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Original Research Paper

Antimicrobial Stewardship in Bacterial Meningitis: A Case-Control Study

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ABSTRACT:

Background: Inappropriate use of antimicrobials leading to the exponential increase in antimicrobial resistance has been a matter of global concern for the last several years. The antimicrobial stewardship program (ASP) aims to optimize the antimicrobial prescribing via multidisciplinary institutional approach to improve patient's prognosis, reduce the chances of antimicrobial resistance, and reduce hospital's financial burden. **Objective:** The aim of this study is to apply the principles of antimicrobial stewardship and then analyze the response of two groups of meningitic patients to the empirical treatment and CSF culture & sensitivity specific treatment, respectively. **Study Design:** This case control study is based on 100 confirmed cases of bacterial meningitis of pediatric age group with over the period of one year at General medicine ward, Children Hospital & Institute of Child Health, Faisalabad. **Results:** There was male predominance with M:F ratio of 1.4:1. Most of the patients (n=55) were ≤ 1 year of age. The main causative agents were S. pneumoniae, S. aureus, and S. epidermidis. A considerable number of patients were resistant to 3rd generation antibiotics including ceftriaxone R=77% (G+) R=41% (G-) and ceftazidime R=59% (G+), R=26% (G-). In terms of duration of hospital and ICU stay and condition at the time of discharge, case group (n=50) showed better prognosis. **Conclusion:** Early (<24hrs) administration of appropriate antibiotic in adequate dose for optimal duration is essential in quality management of pediatric bacterial meningitis with limited morbidity and complications.

Keywords: Antimicrobial stewardship program (ASP), bacterial meningitis, pediatric neurology, cerebrospinal fluid, drug resistance

INTRODUCTION:

Bacterial meningitis is a life-threatening global health challenge having significant mortality rate in children. [1] The incidence of meningitis varies greatly across the geographical regions however, it is estimated to be 20 cases per 100,000 people, which rounds up to 1.2 million patients worldwide. [2] Risk of bacterial meningitis decreases with age, peaking postnatally during neonatal period (age<30 days) with 0.25-1 case per 1000 live births or 25-100 cases per 100, 000 live births (95%

confidence interval (CI) = 0.80-1.60). [3, 4] Despite of improved availability of vaccination, the incidence of meningitis is persistently increasing with estimated 34% more deaths due to meningitis in 2017 as compared to WHO survey-2015. [5] Bacterial meningitis is the inflammation of meningeal layers which completely cover the brain parenchyma and spinal cord. If left unmanaged, it can disrupt the blood brain barrier, penetrating into CNS causing brain abscess, septicemia, and septic shock. [6, 7] Classical signs and symptoms of meningeal irritation or meningitis are fever, vomiting, headache, and neck stiffness. Additional symptoms can be fits, dizziness, or even loss of consciousness. For a long period, ampicillin, fluoroquinolones, cephalosporins, and aminoglycosides were included in the empirical treatment for meningitis. Nevertheless, these antibiotics will be ineffective against the resistant strains. About 50% of the antibiotics prescribed in a hospital setting are considered unnecessary. The unjustified prescription of antimicrobials contributes significantly to the development of drug resistance. [8, 9] The commonly known causative agents for bacterial meningitis in children are Streptococcus pneumoniae, Staphylococcus aureus, Staphylococcus epidermidis, Enterococcus species, Hemophilus influenza, Neisseria meningitis, Escherichia coli, and Klebsiella pneumoniae. [10] To identify the pathogen, CSF analysis is a gold standard investigation. Antibiotic treatment prior to CSF analysis can significantly alter the results. WBC and neutrophil count would be remarkably low after intravenous antibiotics but still the values will be higher than the normal range. [11, 12] However, it is preferred to prescribe medicine within the first 24 hours of infection without compromising on the drug specificity. [13] The emergence of multidrug resistant strains is the biggest threat to the global healthcare system. To spread awareness regarding the judicious use of antibiotics in appropriately calculated doses, the concept of antibiotic stewardship was introduced. This narrative has become popular and widely accepted lately. This article is about implementing this idea and observing the change in outcome by comparing case and control groups.

Inclusion criteria:

- Patients of pediatric age group (up to the age of 14 years) with suspected meningitis
- Patients with no history of infection/sepsis, otherwise healthy children
- Patients with CSF samples positive for causative microorganisms
- Cases with bacterial meningitis confirmed on LP are included in this study.

Exclusion criteria

- Children with premature birth, low birth weight, immunocompromised state, diagnosed chronic pathology, or those who were intellectually compromised.
- Cases in which attendants who did not give consent for lumbar puncture were not included in this study.

MATERIAL AND METHODS:

