Journal of Medicine, Physiology and Biophysics
ISSN 2422-8427 An International Peer-reviewed Journal
Vol.42, 2018

Culture Sensitivity Pattern of Infectious Meningitis in Pediatric Population at a Tertiary Care Hospital

Dr. Abdul Aleem Dr. Muhammad Sohail Ahmad Dr. Muhammad Kaleem
House Officer Nishtar Hospital Multan

Abstract
Objective:
This study aims to determine the culture sensitivity pattern and clinical features of patients suffering from infectious meningitis presenting at Nishtar medical university hospital Multan, Pakistan.
Study design:
Descriptive cross-sectional study
Place and duration of study:
Pediatric department, Nishtar Hospital Multan the duration of the study was January 01, 2017 to December 31, 2017.
Method
All the children of age 1 month to 12 years with suspected meningitis were included in our study. The patients who were critically ill or immune compromised were not included in the study. All these cases were evaluated by detailed history, thorough physical examination and the necessary investigations. All the demographic data and other variables related to clinico-epidemiological features were measured and recorded using a specifically designed Proforma. The data were analyzed by using computer program SPSS 21 version.
Result
Of the 178 patients included in the final analysis, 113 (63.6%) were females and 65 (36.4%) males. The age ranged from 1 month to 12 years with a median of 31 months (6.00 - 72.50). Seventy-five percent of them were below 5 years. On the basis of investigations, bacterial meningitis was diagnosed in 91, viral meningitis in 27, tuberculous meningitis in 21 and cryptococcal meningitis in 15 patients. The most common clinical presentations of meningitis were fever, vomiting, headache, irritability, neck stiffness and altered level of consciousness. While the photophobia and fits were less common. The GCS score was more than 13 in 33 patients (18.8%) and 8-13 in 93 patients (52%). Whereas, less than eight GCS score was observed in 52 children (29.2%). Most of the complications were observed in the initial 48 hours of admission. The commonly observed complications were an altered level of sensorium, seizure, and shock. The minimum length of hospitalization was three days and the maximum was 36 days with median (IQR) of 12 days (4-15). The mortality was observed in 29 patients (16.2%) of Pediatric Department.
Conclusion
Infectious meningitis is a common disease of Pakistani pediatric population. The female children of rural areas, having age less than 5 years are more prone to suffer from this disease. For effective management of infectious meningitis, the antimicrobial sensitivity data should be continuously monitored.
Keywords: Meningitis, children, culture sensitivity patterns, clinical features

Introduction:

Infections of the central nervous system are life-threatening. Meningitis is an infection involving the meninges of the brain and subarachnoid space. This infectious disease may result in impaired consciousness, seizures, increased intracranial pressure and stroke (1). It is estimated that approximately 75 % of meningitis cases occur in children under the age of five years (2-4). In the United States, the incidence of bacterial meningitis has been reported to be 5 to 10 cases per 100,000 populations (4). Bacterial meningitis incidence in children of tropical countries such as Africa and Asia is very high (5). A careful review of the recent medical literature reveals that the rate of incidence in these developing countries is 80.69 cases per 100 000 children (5). Unfortunately, exact estimates and epidemiology of infectious meningitis are lacking in Pakistan. But a much higher burden of disease is considered in the countries like Pakistan. Thus, a huge load of this infectious disease results in increased rate of morbidity, mortality and economic burden.

Meningitis is usually characterized by fever, headache, and intolerance to light and sound, and neck stiffness. The etiological factors for this central nervous system infection differ greatly by a change in geographical area and age group (6). The studies have shown that bacterial meningitis alone is responsible for about 30%– 40% of central nervous system infections (7, 8). A report by WHO estimates that over 1.2 million cases of bacterial meningitis occur worldwide each year (8). Consequently, meningitis is considered a leading cause of neurological dysfunction. Hence, it requires a comprehensive management plan with special focus on the eradication of the specific etiological factor. Unfortunately, both the epidemiology of meningitis and the sensitivity to various groups of antimicrobials are changing as a result of widespread misuse of antimicrobials

(9). The data regarding the specific epidemiology and clinical presentation of meningitis in Pakistani children, and the susceptibility of causative microbes to various antimicrobial groups is quite inconclusive and controversial. Currently, the available medical literature is quite insufficient to address this burning question in a comprehensive way. So the present study aims to determine the common clinico-epidemiological features of children suffering from infectious meningitis.

