ORIGINAL ARTICLE

PROTOCOLS OF TREATMENT OF MENINGITIS IN MEDICAL DEPARTMENT: ARE THERE ANY?

Saqib Malik, Najma Rehman, Farhat Naz, Zainab Syed, Zarnab Zainab, Romana Irshad*

Department of Medicine, *Department of Pathology, Ayub Medical College, Abbottabad-Pakistan

Background: Meningitis, whether viral or bacterial is associated with high mortality rate and risk of severe lifelong disability. Early antibiotics administration and favourable outcomes have been demonstrated by previous studies. The purpose of the study was to evaluate whether the patients with suspected meningitis in general medicine department of Ayub Teaching Hospital Abbottabad were being managed according to protocols. **Methods:** This cross-sectional study was carried out in the Medical Department of Ayub Teaching Hospital Abbottabad from March 2018-March 2019 in which data was retrospectively collected from the hospital records of all patients with suspected meningitis admitted in Medical Ward. SPSS version 20.0 was used for data analysis. **Results:** Out of 41 patients in the study 19 (51.74%) were male. Viral encephalitis accounted for 23 (56.1%) tuberculous meningitis for 14 (34.1%), and 4 (9.8%) patients had septic meningitis. Lumbar puncture for CSF examination was performed in 38 (92.7%). Out of 41 patients, 19 (46.3%) received a combination of Ceftriaxone, Acyclovir and Dexamethasone, 16 (39.0%) patients received anti tuberculous treatment (ATT), Dexamethasone and Streptomycin combination, 3 (7.35%) patients were given Ceftriaxone (2g) and Dexamethasone and 1 (2.45%) patient was given a combination of Ceftriaxone(2gm) along with Vancomycin (1gm) and Dexamethasone; while 2(4.9%) patients were given a combination of Acycolvir and Dexamethasone. **Conclusion:** This study identified practice gaps in the management of patients with suspected meningitis according to guidelines, as lumbar puncture and CSF-RE were not timely done and proper laboratory records were not maintained. Secondly blood culture facilities were not available in the hospital.

Keywords: Tuberculous Meningitis; Viral Encephalitis; Lumbar Puncture

Citation: Malik S, Rehman N, Naz F, Syed Z, Zainab Z, Irshad R. Protocols of treatment of meningitis in medical department: Are there any? J Ayub Med Coll Abbottabad 2020;32(3):369–72.

INTRODUCTION

Meningitis is a major global public health challenge associated with high mortality and long-term adverse sequelae in survivors. It can pathologically be defined as the inflammation of the coverings (meninges) of the central nervous system (brain and spinal cord) chiefly caused by infection with bacteria and viruses. Characteristic feature of meningitis is the elevation of white blood cells in the cerebrospinal fluid usually >5 leucocytes/μL.[1]

Patients with meningitis typically present with signs and symptoms of fever, headache, neck stiffness and altered mental state. Majority of these patients have at least two of these features and demand urgent work up for diagnosis of meningitis.[2]

Guidelines recommend that lumbar puncture (LP) should be performed in suspected cases of meningitis within the 1st hour of arrival of patient at the hospital, provided there are no contraindications to the procedure. This should immediately be followed by commencement of treatment. If LP cannot be performed within the first hour, treatment should be started as soon as blood is drawn for cultures, and LP should still be performed within 4 hours of commencing antibiotics for identification of causative organism. The time available to sample blood culture is limited and should be done promptly as it can become difficult to identify the causative bacteria in the sample after commencement of treatment.[3]

On the basis of duration of symptoms meningitis is classified as acute (<5 days) and subacute (>5 days). Typically, patients with Tuberculous and fungal meningitis present with subacute and chronic symptoms whereas bacterial and viral meningitis present with less than 5 days history of symptoms. Acute bacterial meningitis has a high mortality rate and sinister neurological sequelae. It requires urgent antibiotic therapy and adjuvant corticosteroids therapy especially in cases of pneumococcal meningitis therefore, it should always be considered in differential diagnosis.[4] Cases of tuberculous meningitis are difficult to diagnose and manage as cultures for acid fast bacillus (AFB) are insensitive and can take several weeks to grow the organism, but patients require prompt treatment in the form of anti-tuberculous treatment (ATT) and steroids to get a favourable clinical outcome.[5]

According to the WHO bacterial meningitis was estimated to be responsible for about 300,000,

deaths in all ages in the year 2015, with highest number of deaths in infants and young children.[6] In spite of improvements in health care, acute bacterial meningitis presents a worldwide public health problem, especially in developing countries with inadequate health care systems, poverty and unhygienic living conditions making people vulnerable to contract the disease and reduce their chances of getting optimal treatment.[7]

