International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319 – 6505, Impact Factor: SJIF: 5.995
Available Online at www.journalijcar.org
Volume 6; Issue 5; May 2017; Page No. 3933-3936
DOI: http://dx.doi.org/10.24327/ijcar.2017.3936.0400

Research Article

ACUTE BACTERIAL MENINGITIS IN A TERTIARY CARE CENTRE IN SOUTH INDIA –A STUDY

Lizy Mathew., Bhargavi.L and Sumangala Bai

Govt. Medical College, Thiruvananthapuram, Kerala, India

A R T I C L E I N F O

Article History:

Received 12th February, 2017
Received in revised form 20th March, 2017
Accepted 7th April, 2017
Published online 28th May, 2017

Key words:

Bacterial meningitis, cerebrospinal fluid, heated chocolate agar.

A B S T R A C T

Amongst infectious diseases that continue to plague children and adults in both industrialized and developing countries, bacterial meningitis has a unique place.
Objective: Aim of the study was to study the cases of bacterial meningitis during one year, by isolating and identifying the common pathogens, their antibiotic sensitivity patterns, the common age groups affected, seasonal variation, clinical outcome etc.
Methods: 668 patients admitted with symptoms of acute bacterial meningitis were included in the study.
Results: Primary pathogens still rank first among the etiological agents of acute bacterial meningitis. Precentrifugation of cerebrospinal fluid (CSF) samples increased the isolation rate. Heated chocholate agar was superior to ordinary chocholate agar for isolation of *Hemophilus influenzae* and for performing antibiotic sensitivity.

INTRODUCTION

Meningitis is an inflammation of the meninges - membranes that cover the brain and spinal cord. In spite of the advances in medical care and wide spread use of antibiotics, meningitis still has high morbidity and mortality. It could be due to infectious or non infectious causes. Infectious meningitis may be due to bacterial, viral or fungal etiology. According to WHO, the incidence of bacterial meningitis is exceeding 1.2 million cases each year worldwide. (WHO1988).

This prospective study was conducted to find out the incidence of acute bacterial meningitis in our setting, to find the common etiological agents of meningitis, the age groups affected, the symptomatology and also to evaluate heated chocolate agar for the isolation of *Haemophilus influenzae*. The study was conducted in the Government Medical College Hospital Thiruvananthapuram from May 1998 to April 1999.

MATERIALS AND METHODS

A total of 668 CSF samples were studied during this period. All patients admitted with symptoms of acute bacterial meningitis and an elevated CSF polymorph count was included in the study excluding patients with CSF leak or fistula and all cases of traumatic meningitis. In each case, the age, sex, brief history of the patient, signs and symptoms & previous antibiotic treatment were recorded. Follow up of proven cases of bacterial meningitis was also done.

Corresponding author:* **Lizy Mathew
Govt. Medical College, Thiruvananthapuram, Kerala, India

The CSF samples were subjected to naked eye examination to see whether the sample was clear, turbid, xanthochromic or blood stained. A cell count was performed on all CSF samples using a Naeubaeurs counting chamber. A drop of well mixed sample of CSF was transferred to clean glass slide. To this a small loopful of methylene blue was added and mixed. Using a sterile Pasteur pipette, Neubauer's counting chamber was charged with the stained sample of CSF and the cells in the four corner squares were counted under high power objective.

The samples were inoculated on 5% Sheep blood agar, Heated chocolate agar, MacConkey Agar and Brain heart infusion broth. Heated chocolate agar was prepared by heating ordinary chocolate agar at 85^0C for 10 minutes. The organisms isolated were identified by routine laboratory methods.[1]

RESULTS

Among 668 patients included in the study, 378 (56.6%) were males and 290 (43.4%) were females. 23 (3.44%) cases were confirmed by culture. Out of the 23 culture positive cases 15(65.2%) were males and 8(34.8%) were females.