Material and Method

This descriptive cross-sectional study was conducted at Department of Pediatric Medicine, Nishtar Hospital Multan, Pakistan, which is a tertiary care teaching hospital. Our hospital receives referrals from various hospitals of adjacent areas with a catchment population of about 3.5 million. The duration of the study was January 01, 2017 to December 31, 2017. All the children of age 1 month to 12 years with suspected meningitis presenting to Pediatric Department, Nishtar Hospital Multan, Pakistan were included in our study.

Inclusion criterion:

Children of age 1 month to 12 years who presented with suspected meningitis.

Exclusion criteria:

- ✓ Critically ill patients.
- ✓ Patients who were immune compromised.
- ✓ Patients whose parents not giving consent.

Written informed consent was taken from parents. All these cases were evaluated by detailed history, thorough physical examination and the necessary investigations. According to needs of patients, various laboratory investigations and imaging studies e.g. complete blood count, renal parameters, liver function tests, serum electrolytes, chest X-ray, CT scan brain, lumbar puncture for cerebrospinal fluid analysis and culture sensitivity were performed. Furthermore, the disease specific investigations such as gram staining, acid-fast staining, PCR, and detection of cryptococcal antigen (CrAg) in CSF were also performed to detect for the specific etiological factor of infectious meningitis. Patients were sub-categorized into different types of infectious meningitis on the basis of results of CSF analysis. Different variables such as age, sex, residential area, prominent symptoms, and the grades of the complications were recorded in a specifically designed Proforma. The data were analyzed by using computer program SPSS 21 version. The descriptive statistics were used to calculate mean ± SD for the age of the patients. Frequencies and percentages were calculated for all the variables included in the study.

Results

A total of 204 patients with clinical suspicion of meningitis were enrolled. Twenty six patients were excluded; out of these twenty six cases, 16 did not have infectious meningitis. In four cases, the parents did not give consent, while six patients did not have a clear final diagnosis. Of the 178 patients included in the final analysis, 113 (63.6%) were females and 65 (36.4%) males. The age ranged from 1 month to 12 years with a median of 31 months (6.00 - 72.50). Seventy-five percent of them were below 5 years. On the basis of investigations, bacterial meningitis was diagnosed in 105 (59.1%), viral meningitis in 31 (17.53%), tuberculous meningitis in 25 (13.63%) and cryptococcal meningitis in 17 (9.7%) patients. The common presenting complains were fever (n=140, 76.2%), irritability (n= 99, 55.6%), vomiting (n=76, 42.7%), headache (n=62, 34.8), and drowsiness (n=47, 26.5%). The common signs observed in these patients were neck rigidity (n=43, 24.1%), Brudzincski's sign (n=29, 16.3%), Kerning's sign (n=22, 12.4%), bulging fontanels (n=14, 7.86 %), focal neurological signs (n=11, 6.2%) and dilated poorly reactive pupils (n=4, 2.2%). The GCS score was more than 13 in 33 patients (18.8%) and 8-13 in 93 patients (52%). Whereas, less than eight GCS score was observed in 52 children (29.2%). The commonly observed complications were an altered level of sensorium, seizure, and shock. Mechanical ventilation was required in 71 (39.6%) and inotropic support in 50 (27.9%) patients. The outcome of meningitis was analyzed in terms of patient survival and length of hospital stay. The minimum length of hospitalization was 3 days and the maximum was 36 days with median (IQR) of 12 days (4-15). As far as the mortality is concerned, it was observed in 29 patients of Pediatric Department (16.2%).