A total of 100 patients of bacterial meningitis were enrolled in this study from 1st Jan 2022 to 1st Jan 2023. The patients were received in medical emergency and were admitted in neonatology/general pediatric medicine ward at The Children's Hospital and Institute of Child Health, Faisalabad. It is a government hospital, a tertiary healthcare facility located in Faisalabad, Punjab, Pakistan. Oral and written consent was taken from the guardians/parents of the children, separately for intravenous treatment, lumbar puncture, and mechanical ventilatory support (if and when indicated). One CSF sample of 1-3ml was aseptically collected from each patient in a sterile test tube for culture and sensitivity. The collected samples were immediately sent for analysis and reporting in the local hospital laboratory. To collect the demographic information of the patients, a pre-structured questionnaire was used. The collected data included patient's gender, residency, literacy rate of attendants, medical history since birth, prenatal, perinatal, or postnatal complications, and treatment history for the current episode of meningitis. It also included the signs and symptoms at the onset of infection and time taken from the onset of the symptoms and presentation to the hospital. A detailed neurological examination was done by medical specialists and neurologists to confirm the diagnosis of meningitis. Elaborative CSF analysis included CSF pH, appearance, WBC count, glucose, protein level, neutrophil count, nature of organism, and its gram staining. The CSF samples were inoculated on blood and chocolate agar to identify the organisms. The inoculated plates were incubated for 48 hours at 37˚C with 5% CO_2. After the colonization of the organisms, the isolates were identified by using gram staining and standard PCR method. The antibiotic susceptibility test was performed according to the standardized CLSI method. We used 13 commonly used antibiotics; Vancomycin (30), Tazobactam-piperacillin (30), Oxytetracycline (30), Meropenem (10), Ceftriaxone (30), Erythromycin (15), Levofloxacin (05), Rifampicin (05), Salbactam-cefoperazone (30), Amoxicillin (25), Amikacin (10), Ceftazidime (30), and Ciprofloxacin (05). The doses of antibiotics were in micrograms and the results of antibiotic sensitivity were recorded in millimeters.

Data Analysis:

The results were tabulated, and the statistical Analysis was performed using Statistical Package for Social Sciences Version 25 (SPSS v25). The Quantitative data analysis e.g., Age, gender, demographic features etc., of the patients was done by means and standard deviations. The Qualitative data analysis has variable outcomes e.g., components of clinical history, physical examination, CSF characteristics etc. which were calculated by percentages and frequencies. The level of significance was determined at $P < 0.05$ and two-tailed level at 95% Confidence interval.

RESULTS:

Out of 100 BM positive patients selected for this study (considering the inclusion and exclusion criteria), 59% were male and 41% were female with Mean±SD of 11.8±0.02 and 8.2±0.5. There was a significant male predominance with male to female ratio of 1.4:1 with *P*-value < 0.001. The patients are subdivided into 5 groups depending on their age. The number of male and female patients in respective groups were described as follows; 1 month-3 month (M=14, F=12), 4 months-1 year (M=17, F=12), 1 year-5 years (M=9, F=10), 5 years-10 years (M=12, F=6), and 10 years-14 years (M=7, F=2). Most of the patients belonged to rural areas (n=71, 71%, Mean±SD 14.2±0.07, *P*-value=0.01), whereas 29 patients were urban residents (29%, Mean±SD 5.8±0.04). Most of the patient's attendants belonged to rural areas, were illiterate and did not have any previous record or could not recall the treatment that the patient had before presentation, accounting for 19 patients with unknown prior treatment Mean±SD 3.8±0.5. Out of total, 42 patients did not take any prior treatment (Mean±SD 8.4±0.6, *P*-value 0.03), and 39 patients were referred from other facilities with ongoing empirical treatment (Mean±SD 7.8±0.09, *P*-value 0.007). Table 1

Characteristics	**1 month-3 months**	**4 months-1year**	**1 year - 5 years**	**5 years - 10 years**	**10 years - 14 years**	**mean ± SD**	***P* – value**
Gender							
Male	14	17	9	12	7	11.8±0.02	<0.001
Female	12	11	10	6	2	8.2±0.5	
Resident							
Rural	18	21	12	14	6	14.2±0.07	0.01
Urban	8	7	7	4	3	5.8±0.4	
Treatment History							
Took prior treatment for the recent episode but no record available	5	4	7	2	1	3.8±0.5	0.64
Did not take any prior treatment	9	11	8	11	3	8.4±0.6	0.03
Taking empirical treatment	12	13	4	5	5	7.8±0.09	0.007

Table 1. Demographic characteristics of selected patients

On presentation, patients had a variety of signs and symptoms including fever 93%, headache 42%, fits 59%, vomiting 61%, delirium 34%, loss of consciousness 28%, photophobia 52%, phonophobia 31%, and neck stiffness 84%. Fig. 1.

