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RESEARCH ARTICLE

Hospitalized Adults with Acute Bacterial Meningitis: Etiology and Antimicrobial Susceptibility Profiles

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Abstract

Eeffective management of acute bacterial meningitis depending on the diagnosis of bacteria that cause disease, as well as, identification of the effective antibiotic or antibiotics against most of these causative agents, the objective of this study was to detect the causative agents of acute bacterial meningitis isolated from C.S.F of inpatients adults. Since June 2017 and July 2018; 135 C.S.F. specimens were collected, 53 (39.26 %) were positive for C.S.F culture, and 71 specimens were negative. Of 53 acute meningitis patients, there were 66% male and 34% female, predominant causative agents was *S. pneumoniae* (20.8%), followed by *N. meningitides* (18.9%) and *K. pneumoniae* (15.1%). Antimicrobial susceptibility profiles differ depending on the causative agents, the results shows a high sensitivity to Amikacin, Vancomycin, Gentamicin, and Ciprofloxacin, *S. pneumoniae* were high sensitive to Vancomycin, Gentamicin, Chloramphenicol, as well as, Ciprofloxacin, While *H. influenzae* and *N. meningitides* exhibited considerable susceptibility to Chloramphenicol.

Key words: *Meningitis; C.S.F; Antibiotics.*

Introduction

Meningitis is result of the microbial agent's intrusion in to the brain and spinal cord meninges membranes. Acute bacterial meningitis is a major worldwide lethal health problem, characterized by potentially devastating and the rapid progression of symptoms effects including fever, headache, hypothermia, nausea, vomiting, photophobia, confusion, lethargy, irritability, poor feeding, respiratory distress, diarrhea, bulging fontanelles and seizures [1,2]. The efficiency of meningitis treatment may be limited because of bacterial strains resistant to antibiotics and the widespread use of antibiotics for upper respiratory tract infections, so, rapid identification and suitable therapy very important for avert the complications and reviews of meningitis cases must make periodically determining the antimicrobial susceptibility profile of meningitis causative pathogens is an important part of clinical practices can produce an important data to upgrade therapeutic decisions and instructs prevention strategies. The relative frequencies of meningitis bacterial causative agents of adult are varying during various seasons, countries, patient's age, undergoing clinical and/or surgical situations of patients, state of vaccines intake, antibiotics usage in the community, and the way the pathogens are acquired [3, 6]. However; *S. pneumoniae*, *N. meningitidis*, *H. influenzae* type b and *K. pneumonia* reported as the major common pathogens that cause meningitis [7, 9], other important reasons are the increasing of multi-antibiotic resistant isolates like methicillin resistant *Staphylococcus aureus*, and recently rising of ß-lactamases producer isolates [10], possible main reason could be due to neo-generation of Vancomycin and anti-pseudomonal ß-lactam antibiotics wide usage [11], for this, antimicrobial susceptibility profile for meningitis pathogens is essentially for effective management for meningitis patients in the early crucial hours of treatment. In patients suspected of having acute bacterial

meningitis, the diagnosis needs a high degree of medical suspicion and must obtains the Cerebrospinal Fluid (C.S.F.) via lumbar puncture for culturing, and antimicrobial therapy started without late. Treatment of Acute bacterial meningitis accumulates by two parts, first confirming the infection by C.S.F. culturing "gold way" and second, obtains the antimicrobial susceptibility profile for bacteria. [12, 13].For all above, our study was aims at investigating the frequency of bacterial organisms isolated from C.S.F., as well as their antimicrobial susceptibility profiles.

Patients and Methods

Since June 2017 and July 2018; 135 C.S.F. specimens were collected by lumbar puncture as a first step of ordinary medical dealing with suspected acute meningitis cases, who entering to Al-Ramadi Teaching Hospital. All specimens were collected in sterilized disposable test tubes by specialist doctor and transmitted to bacteriology laboratory within 30 minutes. The specimens were dealt according to typical methods of medical bacteriology, by centrifugation at 5000 rpm for 7 minutes; and the precipitates were analyzed by Gram's stain and inoculated on blood agar, chocolate agar, and MacConkey's agar plates, and incubated at 35-37 Celsius aerobically: While chocolate agar plates incubated within anaerobic jar with CO_2 gas pack systems, to generate micro-areophilic atmosphere (5 - 10% CO_2 conc.) for fastidious bacteria. After 18 - 24 hrs .Of incubation, checked the existence of bacterial growth on the plates, plates which did not contain any growth, were incubated for further 24 hrs. Isolates were characterized by microbiological procedures, included colonies characteristics, Gram's stain, bio-chemical, serological tests and using the Vitek-32 system (BioMerieux). Antibiotic-sensitivity test was performed for pure isolates using the Kirby Bauer disc diffusion technique on Mueller Hinton agar medium, results were compared with Clinical and Laboratory Standards Institute (CLSI) instructions. [14] Isolates that developing intermediate inhibition zones were counted as non-susceptible. Statistical analysis was done by SPSS system, version 22.

