

Risk Factors Associated with Development of Post-Meningitic Hydrocephalus

1. Habibullah Babar 2. Asghar Khan Babar 3. Ismat Durrani

1. Asstt. Prof. of Pediatrics, 2. Dept. of Neurosurgery 3. Dept. of Pediatrics, Bolan Medical Complex Hospital, Quetta

ABSTRACT

Objective: To determine the frequency and risk factors associated with the development of post-meningitic hydrocephalus in children suffering from pyogenic meningitis.

Study Design: A descriptive as well as case control study.

Place and Duration of Study. Children admitted with the diagnosis of pyogenic meningitis from December 2010 to July 2011 in the Pediatric unit-2 of Bolan Medical Complex Hospital Quetta.

Patients and Methods: All the children admitted to the Pediatric Unit-2 of Bolan Medical Complex Hospital (BMCH) from December 2009 to July 2011 with the diagnosis of bacterial meningitis. The diagnosis of bacterial meningitis was based on history and examination suggestive of meningitis with at least one of the following items be present, positive CSF culture or positive gram stain (for hemophilus influenza, Streptococcus Pneumoniae, or Neisseria meningitides.), or CSF TLC10/ML and positive blood culture for above mentioned organism or CSF culture and gram stain negative for the organism but CSF WBC100/ML with >50% polymorphonuclear cells. Patients below 2 month of age and patient with Tuberculous meningitis were excluded from the study. The data collected on a specific Performa having different variables such as age, sex, seizure, duration of treatment ect. Then the data was analyzed on Epi info version 6 simple frequencies were calculated for each variable. Chi square analysis was done to see any correlation between the risk factors and post-meningitic hydrocephalus. Odds ratio was calculated for the risk factors.

Results: The mean age of study subjects was 7.2 years with 60% males and 40% females. Gram stains were positive in 37.5% of patients, CSF culture was positive in 27.5% of the patients, in 17.5% of the patients hydrocephalus was the main complication of bacterial meningitis and 25% had other type of sequelae including seizures, hearing loss, hemiparesis etc. Significant association was found between seizure at admission (p-value<0.040), duration of illness (p-value<0.01%), age on admission (p-value<0.01). 68.8% patients came for follow up 2.5% patients left against medical advice (LAMA) and 2.5% expired.

Conclusion: The association was found between the development of post-meningitic hydrocephalus and variables such as seizure, duration of illness (patients having duration of symptoms like fever, headache, vomiting, cerebrospinal fluid leukocyte count and duration of antibiotic treatment.

Key Words: Pyogenic meningitis, Hydrocephalus, Computed tomography, Magnetic resonance imaging, Cerebrospinal fluid, Prognosis.

INTRODUCTION

Fifty years after the advent of antibiotics for clinical use, bacterial meningitis remains an important cause of morbidity and mortality. As such, it represents a unique human infectious disease, because the pathophysiologic effects of the disease progression and sub-optimal outcomes occur despite bacteriologic cure of the infection.¹ Bacterial meningitis is the most destructive of acute infections in normal individuals. With the use of appropriate antimicrobials mortality from bacterial meningitis has been reduced from greater than 90% to less than 10%, although mortality in the neonate remains between 15 and 20%.^{2,3} The three most common aetiologic bacteria, Hemophilus Influenza, Streptococcus Pneumoniae and Neisseriae Meningitidis account for 90% of reported cases occurring in infants and children more than 60 days of age.^{4,6} Before the use of the Haemophilus conjugate vaccines, the annual incidence of bacterial meningitis in children 0 to 5

years of age was between 30 and 70 per 1000000.^{4,6-9} However, because the morbidity and mortality of bacterial meningitis vary with etiologic organism, the substantial reduction in prevalence of meningitis caused by Haemophilus vaccine may not lead to as striking a reduction in the incidence of neurologic sequelae of this disease¹⁰⁻¹⁴. Meningitis is still the most serious infectious disease for many developing countries, including Pakistan. In a local study done at Sheikh Zayed Medical Institute Lahore, the incidence of pyogenic meningitis was 1.2% cases per 100 admissions.¹⁵ In developed countries, the focus in managing bacterial meningitis has been shifted from reduction of mortality to reduction of sequelae¹⁶, but developing countries are still burdened by excessive mortality and sequelae rates^{17,18}, compared with those in developed countries.^{1,4,16,19} According to various studies done abroad, the incidence of post-meningitic hydrocephalus ranges from 21-41% in new born babies^{20,21}, and 7-9% in infants and school age

children.^{23,24} In two other studies done in Arizona and Canada the serious sequelae of pyogenic meningitis including hydrocephalus among the survivors were 44% and 33% respectively.^{24,25}