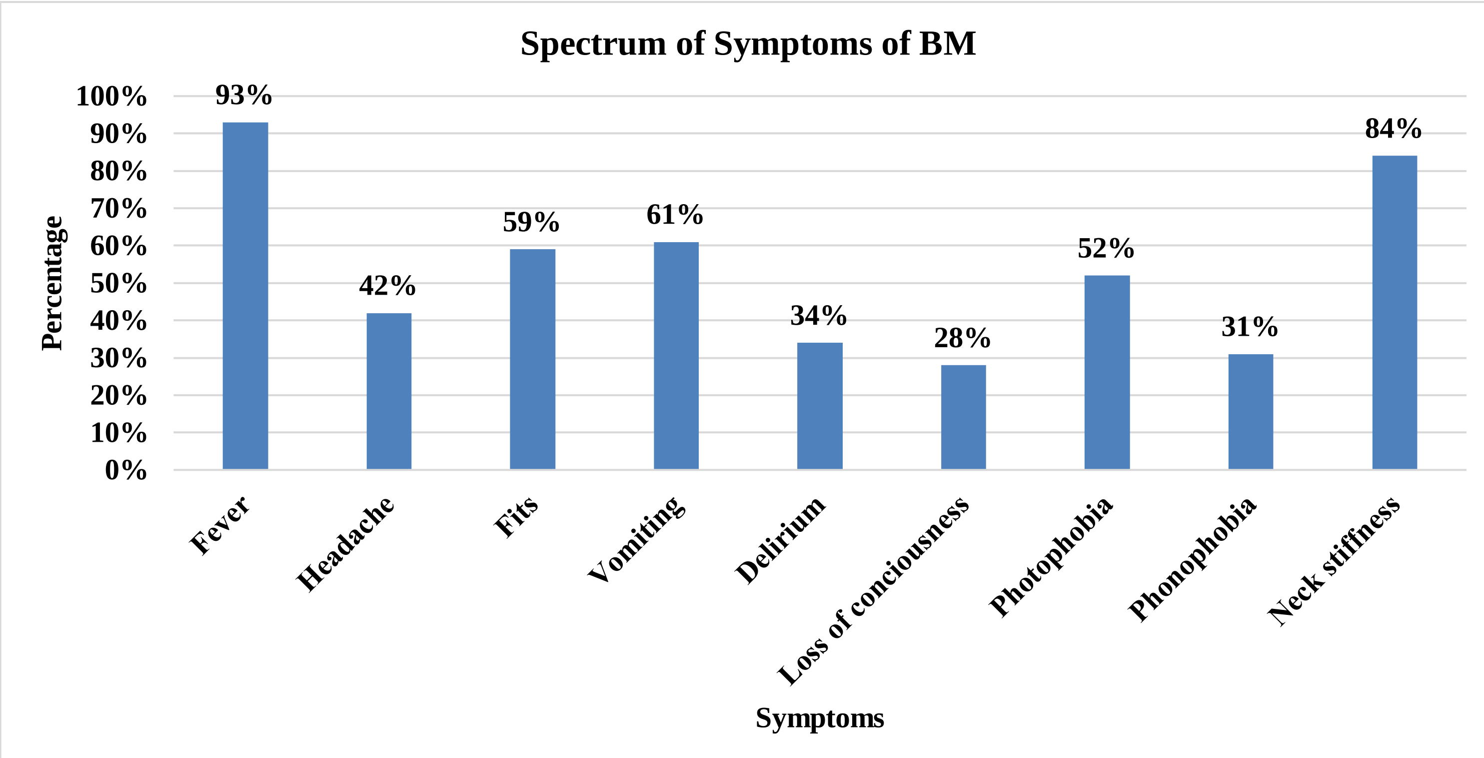


Fig 1. Spectrum of signs and symptoms of bacterial meningitis in selected patients (n=100).

After the admission of the patients in medical emergency, the patients were divided into two groups; 50% Case and 50% control. Case (n=50%) included 32 (0.64) male and 18 (36%) female patients, while Control group (n=50%) comprised of 24 (48%) male and 26 (52%) female patients. The patients of case and control groups were compared on several clinical aspects mentioned in table 2. Case (n=50, M=32, F=18) were the patients that were presented to the specialized clinic within 24 hours of onset of symptoms of meningitic irritation and received proper treatment including lumber puncture for CSF analysis for specific antimicrobial regimen. However, 50% of control group patients (M=24, F=26) presented late, after the first 24 hours of onset of symptoms and the empirical treatment was started without waiting for the CSF analysis report. However, LP was done later to analyze the appropriateness of the ongoing treatment and the CSF characteristics are featured in detail in Table 2.

Commencement of Antimicrobial Therapy (with respect to onset of symptoms)	**Case (n=50)**		**Control (n=50)**		**Total**	**P-value**	**Odds Ratio**	**95% Confidence Interval**	
	Male	**Female**	**Male**	**Female**				**Upper Limit**	**Lower Limit**
Within 24 H	32	18	0	0	50	0.001	0.43	0.023	1.8
After 24 H	0	0	24	26	50	0.002	0.56	0.076	2.1
LP (with respect to onset of symptoms)									
Within 24 H	32	18	0	0	50	0.005	0.72	0.046	2.8
After 24 H	0	0	24	26	50	0.03	0.45	0.057	3.5
CSF pH									
7.32-7.50	23	7	16	11	57	0.04	0.23	0.029	3.1
7.6-8.0	9	11	8	15	43	0.37	0.41	0.031	2.9

CSF Protein Level									
14-45 mg/dL	24	6	14	11	55	0.09	0.43	0.058	2.7
46-2500 mg/dL	8	12	10	13	43	0.05	0.59	0.041	3.4
CSF Glucose level									
Low 0-44 mg/dL	14	8	13	10	45	0.04	0.21	0.041	4.3
45-100 mg/dL	10	6	9	6	31	0.61	0.34	0.052	3.9
>100 mg/dL	8	4	2	8	22	0.92	0.42	0.063	2.8
CSF Appearance									
Clear	25	12	9	12	58	0.32	0.58	0.048	1.4
Turbid	7	6	15	14	42	0.59	0.82	0.072	1.6
CSF WBC Count									
21-100 cells/mm^3	3	4	7	6	20	0.61	0.73	0.062	2.4
101-2000 cells/mm^3	14	9	5	12	40	0.48	0.95	0.094	3.6
>2000 cells/mm^3	15	5	14	8	42	0.82	0.83	0.031	1.4
Neutrophils									
10%-30%	14	7	8	5	34	0.31	0.74	0.053	2.7
31%-60%	8	5	3	7	23	0.67	0.72	0.061	1.4
61%-90%	7	3	9	4	23	0.39	0.95	0.073	3.4
>90%	3	3	4	10	20	0.51	0.72	0.671	2.5

Table 2. Comparative analysis of case (n=50) and control (n=50) groups based on CSF characteristics stratified further based on gender. Value =*p* <0.05 considered significant.