Results

Of 135 C.S.F specimens, 11 isolates were excluded due to contamination, while 53 (39.26 %) were positive for C.S.F culture, and 71 specimens were negative for C.S.F culture. The predominant isolate was *Streptococcus pneumoniae* (20.8%), followed by *Neisseria meningitides* (18.9%) and *Klebsiella pneumoniae* (15.1%), followed by *Pseudomonas aeruginosa* and *E. coli* (13.2%) for each and *Himophilus infleunzae* (11.3%) finally *Staphylococcus aureus* (7.5%). 53 acute meningitis patients, there were 35 male and 18 female; table 1 show in general that the male group was more susceptible to acute meningitis bacterial pathogens than the female group with exception of *Pseudomonas aeruginosa* which caused 57.1 % infections in female group and the infections with *Himophilus infleunzae* were divided equally between the two groups. In general, male patients were more susceptible to acute bacterial meningitis pathogens (Fig. 1).The results of susceptibility of bacterial isolates to tested antibiotics showed that; *Streptococcus pneumoniae* were 100% (11 isolates) sensitive to Vancomycin, 10 isolates (90.9%) sensitive for Gentamicin and Chloramphenicol, 9 isolates (81.80%) were sensitive for Ciprofloxacin, 8 isolates (72.7%) were sensitive to Tetracycline and Clindamycin, while 9 isolates (81.8%) were resistant to Cefepime and Penicillin. 4 isolates (100%) of *Staphylococcus aureus* were resistant to Ciprofloxacin, while 3 isolates (75%) were sensitive to Gentamicin and Ceftriaxone.

Table 1: The Characteristics of 53 Patients with Positive C.S.F Cultures

Name of isolate	Female		Male		P value	Total
	N	%	N	%		
Streptococcus pneumoniae	3	27.3	8	72.7	0.000**	11
Neisseria meningitidis	3	30.0	7	70.0	0.000**	10
Klebsiella pneumoniae	2	25.0	6	75.0	0.000**	8
Pseudomonas aeruginosa	4	57.1	3	42.9	0.193	7
E. coli	2	28.6	5	71.4	0.000**	7
Himophilus infleunzae	3	50.0	3	50.0	0.000**	6
Staphylococcus aureus	1	25.0	3	75.0	0.000**	4
Total	18	34.0	35	66.0	0.002**	53

The analysis with Binomial Test for proportions, ** the difference are significant at the 0.01 level

