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Characteristics, Patterns of Pathogens, and Antibiotics Resistance of Bacterial Meningitis at RSUP dr. Mohammad Hoesin Palembang

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Abstract

Bacterial meningitis is an inflammation of the meninges, especially arachnoid and pia mater, which occurs due to the invasion of bacteria into the subarachnoid space. Bacterial meningitis cases are distributed throughout the world, with an incidence of 2-6 / 100,000 people per year with a peak incidence in infants, adolescents, and the elderly. This study was a retrospective cross-sectional descriptive study to look for sociodemographic characteristics, pathogens and resistance patterns, and clinical outcomes of bacterial meningitis patients at dr. Mohammad Hoesin Palembang. There were 43 cases of bacterial meningitis, and only 13 cases met the inclusion and exclusion criteria. Most cases of bacterial meningitis were in the 30-45 years (30%) and 46-55 years (30%) age groups, with predominantly female patients (69%). The most noted clinical manifestations were fever and neck stiffness (100%). decreased consciousness (92%), hemiparesis (77%), headache (70%) and seizures (54%). The mortality rate of bacterial meningitis patients reached 53% with a disability rate reaching 39%. Pathogens found based on culture results were Staphylococcus sp. (69%), Acinetobacter baumanii (5.3%), Klebsiella pneumonie (15%), Shigella somnei, and E. coli (5.3%). Antibiotic resistance to Staphylococcus sp. Was quite high, namely Erythromycin and Oxacillin reaching 77%, Trimethoprim / Sulfamethoxazole 55%, Ciprofloxacin, Clindamycin, levofloxacin reached 33%. Higher mortality was found in patients with drug resistance.

Keywords: bacterial meningitis, drug resistance, Staphylococcus sp.

Abstrak

Meningitis bakterial merupakan inflamasi meningen terutama arachnoid dan piamater yang terjadi karena invani bakteri ke dalam ruang subarachnoid. Kasus meningitis bakterial terdistribusi di seluruh dunia, dengan insiden mencapai 2-6/100.000 jiwa per tahun dengan puncak kejadian pada kelompok bayi, remaja, dan lansia. Penelitian ini merupakan penelitian deskriptif potong lintang retrospektif dengan tujuan mencari karakteristik sosiodemografi, pola kuman dan resistensi, serta luaran klinis pasien meningitis bakterialis di RSUP dr. Mohammad Hoesin Palembang. Tercatat 43 kasus meningitis bakterial, dan hanya 13 kasus yang memenuhi kriteria inklusi dan ekslusi. Usia kasus meningitis bakterial terbanyak yaitu pada kelompok usia 30-45 tahun ((30%) dan 46-55 tahun (30%), dengan didominasi pasien wanita (69%). Manifestasi klinis yang banyak tercatat yaitu demam dan kaku kuduk (100%), penurunan kesadaran (92%), hemiparese (77%), nyeri kepala (70%) dan kejang (54%). Angka kematian pasien meningitis bakterial mencapai 53% dengan angka kecatatan mencapai 39%. Patogen yang ditemukan berdasarkan hasil kultur yaitu Staphylococcus sp. (69%), Acinobacter baumanii (5,3%), Klebsiella pneumonie (15%), Shigella somnei dan E. coli (5,3%). Resistensi antibiotik terhadap Staphylococcus sp. cukup tinggi yaitu Eritromisin dan Oxacilin mencapai 77%, Trimetoprim/Sulfamethoxazole 55%, Ciprofloxacin, Clindamycin, Levofloxacin mencapai 33%. Angka kematian lebih tinggi ditemukan pada pasen dengan resistensi obat. Penelitian ini menunjukkan angka resistensi antibiotik cukup tinggi dan diduga berhubungan dengan mortalitas dan morbiditas tinggi.

Kata kunci: meningitis bakterial, resistensi obat, Staphylococcus sp.

1. Introduction

Bacterial meningitis is inflammation of the meninges due to the invasion of bacteria into the subarachnoid space. The inflammatory process is not limited to the meninges, but can also spread to the brain parenchyma, ventricles, and spinal cord. Neuronal damage, especially to the hippocampal structure, is thought to be a potential cause of persistent neuropsychological deficits in patients recovering from bacterial meningitis.[1] Bacterial meningitis are distributed worldwide, with the peak incidence in infants, adolescents, and the elderly.