Heated chocolate Agar

Heated chocolate agar was a more enriched medium for *H. influenzae* than ordinary chocolate agar. In this medium, *H. influenzae* strains produced larger colonies even without staphylococcal touch colonies. It was also a better medium for performing antibiotic sensitivity tests for *H. influenzae*.

Table 2 Age wise analysis of patients included in the study

Age	Total no. of patients	Culture positives
0- 1 months	178 (26.6)	1(4.4)
> 1-3months	33 (5.0)	2(8.7)
>3m -5yrs	160 (24.0)	10 (43.5)
>5yrs- 12yrs	48 (7.2)	2(8.7)
>12-40 yrs	137(20.5)	3(13.0)
>40yrs	112(16.8)	5(21.7)

The maximum number of patients included in the study belonged to two age groups 0-1 month (26.6%) and >3m-5yr (24%). 10 out of 23 (43.5%) culture positive cases belonged to the latter age group. The next highest occurrence of the disease was seen in >40yrs group (21.7%) (Table-2)

Table 3 Correlation between Gram stain and culture

Gram stain +ve Culture +ve	Gram stain +ve Culture –ve	Gram stain -ve Culture +ve
23	4	0

It was seen that gram stain was 100% sensitive. Among the analysed cases none was gram stain negative and culture positive. Gram stain positive and culture negative cases were due to prior antibiotic therapy.

Table 4 Analysis of symptomatology

Symptom	Frequency (%)
Fever	18 (78.2)
Vomiting	11(47.8)
Neck stiffness	11(47.8)
Seizures	9 (39.1)
Altered behavior	6 (26)
Headache	5(21.7)
Torticollis	1 (4.3)
Nerve palsies	1 (4.3)

The common symptoms seen in patients with acute bacterial meningitis were fever, vomiting and neck stiffness. Rare symptoms like torticollis and multiple nerve palsies were seen in one case each – both were children (Table-4)

Table 5 Bacterial agents isolated in the study

Organism	No.(%)
S.pneumoniae	11(47.8)
H.influenzae	7 (30.4)
E.coli	2 (8.7)
Klebsiella sp.	1 (4.3)
S.typhimurium	1 (4.3)
β haemolytic Streptococci	1 (4.3)
Total	23

The common pathogens isolated were *S.pneumoniae* and *H.influenzae*. Enteric gram negative organisms constituted 17% of the isolates. *β haemolytic Streptococcus* was isolated from one case of neonatal meningitis.

Table 6 Distribution of pathogens in paediatric and adult population

Etiological agent	Paediatric	Adult	Total
S.pneumoniae	5	6	11
H.influenzae	7	-	7
Enteric gram negative bacilli	2	2	4
β-haemolytic Streptococci	1	-	1

Among adults, *S.pneumoniae* was the commonest etiological agent of acute bacterial meningitis. In children the predominant pathogen was H. *influenzae* followed by S.*pneumoniae.* (Table-6)

Table 7 Clinical outcome of patients

	≤12 yrs			>12 yrs		
Etiology	Recovered	Expired	Total	Recovered	Expired	Total
S. pneumonia	3	2	5	5	1	6
H. influenza	7	-	7	-	-	-
E. coli	1	-	1	-	1	1
Klebsiella sp	-	-	-	-	1	1
S.typhimurium	1	-	1	-	-	-

Five out of the 23 culture positive cases expired giving an overall mortality of 22% . In the paediatic group only 2 deaths occurred, both of which were cases of pneumococcal meningitis. But in the adult population, enteric gram negative bacillary meningitis was the predominant cause of death. (Table-7)

All the *S.pneumoniae* strains were sensitive to penicillin as detected by oxacillin 1μg disc diffusion method. *H.influenzae* strains were uniformly sensitive to ampicillin, chloramphenicol and ceftriaxone. β haemolytic Streptococus was also sensitive to penicillin.