Lumber puncture was performed on all the patients either within or after 24 hours of onset of symptoms. Depending on the clinical history, patients were divided into 3 groups. Patients who were already taking empirical treatment (n=29) and the patients who took antibiotics with no previous record available (n=21) were included in control group (n=50). Whereas the patients who did not take any prior treatment and specific antibiotic treatment was given to them after LP were taken as case (n=50%). Based on frequency in all groups, the causative organisms are mentioned in descending order: Streptococcus pneumoniae n=31, Staphylococcus aureus n=20, Staphylococcus epidermidis n=11, Enterococcus species n=11, Hemophilus influenza n=10, Neisseria meningitis n=9, Escherichia coli n=5, and Klebsiella pneumoniae n=3 (Table 3). The frequency of all the bacterial pathogens was almost constant in all 3 groups. (*P*<0.34)

Categories		**Isolated Organisms**	**Frequency**	**Percentage**
Case	**Patients without any prior antimicrobial treatment (n=50)**	Streptococcus pneumoniae	17	17.0%
		Staphylococcus aureus	9	9.0%
		Staphylococcus epidermidis	5	5.0%
		Enterococcus species	7	7.0%
		Neisseria meningitis	4	4.0%
		Hemophilus influenza	5	5.0%
		Escherichia coli	2	2.0%
		Klebsiella pneumoniae	1	1.0%
Control	**Patients on Empirical Treatment (n=29)**	**Isolated Organisms**	**Frequency**	**Percentage**
		Streptococcus pneumoniae	9	9.0%
		Staphylococcus aureus	5	5.0%
		Staphylococcus epidermidis	3	3.0%
		Enterococcus species	2	2.0%
		Neisseria meningitis	3	3.0%

		Hemophilus influenza	4	4.0%
		Escherichia coli	2	2.0%
		Klebsiella pneumoniae	1	1.0%
	Partially treated by unknown antimicrobials (n=21)	**Isolated Organisms**	**Frequency**	**Percentage**
		Streptococcus pneumoniae	5	5.0%
		Staphylococcus aureus	6	6.0%
		Staphylococcus epidermidis	3	3.0%
		Enterococcus species	2	2.0%
		Neisseria meningitis	2	2.0%
		Hemophilus influenza	1	1.0%
		Escherichia coli	1	1.0%
		Klebsiella pneumoniae	1	1.0%

Table 3. Frequency of bacterial isolates in different treatment groups based on CSF analysis.