The selection of appropriate antibiotics in the management of bacterial meningitis is a crucial step because it is related to the potential for drug resistance and the speed of pathogen development. In immunocompetent adults, S. pneumoniae and N. meningitides are the main pathogens causing bacterial meningitis, because these two bacteria can colonize the nasopharynx and cross the blood-brain barrier. Gram-negative bacilli such as Escherichia coli, Klebsiella spp, Staphylococcus aureus, Staphylococcus epidermidis, and Pseudomonas spp are usually the cause of nosocomial bacterial meningitis, which usually occurs in patients with craniotomy, internal or external ventricular catheterization, and head trauma. In several pathogens, the occurrence of resistance while receiving antibiotic therapy or prophylaxis is thought to be a more likely factor in the incidence of additional infection by resistant organisms, than the transfer of organisms from one patient to another.[2] The choice of empiric antibiotics in bacterial meningitis patients must also be based on local epidemiology, patient age, and presence of any underlying disease or comorbid factors. If the pathogen and antibiotics resistance is not known it will be difficult to determine first-line antibiotics in patients with suspected sepsis until culture results are obtained so that each unit of care should ideally have its pattern of pathogens and resistance.

This study aims to find sociodemographic characteristics, pathogens and resistance patterns, and clinical outcomes of bacterial meningitis patients at dr. Mohammad Hoesin Palembang.

2. Method

This is a retrospective descriptive cross-sectional study using secondary data from the Microbiology Laboratory of dr. Mohammad Husein Palembang January - December 2018. Sampling was carried out by the total sampling method of all medical records of bacterial meningitis patients who were treated at the Neurology Department. Patients were excluded from the study if data were incomplete. the patient did not undergo lumbar puncture and sterile CSF cultures. The study variables were age, gender, awareness, neurological deficit, clinical outcome, pathogens that cause bacterial meningitis, and level of resistance/sensitivity of pathogens to antibiotics. The data that has been collected will be processed in statistical form using the SPSS for Windows program.

3. Results

During the observation period, there were 43 patients recorded with bacterial meningitis and bacterial meningoencephalitis. Four samples were excluded due to incomplete medical records, 9 samples died before lumbar puncture was performed, 4 samples rejected lumbar puncture, 13 samples were sterile culture results. So that only 13 samples were obtained that met the inclusion and exclusion criteria.

From table 1, the highest number of cases of bacterial meningitis based on age levels is found in 2 age groups, namely the age group 36 - 45 years and 46 - 55 years, namely 4 cases (30%), then the 26 - 35 age group. years as many as 3 cases (23%), 18-25 years as many as 1 case (8.5%), and the age group 56-65

years as many as 1 case (8.5%). The bacterial meningitis cases were dominated by 9 cases (69%) for women, while for men (4 cases) (31%).

The clinical manifestations in meningitis patients in this study are unconsciousness in 12 cases (92%), hemiparesis 10 cases (77%), seizures in 7 cases (54 %), neck stiffness in 13 cases (100%), headache in 9 cases (70%), vomiting in 6 cases (46%) and fever (100%).

Table 1. Characteristic Bacterial Meningitis Patients

No.	Variables	n	Percentage (%)
1.	Age		
	1. 18 – 25 y.o	1	8,5
	2. 26 – 35 y.o	3	23
	3. 36 – 45 y.o	4	30
	4. 46 – 55 y.o	4	30
	5. 56 – 65 y.o	1	8,5
	6. > 65 y.o	0	0
2.	Sex		
	1. Male	4	31
	2. Female	9	69
3.	Clinical manifestations		
	1. unconsciousness	12	92
	2. hemiparesis	10	77
	3. seizure	7	54
	4. neck stiffness	13	100
	5. headache	9	70
	6. vomiting	6	46
	7. fever	13	100
4.	Clinical outcome		
	1. without sequelae	1	8
	2. with sequelae	5	39
	3. Died	7	53

From the CSF culture, it was found that the highest number of pathogens in bacterial meningitis was Staphylococcus sp. in 9 cases (69%), followed by Klebsiella pneumonia in 2 cases (15%), 1 case of Acinetobacter baumannii (5.3%), 1 case of Shigella sonnei (5.3%), and 1 case of Escherichia coli (5.3%) (Table 2). Antibiotic resistance of Staphylococcus sp meningitis in 9 patients, namely Erytromicin and Oxacillin in 7 cases (77%), benzylpenicillin in 6 cases (66%), Trimethoprim/Sulfamethoxazole 5 cases (55%), Ciprofloxacin, Clindamycin, Levofloxacin in 3 cases (33%).