In a local study done at Lahore (Mayo Hospital) the incidence of post-meningitic residual sequelae was 7% at the time of discharge and the most common residual defect was found to be hydrocephalus and deafness²⁷. Several risk factors have been described to have association with the development of hydrocephalus in children suffering from pyogenic meningitis. These include age, coma, temperature, seizure at admission, duration of symptoms, type of organism, cerebrospinal fluids findings and gender^{22,27}. Very few studies have been carried out on this subject. Furthermore, almost all the studies have been carried out in Europe and America, while local data is lacking in this regard. Thus this study will be of immense help to our clinicians to find out the magnitude of the problem and to predict the development of hydrocephalus in these children.

PATIENTS AND METHODS

This study was conducted at the Department of Pediatrics Unit-2, Bolan Medical Complex Hospital (BMCH), Quetta. All the children (>2month age) admitted to the pediatric unit-2 ward of (BMCH) from December 2009 to July 2011 with the diagnosis of bacterial meningitis, were included in the study. The diagnosis of bacterial meningitis was based on history and examination suggestive of meningitis with at least one of the following three items should be present.

- Positive CSF culture, gram stains for Hemophilus Influenza, Streptococcus pneumoniae, Neisseria meningitides.
- If CSF Leukocyte counts 10/ml and blood culture positive by day three of admission for Hemophilus influenza, Streptococcus pneumoniae, Neisseria meningitides.
- If CSF culture and gram stain negative, but CSF Leukocyte count 100/ml with >50% polymorphonuclear cells and CSF glucose <50% of blood glucose or if no blood glucose, CSF glucose <30mg/dl; OR CSF Leukocyte>1000/ml with >50% polymorphonuclear cells.

The diagnosis of hydrocephalus was based on increased fronto-occipital circumference, ultrasound head, computed tomography (CT) and Magnetic resonance imaging (MRI). The exclusion criteria were age<2mont and >15years, tuberculous meningitis, Arnold-chiari malformation, intraventricular tumours. During the study period, 87 patients were admitted to our ward with the diagnosis of bacterial meningitis. Out of these, seven patients were excluded based on the above mentioned criteria, leaving 80 patients. The mean age

of study subjects was 7.2 years with a range of 2months to 15 years. Males were 60 percent and females 40%.the data was collected on a performa noting, variables such as age, sex, duration of illness on admission (>3 or<3days), seizure on admission (present or absent), CSF examination, duration of antibiotic treatment, ultrasonography brain, CT and MRI brain. 42 out of 80 patients (52%) suffering from bacterial meningitis had no imaging done and therefore, were presumed to have no hydrocephalus. Outcomes were evaluated at the time of discharge from the Hospital and their follow-up at the out patient department (OPD). Outcome measures were described as follows; complete recovery, recovery with sequelae, such as, hydrocephalus, seizures, paresis, hearing loss and others and death

The data was analyzed on Epi info version 6. Simple frequencies were calculated for each variable. Chi square analysis was done to see any correlation between the risk factors and post-meningitic hydrocephalus. Odds ratio was calculated for the risk factors.

RESULTS

The mean age of study subjects was 7.2 years with 60% males and 40% females. Gram stains were positive in 37.5% of patients, CSF culture was positive in 27.5% of the patients, in 17.5% of the patients hydrocephalus was the main complication of bacterial meningitis and 25% had other types of sequelae including seizures, hearing loss, hemiparesis ect. In 48% (32 patients) patients neuroimaging was done, ultrasonography was 1.3%, CT scan head was 41.3% and MRI head was 5.0%, in 63.2% patients, neuroimaging did not show any abnormality. In 68.8% patients only Ceftriaxone was given. Ceftriaxone and others antibiotics in combination were given in 25% of patients. Significant association was found between seizure at admission (p-value<0.040), duration of illness (p-value<0.01%), age on admission (p-value<0.01). 68.8% patients came for follow up. 2.5% patients left against medical advice (LAMA) and 2.5% expired.

