Open Access

Original Article

Exploring the Etiological Profile and Sensitivity Pattern of Bacterial Pathogens Isolated from Cerebrospinal Fluid in Meningitis Patients: A Tertiary Care Center Study

Aneela Khawaja, Faiqa Arshad*, Nusrat Alavi, Asma Ejaz, Umaira Ahsan, Namra Yunus***, Aina Farooq**

Department of Pathology, RMDC/PRTH, Lahore Pakistan, *Department of Pathology, Gujranwala Medical College, Gujranwala Pakistan, **Department of Pathology, Al Aleem Medical College, Gulab Devi Educational Complex, Lahore Pakistan, ***Department of Pathology, Fatima Memorial College of Medicine and Dentistry, Lahore Pakistan

ABSTRACT

Objective: To explore the etiological profile and sensitivity pattern of bacterial pathogens isolated from cerebrospinal fluid (CSF) in meningitis patients at a tertiary care center.

Study Design: Cross sectional study.

Place and Duration of Study: The study was conducted at a tertiary care center, Lahore, Pakistan, from Jun 2021 to May 2022.

Methodology: CSF samples obtained from hospitalized patients were processed according to standard microbiological protocols. Preliminary identification of pathogens was based on colony morphology, Gram staining, and biochemical testing. Gram-negative organisms were confirmed using API 10s. Antimicrobial susceptibility testing was performed using the standard Kirby Bauer disc diffusion method and interpretation was done according to CLSI guidelines (2023). E- Test method was used to determine the minimum inhibitory concentrations (MICs) of Penicillin and Vancomycin.

Results: Out of 460 suspected cases, 94 (20.43%) were confirmed positive for meningitis. Streptococcal species were predominant among gram-positive organisms, while lactose fermenters, including *E-coli* dominated among gram-negative organisms. Lactose fermenters depicted poor sensitivity towards beta-lactams, extended generation cephalosporins and quinolones. Most of the non-lactose fermenters were sensitive to colistin.

Conclusion: The study identified high prevalence rates of both gram-positive and gram-negative bacteria in CSF samples from bacterial meningitis. Additionally, low susceptibility to various tested drugs was observed. These findings emphasize the importance of accurate diagnosis and appropriate antibiotic management based on local antimicrobial resistance patterns, guiding antimicrobial stewardship and infection control practices.

Keywords: Bacterial meningitis, Cerebrospinal fluid, Antimicrobial susceptibility, Lactose fermenter, Non Lactose fermenter.

How to Cite This Article: *Khawaja A, Arshad F, Alavi N, Ejaz A, Ahsan U, Yunus N, Farooq A. Exploring the Etiological Profile and Sensitivity Pattern of Bacterial Pathogens Isolated from Cerebrospinal Fluid in Meningitis Patients: A Tertiary Care Center Study. Pak Armed Forces Med J 2023; 73(Suppl-2): S474-477. https://doi.org/10.51253/pafmj.v73iSUPPL-1.11858*

INTRODUCTION

Meningitis, a potentially fatal illness characterized by inflammation of protective membranes around the brain and spinal cord.[1] It is a major public health concern globally mostly in the form of bacterial meningitis which is notorious for its sudden onset, severity, and high morbidity and fatality. Understanding the etiology and sensitivity patterns of meningitis -causing bacterial organisms is critical for successful disease management and control.[2]

The diversity of bacterial pathogens involved in meningitis emphasizes the significance of ongoing surveillance and research efforts to stay ahead of new trends and evolving resistance patterns. *Streptococcus pneumoniae, Neisseria meningitidis,* and *Haemophilus influenzae* type b (Hib) have been identified as the primary causes of bacterial meningitis, particularly in children and adults.[3] However, the introduction of vaccinations targeting these capsular pathogens has resulted in modifications in the epidemiology of bacterial meningitis, needing continued observation and adaptation of preventive methods.[4]

In accordance with antibiotic stewardship guidelines, the emphasis is on the use of antibiotics capable of penetrating the blood-brain barrier, thereby enhancing treatment efficacy. However, the widespread use of broad-spectrum antibiotics has contributed to the development of antimicrobial resistance (AMR).[5] This indiscriminate antibiotic usage puts selection pressure on bacterial populations, worsening the spread of AMR. The increasing prevalence of multidrug-resistant (MDR) strains, combined with diminishing treatment options, has raised worries about therapeutic failure and unfavorable clinical consequences in cases of meningitis.[6] Thus, surveillance studies that reveal the sensitivity patterns of bacterial isolates to routinely

Correspondence: Dr Faiqa Arshad, Assistant Professor Pathology, Gujranwala Medical College, Gujranwala Pakistan
Received: 08 Jun 2022, revision received: 11 Jul 2022; accepted: 20 Jul 2022

used antibiotics are crucial in guiding empirical therapy and preventing the emergence of resistance.[7]

Against this backdrop, our study investigated the etiological profile and sensitivity patterns of bacterial pathogens isolated from CSF samples collected from meningitis patients at a tertiary care hospital. By combining accessible data and insights from clinical practice and research, we hope to shed light on current trends, difficulties, and consequences for patient care and public health. To reduce morbidity and mortality, meningitis must be diagnosed accurately and treated with suitable antimicrobials. The efficacy of treatment is dependent on understanding the prevalent bacterial species that cause meningitis and their susceptibility to antimicrobial agents.