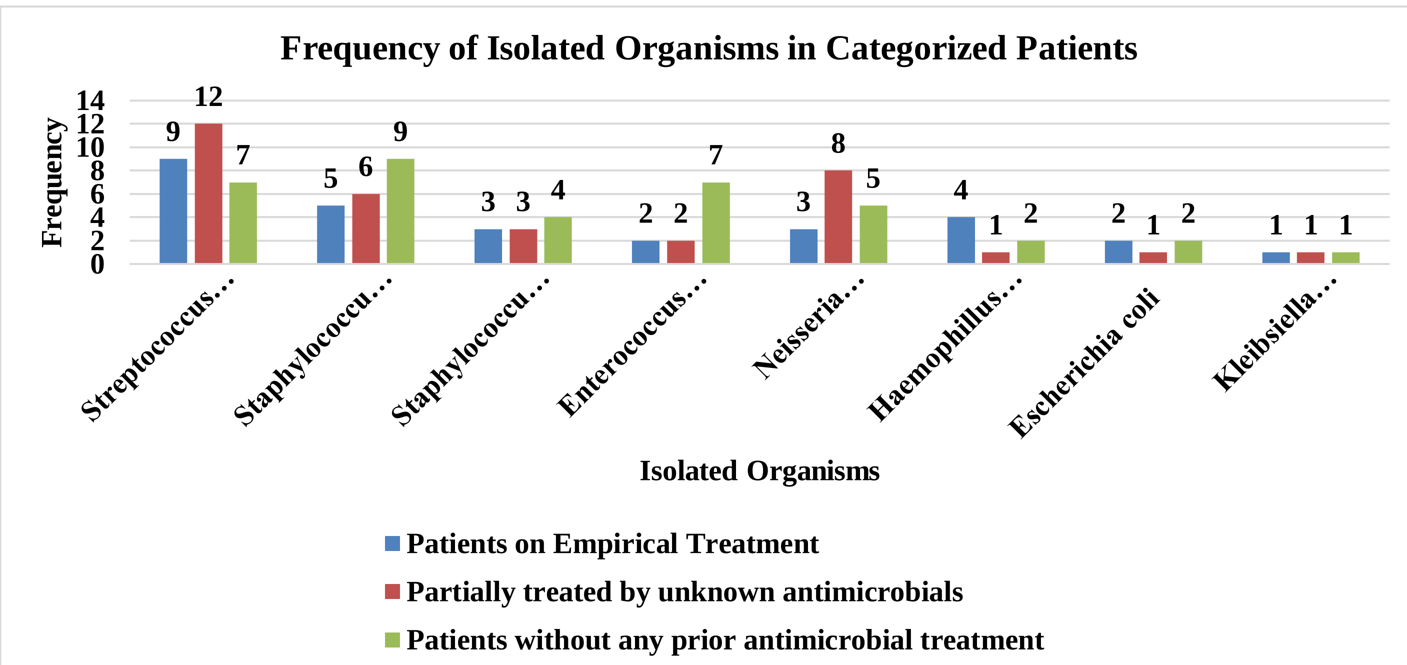


Figure 2. Frequency of Isolated Organisms in Categorized Patients

The CSF samples (n=100) were taken for the antibiotic sensitivity test. Out of 100, 50 samples (case) were taken before the commencement of antimicrobial therapy and 50 (control) were taken after 24 hours of empirical or unidentified antimicrobial treatment. The bacterial isolates were divided into 2 groups depending on their gram staining. Gram positive organisms included Strep. Pneumoniae (n=28), S. aureus (n=20), Enterococcus spp. (n=11), and S. epidermidis (n=10). The average % sensitivity of Gram-positive strains against different antibiotics was as follows; Vancomycin (90%), Tazobactam-piperacillin (80%), Oxytetracycline (80%), Meropenem (78%), Ceftriaxone (77%), Erythromycin (75%), Levofloxacin (75%), Rifampicin (71%), Salbactam-cefoperazone (69%), Amoxicillin (67%), Amikacin (67%), Ceftazidime (59%), and Ciprofloxacin (56%). Table 4.

Gram Positive Isolated Bacteria																
Antibiotics (Conc. µg)	**Streptococcus pneumoniae (N=28)**				**Staphylococcus aureus (N=20)**				**Staphylococcus epidermidis (N=10)**				**Enterococcus spp. (N=11)**			
	S(n)	**%**	**R(n)**	**%**	**S(n)**	**%**	**R(n)**	**%**	**S(n)**	**%**	**R(n)**	**%**	**S(n)**	**%**	**R(n)**	**%**
Amoxicillin (25)	26	93%	2	7%	1	3%	27	135%	8	80%	2	20%	10	91%	1	9%
Rifampicin (5)	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	7	70%	3	30%	8	73%	3	27 %
Oxytetracyclin (30)	28	100%	0	0%	14	47%	6	30%	9	90%	1	10%	9	82%	2	18%
Vancomycin (30)	28	100%	0	0%	18	60%	2	10%	10	100%	0	0%	11	100%	0	0%
Erthyromycin (15)	26	93%	2	7%	N.A	N.A	N.A	N.A	6	60%	4	40%	8	73%	3	27%
Levofloxacin (5)	28	100%	0	0%	17	57%	3	15%	8	80%	2	20%	7	64%	3	27%
Ceftazidime (30)	23	82%	5	18%	15	50%	5	25%	6	60%	4	40%	5	45%	6	55%
Ceftriaxone (30)	27	96%	1	4%	18	60%	2	10%	7	70%	3	30%	9	82%	2	18%
Sulbactam - Cefoperazone (30)	25	89%	3	11%	16	53%	4	20%	8	80%	2	20%	6	55%	5	45%
Ciprofloxacin (5)	19	68%	9	32%	15	50%	5	25%	7	70%	3	30%	4	36%	7	64%
Meropenam (10)	21	75%	7	25%	20	67%	0	0%	9	90%	1	10%	9	82%	2	18%
Amikacin (10)	27	96%	1	4%	N.A	N.A	N.A	N.A	6	60%	4	40%	5	45%	6	55%
Tazobactam-Piperacillin (30)	24	86%	4	14%	19	63%	1	5%	8	80%	2	20%	10	91%	1	9%

Table 4. Elaborative analysis of results of antimicrobial susceptibility test showing drug sensitivity against the Gram-positive isolates from CSF analysis of bacterial meningitis patients