Regarding the enteric gram negative organisms, S. typhimurium was sensitive to ampicillin, chloramphenicol, co-trimoxazole, ciprofloxacinand ceftriaxone. *K.pneumoniae* was sensitive to gentamicin, co-trimoxazole and ceftriaxone and resistant to ampicillin. Two strains of E. coli isolated were resistant to gentamicin and ampicillin but were sensitive to amikacin and ceftriaxone.

DISCUSSION

In the present study, maximum number of patients screened were in the neo-natal age group - 178 (26.6%), followed by the age group (3m – 5 yrs) – 160 (24%). When the patients were categorized into paedriatic (≤ 12 yrs) and adult (>12 yrs) groups, of the 23 confirmed cases of acute bacterial meningitis, 65% were in the paediatric group and 35% were in the adult group. Analysis of bacterial meningitis in the same center in 1995 showed the corresponding percentages to be 56% and 44% respectively showing an increase in the occurrence of the disease in children. Other centers Kottayam, Alappuzha and Calicut showed a much higher occurrence of the disease in children than our center in the year 1995. The percentages were 100%, 85% and 98% respectively[2].

Prior respiratory infection was a common finding in most of the cases. This was observed in 80% of children and in 50% of adults with acute bacterial meningitis. In adults, other common predisposing factors were immunosuppression (25%) and alcoholism (13%). In a study on gram negative bacillary meningitis in adults by Cuenca *et al* (1997) it was concluded that >90% of cases had some underlying disease and immunosuppression was also noticed to be an important predisposing factor. In the present study, 70% of cases were having some underlying illness[3].

In the present study, 43 % of cases occurred during the months of December, January and February – coolest months of the year and only 9% of cases occurred in March, April and May. During the rest of the year, the distribution was rather uniform. Further observations are necessary to substantiate the seasonal distribution of cases.

A wide range of cell counts were observed in the cases studied. No relationship was observed between cell count and age of the patient. The highest cell count recorded in this

study was 6000 cells/cumm. This was in a 30 day old baby with streptococcal meningitis .There were two cases with very low cell count, of which one patient expired and the other escaped with severe sequelae like obstructive hydrocephalus. This points to the fact that low cell count is associated with a bad prognosis.Differential counts showed neutrophilic pleocytosis in all the cases. Lymphocyte predominance was not seen in this study. William. J. Powers has reported confirmed cases of bacterial meningitis with lymphocytic predominance[4]. Previously CSF lymphocytosis in acute bacterial meningitis was attributed to unusual circumstances or atypical organisms like *L.* monocytogenes.[5,6]

In the present study it was observed that centrifuged deposit of CSF was superior to uncentrifuged CSF for gram stain. The interpretation of gram stain was easier, took less time and examination of a few fields itself gave a good picture of the infecting agent. Difficulty' was observed when a highly cellular CSF contained only a few gram negative bacilli.

In the WHO manual of Basic Laboratory procedures in Clinical bacteriology 1991, it has been suggested that a centrifuged deposit should be examined if the CSF is not cloudy[7]. A recent study by Sherry. A. Dunbar *et al* (1998) have also concluded that microscopic examination of a gram stained concentrated CSF is highly sensitive and specific in the early diagnosis of bacterial or fungal meningitis[8].

Among the samples studied, 27 samples showed a positive gram stain but only 23 samples gave a positive culture. The remaining 4 samples were from patients with partially treated meningits. Sohet I *et. al.* (1985) states in their study on diagonsis of partially treated meningitis that 17% of patients who received antimicrobial agents before hospitalisation had negative CSF cultures.[9]

The predominant pathogen isolated in this study was S. *pneumoniae* when both adult and paediatric populations were taken together. Of this 45% occurred in paediatric group and 55% occurred in adults (Table No. X). In a study conducted by Phillips E.J *et al* of Sunnybrook Health Science Centre, Ontario, Canada in 1998, *S. pneumoniae* was identified as the most common etiological agent in children and adults overall[10]. *H. influenzae* was the most common organism implicated to cause meningitis in children <13 yrs followed by *S. pneumoniae* (33%). According to Fothergill *et al* (1933), *H. influenzae* meningitis was rare after 6 yrs and before 2 months of age[12]. In the present study, lowest age recorded for *H. influenzae* meningitis was 3'/$_2$ months and the highest age recorded was 8 yrs.