The incidence rate of meningitis has increased over the years. According to a systematic analysis the incidence of meningitis globally increased from 2.5 million in 1990 to 2.82 million in 2016.[1] An estimated 4100 cases and 500 deaths from bacterial meningitis were reported in the USA from 2003 to 2007, while developing countries face the most burden of disease. The Sub-Saharan region of Africa is faced with the highest incidence rate of meningitis with a report estimating 80,000 suspected cases of meningitis, resulting in more than 4000 deaths alone in the year 2009.[8,9]

Studies have shown *S. pneumoniae* to be the leading agent in the cases of bacterial meningitis, especially in areas where there is high vaccination rate such as North America.[10] In recent times serogroup B *N. meningitides* has been the agent for majority cases of meningococcal diseases in Europe, whereas serogroup C has taken the lead in US.[11]

Among viruses, enteroviruses and herpes viruses are commonly reported agents for meningitis but their epidemiology varies in different countries. Herpes virus meningitis has a high incidence rate in Finland, whereas enterovirus is the leading cause of viral meningitis in Spain. As antibiotics are often used prior to diagnosis of viral meningitis, it can result in unnecessary long courses of antibiotics and prolongation of hospital stay for patients.[12]

Encephalitis caused by herpes simplex and varicella zoster is often treated with antivirals such as acyclovir, but its effectiveness in cases of acute disease is yet to be determined. Once a diagnosis of viral meningitis is made, symptomatic treatment should be initiated and efforts should be made to reduce the length of hospital stay for the patients. Theoretically, quick diagnosis can be made as it only takes a few hours to perform lumbar puncture and PCR.[13]

This study was undertaken to determine that whether meningitis is being treated as per internationally accepted guidelines or not. We could not perform blood and CSF cultures to detect the causative organisms of meningitis due to limited availability of resources including bacteriological culture facilities; lack of BACTEC automated culture system and viral studies in our setup. Thus, all patients with acute meningitis were empirically treated with antibiotics such as ceftriaxone and acyclovir and then specifically on the basis of report of just CSF-RE.

MATERIAL AND METHOD

This cross-sectional study was carried out in the Medical Unit of Ayub Teaching Hospital Abbottabad from March 2018-March 2019 in which data was retrospectively collected from the hospital records of all patients with suspected meningitis admitted in Medical Ward. Variables of the study were patient's name, age, gender, diagnosis, lumbar puncture, CSF-RE, blood culture, CT brain, treatment given, outcome and guidelines followed for treating meningitis. After ethical approval, data was collected and SPSS version 20.0 was used for its analysis.

RESULTS

A total of 41 patients were included in the study. Mean age was 45.56±22.316 ranging from 12 to 90 years. Nineteen (51.74%) out of 41 patients in the study were male and 22 (40.23%) were female. Tuberculous meningitis accounted for 14 (34.1%) cases, viral encephalitis 23 (56.1%) and 4 (9.8%) patients had septic meningitis.

As shown in table-1, the proportion of patients upon whom LP for CSF examination was performed. CT scan brain was carried out in 38(92.7%) patients. Blood culture was not performed in any of the patient. Table-2 shows different treatment regimens used.

There were 8 (19.5%) expiries, 32 (78.0%) patients improved without any disability and 1 (2.4%) patient improved after suffering third cranial nerve palsy.

Table-1: CSF-RE

	Frequency	Percent
Done	38	92.7
Not done	3	7.3
Total	41	100.0

Table-2: Treatment Received

	Frequency	Percent
Ceftriaxone, acyclovir, Dexamethasone	19	46.3
ATT, Decadron, Streptomycin	16	39.0
Ceftriaxone 2gm, Dexamethasone	4	9.8
Acyclovir, Dexamethasone	2	4.9
Total	41	100.0

DISCUSSION

Meningitis is a disease that requires urgent diagnosis and treatment in order to avoid its life-threatening consequences. Following set protocols is essential for optimum management and prevention of complication of meningitis. This study was conducted to assess how adult patients having meningitis were managed in the medical department

of Ayub Teaching Hospital, in correspondence with internationally accepted protocols.

In our study viral meningitis had the highest proportion of cases at 56.1%, followed by tuberculous at 34.1% and bacterial meningitis had the lowest proportion of 4%. This gives an overview of epidemiology of the different types of meningitis in our region and is in contrast to a study conducted in the United States[14] where viral and bacterial meningitis accounted for 61.8%, 21.4% (unknown) and 14.1% of the cases respectively. The difference in the studies is due to the different epidemiological factors in the two regions.