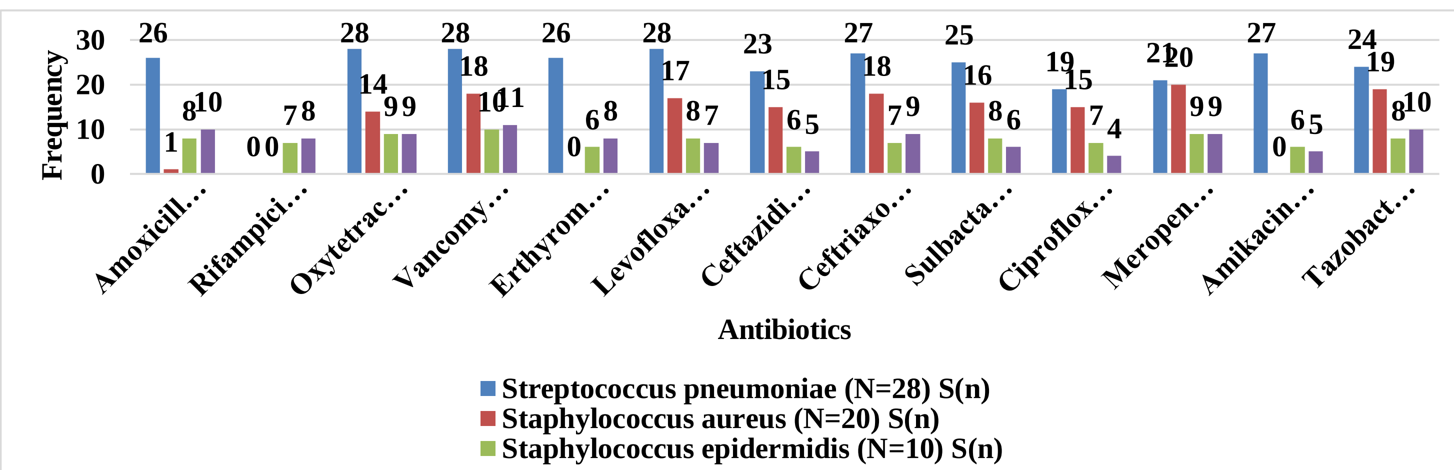
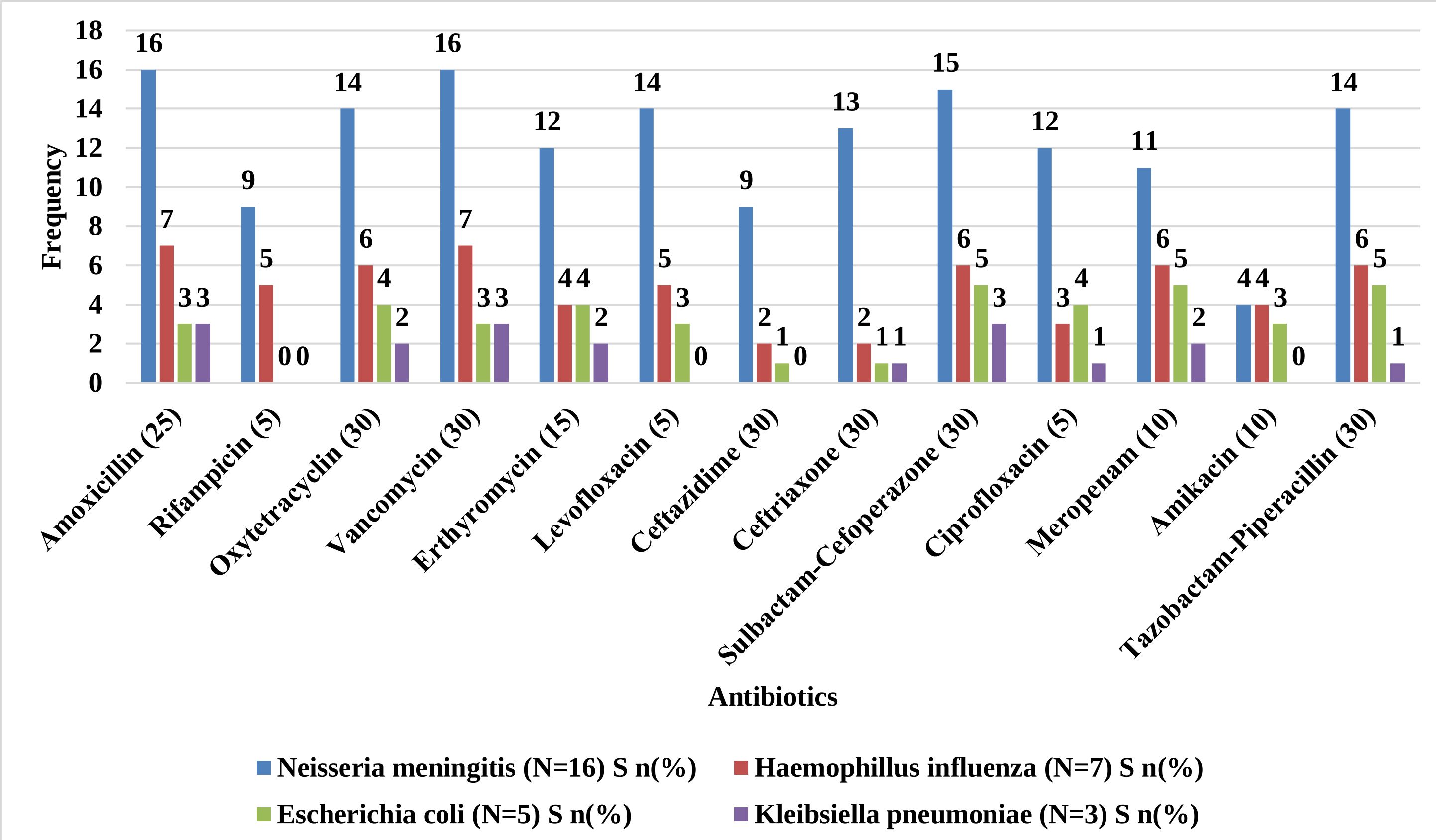


Figure 3. Elaborative analysis of results of antimicrobial susceptibility test showing drug sensitivity against the Gram-positive isolates from CSF analysis of bacterial meningitis patients

Likewise, the antibiotic susceptibility test was performed on Gram-negative isolates as well, including N. meningitidis (n=16), H. influenza (n=7), E. coli (n=5), and K. pneumoniae (n=3). The average % sensitivity of Gram positive strains against different antibiotics was as follows; Vancomycin (90%), Tazobactam-piperacillin (77%), Oxytetracycline (80%), Meropenem (80%), Ceftriaxone (41%), Erythromycin (70%), Levofloxacin (55%), Rifampicin (64%), Salbactam-cefoperazone (95%), Amoxicillin (90%), Amikacin (36%), Ceftazidime (26%), and Ciprofloxacin (58%). Table 5.

