

Pediatric Meningoencephalitis; A Research on Patients Hospitalized in Zahedan, Southeastern Iran

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Background: Meningitis is a life-threatening disease and can lead to significant sequelae. Pediatric bacterial meningitis leaves some survivors with more significant sequelae if not treated, promptly. The advent of vaccine has changed the incidence of pediatric bacterial meningitis but these vaccines have not been used in routine childhood immunization schedule.

Objectives: The current study aimed to investigate the epidemiology, clinical features, etiologic agents and clinical outcome of meningoencephalitis among the pediatric group in Zahedan, Iran.

Patients and Methods: The current cross-sectional and descriptive study investigated the medical records of the patients with meningitis from May 2010 to May 2014. Then, the patients were evaluated according to sex, age, clinical feature, risk factor, etiologic agents, acute or chronic form, and clinical outcome.

Results: Among 55 patients with meningitis (42% girls and 58% boys; mean age of 8.5 months, age range of 45 days to nine years), 55 cases (98%) had acute meningoencephalitis and only one case (2%) had chronic tuberculous (TB) meningitis. Out of the 54 cases with acute disease, only six cases showed a positive test for etiologic agent. Forty-eight patients had negative CSF culture. The most common clinical symptom was fever (95%) and the least was seizure (16%). Mortality rate was 7.2% (four cases). There were no significant risk factors in children with illness, but there was a history of pulmonary TB in grandmother of the case with TB meningitis.

Conclusions: According to the obtained results, and finding a high negative cerebro-spinal fluid (CSF) culture in acute meningitis, it is recommended to use systems to detect the bacteria more, particularly in the patients whose parents use antibiotics before referring to a physician. Also, more specific viral tests are needed to detect the etiologic agents of viral meningitis.

Keywords: Acute Bacterial Meningitis; Meningoencephalitis; Outcome

1. Background

Bacteria and viruses cause a great majority of meningoencephalitis in the pediatric group. Bacterial meningitis is the most common factor among the children younger than four years, with a peak incidence in children between three to eight months (1-3). Male infants have a higher incidence of Gram-negative neonatal meningitis but, female infants are more susceptible to *Listeria monocytogenes* infection (2-4). Overall mortality for bacterial meningoencephalitis is about 5% to 10% and it is different according to the etiologic microorganism, patient's immunity level, and also the patient's age. In neonates, mortality is higher and it is 15% to 20%. Of the meningitides caused by the most common pathogens, *Streptococcus pneumoniae* meningitis has the highest mortality rate (26.3% to 30%), *Haemophilus influenzae* (Hib) meningitis has the next highest rate (7.7% to 10.3%), and *Nisseria meningitidis* has the lowest (3.5% to 10.3%). For tuberculous meningitis, morbidity and mortality are related to the stage of the illness. The rate of significant morbidity is 30% for stage I, 56% for stage II, and 94% for stage III. About 30% of

children with meningoencephalitis have neurologic sequelae (4-8). This rate varies by microorganisms and diseases, since *S. pneumoniae* has the highest rate of complications. Complications include seizures, bilateral hearing loss, and functionally important behavior, or neuropsychiatric disorders. Therefore, many of the children who get meningoencephalitis are very young and lack mature cognitive and motor skills, some of these sequelae may not be diagnosed for years (1-5). The causative agents, risk factors, and clinical outcomes were studied by researchers and the results were different according to the age and setting (1-8). Risk factors for meningitis include: skipping vaccinations, age (viral meningitis mostly occurs in children younger than five years and bacterial meningitis commonly affects people under 20), community settings (children in boarding schools and child care facilities are at higher risk), and factors that may compromise patient's immune system including: acquired immune deficiency syndrome (AIDS), use of immunosuppressant drugs, spleen removal, end-stage renal disease, and dia-

betes (2-6). In a follow-up study on the children who recovered from meningitis for five to ten years, one out of four school-aged meningitis survivors had either serious and disabling sequelae or an auditory dysfunction that impaired their performance in school (3). In infants, the signs and symptoms of meningitis are not always obvious due to the infant's inability to communicate symptoms. Therefore, parents, relatives, and kindergarten staff must pay very close attention to the infant's overall condition. If meningitis is suspected, several tests and procedures are needed to determine the diagnosis. However, early intravenous (IV) antibiotic treatment is often started before the tests (8-12). There are many reports about epidemiology of meningitis, risk factors, etiologic agents and clinical outcomes (5-17). Recently, etiologic agents and case fatality rates were evaluated in two studies in Iran by Mahmoudi et al. and Azadfar et al. (8, 17).

2. Objectives

The current research aimed to study the etiological agents of meningoencephalitis, the most common clinical manifestations, risk factors, and clinical outcomes among children and young adults who were admitted to a referral regional hospital in Zahedan, Iran.

3. Patients and Methods

The current cross-sectional and descriptive study investigated all the patients' medical records with meningoencephalitis from May 2010 to May 2014 in Ali-ibn-Abitaleb Hospital in Zahedan (Sistan and Baluchestan Province) in the Southeast of Iran. All patients who were evaluated in this study had been diagnosed with meningitis according to clinical features and Lumbar Puncture (LP). Inclusion criteria were: age younger than 18 years and those who had clinical manifestation for meningitis and underwent LP. Gram staining and microbiological diagnostic tests were used to detect etiologic microorganisms and when Tuberculosis and viruses were suspected as etiologic agents, the polymerase chain reaction method was also used. Imaging tests including brain magnetic resonance imaging (MRI) and computer tomography scan (CT-scan) were used before LP (in the suspected cases of brain edema or mass) or when the patients were suspected to have complication. Then, the patients were evaluated according to sex, age, clinical feature, risk factor, pathogenic microorganism, acute or chronic form, and clinical outcomes.

