	-	1(100)	0	1(100)
Vancomycin	-	-	10(100)	-	-	-	-	-	-	1(100)	-	-	-	-	-	-
Linezolid	-	-	10(100)	-	-	-	-	-	-	-	-	-	-	-	-	-
Fosfomycin	0	27	0	100	100	-	-	-	-	0	-	-	1(100)	-	-	-

In the istribution of bacteria, it appears that *Acinetobacter baumannii* is the most common species of bacteria found in the microbiological examination of infected open fracture patients, which is 15.84%. The same results were reported in a study by Kale *et al*. (2017). It was stated that the bacteria often found in open fractures is *Acinetobacter baumannii*, 14.06% of all swab culture results.[11] Another study by Zhu *et al*. (2017) in 337 cases of an open fracture shows that the isolation of *Acinetobacter baumannii* culture was found in 16 cases out of 201 cases contaminated with seawater. Based on the research results described above, it appears that *Acinetobacter baumanni*i, as the species of pathogen most often found in culture isolations of

patients with open fracture grade III post debridement, showed low susceptibility to the kinds of antibiotics tested. On examination, susceptibility was found to 2 kinds of antibiotics, namely Trimethoprim-Sulfamethoxazole (13%) and Tigecycline (22%). The genus *Acinetobacter* includes non-lactose-fermenting, catalase-positive, non-motile, non-fastidious, oxidase-negative, and aerobic Gram-negative coccobacilli. *Acinetobacter baumannii* is clinically significant because it involves nosocomial infections and intrinsically resistant to wider classes of antimicrobials with a high propensity to develop resistance. It is caused by the unique ability of *Acinetobacter baumannii* to survive desiccation, renders its viability in inanimate objects for months, and thus facilitates its spread in the hospital.[12,13] *Acinetobacter* species are capable of accumulating multiple antibiotic resistance genes, leading to the development of multidrug-resistant or extensively drug-resistant strains through the production of β lactamases, efflux pumps, lower permeability of the outer membrane, mutations in antibiotic targets (e.g., for quinolones), production of enzymes inactivating aminoglycosides .[14,15,16]

The first line antibiotics for infection caused by *Acinetobacter baumannii* including a broad-spectrum cephalosporin (ceftazidime or cefepime), a combination beta-lactam/beta-lactamase inhibitor (i.e., one that includes sulbactam), or a carbapenem (e.g., imipenem, meropenem, or doripenem). Carbapenems are highly bactericidal against susceptible strains of *Acinetobacter*, but isolates that are susceptible to imipenem may be resistant to meropenem, and vice versa, susceptibility to the specific carbapenem should be confirmed before its use.[16] *Acinetobacter baumannii* that resistance to the above agents have limited therapeutic options, certain Tetracyclines (Minocycline and Tigecycline) may also have a role, Polymyxins (Polymyxin B and colistin [polymyxin E]) are the most commonly used agents for *Acinetobacter* isolates resistant to first-line agents. [16,17]

E. coli ESBL the second most common bacteria found in isolates of patient specimens with open grade III fractures, namely 11.88%. It is not much different from the findings in the study by Abraham and Wamisho (2009), which showed a total of 17 cases (10.5%) of patients with *E. coli* isolates. *E. coli* obtained in this study are ESBL-producing bacteria. Extended Spectrum β-Lactamase (ESBL) is a plasmid enzyme that mediates the hydrolysis and inactivation of beta-lactam antibiotics including third-generation Cephalosporins, Penicillin, and Aztreonam.[18] In this study, several kinds of antibiotics showed susceptibility values of up to 100%, namely Ampicillin, Amoxicillin-clavulanic acid, Amoxicillin, and Trimethoprim-Sulphamethoxazole.[19] In this study, results have obtained 100% susceptibility in the test against the antibiotic Amikacin and Clindamycin.