Gram Negative Isolated Bacteria																
Antibiotics (Conc. µg)	**Neisseria meningitis (N=16)**				**Haemophillus influenza (N=7)**				**Escherichia coli (N=5)**				**Kleibsiella pneumoniae (N=3)**			
	S(n)	**%**	**R(n)**	**%**	**S(n)**	**%**	**R(n)**	**%**	**S(n)**	**%**	**R(n)**	**%**	**S(n)**	**%**	**R(n)**	**%**
Amoxicillin (25)	16	100%	0	0%	7	100%	0	0%	3	60%	2	40%	3	100%	0	0%
Rifampicin (5)	9	56%	7	44%	5	71%	2	29 %	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A
Oxytetracyclin (30)	14	88%	2	13%	6	86%	1	14 %	4	80%	1	20%	2	67%	1	33%
Vancomycin (30)	16	100%	0	0%	7	100%	0	0%	3	60%	2	40%	3	100%	0	0%
Erthyromycin (15)	12	75%	4	25%	4	57%	3	43 %	4	80%	1	20%	2	67%	1	33%
Levofloxacin (5)	14	88%	2	13%	5	71%	2	29 %	3	60%	2	40%	0	0%	3	100%
Ceftazidime (30)	9	56%	7	44%	2	29%	5	71 %	1	20%	4	80%	0	0%	3	100%
Ceftriaxone (30)	13	81%	3	19%	2	29%	5	71 %	1	20%	4	80%	1	33%	2	67%
Sulbactam-Cefoperazone (30)	15	94%	1	6%	6	86%	1	14 %	5	100%	0	0%	3	100%	0	0%
Ciprofloxacin (5)	12	75%	4	25%	3	43%	4	57 %	4	80%	1	20%	1	33%	2	67%
Meropenam (10)	11	69%	5	31%	6	86%	1	14 %	5	100%	0	0%	2	67%	1	33%
Amikacin (10)	4	25%	12	75%	4	57%	3	43 %	3	60%	2	40%	0	0%	3	100 %
Tazobactam-Piperacillin (30)	14	88%	2	13%	6	86%	1	14 %	5	100%	0	0%	1	33%	2	67%

Table 5. Summary of antimicrobial sensitivity test results showing drug sensitivity against Gram-negative isolates of CSF analysis in patients of bacterial meningitis



Lastly, the case and control groups were compared based on severity of the disease and associated morbidity (Table 6). Duration of stay in hospital, ICU, and mechanical ventilation (if required) was slightly lesser in case group (*P*-value >0.05). Likewise, the condition at the time of discharge was slightly better for case group with *P*-value 0.045. The results are comprehensively explained in table 6.

Prognostic Factors	**Case (n=50)**	**Control (n=50)**	**Mean±SD**	**P-value**
Mean duration of hospital stay	24.3	26.9	25.6±0.04	0.471
Mean duration of ICU stay	6.5	9.2	8.35±0.07	0.059
Mean duration on Mechanical ventilation	5.8	6.1	5.95±0.05	0.095
Condition at the time of discharge				
Alive and healthy	37	31	34±0.45	0.045
Alive with neurological deficit	9	14	11.5±0.92	0.569
Expired (during treatment)	4	5	4.5±1.26	0.432

Table 6. Comparative evaluation of prognostic factors in case and control groups

DISCUSSION:

In this study, we analyzed the outcomes of antibiotic treatment in case and control groups. The case group patients received antibiotics according to their CSF analysis and antibiotic susceptibility report. Whereas the control group took empirical treatment without any specific investigation. There is consensus at a large scale that the antibiotic treatment should be started within the first 24 hours of onset of symptoms of meningitis to ensure better prognosis. The first 24 hours of onset of infection are considered golden hours. In that case, LP can be postponed, or its results should not be awaited to start the treatment. However, there are several possible uncertainties regarding non-specific treatment including incomplete antibiotic treatment or inadequate dose calculations which can result in increased antibiotic resistance and hence difficult eradication of causative organism. [14] The patients with incomplete medical record and treatment history received few doses of unknown antibiotics. The treatment could not be pursued, and empirical treatment was started on their arrival at emergency. This abrupt change in regimen can significantly increase antibiotic resistance and decrease efficacy in treating meningitis. [2-6, 15] Worldwide, the empirical treatment of meningitis is done via intravenous ampicillin and ceftriaxone. These drugs are first line treatment for a few diseases and their prescriptions by general practitioners goes unchecked. The common cause of rapidly increasing antibiotic resistance is the multiple exposures of inadequate antibiotic doses to the causative strains resulting in multidrug resistant microorganisms. This article highlights the need of implementation of antimicrobial stewardship principles with appropriate antibiotic prescription in adequate doses. [12-16] Results did not show any gender bias. A slight male preponderance was noticed with insignificant P value (>0.05). Most of the patients belonged to rural areas where inadequate healthcare facilities, deplorable hygiene, lack of education, low socioeconomic status, and lack of convenience were the major factors contributing to inadequate disease control and management. The disease predominantly affected children under the age of one year. The risk of bacterial meningitis is higher in neonates and infants because the maternal antibodies are unable to cross placenta after 32 weeks of gestation and the immune system weakens after birth due to optimal neutrophil-macrophage activity meanwhile, partial vaccination (according to age) will be insufficient to provide efficient cover against causative agents of meningitis. [17]Other factors that can precipitate meningitic infection are low birth weight, premature birth, perinatal or postnatal infections/sepsis or other co-morbidities. Such patients were not included in this study to keep the results unaffected by additional factors. [17, 18] A major health system crisis that the world is facing today is antibiotic resistance. In this study, we have evaluated antimicrobial resistance (AMR) and susceptibility of the causative agents against the commonly available antibiotics that are used against meningitis. Those 13 antimicrobials included all the generation of drugs: 1st (amoxicillin, oxytetracycline), 2nd (levofloxacin, ciprofloxacin), and 3rd (Ceftriaxone, ceftazidime). We have found a significant number of cases resistant to even 3rd generation of antibiotics ceftriaxone S=41% (gram positive) S=77% (gram negative) and Ceftazidime S=59% (gram positive) S=26% (gram negative). Amoxicillin is the most prescribed drug in pediatric bacterial meningitis which was also resistant to multiple pathological stains accounting for sensitivity S=67% (gram positive), S=90% (gram negative). Table 4 & 5

CONCLUSION:

This case-control study compared both groups based on treatment regimen, resultant prognosis, and associated morbidity. It is a mutual consensus among peers that the antibiotic treatment should be started in suspected cases of meningitis empirically, without waiting for CSF report. However, this study reveals that the patients who took organism specific antibiotics experienced slightly better outcomes with significant p value. Hence the implementation of the principles of antibiotic stewardship with the prescription of appropriate antibiotic in meningitic doses can greatly improve the prognosis.