Almost all patients in the study underwent CT scan (38/41), this is in contrast to the ESCMID guidelines[15] which recommend imaging study to be performed only in patients with signs and symptoms of focal neurological deficits, new-onset seizures, severely altered mental status and immune-compromised state. However, CT scan is performed as a routine investigation in our clinical setting before doing lumbar puncture whether it is indicated or not. Previous studies show that unfavourable outcome is largely due to a failure to start antibiotic regimen on time because of the delay caused by unnecessary cranial imaging.

In line with the UK joint specialist guidelines[3] for meningitis, lumbar puncture was performed for majority of the patients (38 out of 41) in our study. The guidelines recommend that lumbar puncture should be performed within the initial 1-hour period of patient's arrival to the hospital, however, in our study the exact timing of lumbar puncture was not known due to scarcity of clinical record of the patients. However, it was noted that sometimes lumbar puncture performed after 24-48 hours of admission of patients to the hospital and sometimes it was refused by the attendants delaying the accurate diagnosis and management.

The diagnostic test for bacterial meningitis is blood culture. A positive blood culture helps in determining the susceptible microbes along with suitable antibiotics. The same UK joint specialist guidelines[3] for meningitis recommend blood culture to be taken before commencing antibiotic treatment and also recommend PCR for diagnosis of different strains of viral meningitis, but in our study blood cultures and PCR were not performed for any of our patients mainly due to unavailability of facilities at the hospital and financial constraints of the patients.

For empirical treatment, before availability of CSF-RE reports, the guidelines recommend initiating IV ceftriaxone in a dose of 2 grams twice a day and its administration should not exceed 1 hour. Treatment at medical department of ATH is in accordance with the set treatment protocols. Thirty-nine patients in our study received IV ceftriaxone. The specific treatment regimen for bacterial meningitis patients should be determined by the blood culture and sensitivity, but this was never determined in our set up. According to guidelines when ceftriaxone is administered in combination with either vancomycin or rifampicin it yields adequate CSF sterilization after 24 hours as compared to ceftriaxone alone. But vancomycin was given only to one patient due to non-availability in hospital but it was observed that our patients still did well with ceftriaxone alone. The advised duration of treatment is 10–14 days and our patients were managed accordingly.[15]

The guidelines also strongly recommend starting dexamethasone (10 mg QID for 4 days) for all adults either shortly before or simultaneously with the first dose of antibiotic. In our study, IV Dexamethasone was given to all patients but not in a recommended dose, majority of the patients were given 4 mg dexamethasone twice or thrice a day. In viral meningitis the guidelines show treatment with acyclovir is controversial and has no proven effects on the outcome of the patients. Treatment recommended for viral meningitis is simple analgesics and fluids however in our study cases of CSF-RE based viral meningitis all received treatment with acyclovir.

For uncomplicated cases of TBM (including cerebral tuberculomas without meningitis). United Kingdom guidelines recommend treatment with rifampicin, isoniazid, pyrazinamide and a fourth agent (streptomycin, ethambutol, or prothionamide) for the first two months followed by rifampicin and isoniazid for 10 months.[16] Our patients were started on ATT as per guidelines but were lost to follow up.

Bacterial meningitis is almost always fatal if not properly treated, whereas viral meningitis usually resolves spontaneously and is rarely fatal. In adults, meningitis is associated with mortality rate of 19–37%.[17] The data from our study showed overall mortality of meningitis for all recorded cases in medical department of Ayub Teaching Hospital to be 19.5%. Study conducted by Namani *et al* showed a 2% mortality rate and 16% incidence of neurological complications in children. On the other hand, the same study showed the figure was 10% and 35% in adults.[18] In our study only 1 patient developed 3rd nerve palsy while rest of the patients were discharged without any disability.

This study has the following limitations. First, due to retrospective study design it was impossible to standardize the quality of information documented in the patients' folders and the clinical record of most of the patients was not complete. This structure of study design did not enable us to acquire

extra details, for example seriousness of the ailment and long-term follow-up to assess the long-term sequelae of meningitis in our patients. Secondly, data was gathered from a single hospital, so the results may not be relevant to population on a broader scale. Thirdly, we included patients who had presented to a single medical unit. Fourthly etiological agent was not confirmed in our patients and this result is due to non-availability of specific laboratory tests, specific culture medium and viral studies in our setup. In addition, hospital laboratory is not providing 24 hours service even for simple CSF-RE and administratively after the working hours of our hospital, i.e., 6 p.m. the specimen is not usually accepted.

Although there have been many limitations, but this study remains the biggest, we believe, till date, to provide information regarding the epidemiology, management and outcome of patients with meningitis in a setting located in a poor socioeconomic place like Abbottabad.