Meanwhile, the pattern of antibiotic resistance in patients with bacterial meningitis caused by Acinetobacter sp is resistant to all antibiotics except Tygecicline. The pattern of antibiotic resistance of patients with bacterial meningitis caused by Klebsiella pneumonia is Nitrofurantoin, Gentamicin, Trimethoprim / Sulfamethoxazole, Aztreonam, namely 2 cases (100%), Ciprofloxacin, Tygecicline, Cefepime, Meropenem, Piperacillin / Tazobactam, 1 case (50%). (Table 3)

Table 2. Pathogens in bacterial meningitis

No.	Pathogen	n	Percentage (%)
1.	Staphylococcus sp.	9	69
2.	Acinetobacter baumannii	1	5,3
3.	Klebsiella pneumoniae	2	15
4.	Shigella somnei	1	5,3
5.	Escherichia coli	1	5,3

Table 4. Antibiotics Resistance and Clinical Outcome of Bacterial Meningitis due to Staphylococcus sp.

No.	Antibiotic resistance	n (%)	health	With sequelae	Died
1.	Oxacillin	7 (77)	1 (14)	3 (43)	3 (43)
2.	Erythromycin	7 (77)	1 (14)	3 (43)	3 (43)
3.	Benzylpenicillin	6 (66)	1 (17)	3 (50)	2 (33)
4.	Trimethoprim/ Sulfamethoxazole	5 (55)	1 (20)	2 (40)	2 (40)
5.	Ciprofloxacin,	3 (33)	-	2 (66)	19 (34)
	Clindamycin,		-	1 (34)	2 (66)
	Levofloxacin		-	2 (66)	1 (34)

The mortality and disability rate of bacterial meningitis due to Staphylococcus sp. those experiencing antibiotic resistance were noted to be quite high. The mortality rate for resistant Oxacillin reached 43%, Erythromycin

43%, Benzylpenicillin 33%, Trimethoprim / Sulfamethoxazole 40%, Ciprofloxacin 34%, Clindamycin 66%, Levofloxacin 34% (table 4). The mortality rate for bacterial meningitis due to Acinetobacter sp, Klebsiella pneumoniae, E. coli, and Shigella somnei reaches 100%.

Tabel 3. Pola resistensi antibiotik Pasien Meningitis Bakterial

No.	Antibiotik	Staphylococcus sp. (N=9)	Acinetobacter sp. (N=1)	Klebsiella pneumonia (N=2)	Shigella sp. (N=1)	Escherichia coli (N=1)
1.	Ciprofloxacin	3 (33 %)	1 (100%)	1 (50%)	0	0
2.	Clindamycin	3 (33%)				
3.	Erythromycin	7 (77 %)				
4.	Nitrofurantoin	0 0		2 (100%)	0	0
5.	Gentamicin	2 (22 %)		2 (100%)	0	0
6.	Inducible Clindamycin Resistance	0				
7.	Levofloxacin	3 (33 %)				
8.	Linezolid	0				
9.	Moxifloxacin	3 (33 %)				
10.	Oxacillin	7 (77 %)				
11.	Cefoxitin Screen	1 (11 %)				
12.	Benzylpenicillin	6 (66 %)				
13.	Quinupristin/Dalfopristin	0				
14.	Rifampicin	1 (11 %)				
15.	Trimethoprim/Sulfamethoxazole	5 (55 %)		2 (100%)	0	0
16.	Tetracycline	1 (11%)				
17.	Tigecycline	0	0	1 (50%)	0	0
18.	Vancomycin	0				
19.	Amikacin		1 (100%)	0	0	0
20.	Ceftazidime		1 (100%)	0	0	0
21.	Ceftriaxone		1 (100%)	0	0	0
22.	Cefazolin		1 (100%)	0	0	0
23.	Cefepime		1 (100%)	1 (50%)	0	0
24.	Gentamicin		1 (100%)		0	0
25.	Meropenem		1 (100%)	1 (50%)	0	0
26.	Ampicillin/Sulbactam		1 (100%)	0	0	1 (100%)
27.	Trimethoprim/Sulfamethoxazole		1 (100%)	0	0	0
28.	Piperacillin/Tazobactam		1 (100%)	1 (50%)	0	0
29.	Ertapenem			1 (50%)	0	0
30.	Aztreonam			2 (100%)	0	0
31.	ESBL				0	0