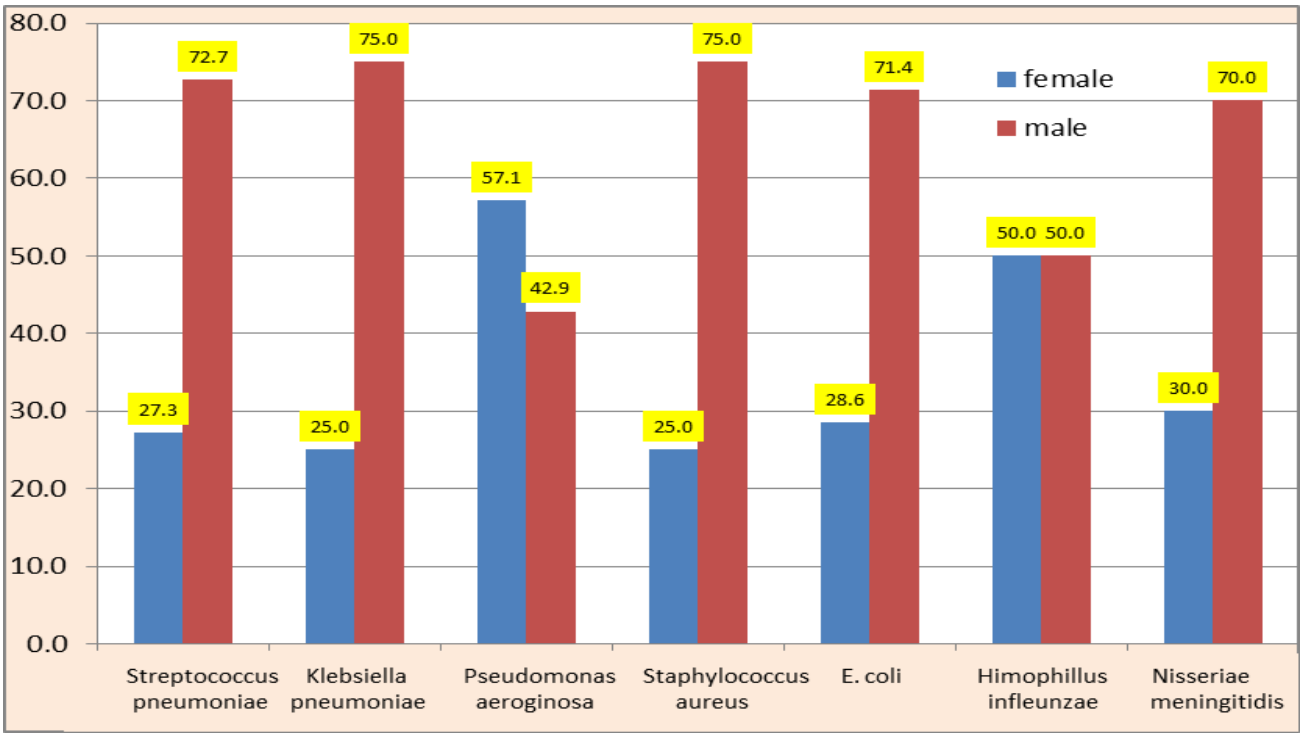

Fig. 1: Distribution of Acute Meningitis Pathogens According to the Patients Gender

90% *Neisseria meningitidis* isolates were sensitive to Penicillin and Chloramphenicol, 6 isolates (100%) of *Himophilus infleunzae* were sensitive to Chloramphenicol, 5 isolates (83.3%) were sensitive to Tetracycline, while (50%) were resistant to Ceftriaxone. 8 isolates (100%) of *Klebsiella pneumoniae* were sensitive to Colistin, 7 isolates (87.5%) were sensitive to Meropenem and Ciprofloxacin, 6 isolates (75%) were sensitive to Amikacin, while 8 isolates (100%) were resistant to Aztreonam, Gentamicin and Ceftazidime, and 6 isolates (75%) were resistant to Cefepime.6 isolates (85.7%) of *Pseudomonas aeruginosa* were sensitive to Cefepime and Ciprofloxacin, 5 isolates (71.4%) were sensitive to Amikacin, while 100% were resistant to Imipenem, Ceftazidime, and Meropenem. 6 isolates (85.7%) of *E. coli* were sensitive to Amikacin, 5 isolates (71.4%) were sensitive to Ciprofloxacin, and 4 isolates (57.1%) were sensitive to Gentamicin.

Table 2: Antibiotics Susceptibility Profile of Bacterial Isolates

Pathogens / Antibiotics		*Strep. pneumoniae*		*K. pneumoniae*		*N. meningitidis*		*P. aeruginosa*		*Staph. aureus*		*H. infleunzae*		*E. coli*	
		N	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
Amikacin	S		0.0	6	75		0.0	5	71.4		0.0		0.0	6	85.7
	R		0.0	2	25		0.0	2	28.6		0.0		0.0	1	14.3
Gentamicin	S	10	90.9	0	0.0		0.0		0.0	3	75		0.0	4	57.1
	R	1	9.1	8	100		0.0		0.0	1	25		0.0	3	42.9
Ciprofloxacin	S	9	81.8	7	87.5		0.0	6	85.7	0	0.0		0.0	5	71.4
	R	2	18.2	1	12.5		0.0	1	14.3	4	100		0.0	2	28.6
Imipenem	S							0							
	R		0.0		0.0		0.0	7	100.0		0.0		0.0		0.0
Ceftriaxone	S	6	54.5		0.0	5	50		0.0	3	75	3	50		0.0
	R	5	45.5		0.0	5	50		0.0	1	25	3	50		0.0
Ceftazidime	S			0				0							
	R		0.0	8	100		0.0	7	100		0.0		0.0		0.0
Tetracycline	S	8	72.7		0.0		0.0		0.0		0.0	5	83.3		0.0
	R	3	27.3		0.0		0.0		0.0		0.0	1	16.7		0.0
Meropenem	S		0.0	7	87.5		0.0	0	0.0		0.0		0.0		0.0

	R		0.0	1	12.5		0.0	7	100		0.0		0.0		0.0
Cefepime	S	2	18.2	2	25		0.0	6	85.7		0.0		0.0		0.0
	R	9	81.8	6	75		0.0	1	14.3		0.0		0.0		0.0
Aztreonam	S			0											
	R		0.0	8	100.0		0.0		0.0		0.0		0.0		0.0
Colistin	S		0.0	8	100.0		0.0		0.0		0.0		0.0		0.0
	R			0											
Penicillin	S	2	18.2		0.0	9	90		0.0		0.0		0.0		0.0
	R	9	81.8		0.0	1	10		0.0		0.0		0.0		0.0
Chloramphenicol	S	10	90.9		0.0	9	90		0.0		0.0	6	100		0.0
	R	1	90.1		0.0	1	10		0.0		0.0	0	0.0		0.0
Vancomycin	S	11	100		0.0		0.0		0.0		0.0		0.0		0.0
	R	0													
Clindamycin	S	8	72.7		0.0		0.0		0.0		0.0		0.0		0.0
	R	3	27.3		0.0		0.0		0.0		0.0		0.0		0.0