4. Results

Among 55 patients with meningitis (42% girls and 58% boys; mean age of 8.5 months, age range of 45 days to nine years), 55 cases (98%) had acute meningoencephalitis and only one case (2%) had chronic Tuberculous (TB) meningitis. Out of 54 cases with acute disease, one case had positive cerebro-spinal fluid (CSF) culture for *Streptococcus pneumoniae*, another case was positive for *Enterococcus*

sp., two cases were negative for *Staphylococcus coagulase* test, and one was positive for Herpes simplex virus (HSV) (detected by PCR). Forty-eight patients had negative CSF cultures. The most common clinical symptoms were fever 95%, vomiting 83%, altered level of consciousness 53%, neck stiffness 26%, profound fontanelle 26%, and the least was seizure 16%. Mortality rate was 7. 2% (4 cases). These four cases were treated late because they had referred to the hospital late. There were no significant risk factors in children with illness, but there was a history of pulmonary TB in grandmother of the case with TB meningitis. Brain edema was observed in five cases and four patients had hydrocephalus. Hemiplegia was observed in four cases and subdural empyema was reported in three cases.

5. Discussion

Meningitis disease is an inflammation of the meninges that surround the brain and spinal cord. The inflammation is most commonly caused by a virus or a bacterium, which get to the meninge from an infection in another part of the body through the bloodstream or from a site near the brain (1-5). The treatment and clinical outcomes are different according to the cause, age, and the risk factors (10-12). Results of the current study showed that among 54 cases with acute disease, one case had positive cerebro-spinal fluid (CSF) culture for *Streptococcus pneumoniae*; one case was positive for *Enterococcus* sp.; two cases were negative *Staphylococcus coagulase* test, and one case was positive for HSV. Unfortunately, forty-eight patients had negative CSF cultures but treated as bacterial meningitis by ceftriaxone and vancomycin and in the infant group ampicillin was added to this regimen. A high number of negative cultures in the hospital can be due to unsuitable sampling and also using antibiotic as self-treatment by parents, before being referred to the hospital. In the research by Beneteau, among 4806 cases of bacterial meningitis, 23 cases were caused by *S. bovis* (0. 5%). All cases with this infection were infants and among them, 15 cases (65. 2%) occurred in the neonatal period. The majority of infections with *S. bovis* occurred in premature infants (73.9%). In 21 cases, the diagnosis was based on a positive CSF culture (16). Unfortunately, in the current study, only seven cases had positive results for CSF test and 48 cases had negative cultures. Levy et al. conducted a survey from 2001 to 2012. They found that among 4808 patients with bacterial meningitis, 1406 cases had pneumococcal infection (29. 2%). The number of patients with this infection significantly decreased by 27.4% ($P = 0. 041$) after pneumococcal vaccination in children (from 2009 to 2012). For children younger than two years, the decrease was 28. 2% ($P = 0. 039$) (4). Patients in the current study did not receive any vaccine against Hib, pneumococcal and meningococcal infections because Iranian healthcare system does not immunize children against these pathogens. The study by Mahmoudi showed that the most common microorganisms associated with bacterial meningitis in children were *Streptococcus pneu-*

moniae (22.5%), *Haemophilus influenzae* (10%), and *Neisseria meningitidis* (10%). He reported the rate of mortality and sequelae as 10% and 35%, respectively. Ventriculomegaly hydrocephalus was found in one case positive for *Mycobacterium tuberculosis* meningitis (8). Another study in Iran by Azadfar et al. showed that among 45 CSF samples taken from children, HSV-1 was detected in four (8.8%) samples without any HSV-2 infections. To detect the virus, DNA extraction and PCR were performed (17). In the present study, 2% of the cases had positive results for HSV-1. In the study by Morrill, the incidence of pneumococcal diseases decreased significantly by 3.5% per year. Among the hospitalized patients, risk factors for pneumococcal infection included: respiratory disease, diabetes, and renal failure and invasive disease (37.4% versus 35%, $P = 0.004$) and mortality rate (14.0% versus 12.7%, $P = 0.045$) were higher in non-vaccinated patients when compared to those vaccinated (13). Among the current study patients, only one case had a significant risk factor and this patient was in close contact with his grandmother who had positive pulmonary TB smear. In the survey by Namani et al. *Neisseria meningitidis* was the most common pathogen of bacterial meningitis and bacterial meningitis was the most common in the pediatric population. In this study, the mean age of pediatric cases was 3.2 years, while for adults it was 41 years (15). Mean age was 8.5 months and age range was 45 days to nine years. In all the conducted studies, fever and vomiting were the most common features and seizure was the least. The current study had a major limitation like other studies in this city because, the etiology was confirmed only in seven patients and this result was due to the limited laboratory test and specific culture medium. The other cause for negative culture can be due to administration of antibiotics at the time or before the time of specimen collection.

According to negative CSF cultures in children with acute meningitis, CSF culture using the new systems such as BACTEC (a blood culture system) and PCR are recommended to detect the etiologic agents of bacterial meningitis, particularly in the population under study which patients had used antibiotics without prescription.

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