Post-Traumatic Bacterial Meningitis in Head Injury Patients and Detection of Antibiotic Resistance Patterns

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ABSTRACT

Post-traumatic meningitis classified as one of the serious complications that requires urgent treatment. However, emergence of antibiotic resistance and the difficulty of choosing the appropriate treatment directly and seriously affected the lives of infected patients. This study aimed to identify the bacterial species associated with post-traumatic meningitis among traumatic head injury patients and detect their antibiotics resistance. Clinical samples of cerebral spinal fluid collected from patients suffering of head accidents. These specimens were cultured on MacConkey agar and blood agar. Bacteria diagnosed according to traditional methods and biochemical tests to examine cerebral spinal fluid samples. In addition, the VITECK-2 system used to confirm the diagnosis and susceptibility test. Results showed that 71 patients (57.7%) diagnosed with post-traumatic meningitis out of 123 patients. Most cases of meningitis were emergence within 1-2 days after trauma. Gram-positive bacteria are more common than gram-negative ones. The results of the study showed the presence of multidrug resistant bacterial strains. Staphylococcus aureus was the most common cause of post-traumatic meningitis. Vancomycin and levofloxacin gave excellent results in eliminating gram-positive bacteria, Meropenem and levofloxacin are appropriate to kill gram-negative.

Keywords: Bacterial meningitis, Post-traumatic meningitis, Cerebrospinal fluid inflammation, Multidrug resistant bacterial.

INTRODUCTION

Meningitis known as an acute or chronic infection that occurs in the protective membranes that cover the brain and spinal cord called the meninges[1]. An inflammation classified as a life-threatening infection due to its proximity to the brain and spinal cord[2]. Head injury accidents are cause bacteria in the nasal cavity to enter the meningeal space, causing post-traumatic meningitis. A serious complication is likely to lead to a high death rate or stay in the hospital for a long time[3]. Post-traumatic meningitis is associated with several factors, such as cerebrospinal fluid (CSF) fistula and basilar skull fracture, but there are other factors whose role is still unclear, such as pinhole surgical procedures performed in the emergency department and hypotensive craniotomy[4,5]. In addition to cerebral shunts or extra ventricular drains, which may increase the risk of post-traumatic meningitis. In these cases, the patient is more susceptible to infection with Staphylococcus, Pseudomonas, etc.[6]. It is worth noting that patients undergoing cochlear implants for ear are also people at risk of infection with meningitis, which may be occur post-surgery[3]. Post-traumatic meningitis classified as one of the serious complications that requires urgent treatment, the emergence of antibiotic resistance and the difficulty of choosing the appropriate treatment directly and seriously affected the lives of infected patients[7]. Antibiotics are natural organic substances have the ability to inhibit the growth of other organisms and produced by microorganisms in certain concentrations[8]. Bacterial antibiotics resistance is a public health problem as the indiscriminate use of antibiotics to treat infections has led to the emergence of strains with multiple resistance to different antibiotics[9]. It has become one of the major problems, especially among hospitalized patients, causing economic loss in healthcare centers because it leads to use larger amounts of treatment and longer time[10]. This resistance occurs for several reasons, including the production of beta-lactamase enzymes and the impermeability of its cell wall, as well as the possibility containing and acquiring resistance genes from other bacterial species through plasmids and elements transferable by bacterial conjugation[11]. The occurrence of genetic mutations in genes that lead to the development of resistance to these antibiotics and causing failure and less of response to treatment[12]. Recently, a high rate of traffic accidents has recorded, especially among motorcycle drivers in Diyala Governorate. However, no previous study has conducted in the governorate to determine the possibility of developing post-traumatic meningitis. This may be due to the difficulty of taking the sample or continue giving antibiotics in order to speed up the patient's recovery. However, many studies have recorded high rates of antibiotic resistance among various types of bacteria, which makes it difficult for health workers to make the right decision in prescribing appropriate treatment. This study aimed to identify bacterial species associated with post-traumatic meningitis among traumatic head injury patients and detect their antibiotics resistance.

MATERIALS AND METHODS

Collection of samples:

During the period from March 2023 to February 2024. The samples collected from patients suffering of head accidents (basal skull fracture and spinal fluid leak) who admitted to the intensive care unit in Baqubah Teaching Hospital in Diyala governorate. These samples cultured on MacConkey agar and blood agar. Bacteria diagnosed according to the morphological and biochemical characteristics. In addition, the VITECK-2 system used.