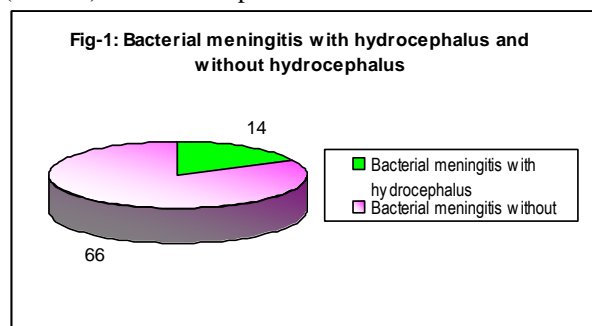


Table 1: Risk factors associated with post-meningitic hydrocephalus (n = 80)

Variable	Hydrocephalus	No hydrocephalus	Odds ratio	95% CI	*P-Value
Age 2 month-1year >1year – 15year	12 02	15 51	20.4	3.6-149	<0.01
Duration of symptoms (Fever, vomiting, headache, seizure) ≥3days <3days	12 02	33 33	06	1.2-42	<0.01
Seizure on admission Present Absent	07 07	15 51	3.4	0.89-13.2	<0.03
Cerebrospinal fluid, total leukocyte count (TLC) <500 cells/cumm >500 cells/cumm	09 05	26 40	2.7	0.73-10.8	<0.08
Duration of antibiotic 14 days 7-10 days	05 09	08 58	4.03	0.0-1.1	<0.02

*P-value determined by chi-square test.

DISCUSSION

Bacterial meningit (BM) results in substantial morbidity and mortality. Hemophilus Influenza, Streptococcus pneumoniae and Neisseriae meningitides account for 90% of reported cases occurring in infants and children more than 60 days of age.^{4,6} Hydrocephalus following bacterial meningitis is a common and major complication in children. It presents as a challenge for the physicians and has considerable effect on the effectiveness of the treatment and outcome of patients. Outcome of bacterial meningitis has significantly improved with advent of antibiotics. In spite of appropriate treatment with antibiotics some of the patients develop major as well as minor sequelae associated with bacterial meningitis. However, few of the studies have been done to find out the modalities to intervene in the pathophysiology of bacterial meningitis to decrease the worst outcome of bacterial meningitis. Studies also have been done to find out certain risk factors at the time of presentation of bacterial meningitis which could be associated with development of post-meningitic sequelae, including hydrocephalus, e.g. age, sex, seizure at admission, duration of illness, type of organism, type of antibiotic used. Therefore, we can predict the development of post-meningitic sequelae at the time of presentation and refer the patients to tertiary care hospital, our study shows a statistically significant correlation between certain risk factors such as seizure at admission (p-value 0.03) and duration of symptoms (p-value 0.01) with development of post-meningitic hydrocephalus, which is consistent with the results of the literature.^{23,28} In our study frequency of post-meningitic hydrocephalus was much higher (17.5%) than reported in literature (7.9%)^{20,21}, the reason of

which is difficult to explain. Even in a local study²⁷ done (at Mayo Hospital Lahore) the incidence of post-meningitic sequelae was much lower i.e. 7% than our study. However, other sequelae such as seizures, hemiparesis and hearing loss were less common in our study as compared to the reported from Arizona and Canada.^{24,25}

In a meta analysis of prospective cohort studies from developed countries the least favorable outcome was with streptococcus pneumoniae meningitis, the most favorable with Neisseriae meningitides while outcome with Hemophilus influenza meningitis was intermediate.¹¹ According to our study post-meningitic hydrocephalus developed in 26.6%, 10% and 40% of patients with Streptococcus pneumoniae, Neisseriae meningitides and Hemophilus influenza meningitis respectively. As the wide spread use of Hemophilus conjugate vaccine results in the virtual elimination of meningitis caused by Hemophilus influenza type b, Streptococcus pneumoniae become the predominant cause of bacterial meningitis in developing countries. Our study shows that Hemophilus influenza is the predominant cause of post-meningitic sequelae following bacterial meningitis. This is probably due to the low use of Haemophilus vaccine in our country. Our study is mainly focusing on the development of post-meningitic hydrocephalus at the time of discharge. Another study needs to be done to look at the remaining post-meningitic sequelae (seizures, hearing loss, paresis) and the duration of cohort of patients with bacterial meningitis needs to be extended, because some of the post-meningitic sequelae in many patients improve with time and may resolve completely.²⁸ Feigin et al²⁸ reported that neurologic or audiometric abnormalities were present in 42% of children with

Hemophilus influenza meningitis at discharge, 38% at 1 month, 26% at 3 months, 13% at 6 months and 5% at 1 year. No child had developed late onset deafness or had a late recovery of Audiometry function.

CONCLUSION

The association was found between the development of post-meningitic hydrocephalus and variables such as seizure, duration of illness (patients having duration of symptoms like fever, headache, vomiting, cerebrospinal fluid leukocyte count and duration of antibiotic treatment. We have also observed that the smaller the age of the patient the more he is prone to develop hydrocephalus and other post-meningitic sequelae

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