Pseudomonas aeurigenosa is the third most common bacteria isolated in this study, with a percentage of 9.90%. *Pseudomonas aeruginosa*

is a gram-negative bacillus found widely in nature, soil, and water. *Pseudomonas aeruginosa* infrequently found as part of the human microflora in healthy individuals is a gram-negative, non-glucose fermenter rod. *Pseudomonas aeruginosa* is widespread in natural environments, and it is an opportunistic pathogen for humans, leading to a broad spectrum of diseases such as urinary, burn, respiratory infections, and septicemia.[20] It is the primary cause of ventilated, associated pneumonia in the intensive care unit.[21] In recent years, nosocomial infections caused by *Pseudomonas aeruginosa* have been recognized as an acute problem in hospitals due to its intrinsic resistance to many antibiotic classes and its capacity to acquire practical resistance to all effective antibiotics.[22] All these features in *Pseudomonas aeruginosa* characterize it as a major microorganism to monitor antibiotic resistance in the clinical specimens. On the other hand, the spread of these bacteria in hospital personnel, wet places could be a reservoir. Therefore, it is necessary to evaluate the contribution of hospital equipment and personnel in the dissemination route of multidrug resistance *Pseudomonas aeruginosa.*[23]

The choices for treatment for *Pseudomonas aeruginosa* infections include the following antimicrobial agents, with the fluoroquinolones being the only oral options: Aminoglycosides, Cephalosporins, third-generation, Cephalosporins fourth-generation, Fluoroquinolones, Monobactam, Extended-spectrum penicillins (Ticarcillin and/or Ticarcillin-Clavulanate, Piperacillin and/or Piperacillin–Tazobactam, Azlocillin), Polymyxin B/Colistin. In systemic infection with shock/sepsis, antimicrobial therapy should consist of two intravenous antimicrobial agents, with one of these being an aminoglycoside.[24]

Acinetobacter baumannii, E. Coli ESBL, and *Pseudomonas aeruginosa* are nosocomial bacterial that is often found in intensive care unit environments.[25] In Dr. Soetomo General Hospital Surabaya, all patients with open fractures who underwent emergency surgery will be admitted to the intensive care unit for postoperative observation. That procedure could contribute to why *Acinetobacter baumannii, E. Coli ESBL,* and *Pseudomonas aeruginosa are* the most species found in this study.

Several studies reported different things; the most common bacteria found were *Pseudomonas aeruginosa* and *Staphylococcus capitis*.[26,27] In a prospective study of infection in open fractures, 78.7% of all open fractures were contaminated with bacteria. The rate of infection correlated directly with the fracture type, according to Gustillo *et al.* (1984), 24.5% in type I open fractures and 86.8% in type IIIC open fractures. Infection is usually caused by various bacteria dominated by *Staphylococcus aureus* (52.8%), *E. coli* and *Enterobacter* (32.5%), *Streptococcus* (26.0%), *Pseudomonas* (17.1%) and *Proteus* (1.6 %).[28]

Based on the average antibiotic susceptibility for the top 5 most common Gram-positive bacteria, the most effective antibiotic

includes Linezolid, Vancomycin, Levofloxacin, Chloramphenicol Erythromycin, respectively. Meanwhile, the most effective antibiotic for Gram-negative bacteria includes Meropenem, Amikacin, Tazobactam, Tigecycline, and Levofloxacin.

The use of Cefazolin as an antibiotic in grade III open fractures shows a low susceptibility value in this study, its difference with the study by Patanwala *et al*. (2019) showed that Cefazolin monotherapy in cases of grade III open fractures was as effective as the use of Cefazolin with Aminoglycosides in the incidence of infection at the fracture site with a lower risk of kidney problems.[29]

Meanwhile, the evaluation of ceftriaxone's susceptibility as a recommended antibiotic for grade III open fracture cases at Dr. Soetomo General Hospital Surabaya showed different susceptibility values, namely 22% (*Pseudomonas aeruginosa*) and 100% (*E. Coli*). Research by Abraham and Wamisho (2009) showed an excellent susceptibility value to the use of ceftriaxone in open fracture cases with various degrees, namely between 66.7 to 100% in different species of bacterial isolates.[19]

In this study, the most bacteria isolated were nosocomial bacteria which were multi-resistant bacterial. Hence infection control measures to prevent nosocomial infections are essential. Infection measure control including hand-hygiene protocols, routine cultures from healthcare personnel and environment, identification of environmental sites serving as common sources of transmission, closure of hospital units/wards for sterilization, disinfection of potentially contaminated medical equipment, use of individual medical equipment, minimize time on intensive care unit after post-emergency surgery on open fracture patient.

CONCLUSION

The rational use of antibiotics and supported by the selection of antibiotics based on culture and antibiotic susceptibility tests and the prevention of nosocomial infection are the main pillars in preventing grade III open fracture complications.

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