Discussion

The study estimated the bacterial organisms causing acute meningitis, its antibiotics susceptibility and the relationship between the gender and acute meningitis infections in order to provide data for bacterial causative agents, monitoring antibiotics susceptibility profile for inpatients adults. *Streptococcus pneumoniae* and *Neisseria meningitides* were the predominant causative agents followed by *Klebsiella pneumoniae*, *Pseudomonas aeruginosa, E. coli, Himophilus infleunzae*, and *Staphylococcus aureus.*

Many studies on acute bacterial meningitis have often shown a predominance of *S. pneumoniae* (3), a second study conducted in 2013 at the national level has confirmed the predominance of *S. pneumoniae* (60 %), followed by *N. meningitidis* (11%) and *H. infleunzae* (9.5 %) (2), while the inconsistency by some studies [4, 5] with our results could be explained by the fact of the differences in weather conditions and geographical locations, the way the bacteria are acquired and many other reasons [3, 6].

Depending on the data obtained from the current study, the number of adult males with acute bacterial meningitis varies significantly from female patients (Fig. 1). A recent retrospectively studies also recorded that the acute bacterial meningitis were more common in male patients [16, 17], reasons for an greater occurrence in men could conceivably be rely on contrast in nutrition manners for men and women [18], with men, probability of risk foods consuming is higher [19], While we think that the main reason for this, is to increase the number of males in society compared to females.

Antibiotics susceptibility testing is important for monitoring susceptibility profile in circulating strains of acute meningitis causing bacteria and it's a part of monitoring the emergence and spread of strains with reduced susceptibility to antibiotics.[15]. In this study *Streptococcus pneumoniae* 11, *Neisseria meningitides* 10, *Klebsiella pneumoniae* 8, *Pseudomonas aeruginosa* and *E. coli* 7 isolates for each, *Himophilus infleunzae* 6, and *Staphylococcus aureus* 4 isolates were obtained and tested for antibiotics susceptibility.

Recording the antibiotics susceptibility profile for bacteria causing acute meningitis is important since the use of antibiotics in therapy and it's an important point to consider since the initial antimicrobial treatment detection is depending on bacteria frequently causing the infection and also depending on patient age, medical preparation and profile of antibiotics susceptibility. Combination antibiotics is recommended to treat acute meningitis [20].

In this study antibiotics susceptibility was implemented via Kirby-Bauer method, the data shows a high sensitivity to antibiotics like Vancomycin, Gentamicin, Ciprofloxacin except for routinely used antibiotics like Ceftriaxone Ceftazidime and Tetracycline (table 2), which were also recorded as resistant in a previous study [21], this could be attributed by the use of these antibiotics routinely and also its common use in local clinics. *Streptococcus pneumoniae* isolates

were high sensitive to Vancomycin, Gentamicin, Chloramphenicol, as well as, Ciprofloxacin and show high resistant to Cefepime and Penicillin, precedent studies have, however, recorded Penicillin resistance percentage for *S. pneumoniae* about 68.8% and Chloramphenicol resistance percentage of 78.5% [22].Therefore, Ciprofloxacin regarding as one of initial choice antibiotic for *S. pneumoniae* meningitis.

Depending on the data obtained from the current study, *Haemophilus influenzae* and *Neisseria meningitidis* showing high susceptibility to Chloramphenicol. *Klebsiella pneumoniae* isolates show high sensitivity to Ciprofloxacin, these antibiotics can still be very effectively used against acute meningitis in adults. In addition, *E. coli* isolates exhibited intermediate sensitivity to Gentamicin and they were sensitive to Amikacin and Ciprofloxacin (table 2), while 100% of *S. aureus* were resistant to Ciprofloxacin, *Himophilus infleunzae* isolates were resistant to Ceftriaxone may due to beta lactamase producing, *Klebsiella pneumoniae* isolates show high resistant to Aztreonam, Gentamicin and Ceftazidime, and 100% of *Pseudomonas aeruginosa* were resistant to Imipenem, Ceftazidime, and Meropenem. *Pseudomonas aeruginosa* developing resistant to several groups of antibiotics is well known, and several molecular mechanisms for its self and acquired resistance have been recorded.

Conclusion

Percentage of adult male patients differs significantly comparing to female patients, and *S. pneumoniae* and *N. meningitides* were the predominant causative agents of acute meningitis followed by *K. pneumoniae*, *P. aeruginosa, E. coli, H. infleunzae*, and *S. aureus*. According to Antibiotics susceptibility profiles, the data shows a high sensitivity to antibiotics like Vancomycin, Gentamicin, and Ciprofloxacin except for routinely used antibiotics like Ceftriaxone Ceftazidime and Tetracycline.

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