Phenotypic and microscopic diagnosis of bacterial isolates:

Bacterial colonies characterized by several apparent feature, such as shape, size, color, and odor emitted by the colonies. Through it, a distinction made between different bacterial species as a primary diagnosis of bacteria. After that, microscopic examination of the isolates performed using a gram smear and then examined with an

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optical microscope and using an oil lens to observe their interaction with the dye as well as the shape and arrangement of the cells[13].

Diagnosis by the VITECK-2 system:

Biochemical tests performed for all bacterial isolates to identifying the bacterial species using the diagnostic kit prepared by the VITECK-2 system. Susceptibility testing was also performed with the same device and using the appropriate kit from the manufacturer[14].

Statistical analysis:

Excel 2016 software was used to analysis the data we collected. We expressed the quantitative data by frequencies and percentages.

RESULTS

The results of this study showed that 71 patients (57.7%) diagnosed with post-traumatic meningitis out of 123 patients suffered from head accidents, their ages ranged between (<10 -50) years. as shown in table (1).

Table 1: Distribution of injuries according to age groups

No.	Age	Isolates No.
1	<10	5
2	(11-20)	14
3	(21-30)	20
4	(31-40)	15
5	(41-50)	17
Total		71

Post-traumatic meningeal symptoms occurrence coincided with the patient's failure respond to the prescribed treatment. There was a time interval between head injury and appearance symptoms for mentioned seventy-one cases as shown in the table (2). However, most cases of meningitis diagnosed within 1-2 days after trauma.

Table 2: The relationship between the time and the number of cases

Time	No. of cases
< 24 hour	11
After 24-48 hour	56
1 week	4
Total	71

In this study, most cases of meningitis caused by gram-positive bacteria, as shown in table (3). The incidence rate in *Staphylococcus aureus*, *S. pneumonia* and *S. hemolytica* were (43.6%), (23.9%) and (12.6%), respectively. Bacterial species identified based on the phenotypic characteristics of the isolates in each culture medium used for diagnosis. *Staphylococcus aureus* classified as gram-positive, coagulase-positive, has a high ability to lyse blood, it spherical cells with a diameter of 1mm non-motile, and does not form spores[15]. While the initial diagnosis of *Streptococcus pneumoniae* based on the shape the colony on the plate, it was spherical, alpha-hemolytic, and appeared under the microscope as binary cocci[16]. Colonies of *Staphylococcus hemolyticus* bacteria appeared spherical shapes, white in color, non-motile and non-spore-forming, with a diameter ranging between 0.8-1.3 micrometers[17].

The results of the current study indicate a decrease in the proportion of gram-negative bacteria, as shown in table (3). The percentages of *Haemophilus influenzae*, *Enterobacter spp* were (15.4%) and (4.2%), respectively. Initial results for the diagnosis of *Haemophilus influenzae* indicated that is a gram-negative, non-motile, bacillary, facultatively anaerobic bacterium[18]. While *Enterobacter spp* bacteria appeared under the microscope as rod-shaped, gram-negative bacteria, facultative, anaerobic, and motile[19].

Table 3: Numbers and percentages of bacterial isolates

No.	Bacterial isolates	Isolates	
		No.	%
	S. aureus	31	43.6
	S. pneumonia	17	23.9
	S. hemolytica	9	12.6
	H. influenza	11	15.4
	Enterobacter spp.	3	4.2
Total		71	

Antimicrobial susceptibility tests conducted on 71 different isolates using the special kit prepared for VITECK-2 system, and the results compared according to Clinical & Laboratory standards institute [20]. As shown in table (4), the results showed the presence of multi-drugs resistant bacteria to three or more classes of antimicrobials. The cephalosporin group, especially (Ceftazidime, Cefuroxime, Cefotaxime), the aminoglycosides group, the aminopyrimidine-Sulfamethoxazole group, and fluoroquinolones group especially Ciprofloxacin showed high resistance to all type of bacteria in this study.