Table I: Demographic features of children with meningitis

Variable	N (%)
Age	
< 5 years	134 (75.3%)
> 5 years	44 (24.7%)
Median(IQR)	31 (6.00-72.50)
Gender	
Male	65 (36.4%)
Female	113 (63.6%)
Residential area	
Rural	146 (82.4%)
Urban	32 (17.53%)

Table II: Clinical features of patients with meningitis

Diagnosis	
Bacterial meningitis	106 (59.1%)
Viral meningitis	31(17.53%)
Tuberculous meningitis	24 (13.63%)
Cryptococcal meningitis	17 (9.7%)
Major sign and symptoms	
Fever	140 (76.2%),
Irritability	99 (55.6%)
Vomiting	76 (42.7)
Headache	62 (34.8)
Drowsiness	47 (26.5%)
Neck stiffness	43 (24.1%)
Brudzincski's sign	29(16.3%)
Kerning's sign	22 (12.4%)
Photophobia	17 (10%)
Bulging fontanels	14 (7.86%)
Focal neurological signs	11 (7.1%)
Dilated poorly reactive pupils	4 (2.2%)
GCS at presentation	
More than thirteen	33 (18.8%)
8-13	93 (52%)
Less than 8	52 (29.2%)
Complications	
Altered level of consciousness	127 (82.5)
Convulsions	99 (64.2)
Shock	56 (36.4)
Mechanical ventilator support	61 (39.6%)
Ionotropic support	43 (27.9%)
Length of first hospital stay (Days)	
Minimum	3
Maximum	36
Median(IQR)	12 days (4-15)
Outcome	
Survivors	132 (85.7)
Expired	29 (16.2%)

Table III: Frequency of organisms isolated from CSF

Organism	N (%)
Bacterial Meningitis	
Streptococcus pneumonia	29 (32.1%)
Nesseria species	20 (22.3%)
Haemophilus species	16 (17.6%)
Staphylococcus aureus	10 (11.3%)
Escherichia coli	6 (6.6%%)
Enterococcus species	4 (4.4%)
Klebsiella pneumonia	2 (2.2%)
Acinetobacter species	2 (2.2%)
Pseudomonas species	1 (1.1%)
Viral Meningitis	27(17.53%)
Coxsackie Virus	11 (40.7%)
Herpes viruses	8 (29.6%)
Measles virus	5 (18.5%)
Influenza virus	3 (11.1%)
Tuberculous Meningitis	
Mycobacterium tuberculosis	21 (13.63%)
Fungal Meningitis	
Cryptococcus species	15 (9.7%)