In a 11 year review of 618 cases of bacterial meningitis in children by Chotpiyasunondh.T. of Children's Hospital, Bangkok in 1994, *H. influenzae* was the most common causative agent (42.3%)[11].

The gram negative organisms isolated in adults were *E. coli* and *K. pneumoniae.* According to Cuenca M *et al* of Madrid, *E. coli* was the most common organism recovered from adult patients with gram negative bacillary meningitis[3].

Of the 23 culture confirmed cases of acute bacterial meningitis, 5 patients expired. Among these, three (60%) cases were due to ***S.*** *pneumoniae* and two (40%) cases were due to enteric gram negative bacilli. The case fatality rate observed for pneumococcal meningitis was 27%. It was much higher for gram negative bacillary meningitis (50%) No fatality was associated with *H. influenzae* meningitis. But a case of *H. influenzae* meningitis. That patient later on presented with obstructive hydrocephalus for which surgical intervention was taken by the Neurosurgery department.

The Salmonella meningitis recovered completely with third generation cephalosporin for 3 weeks. The average duration of hospital stay ranged from two to three weeks. The specific antibiotic therapy given were penicillin for streptococcal and pneumococcal meningitis, ceftriaxone for *H. influenzae* and third generation cephalosporin for enteric gram negative bacilli.

Regarding the antibiotic sensitivity patterns all the pneumococcal isolates were uniformly sensitive to penicillin as detected by disc diffusion method (oxacillin lμg). The study by Kragsbjerg P. *et al* 1994 also records that all pneumococcal isolates were fully sensitive to penicillin[13].

All the *H. influenzae* strains were sensitive to ampicillin and chloramphenicol. The *E.coli* strains were resistant to ampicillin, chloramphenicol and trimethoprim-sulphamethoxazole combination. The *S. typhimurium* isolated was sensitive to ampicillin, chloramphenicol (Table No. XII). In a 4 year study on neonatal meningitis by Adhikari *et al* (1995), University of Natal, Durban, they have observed gram negative isolates to be resistant to ampicillin, chloramphenicol and trimethoprim - sulfamethoxazole combination. They have also reported *Klebsiella* strains resistant to Amikacin[7I]. But in the present study, only one strain of *K. pneumoniae* was isolated and it was sensitive to gentamicin, trimethoprim-sulfamethoxazole combination, chloramphenicol and cefriaxone. All the gram negative strains were uniformly sensitive to ceftriaxone.

Summary

Findings of the study showed that primary pathogens still rank first among the etiological agents of acute bacterial meningitis The commonest etiological agents isolated were *S. pneumoniae* followed by *H. influenza,* enteric gram negative bacilli and β *haemolytic streptococci* (4%.). *N. meningitidis* was not isolated in this study. An increase in incidence was observed during the winter months December, January and February.

Five out of the twenty three cases expired giving an overall mortality of 22%. Three were cases of pneumococcal meningitis and the remaining two were due to gram negative bacilli.

Precentrifugation of CSF samples for gram stain and culture increased the isolation rate and made interpretation of gram stain easier. Heated chocolate agar was superior to ordinary chocolate agar for the isolation and also for performing antibiotic sensitivity tests for *H. influenzae.* By analysing the data from this study, it is clear that proper centrifuged CSF gram stain examination is quite mandatory for starting prompt and proper therapy in acute bacterial meningitis.

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How to cite this article:

Lizy Mathew *et al* (2017) ' Acute Bacterial Meningitis In A Tertiary Care Centre In South India –A Study', *International Journal of Current Advanced Research,* 06(05), pp. 3933-3936.
DOI: http://dx.doi.org/10.24327/ijcar.2017.3936.0400

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