4. Discussion

Based on this study the mean age of the patients was 41 ± 10.59 years. This is similar to the results of a study by Handojo et al. In Bali which stated that the average age of bacterial meningitis patients was 43 years. Based on the age level, it was found in 2 age groups, namely the age group 36-45 years and 46-55 years, which were both 4 cases (30%). This is following the meningitis data published by WHO that the most age group for adult meningitis patients is the age group 15 - 44 years. Mosavi-jarrahi et al where the incidence rate of women is more than men.[6] A study of Dharmarajan, et al. found that from 619 subjects, there were 52.8% of cases of women, the remaining 47.2% were men. Men are said to be more often accompanied by other comorbid, fever, abnormal microbiological examination results, and abnormal CT scans, while women experience more frequent neck stiffness.[7] According to the results of research by Rabbani et al in several developing countries, men are more dominant than women.[2] The differences with some of these studies may be due to differences in the basic characteristics of the subject, the length of the study, and the number of samples taken.

Of the 13 patients who met the inclusion criteria, the most distribution of clinical manifestations was neck stiffness (100%), fever (100%), decreased consciousness (92%), hemiparesis (77%), headache (70%), seizures (54%).) and projectile vomiting (46%). Handoyo et al's study found fever in 46 people (85.18%), the headache was found in 37 people (68.51%), seizures were found in 15 people (27.78%), vomiting was found in 20 people (37.03%). In this study also obtained a level of consciousness (GCS) 15 in 13 people (24.07%), and the rest had decreased levels of consciousness with GCS 12-14 by 10 people (18.51%), GCS 8-11 as many as 10 people (18.51%), and GCS <8 as many as 4 people (7.4%). Neck stiffness was found in 49 patients (90.75%), cranial N paresis was found in 12 patients (22.22%), and hemiparesis in 17 people (31.48%).[3] Fever, neck stiffness, decreased consciousness, headache, and hemiparesis are found in almost all meningitis patients. This was also found in the previous study conducted by Jannis and Hendrik at Dr. Cipto Mangunkusumo Hospital. According to Jannis, meningitis classic triad, namely headache, fever, and neck stiffness were found in 271 patients (99.3%). Only 2 patients were without the classic triad of meningitis.8 According to Van de Beek's study, 51% of acute meningitis patients presented with the classic triad.

In this study, the most clinical outcomes after treatment were 7 cases (53%) died, 5 cases (39%) lived with sequelae and 1 case (8%) lived without sequelae. The results of this study are following Handojo et al's research, it was found that the proportion of meningitis patients who died was 57.4% and the proportion of meningitis patients who lived was only 42.6% .27 Similar results were also reported by Wall, et al, who got 715 cases of adult bacterial meningitis, the mortality rate was 45% on the 10th day and 54% on the 40th day. The differences with some of these studies may be due to differences in the characteristics of the subject, the length of the study, the number of samples taken, and differences in the causative bacteria between the previous study and this study.