In a country like Pakistan where there is no control over sale of antibiotics without prescription, blood and CSF culture, and diagnostic PCR remains the investigations of choice for identifying the causative agent of meningitis.

CONCLUSION

From this study we conclude that in Medical department of Ayub Teaching Hospital, guidelines for clinical management of meningitis were not completely followed.

AUTHORS' CONTRIBUTION

SM: Concept and design of study, main article writing, final approval of version. NR, ZS: Data collection. FN, RI: Statistical analysis. ZZ: Revisiting critically.

REFERENCES

1. Zunt JR, Kassebaum NJ, Blake N, Glennie L, Wright C, Nichols E, *et al*. Global, regional, and national burden of meningitis, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol 2018;17(12):1061–82.
2. van de Beek D, de Gans J, Spanjaard L,Weisfelt M, Reitsma JB, Vermeulen M. Clinical features and prognostic factors in adults with bacterial meningitis. N Engl J Med 2004;351(18):1849–59.
3. McGill F, Heyderman RS, Michael BD, Defres S, Beeching NJ, Borrow R, *et al*. The UK joint specialist societies guideline on the diagnosis and management of acute meningitis and meningococcal sepsis in immunocompetent adults. J Infect 2016;72(4):405–38.
4. Koster-Rasmussen R, Korshin A, Meyer CN. Antibiotic treatment delay and outcome in acute bacterial meningitis. J Infect 2008;57(6):449–54.
5. Hasbun RO. Cerebrospinal fluid in central nervous system infections. Chapter 2. In: Infections of the Central Nervous System. 4th ed. Edited by Scheld, Whitley & Marra: 2014; p.4–23.
6. WHO. Defeating meningitis by 2030: baseline situation analysis. Geneva: World Health Organization; 2019.
7. Miller R, Houlberg K. Meningitis service-age personnel. J Royal Nav Med Serv 2015;101(1):63–8.
8. WHO. Meningococcal meningitis: Fact sheet 2017. [Internet]. World Health Organization updated December 2017 [cited 2017 Nov 9] Available from: http://www.who.int/mediacentre/factsheets/fs141/en/
9. WHO. Number of suspected meningitis cases and deaths reported 2010 epidemiological season. [Internet]. World Health Organization [cited 2017 Nov 9]. Available from: https://www.who.int/gho/epidemic_diseases/meningitis/suspected_cases_deaths_text/en/
10. Gounder PP, Zulz T, Desai S, Stenz F, Rudolph K, Tsang R, *et al*. Epidemiology of bacterial meningitis in the North American Arctic, 2000–2010. J Infect 2015;71(2):179–87.
11. Pelton SI. The Global Evolution of Meningococcal Epidemiology Following the Introduction of Meningococcal Vaccines. J Adolesc Health 2016;59(2 Suppl):S3–11.
12. de Ory F, Avellon A, Echevarria JE, Sacnhez-Seco MP, Trallero G, Cabrerizo M, *et al*. Viral Infections of the central nervous system in Spain: a prospective study. J Med Virol 2013;85(5):554–62.
13. Landry ML, Greenwold J, Vikram HR. Herpes simplex type-2 meningitis: presentation and lack of standardized therapy. Am J Med 2009;122(7):688–91.
14. Hasbun R, Rosenthal N, Balada-Llasat JM, Chung J, Duff S, Bozzette S, *et al*. Epidemiology of Meningitis and Encephalitis in the United States, 2011-2014. Clin Infect Dis 2017;65(3):359–63.
15. van de Beek D, Cabellos C, Dzupova O, Esposito S, Klein M, Kloek AT, *et al*. ESCMID guideline: diagnosis and treatment of acute bacterial meningitis. Clin Microbiol Infect 2016;22(Suppl 3):S37–62.
16. Modi M, Goyal MK, Jain A, Sawhney SS, Sharma K, Vyas S, *et al*. Tuberculous meningitis: Challenges in diagnosis and management: Lessons learnt from Prof. Dastur's article published in 1970. Neurol India 2018;66(6):1550–71.
17. van de Beek D, de Gans J, Tunkel AR, Wijdicks EF. Community-acquired bacterial meningitis in adults. N Engl J Med 2006;354(1):44–53.
18. Namani SA, Koci RA, Qehaja-Bucaj E, Ajazaj-Berisha L, Mehmeti M. The epidemiology of bacterial meningitis in Kosovo. J Infect Dev Ctries 2014;8(7):823–30.

Submitted: November 20, 2019	*Revised: February 3, 2020*	*Accepted: February 21, 2020*

Address for Correspondence:

Najma Rehman, Department of Medicine, Ayub Medical College, Abbottabad-Pakistan
Email: tufflogic2019@gmail.com