DISCUSSION

Head accidents and skull fractures cause to infiltrate bacteria through the blood-brain barrier (BBB) and the nervous system. After Brain and spinal cord injury, there is a primary damage caused by the initial trauma, which settlement neurons cell and instigate a secondary disadvantage cascade, which ultimately leads to more damage during the subsequent period[21]. Antibiotics must give to the patient for treat the damage and avoid complications. But, when the response to treatment fails, the rapid development of the inflammatory response at this stage of infection, combined with damage to the blood-brain barrier allows bacterial entry, resulting in mucosal colonization, invasion and proliferation in the intravascular space, migration above the blood-brain barrier (BBB), and invasion of the meninges and nervous system[3,22]. Which explains increased incidence with post-traumatic meningitis in the first and second day after head accidents. In addition, to possibility of occurrence at all ages. Several studies have indicated that the most common causative gram-positive agents of bacterial meningitis are *Streptococcus pneumoniae*, Group B *Streptococcus*, *Staphylococcus aureus* and *Listeria monocytogenes*[5,8]. The unjustified use of antibiotics, people resorting to self-medication and the lack of laws preventing the dispensing of antibiotics without a prescription have played an effective role in exacerbating the problem of antibiotic resistance around the world, as many of the antibiotics used have become ineffective in treating infections[23]. Which allowed bacteria to survive and reproduce despite the presence of antibiotics, which encourage pharmaceutical companies to fabricate new generations of drugs[24]. However, as the years passed the emergence of resistant bacterial strains has presented a heavy burden and a serious challenge to these medical achievements[9]. Because of inability of several types of drugs to kill or control bacteria, due to the accumulation of a group of genes, each gene encoding resistance to a specific drug[25]. In addition, it caused by elevation of genes encoding multidrug efflux pumps, enzymatic inactivation, and alteration in target structure[26].

In gram-negative bacteria, the most influential mechanism in the emergence of resistance for aminoglycosides is enzymatic inactivation.

Table 4: Resistance percentages in different antimicrobial groups

Antimicrobial groups	Antibiotics	Resistance percentages				
		S. aureus	*S. pneumonia*	*S. hemolytica*	*Enterobacter spp.*	*H. influenzae*
Cephalosporin	Ceftazidime	90.4%	90.4%	90.5%	64.7%	59.9%
	Cefuroxime	81.5%	80.9%	95.5%	61.4 %	62.2%
	Cefotaxime	79.6%	80.8%	98.1%	59.5%	98.2%
	Ceftriaxone	17.2%	**12.3%**	39.8%	68%	51%
Aminoglycosides	Tobramycin	95.8%	88%	98.6%	92.9%	90.1%
	Amikacin	69.6%	83.3%	61.5%	53.7%	62.3%
Carbapenem	Meropenem	23.4%	**4.7%**	18.9%	**5.9%**	**0%**
Fluoroquinolones	Ciprofloxacin	52.8%	45.2%	49.9%	28.9%	39.3%
	Levofloxacin	**13.2%**	**6.1%**	**4%**	**10%**	**9%**
Amino pyrimidine, Sulfamethoxazole	Trimethoprim /Sulfactam	94.4%	100%	84.6%	67.6%	61%
Quinolone	Norofloxacin	21.3%	**5.3%**	31.2%	27.8%	59.9%
Glycopeptide	Vancomycin	**12.8%**	**3%**	**8.5%**	100%	100%

Most often, these enzymes arise from a plasmid or transposon carrying resistance genes[27]. In general, there are many reasons and various mechanisms that explain the emergence of resistance. It may be the result of structural features of the bacteria, such as not having the structure of the target antibiotic, or the antibiotics not reaching their natural target due to their structural characteristics, as in vancomycin, which cannot pass through the outer membrane of gram-negative bacteria, so they are completely resistant[23,28]. As shown in table (4). The spread of antibiotic resistance occurs in different ways. The process of manufacturing and creating new, safe antibiotics requires a long effort and time, in addition to high economic costs. While this problem can be avoided by urging health workers to rational use of antibiotics (right reasons, perfect dose, right method, right time), while taking strict infection control measures in hospitals and the community[29,30,31]. The results indicate the most appropriate antibiotics used to eliminate the *S. aureus* and *S. hemolytica* are (Vancomycin and Levofloxacin). While, several effective drugs can health workers used to eradicate *S. pneumonia* (Vancomycin, Meropenem, Norofloxacin, Levofloxacin and Ceftriaxone). In addition, the most appropriate antibiotics used to eliminate the gram-negative bacteria were (Meropenem and Levofloxacin).

CONCLUSIONS

Meningeal symptoms appeared in recumbent patients in 1-2 days after head injury, despite receiving antibiotics. This is an indication of the ineffectiveness of treatment due to high rates of resistance. *Staphylococcus aureus* was the most common cause of post-traumatic meningitis during the cerebrospinal fluid examination. The antibiotics used in this study showed high resistance in both gram-negative and gram-positive bacteria.

Authorship Contribution: The study designed by Wissam Faleh Hassan, Ph.D. in Neurology and Hanan Raheem Hassooni, Ph.D. in microbiology, edited the final version of the manuscript after reviewed. Ali Shakir Al-Ezee, M.Sc. in microbiology and Enas Ammar Mohammed, M.Sc. in microbiology contributed to carrying out the laboratory work. All authors approved on the final version of the manuscript.

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