Conflict of interest: None

REFERENCES:

1. Wright C, Blake N, Glennie L, Smith V, Bender R, Kyu H, Wunrow HY, Liu L, Yeung D, Knoll MD, Wahl B. The global burden of meningitis in children: challenges with interpreting global health estimates. Microorganisms. 2021 Feb 13;9(2):377.
2. Nakamura T, Cohen AL, Schwartz S, Mwenda JM, Weldegebriel G, Biey JN, Katsande R, Ghoniem A, Fahmy K, Rahman HA, Videbaek D. The global landscape of pediatric bacterial meningitis data reported to the World Health Organization–coordinated Invasive Bacterial Vaccine-Preventable Disease Surveillance Network, 2014–2019. The Journal of infectious diseases. 2021 Sep 1;224(Supplement_3):S161-73.

3. Gonçalves BP, Procter SR, Paul P, Chandna J, Lewin A, Seedat F, Koukounari A, Dangor Z, Leahy S, Santhanam S, John HB. Group B streptococcus infection during pregnancy and infancy: estimates of regional and global burden. The Lancet Global Health. 2022 Jun 1;10(6):e807-19.
4. Park JJ, Narayanan S, Tiefenbach J, Lukšić I, Ale BM, Adeloye D, Rudan I. Estimating the global and regional burden of meningitis in children caused by Haemophilus influenzae type b: A systematic review and meta-analysis. Journal of Global Health. 2022;12.
5. Mwenda JM, Soda E, Weldegebriel G, Katsande R, Biey JN, Traore T, de Gouveia L, du Plessis M, von Gottberg A, Antonio M, Kwambana-Adams B. Pediatric bacterial meningitis surveillance in the World Health Organization African region using the invasive bacterial vaccine-preventable disease surveillance network, 2011–2016. Clinical infectious diseases. 2019 Sep 5;69(Supplement_2):S49-57.
6. Teixeira DC, Diniz LM, Guimarães NS, Moreira HM, Teixeira CC, Romanelli RM. Risk factors associated with the outcomes of pediatric bacterial meningitis: a systematic review. Jornal de pediatria. 2020 May 11;96:159-67.
7. Svendsen MB, Ring Kofoed I, Nielsen H, Schønheyder HC, Bodilsen J. Neurological sequelae remain frequent after bacterial meningitis in children. Acta Paediatrica. 2020 Feb;109(2):361-7.
8. Wang LP, Yuan Y, Liu YL, Lu QB, Shi LS, Ren X, Zhou SX, Zhang HY, Zhang XA, Wang X, Wang YF. Etiological and epidemiological features of acute meningitis or encephalitis in China: a nationwide active surveillance study. The Lancet Regional Health-Western Pacific. 2022 Mar 1;20:100361.
9. Poletto E, Zanetto L, Velasco R, Da Dalt L, Bressan S. Bacterial meningitis in febrile young infants acutely assessed for presumed urinary tract infection: a systematic review. European Journal of Pediatrics. 2019 Oct;178:1577-87.
10. Principi N, Esposito S. Bacterial meningitis: new treatment options to reduce the risk of brain damage. Expert Opinion on Pharmacotherapy. 2020 Jan 2;21(1):97-105.
11. Wall EC, Chan JM, Gil E, Heyderman RS. Acute bacterial meningitis. Current Opinion in Neurology. 2021 Jun 1;34(3):386-95.
12. Xu M, Hu L, Huang H, Wang L, Tan J, Zhang Y, Chen C, Zhang X, Huang L. Etiology and clinical features of full-term neonatal bacterial meningitis: a multicenter retrospective cohort study. Frontiers in pediatrics. 2019 Feb 13;7:31.
13. Pruitt CM, Neuman MI, Shah SS, Shabanova V, Woll C, Wang ME, Alpern ER, Williams DJ, Sartori L, Desai S, Leazer RC. Factors associated with adverse outcomes among febrile young infants with invasive bacterial infections. The Journal of pediatrics. 2019 Jan 1;204:177-82.
14. Julián-Jiménez A, Morales-Casado MI. Usefulness of blood and cerebrospinal fluid laboratory testing to predict bacterial meningitis in the emergency department. Neurología (English Edition). 2019 Mar 1;34(2):105-13.
15. Lien CY, Lee JJ, Tsai WC, Chen SY, Huang CR, Chien CC, Lu CH, Chang WN. The clinical characteristics of spontaneous Gram-negative bacterial meningitis in adults: A hospital-based study. Journal of Clinical Neuroscience. 2019 Jun 1;64:101-5.
16. Siegel JL. Acute bacterial meningitis and stroke. Neurologia i Neurochirurgia Polska. 2019;53(4):242-50.
17. LaPenna PA, Roos KL. Bacterial infections of the central nervous system. InSeminars in Neurology 2019 Jun (Vol. 39, No. 03, pp. 334-342). Thieme Medical Publishers.
18. Hashim QM, Muhssin HJ, Salish NA, Hashim JM, Johny AM, Nasrawi AJ. The role of CSF-CRP in diffrentation between bacterial from nonbacterial meningitis. Current Pediatric Research. 2021 Aug 21;25(8).