METHODOLOGY

This cross-sectional descriptive study was conducted at the Pathology Department, Microbiology section of Rahbar Medical and Dental College in Lahore, Pakistan, from June 2021 to May 2022, following approval from the institutional ethics review committee Ref # 786/21 dated 21-05-2021. Total of 460 CSF samples obtained from admitted patients were processed in accordance with standard microbiological protocols.

CSF samples were centrifuged at 3000 rpm in the microbiology laboratory, and the supernatant was carefully discarded. The resulting pellet (sediment) was then inoculated onto Blood, Chocolate, and MacConkey's agar plates. These inoculated plates were incubated for 24-72 hours at 37°C in ambient air for possible bacterial growth.

Preliminary identification of pathogenic bacteria was done on the basis of colony morphology, gram staining, and biochemical testing. Gram negative organisms were confirmed using API 10s. Following initial identification, antimicrobial susceptibility testing was performed; zones of inhibition were measured and interpretation was done according to CLSI, 2023. E-Test method was used to determine the minimum inhibitory concentrations (MICs) of Penicillin and Vancomycin.

RESULTS

Out of 460 CSF samples of suspected cases of meningitis, culture identified 94 samples (20.43%) to be positive. The male-to-female ratio among positive cases was 62 (65.95%) to 32 (34.04%) respectively. The age distribution of positive cases is illustrated in Table-I. Table-II & III shows the sensitivity profile of Gram positive and Gram negative isolates, respectively.

Table-I: Age Distribution of Positive Meningitis Cases (N=94)

Age group	Total N=94 (%)	Male n=66 (%)	Female n=28 (%)
0-15 yrs	25 (26.59)	17 (25.75)	8 (28.57)
>15- 30 yrs	15 (15.95)	9 (13.63)	6 (21.42)
>30-60 yrs	43 (45.74)	28 (42.42)	15 (53.57)
>60 yrs	11 (11.70)	8 (12.12)	3 (10.75)

Table-II: Sensitivity Pattern of Gram-Positive Organisms (n=24)

	Staph spp. n=7 (%)	Streptococcus spp. n=13 (%)	Enterococcus spp. n=4 (%)
Penicillin	1 (14.28)	13 (100)	2(50)
Ampicillin	1 (14.28)	13 (100)	
Erythromycin	3 (42.85)	10 (76.92)	1(25)
Trimethoprim-sulfamethoxazole	4 (57.14)		-
Clindamycin	5(71.42)	11 (84.61)	2(50)
Cefoxitin	4 (57.14)		-
Vancomycin	7 (100)	13 (100)	4(100)
Linezolid	7 (100)	13 (100)	4(100)
Gentamicin	4 (57.14)	-	*
Amikacin	6 (85.71)	-	-
Doxycycline	2 (28.57)	10 (76.92)	
Ciprofloxacin	3 (42.85)	-	-
Levofloxacin	4 (57.14)	09 (69.23)	-
Chloramphenicol	7 (100)	13 (100)	3 (75)

**high level resistance was checked for Enterococcus spp.*

Table-III: Sensitivity Pattern of Gram-Negative Organisms (n=65)

Antibiotics Tested	Lactose Fermenters n=42 (%)	Non-Lactose Fermenters n= 26 (%)
Ampicillin	3 (7.14)	NT
Amoxicillin-clavulanate	9 (21.4)	NT
Ceftriaxone	11 (26.2)	18 (69.2)
Imipenem	36 (85.7)	11 (42.3)
Meropenem	38 (90.5)	8 (30.7)
Piperacillin-Tazobactem	38 (90.5)	18 (69.2)
Tigecycline	39 (92.8)	23 (88.5)
Gentamicin	35 (83.3)	7 (26.9)
Amikacin	31 (73.8)	7 (26.9)
Colistin	41 (96.7)	24 (92.3)
Ciprofloxacin	11 (26.2)	5 (19.2)
Levofloxacin	35 (83.3)	16 (61.5)
Minocycline	40 (95.2)	20 (80.8)
Ceftazidime	NT	9 (34.6)

DISCUSSION

Meningitis remains a significant public health challenge worldwide, with considerable encumberment. Comprehending the causative etiology and antimicrobial susceptibility patterns of bacterial isolates among CSF samples has a vital role for effectual management and control of the disease.