Discussion

Meningitis is a medical emergency. It is a life-threatening infectious disease associated with fatal complications (10). The recent medical literature reveals that it is prevalent globally but its prevalence is much higher in tropical countries (11). In developed countries the incidence rate of meningitis in children is quite low (11). However, in the developing countries like Pakistan, we still observe a huge burden of ailment caused by meningitis in pediatric population (12). The results of our study revealed that the age of study population ranged from 1 month to 12 years and seventy-five percent of them were below 5 years. This finding is consistent with that a study from Aga Khan University Hospital, Karachi, in which the frequency of children having age less than five years was 67 % (12). In our study the female gender showed a preponderance towards the development of disease, it is in contrast to the study by Farag H et al (13). This Egyptian study revealed that the male gender was a predominant population of their study (62.9%). In our study we also found that 127 patients (82.4%) belonged to the rural areas. This finding can be correlated with the fact that in most of the rural areas of Pakistan, a huge number of children remain un-vaccinated (14). So the high incidence of meningitis in rural areas can be justified due to the vaccination failure or the lack of vaccination against the common causative agents of meningitis. In the current study, it was found that acute bacterial meningitis was the most common entity among various types of infectious meningitis (59.1%). This finding is coherent with the results of studies by Farag H et al and Jawaid A et al, which reported the frequency of acute bacterial meningitis as 65.2% and 56% respectively (9,13). These values are very close to findings of our study. Cryptococcal meningitis is a fungal infection involving CNS. It is the type of infectious meningitis which mainly affects people with immune deficiencies, such as AIDS or people with malignancy. In our study we excluded all the patients having immune deficiencies (15). Despite the exclusion of immune compromised patients, the frequency of cryptococcal meningitis was 9.7% in our study, this finding is strikingly surprising. However, tuberculous meningitis was found in 13.63% of study population. This finding can be compared by another Pakistani study in which its frequency was 16% (12). The discoveries of the above mentioned study are very close to the findings of our study. This high incidence of tuberculous meningitis in Pakistani children can be attributed to the high prevalence of TB in Pakistan. However, further robust studies are required to explore this aspect in a focused manner. In our study the common sign and symptoms of disease were fever (91%), irritability (64.3%), vomiting (49.4%), headache (40.3), drowsiness (30.5%), neck rigidity (27.9%), Brudzincski's sign (18.8%), Kerning's sign (14.3%), bulging fontanels (9%), focal neurological signs (7.1%) and dilated poorly reactive pupils (2.6%). Many of these results of our study are in compliance with a study by Farag H et al (13). In another study by Karanika M et al the presenting complaints were fever 94.4%, vomiting 59.8%, headache 52.1%, irritability 28.1%, fits 20.5% and drowsiness 13.5% (16). The observations of this study also support the findings of our study. However, the mortality rate was quite high in our study (14.3%) in contrast to the studies conducted at highly well equipped and resource-rich centers of America and Canada (17). On the other hand, an Egyptian study reports the overall fatality rate as 10.3% which is relatively close the findings of our study (13). It is recommended that in suspected cases of meningitis, culture should be obtained and empirical antimicrobial therapy should be started without any delay. The diagnosis of

meningitis is confirmed by CSF culture. Consequently, in our study the results of CSF culture revealed that Streptococcus pneumoniae, Nesseria species, Haemophilus species and Staphylococcus aureus are the leading etiological factors of acute bacterial meningitis; and the relative frequency of these organisms which were being isolated from CSF was 32.1%, 22.3%, 17.6%, and 11.3% respectively. This discovery of our study is not consistent with the findings of European studies which describes a paradigm change in the prevalence of Streptococcus pneumoniae, Haemophilus influenzae type b and Neisseria meningitides in developed countries due to the administration of vaccines (18-19). Similarly, in our study, the percentage of E. coli isolated from CSF was only 6.6%, conversely in a study conducted in China reports that E. coli was the most prevalent pathogen, which was identified in 28.5% of isolates obtained from the children included in their study (10). So, the etiological pathogens responsible for infectious meningitis have been found to be relatively diverse. Therefore, antimicrobial sensitivity data should be continuously reviewed to select an appropriate antimicrobial drug for the effective management of infectious meningitis.

Conclusion

Our study concludes that the infectious meningitis is a common disease of Pakistani pediatric population. The female children of rural areas, having age less than 5 years are more prone to suffer from this disease. Fever, irritability, vomiting, headache, drowsiness, and neck stiffness are the common presenting complaints. Among various types of infectious meningitis acute bacterial meningitis is the most common type which can be prevented by proper and complete vaccination of children. The antimicrobial sensitivity data should be continuously monitored, and an appropriate antimicrobial drug should be used for the effective management of this serious CNS infection.