Several scientific publications attempt to explain the factors that influence the clinical outcome of meningitis patients. Based on the results of the univariate analysis of Bodin et al's study, several factors that are thought to increase the risk of death include age> 60 years, decreased consciousness, seizures, shock, papilledema, HIV infection, bacteremia, and Staphylococcus aureus. However,

after a logistic regression test was carried out, only age ≥ 60 years, HIV infection, decreased awareness and shock occurred.[13] According to other sources, it was stated that the most common causes of death were age> 60 years, awareness of admission, and seizures within the first 24 hours.[10] In Indonesia, this has been studied before. From the results of the study at Cipto Mangunkusumo Hospital, Jakarta, there was a decrease in consciousness, hemiparesis had a significant correlation with death.[8] While study at Sanglah General Hospital stated that decreased consciousness, hemiparesis, low sodium levels, cerebral edema, and HIV positive were found mostly in meningitis patients who died. [3]

During the observation period, 44 patients were diagnosed with bacterial meningitis and bacterial meningoencephalitis. However, of the 44 patients, 9 of them died before a lumbar puncture was performed and 4 patients refused to do a lumbar puncture, so only 31 patients had a lumbar puncture performed, and CSF culture was performed. Of the 31 patients who were treated with lumbar puncture and CSF culture, 13 patients obtained sterile CSF culture results so that only 18 patients were obtained from pathogen culture and antibiotic resistance.

The high rate of sterile CSF cultures is a common obstacle. According to Mood et al's study on 47 acute meningitis patients, 46 patients with CSF culture were negative, only 1 patient had CSF positive for meningococcus.14 While the results of Karou et al's study in meningitis endemic areas in South Africa, 279 of 533 samples (52%) CSF were tested negative/sterile. 4 This is due to limited laboratory tests and certain culture media. Other causes may be due to partially treated as a result of antibiotic administration at or before the time of specimen collection. Also, the Department of Microbiology, which is the only unit serving our clinical center, is not open 24 hours. The pathogens that cause meningitis are pathogen-prone and require an immediate process to optimize recovery and identification.[14] Technical challenges, as well as the wide availability of antibiotics (obtained 'without a prescription' or by prescription), have been identified by studies as obstacles to efforts to describe the meningococcal disease in the world primarily in Asia. Economic constraints, lack of laboratory facilities after working hours, lack of laboratory expertise in detecting pathogens, and lack of available techniques apart from Gram stain and culture. The use of polymerase chain reaction (PCR) detection techniques increases the detection sensitivity of N. meningitides, especially in patients who have received antibiotics, but unfortunately, this technique is not routinely available in most of Asia. The percentage of CSF or blood samples in which no bacteria could be identified was generally high in all previously reviewed studies in Asia and is likely to increase over time as access to antibiotics increases.[15]

The negative CSF culture in most cases of meningitis is caused by previous use of antibiotics, delayed lumbar puncture treatment in patients receiving antibiotics, and incompatibility of the pathogen-growing media. A negative CSF culture does not mean there is no pathogen growth. Further examination with polymerase chain reaction (PCR) showed the detection of pathogens such as Haemophilus influenza type b (Hib) and Streptococcus pneumoniae in negative CSF cultures. A negative CSF culture can also indicate that the cause of meningitis is a virus. Based on this, it is recommended to use the BACTEC automatic culture system and specific tests for viruses.

Based on the results of culture carried out at the Clinical Microbiology Laboratory, it was found that the bacteria that caused meningoencephalitis were

Staphylococcus sp. 9 cases (69%), followed by Klebsiella pneumonia in 2 cases (15%), 1 case of Acinetobacter baumannii (5.3%), 1 case of Shigella sonnei (5.3%), and 1 case of Escherichia coli (5.3%). Based on the results of several studies published in the third congress of the European Academy of Neurology, it was found that 53% of the most common causes of meningitis were Streptococcus sp.[9] Similarly, Bodin et al's study also found Staphylococcus sp. was the largest cause of community meningitis as much as 20.3% followed by Klebsiella pneumonia (11.2%)

Staphylococcus Sp. is the most pathogens found in this study. Bacteria in the form of coccids, Gram-positive, alpha-hemolytic (in aerobic conditions) or beta-hemolytic (in anaerobic conditions), and facultative and encapsulated anaerobes have a characteristic morphology on Gram stain, diplococci are lanceolate. They have a polysaccharide capsule which acts as a virulence factor for these organisms; more than 90 different serotypes are known, and these differ in virulence, prevalence, and rates of drug resistance.