In this study, we analyzed the culture sensitivity profile of isolated pathogens, with positivity of n=94

(20.43%). Our results are comparable with previous studies.[8,9] Our findings highlight the importance of continuous surveillance and evaluation of microbiological data to guide clinical decision-making and enhance antimicrobial stewardship efforts.

The male predominance observed in our study aligns with previous literature documenting a higher incidence of meningitis among males. This gender disparity may be attributed to various factors, including differences in immune responses, behavioral patterns, and environmental exposures. A meta analysis revealed higher incidence rates of meningococcal infection observed among young males and the elevated prevalence among females in older age brackets were consistent with most of the continents. Although certain behavioral factors might elucidate some of the gender disparities observed in older age cohorts, the surplus rates among very young males imply that genetic and hormonal distinctions may also play significant roles.[10] However, further research is warranted to reveal the underlying mechanisms driving this gender difference.

Among gram-positive organisms, *Streptococcal species* was unveiled as the predominant etiological agent. This aligns with previous studies in Iran and Africa which also reported *Streptococcus pneumoniae* as a primary causative agent of bacterial meningitis.[11,12] Another study in Europe demonstrated that *Streptococcus pneumoniae*, Neisseria meningitidis, *Staphylococcus aureus* and group B *streptococcus* were the prevailing gram positive organisms.[13] Our neighboring country, India reported comparable results.[14]

Our results depicted lactose fermenters i.e., *E. coli* as the most prevalent gram negative organism. Similar outcomes were also observed in a prior study.[15] However, another study revealed that pseudomonas spp., a nonfermenter, as the most prevalent pathogen in meningitis patients.[16] Additionally, candida species were also identified, emphasizing the need to consider fungal causes of meningitis alongside bacterial pathogens, necessitating distinct management strategies. *Candida* meningitis has also been reported by previous studies.[17] These findings resonate with prior research, further validating the importance of comprehensive pathogen identification in meningitis cases.

Antimicrobial susceptibility testing disclosed concerning trends in antimicrobial resistance among both Gram-positive and Gram-negative bacterial pathogens. The emergence of multidrug-resistant strains poses significant challenges in the treatment of meningitis. The varied pattern of drug susceptibility among different pathogens was observed. Most *streptococcus* isolates were susceptible to commonly prescribed antibiotics such as penicillin, ampicillin, vancomycin, linezolid. A previous study also showed high sensitivity of streptococcus to vancomycin and linezolid.[18] A prior investigation also indicated that vancomycin shows higher efficacy against *Streptococcus pneumoniae*, while clindamycin and rifampicin demonstrate increased sensitivity against *Staphylococcus epidermidis*.[19] This emphasizes the need for prudent antibiotic use and regular monitoring of antimicrobial resistance patterns.

The study also highlighted the emerging drug resistance strains of gram negative with developing resistance in *E. coli*, also raised significant concerns.[20] A previous study also reported a high resistance trends among bacterial pathogens isolated from CSF.[21]

This underscores the importance of ongoing surveillance and appropriate antibiotic stewardship practices to prevent the spread of antibiotic resistance.

CONCLUSION

High prevalence rates were observed for both gram-positive and gram-negative bacteria in CSF of bacterial meningitis cases. The study found Streptococcal species predominant among gram-positive organisms and lactose fermenters, i.e., *E. coli* among gram-negative organisms. Additionally, the organisms showed low susceptibility to various tested drugs. The results of this study highlight the importance of accurate diagnosis, and appropriate antibiotic management tailored to the local antimicrobial resistance patterns. Such surveillance studies not only facilitate empirical treatment, but they also help detect emergent resistance patterns, which can then be used to guide antimicrobial stewardship campaigns and infection control measures.

Conflict of Interest: None

Authors Contribution

AK & FA: Conception, study design, drafting the manuscript, approval of the final version to be published

NA, AE & UA: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

NY & AF: Critical review, data acquisition, drafting the manuscript, approval of the final version to be published.

All Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Le D, Liaw D, Naterelli N, Longbottom B, Preuss C. Recent Developments in the Treatment of Bacterial Meningitis. Infectious Diseases Drug Delivery Systems 2023; 349-81.
2. Asma'a Mutaher Kholood A-S. Bacteriological profile of meningitis in Sana'a, Yemen: two years retrospective study: University of Science and Technology; 2023.
3. Tsang RS. A narrative review of the molecular epidemiology and laboratory surveillance of vaccine preventable bacterial meningitis agents: Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenzae and Streptococcus agalactiae. Microorganisms 2021; 9(2): 449.
4. Koelman DL, van Kassel MN, Bijlsma MW, Brouwer MC, van de Beek D, van der Ende A. Changing epidemiology of bacterial meningitis since introduction of conjugate vaccines: 3 decades of national meningitis surveillance in The Netherlands. Clin Infec Dis 2021; 73(5): e1099-e107.
5. Haddad N, Carr M, Balian S, Lannin J, Kim Y, Toth C, et al. The Blood–Brain Barrier and Pharmacokinetic/Pharmacodynamic Optimization of Antibiotics for the Treatment of Central Nervous System Infections in Adults. Antibiotics 2022; 11(12): 1843.
6. Zheng G, Shi Y, Cao Y, Qian L, Lv H, Zhang L, et al. Clinical Feature, therapy, antimicrobial resistance gene distribution, and outcome of nosocomial meningitis induced by multidrug-resistant Enterobacteriaceae—a longitudinal cohort study from two neurosurgical centers in Northern China. Frontiers Cellular Infec Microbiol 2022; 12: 380.
7. Ali SA, Taj MK, Ali SH. Antimicrobial resistance pattern of bacterial meningitis among patients in Quetta, Pakistan. Infection and drug resistance. 2021:5107-20.
8. Niemelä S, Lempinen L, Löyttyniemi E, Oksi J, Jero J. Bacterial meningitis in adults: a retrospective study among 148 patients in an 8-year period in a university hospital, Finland. BMC Infec Dis 2023; 23(1): 1-10.
9. Awulachew E, Diriba K, Awoke N. Bacterial isolates from CSF samples and their antimicrobial resistance patterns among children under five suspected to have meningitis in Dilla University Referral Hospital. Infection and drug resistance 2020: 4193-202.
10. Green MS, Schwartz N, Peer V. A meta-analytic evaluation of sex differences in meningococcal disease incidence rates in 10 countries. Epidemiol Infec 2020; 148: e246.
11. Zeighami H, Roudashti S, Bahari S, Haghi F, Hesami N. Frequency of etiological agents of acute bacterial meningitis using culture and polymerase chain reaction assay. New Microbes and New Infections. 2021; 43: 100930.
12. Mhlanga B, Katsande R, Toscano C, Cherian T, O'Loughlin R, Rainey J, et al. Pediatric bacterial meningitis surveillance-African Region, 2002-2008. Morbidity and Mortality Weekly Report 2009; 58(18): 493-7.
13. Subbarao S, Ribeiro S, Campbell H, Okike I, Ramsay ME, Ladhani SN. Trends in laboratory-confirmed bacterial meningitis (2012–2019): national observational study, England. The Lancet Regional Health–Europe. 2023; 32.
14. Ghia CJ, Rambhad GS. A systematic literature review on the prevalence and etiology of meningitis among critically ill and hospitalized patients in India. Therap Adv Infec Dis 2021; 8: 20499361211046453.
15. Jeter K, Dang A, Ly A, Jayasekara D. Spontaneous Escherichia coli Meningitis and Brain Abscess in an Immunocompetent Adult. Cureus 2022; 14(9).
16. Nureen Z, Basit Z, Musarat I, Ayesha R, Falk S, Yumna F, et al. Detection of Enterobacteriaceae in cerebrospinal fluid of neonates with meningitis from tertiary care hospitals. Eur Rev Med Pharmacol Sci 2023; 27(21): 10563-8.
17. Xu L, Zhao H, Zhou M, Lang G, Lou H. Single and Repeated Episodes of Candida Species Isolated From Cerebrospinal Fluid for Diagnosing Probable Candida meningitis. Frontiers Microbiol 2021; 12: 742931.
18. Zhang Z, Song Y, Kang J, Duan S, Li Q, Feng F, et al. Epidemiology of patients with central nervous system infections, mainly neurosurgical patients: a retrospective study from 2012 to 2019 in a teaching hospital in China. BMC Infec Dis 2021; 21(1): 1-12.
19. Zhou T, Kuang M, Huang S, Li J, Xie Q. Epidemiological characteristics and drug resistance analysis of cerebrospinal fluid microbial infections in Wenzhou Area. Infection Drug Resistance 2021: 2091-103.
20. Thaver D, Ali SA, Zaidi AK. Antimicrobial resistance among neonatal pathogens in developing countries. The Pediatr Infec Dis J 2009; 28(1): S19-S21.
21. Javaid N, Sultana Q, Rasool K. Trends in antimicrobial resistance amongst pathogens isolated from blood and cerebrospinal fluid cultures in Pakistan (2011-2015): A retrospective cross-sectional study. PLoS One 2021; 16(4): e0250226.

....