Reference

1. Baraff LJ, Lee SI, Schriger DL: Outcomes of bacterial meningitis in children: a meta-analysis. Pediatr Infect Dis J. 1993, 12: 389-394. 10.1097/00006454-199305000-00008
2. Agrawal S, Nadel S. Acute bacterial meningitis in infants and children: epidemiology and management. *Paediatr Drugs*. 2011;13:385-400.
3. de Jonge RC, van Furth AM, Wassenaar M, et al. Predicting sequelae and death after bacterial meningitis in childhood: a systematic review of prognostic studies. *BMC Infect Dis*. 2010;10:232.
4. Kaplan SL. Bacterial meningitis in children older than one month: clinical features and diagnosis. *UpToDate.*www.uptodate.com/contents/bacterial-meningitis-in-children-older-than-one-month-clinical-features-and-diagnosis. Accessed February 28, 2018
5. Luksic I, Mulic R, Falconer R, et al. Estimating global and regional morbidity from acute bacterial meningitis in children: assessment of the evidence. *Croat Med J*. 2013;54:510-518.
6. Brouwer MC, Tunkel AR, van de Beek D. Epidemiology, diagnosis, and antimicrobial treatment of acute bacterial meningitis. Clinical microbiology reviews. 2010 Jul 1;23(3):467-92.
7. Durand, M. L., S. B. Calderwood, D. J. Weber, S. I. Miller, F. S. Southwick, V. S. Caviness, Jr., and M. N. Swartz. 1993. Acute bacterial meningitis in adults. A review of 493 episodes. N. Engl. J. Med. 328:21-28.
8. World Health Organization. Control of epidemic meningococcal disease. WHO Practical Guidelines. Second Edition. 1988. Geneva.
9. Karou SD, Balaka A, Bamoké M, Tchelougou D, Assih M, Anani K, Agbonoko K, Simpore J, de Souza C. Epidemiology and antibiotic resistance of bacterial meningitis in Dapaong, northern Togo. Asian Pacific journal of tropical medicine. 2012 Nov 1;5(11):848-52.
10. Jiang H, Su M, Kui L, Huang H, Qiu L, Li L, Ma J, Du T, Fan M, Sun Q, Liu X. Prevalence and antibiotic resistance profiles of cerebrospinal fluid pathogens in children with acute bacterial meningitis in Yunnan province, China, 2012-2015. PloS one. 2017 Jun 29;12(6):e0180161.
11. Lagunju IA, Falade AG, Akinbami FO, Adegbola R, Bakare RA. Childhood bacterial meningitis in Ibadan, Nigeria--antibiotic sensitivity pattern of pathogens, prognostic indices and outcome. African journal of medicine and medical sciences. 2008 Jun;37(2):185-91.
12. Jawaid A, Bano S, Haque A, Arif K. Frequency and outcome of meningitis in Pediatric Intensive Care Unit of Pakistan. *Journal of College of Physicians and Surgons Pakistan.* 2016;26(8):716.
13. Farag HM, Abdel-Fattah M, Youssri A. Epidemiological, clinical and prognostic profile of acute bacterial meningitis among children in Alexandria, Egypt. *Indian Journal of Medical Microbiology*. 2005;23(2):95.
14. Shaikh AR. Immunization Coverage in a Rural Area. Journal of Rawalpindi Medical College. 2016 Mar 30;20(1):48-52.
15. Sloan DJ, Parris V. Cryptococcal meningitis: epidemiology and therapeutic options. Clinical epidemiology. 2014;6:169.
16. Karanika M, Vasilopoulou VA, Katsioulis AT, Papastergiou P, Theodoridou MN, Hadjichristodoulou CS. Diagnostic clinical and laboratory findings in response to predetermining bacterial pathogen: data from the

Meningitis Registry. PLoS One. 2009 Jul 29;4(7):e6426.
17. Baccarini C, Ternouth A, Wieffer H, Vyse A. The changing epidemiology of meningococcal disease in North America 1945–2010. Human vaccines & immunotherapeutics. 2013 Jan 1;9(1):162-71.
18. Ba O, Fleming JA, Dieye Y, wa Mutombo BM, Ba M, Cisse MF, et al. Hospital surveillance of childhood bacterial meningitis in Senegal and the introduction of Haemophilus influenzae type b conjugate vaccine. The American journal of tropical medicine and hygiene. 2010;83(6):1330–5.
19. Elenga N, Sicard S, Cuadro-Alvarez E, Long L, Njuieyon F, Martin E, et al. Pediatric bacterial meningitis in French Guiana. Medecine et maladies infectieuses. 2015;45(11–12):441–5.