Apart from Staphylococcus, Klebsiella pneumonia is the second most common pathogen found in this study. Klebsiella is the most common bacterial pathogen that causes nosocomial infections due to various virulence factors and resistance to many antibiotics.[17] Meanwhile, according to Jawetz et al, E. coli and streptococci are the main causes of meningitis, especially in infants. E. coli is the cause of about 40% of cases of neonatal meningitis.

The empirical antibiotic therapy used in the inpatient installation of the Department of Neurology, Dr. Moh Hoesin Hospital, Palembang when collecting specimens was ceftriaxone (100%). This cephalosporin class of antibiotics is widely used for bacterial meningitis due to Staphylococcus, Streptococcus, and E. coli. According to the International Society of Neurosurgery in 2016, Cefotaxime and Ceftriaxone are the antibiotics of choice for bacterial meningitis, especially those caused by E. coli. E. coli bacteria are the most common Gram-negative bacteria to cause bacterial meningitis in the United States. This class of antibiotics has a broad spectrum and has a good penetrating activity to penetrate the BBB even in an inflammatory state. Cephalosporin is also an antibiotic recommended for bacterial meningitis caused by both Gram-positive and Gram-negative bacteria. A review conducted by WHO in 2008 stated that the study conducted by Martin et al., And Singi et al., Regarding the administration of ceftriaxone in patients with bacterial meningitis, improved clinical complaints of bacterial meningitis patients seen after 7-10 days of ceftriaxone.

The results of a study conducted in Egypt showed antibiotics of the Meropenem, levofloxacin, ampicillin/ sulbactam, and Piperacillin/tazobactam class had a fairly good sensitivity pattern for Gram-positive and Gram-negative pathogens; thus they are recommended for the treatment of bacterial meningitis. The MIC (minimal inhibitory concentration) results showed that the lowest resistance for MDR (multi-drug resistant) gram-negative isolates was against imipenem, however epileptogenic side effects limit their use in meningitis. It was found that the value of FIC (Fractional Inhibitory Concentration) combination of ampicillin/sulbactam plus Cefepime gave a synergistic or additive effect on Gram-negative MDR isolates, so it is recommended to be used as a treatment option. Meanwhile, Gram-positive MDR shows synergism with the combination of doxycycline plus levofloxacin. Genotype analysis detected that the bacterial antibiotic resistance causing bacterial meningitis was mainly chromosomal, several resistant genes were detected including ESBL/ extended-spectrum beta-lactamases (tem,

ctx-m, shv) which are responsible for resistance to l-lactam antibiotics, and also the resistance Ib gene accounting for resistance to aminoglycosides (amikacin). It is advisable to monitor drug-resistant isolates and to consider the rational use of antimicrobial agents to limit the spread and prevalence of the underlying resistance mechanisms.[18]

Staphylococcus sp. Resistance rate. against antibiotics in this study is quite high. Previous studies by Jiang et al showed that Staphylococcus epidermidis was resistant to antibiotics of the erythromycin class by 5.6%, chloramphenicol by 83.3%, tetracyclines by 33.3%, and rifampicin by 88.9%. Meanwhile, resistance to Vancomycin and linezolid was 100% .[19] Meanwhile, based on the study results of Abdelkader et al, Staphylococcus epidermidis was 100% resistant to the antibiotics Penicillin G, Ampicillin and Levofloxacin, and the remaining 60% were resistant to Ceftriaxone, Cefotaxime, Cipro fl oxacin, Gentamicin, Amoxicillin/clavulanate. Meropenem.[18] Staphylococcus is a form of coccoid, Gram-positive, alpha-hemolytic (in aerobic conditions), or beta-hemolytic (in anaerobic conditions), and this facultative and encapsulated anaerobe has a characteristic morphology on Gram stain, diplococci are lanceolate. They have a polysaccharide capsule which acts as a virulence factor for these organisms; more than 90 different serotypes are known, and these differ in virulence, prevalence, and degree of drug resistance. Also, it is suspected that various substances, both enzymes, and toxins, affect the virulence factors of Staphylococcus.[16, 20]

