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Epidemiology of Meningitis Studied at a University Hospital in Zahedan, South-Eastern Iran

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Background: Meningitis is an inflammation of the membranes, which surround the brain and spinal cord. Early treatment of bacterial meningitis can prevent serious complications. In the last two decades, three vaccines have been developed against the three main bacterial species implicated in meningitis of children in western countries and vaccine-preventable invasive bacterial meningitis has decreased substantially in the past few years. However, none of the developed vaccines are part of our childhood immunization schedule.
Objectives: This study aimed to search the epidemiology of meningitis in Zahedan.
Patients and Methods: In this cross-sectional survey, we studied all patients with meningitis for ten years, from May 2004 to May 2014, who had been referred to our hospital. The patients were evaluated according to their sex, age, clinical features, risk factors, pathogenic microorganisms, form of infection (acute or chronic) and clinical outcome.
Results: Among the 53 patients with meningitis (47% females; 53% males with mean age 36 years) 47 cases (83%) had acute meningitis and six cases (17%) had chronic meningitis (four cases of tuberculosis and two cases of brucellosis). From the 47 cases with acute meningitis, only one case had a positive cerebrospinal fluid (CSF) culture for meningococci and 46 patients had negative CSF culture. The most common clinical symptoms was fever and headache (90%) and the least was seizure (9%). Mortality rate was 7.5% (4 cases). There were no significant risk factors except for two patients with acute meningitis and two cases with chronic meningitis.
Conclusions: According to negative CSF cultures in acute meningitis, CSF culture using the BACTEC automated system and specific viral tests is recommended for detection of the etiological agents of viral and bacterial meningitis, particularly in the Iranian population where patients use antibiotics without prescription.

Keywords: Epidemiology; Meningitis; Acute; Chronic; Outcome; Bacterial; Viral

1. Background

Meningitis is the inflammation of the membranes surrounding the brain and spinal cord. Early treatment of bacterial meningitis can prevent serious complications such as hearing loss, memory difficulty, learning disabilities, brain damage, seizures and death (1-3). Meningitis can be life-threatening and the condition is classified as a medical emergency. Meningitis usually results from a viral infection, yet the cause may also be a bacterial or less commonly, fungal infection (4, 5). Viral meningitis may improve without treatment, yet bacterial meningitis is very serious and requires prompt antibiotic treatment. Since bacterial infections are the most serious and can be life-threatening, finding the source of infection is an important part of the treatment plan (5). Acute bacterial meningitis usually occurs when bacteria enter the bloodstream and migrate to the brain and spinal cord. However, it can also occur when bacteria invade the meninges, as a result of an ear or sinus infection, a skull fracture, or rarely, after a brain surgery. The most common bacteria that can cause acute bacterial meningitis include: *Streptococcus pneumoniae* (pneumococcus), *Neisseria meningitidis* (meningococcus), *Haemophilus influenzae*, and *Listeria monocytogenes* (3-6). Chronic forms of meningitis occur when slow-growing organisms such as mycobacterium tuberculosis invade the membranes and fluid surrounding the brain. Although, acute meningitis occurs suddenly over several hours, chronic meningitis develops over two weeks or more (5). Nevertheless, the signs and symptoms of chronic meningitis such as headaches, fever, vomiting and mental cloudiness are similar to those of acute meningitis. Fungal meningitis is relatively uncommon and causes chronic meningitis (3-5). Cryptococcal meningitis is a common fungal form of the disease which affects people with immune deficiencies, such as AIDS or people with malignancy (6, 7). Risk factors for meningitis include: skipping vaccinations, age (most cases of viral meningitis occur in children younger than five years old and bacterial meningitis commonly affects people under 20), living in a community setting (college students living in dormitories, personnel on military bas-

es, and children in boarding schools and child care facilities are at increased risk of meningococcal meningitis), and factors that may compromise patients' immune system including; AIDS, use of immunosuppressant drugs, and removal of the spleen (3-6). There are many reports about the epidemiology of meningitis and according to the community under study, age of cases and other risk factors, agents and clinical outcome are different (8-16).

2. Objectives

The aim of the present study was to detect the etiological agents of meningitis, clinical features, risk factors, and clinical outcomes of patients who were admitted to a referral regional hospital in Zahedan.

3. Patients and Methods

In this cross-sectional descriptive study, we studied all patients with meningitis for 10 years, from May 2004 to May 2014, who had referred to a regional hospital in Sistan and Baluchestan Province in the Southeast of Iran. The inclusion criteria for patients included having CSF results in their files and being older than 19 years. The patients were evaluated according to their sex, age, clinical features, risk factors, pathogenic microorganism, form of infection (acute or chronic) and clinical outcome.

4. Results

Among 53 patients with meningitis (47% females; 53% males with mean age of 36 years) 47 cases (83%) had acute meningitis and six cases (17%) had chronic meningitis (four cases of tuberculosis and two cases of brucellosis). From 47 cases with acute meningitis, only one case had a positive cerebrospinal fluid (CSF) culture for meningococci and 46 patients had negative CSF culture. The most common clinical symptoms were fever and headache (90%). Other clinical features were vomiting (69%), confusion (11%) and seizure (9%). Mortality rate was 7.5% (4 cases). There were no significant risk factors except in two patients with acute meningitis (army hostel, HIV positive) and two patients with chronic meningitis (one patient had diabetes and the other was a shepherd). Brain edema was found in five cases through MRI and brain CT scan and three patients with chronic meningitis had hydrocephalus.