This study found that the bacteria Acinetobacter sp. resistant to 8 antibiotics namely Ciprofloxacin, Ceftriaxone, Ceftazidime, Cefazolin, Cefepime, Gentamicin, Meropenem, and Trimethoprim/Sulfamethoxazole. Based on Jiang et al's study, Acinetobacter sp was 100% resistant to Piperacillin/ Tazobactam, Imipenem, Meropenem, and 50% to Gentamicin, Piperacillin, Amikacin, Ciprofloxacin, Levo floxacin, Chloramphenicol.[19] Meanwhile, based on the study results of Abdelkader et al. Penicillin, Ampicillin, Chloramphenicol, and 85.7% against the antibiotics Ceftriaxone, Ciprofloxacin, Meropenem. [18]

Acinetobacter baumannii, non-motile, non-fermentative glucose, oxidase negative, gram-negative coccobacillus bacterium, has recently become important due to increased resistance to many of the available antibiotics. The three main mechanisms of resistance in A. baumannii: enzymes that deactivate antibiotics, reduce the entry of bacteria into the target, and change in target or cellular function due to mutations. The mechanism thought to play a major role in antibiotic resistance is the inactivation of the enzyme due to the production of beta-lactamase, which hydrolyzes carbapenem. These hydrolyzing enzymes include metallo-β-lactamases (which have been reported sporadically in some sections) and class D β-lactamases (widely distributed). The main gene clusters responsible for this resistance are blaOXA-23-, blaOXA-24 / 40-, and gene clusters such as blaOXA-58. Multi-drug resistance, A. Baumannii, poses a potential threat to mankind by causing deadly infections, particularly in ICU settings and in patients on ventilators. Multi-drug resistance A. Baumannii was found in 5 antibiotic groups, namely cephalosporin, carbapenem, ampicillin, fluoroquinolone, an aminoglycoside.

Meanwhile, the pattern of antibiotic resistance in CSF patients with meningoencephalitis against Klebsiella pneumonia bacteria is Nitrofurantoin, Gentamicin, Trimethoprim/ Sulfamethoxazole, and Aztreonam by 100% and Meropenem 50%. Based on the results of the study by Jiang et al, Klebsiella pneumonia is 100% resistant

to Ampicillin/sulbactam, Piperacillin/ Tazobactam, Imipenem, Meropenem, Chloramphenicol. 66.6% resistance to Cefepime, Levofloxacin, Ciprofloxacin, and 33.3% resistance to Cefoperazon, Ceftazidime, Ceftriaxone, Amikacin, Gentamicin, Co-trimoxazole.[19]

The emergence of multidrug-resistant (MDR) K. pneumoniae is an important public health challenge worldwide. The overuse and misuse of antibiotics have led to the rapid evolution of antibiotic-resistant bacteria and antibiotic resistance genes. Klebsiella pneumoniae has become the most common bacterial pathogen responsible for nosocomial infections due to its high virulence factor and general resistance to most antibiotics. In several studies mentioned the molecular mechanism of antibiotic resistance of Klebsiella pneumoniae was investigated and the results indicated the involvement of the β-lactamase signaling pathway induced by β-lactamase recruitment. The antimicrobial susceptibility of Klebsiella pneumoniae was assessed using an automated system and extended-spectrum β-lactamase (ESBL) and β-arrestin expression levels in Klebsiella pneumoniae were analyzed by quantitative reverse transcription PCR. The results show that β-arrestin recruitment is increased in Klebsiella pneumoniae with antibiotic resistance. Of note, inhibition of β-arrestin recruitment significantly suppresses ESBL expression and besides, genes encoding β-arrestin and ESBL are upregulated in Klebsiella pneumoniae. Restoration of endogenous β-arrestin markedly increases the antibiotic resistance of Klebsiella pneumoniae to β-lactam. The resistance mechanism is mediated by the loss of porin in the cytomembranes, production of ESBL, carbapenemases and even metallo-β-lactamases to increase antibiotic resistance.[17,25]

5. Conclusion

Bacterial meningitis cases are dominated by the adult age group, with the most manifestations in the form of neck stiffness, fever, and decreased consciousness. The mortality and disability rates of bacterial meningitis patients who experience antibiotic resistance in this study are quite high, but this study cannot conclude whether there is a relationship between mortality and patient morbidity with antibiotic resistance that occurs.

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