5. Discussion

Meningitis is inflammation of the protective membranes covering the brain and spinal cord. The inflammation may be caused by infection with viruses, bacteria, or other microorganisms, and less commonly by certain drugs. The most common symptoms of meningitis are headache, vomiting and neck stiffness associated with fever and altered consciousness. Children often exhibit only nonspecific symptoms, such as irritability and drowsiness. A lumbar puncture diagnoses or excludes meningitis. The first treatment in acute meningitis consists of promptly administered antibiotics and sometimes antiviral drugs. Corticosteroids can also be used to prevent complications from excessive inflammation. Meningitis can lead to serious long-term consequences such as deafness, epilepsy, hydrocephalus and cognitive deficits, especially if not treated quickly. Some forms of meningitis (such as those associated with meningococci, *Haemophilus influenza* type B, pneumococci or mumps virus infections) may be prevented by immunization. Unfortunately, we could not detect microorganisms in patient cultures except for five cases (one bacterial and four mycobacterial). These negative results may be due to use of antibiotics before sampling, or limited number of bacteriological culture facilities and lack of BACTEC automated culture system. Thus, we had no positive cultures and treated all patients with acute meningitis using antibiotic such as ceftriaxone and vancomycin. Classic symptoms and signs of bacterial meningitis in culture-positive patients were fever, headache, vomiting and confusion. Due to limited microbiological culture and viral studies, we had no significant positive cultures. In an American study in 2014, they found that *S. pneumoniae* was the leading identifiable cause of bacterial meningitis, and this is when there has been a significant decrease in the incidence and mortality from meningitis, associated with the introduction of conjugated vaccines. The incidence of *Neisseria meningitidis* infection has decreased from 0.721 per 100000 people in 1997, to 0.123 per 100000 people in 2010 which has placed this pathogen close to common bacterial causes of nosocomial meningitis such as staphylococcus, Gram-negative bacteria and *Haemophilus influenza* (12). In Morrill's study, the incidence of pneumococcal diseases decreased significantly by 3.5% per year in outpatients and increased non-significantly by 0.2% per year in inpatients. Among inpatients with serious infections, risk factors for pneumococcal infection included: respiratory disease, diabetes and renal failure. Invasive disease (37.4% versus 34.9%, P = 0.004) and mortality (14.0% versus 12.7%, P = 0.045) were higher in non-vaccinated patients compared to vaccinated patients (13). Among our patients, only four cases had significant risk factors. Chiang's study was a systematic review and meta-analysis, which evaluated the risk factors and clinical outcomes of 1636 children. Risk of death was 19.3% and probability of survival without neurological sequelae was 36.7%. Among survivors, risk of neurological sequelae was 53.9%. Diagnosis during the most advanced disease stage occurred in 47% of 657 patients in one study and was associated with worse outcomes than was earlier diagnosis. Fatality rate in our study was 7.5% and these patients had referred to the hospital late (14). Namani's study compared meningitis cases in 2000 with 2010 and showed a 35.5% decline in incidence and a decrease fatality rate from 10% to 5% (15). They detected a lower mortality rate (5% versus 2%) and a lower incidence of neurological complications in children (13% versus 16%) as compared to

adults (32% versus 10% and 16% versus 35%, respectively). *Neisseria meningitidis* was the most common pathogen of bacterial meningitis during both study periods and bacterial meningitis was most common in the pediatric population (15). In this study, during the year 2000, the mean age of pediatric cases was 3.2 years, while for adults it was 41 years. In 2010, the mean age of children with bacterial meningitis was 5.5 years while for adults it was 45 years. The median age for all bacterial meningitis cases was seven years (range: one month to 74 years). Most cases were male in both children and adult groups during both study periods, however, differences were not statistically significant ($P > 0.05$). The peak incidence in 2000 was in infants (40%), compared to increased incidence in children of 6–16 years (43%) in 2010. In our study 47% of patients were men and there was no significant difference between males and females ($P < 0/05$). In Mahmoudi et al. (16) study from Iran, among the 31 patients with possible invasive bacterial infections, 20 cases had positive CSF cultures. The isolated bacteria included *S. pneumoniae* (four cases), *H. influenzae* (2), *N. meningitidis* (1), *Klebsiella spp*. (1), *Acinetobacter spp*. (1), *Haemophilus spp* (1), *Staphylococcus aureus* (1), and the other cases had positive test results for *Mycobacterium tuberculosis*. In this study, brain edema was identified in four patients, subdural effusion in four, microabscess in one, and ventriculomegaly hydrocephalus in one patient. All the pneumococcal isolates were resistant to trimethoprim/sulfamethoxazole (SXT), five were resistant to penicillin, and four were resistant to ampicillin and ceftriaxone. All the three *H. influenzae* isolates were resistant to penicillin, and two were resistant to SXT. Among the meningococcal isolates, three were susceptible to ampicillin, ceftriaxone, cefotaxime, ceftizoxime and vancomycin. The *S. aureus* and coagulase-negative staphylococci isolates were susceptible to all antibiotics except SXT. Unfortunately, in our study, only one patient in the acute meningitis group had a positive CSF culture and the infectious agent was susceptible to ceftriaxone and resistant to ampicillin.

Our study has one important limitation: etiology was confirmed only in 13.41% of patients and this result is due to limited laboratory tests and a specific culture medium. The other causes can be due to the practice of partial treatment due to administration of antibiotics at the time or before the time of specimen collection. In addition, the Department of Microbiology, which is the only unit that services our clinical center, is not open 24 hours and does not accept specimens after 8 p.m. The pathogens causing meningitis are fastidious and require immediate processing to optimize recovery and identification.

The findings of this study provide information regarding the epidemiology, clinical features, and outcomes of bacterial meningitis among hospitalized patients in Zahedan. However, according to the negative CSF cultures in acute meningitis, a CSF culture using the BACTEC automated system is recommended for detection of the etiological agents of bacterial meningitis, particularly in our population where patients use antibiotics without prescription.

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