Original Research Article

Study on epidemiology and risk factors for developing bacterial meningitis in children of Odisha, India

Abstract

Objectives: Bacterial meningitis is a leading cause of high childhood transience. It is the foremost cause of fatality in pediatric age group of 0-5 years in India accounting 0.5 to 2.6% of hospital admissions with CFR 16-30%. Based on above scenario, the study was undertaken to address the prevalence, etiology, social determinants of health factors of bacterial meningitis among under five children Odisha, India.

Methods: This was a cross sectional study comprising children under five years of age admitted to tertiary care hospital and teaching institutions in Cuttack with suspected clinical diagnosis of bacterial meningitis during April, 2012 to September 2013. 634 children enrolled into the study after getting appropriate consent from parents or their legal guardians.

Result: 61 children (10.4%) were confirmed with diagnosis of bacterial meningitis after undertaking on confirmatory test of cerebrospinal fluid. Male children (74.7%) were significantly than females (24.3%). The common isolated pathogens were *Streptococcus pneumonia*, *Haemophilus influenzae* type b, *E. coli*, *Pseudomonas aeruginosa*, *Klebseilla pneumoniae* and *Staphylococcus aureus*. *Streptococcus pneumoniae* was observed to be most common pathogen (57.6%) followed by *Haemophilus influenzae* type b (26.2%). The risk factors analyzed showed statistically significant association ($p<0.01$) with household income, mother's education, overcrowding, smoking and poor ventilation of household.

Conclusion: Strengthening early detection and prompt treatment of emergent case at the household level, improvement in mother's education and awareness, transportation to local hospital and facility for treatment and care should be utmost priority in the present scenario. In child vaccine program theses pathogens should be given wide.

Key words: Bacterial meningitis, *Haemophilus influenzae* type b, *Streptococcus pneumoniae*

INTRODUCTION

Bacterial meningitis, an infection of the membranes (meninges) and cerebrospinal fluid (CSF) surrounding the brain and spinal cord, is a major cause of death and disability worldwide[1]. Bacterial meningitis is associated with high mortality and morbidity worldwide, with an estimated 16 million cases in 2013, causing 1.6 million years lived with disability each year [2] and over 21,000 deaths in 2015 in India alone [3]. According to Indian records 0.5 to 2.6% of hospital admissions are of Acute Bacterial Meningitis. In developed countries (with best available facilities), the cases fatality rate is 10% while it is 16-30% in India [4]. *Haemophilus influenzae* type b (Hib), *Streptococcus pneumoniae* (Pneumococcus), and *Neisseria meningitidis* (Meningococcus) are the three main bacteria accounting most cases of bacterial meningitis in infants and young children [5; 6]. Although safe and effective vaccines have existed for years, vaccination rates remain suboptimal in South Asia and the impact of vaccine implementation has been munificent among low and middle-income countries like India [7].

Odisha is an eastern state of India being situated on the coast of Bay of Bengal with a total population of about 38 million and the third least urbanized state with 15% of population residing in

urban area. Around 83.31 percent live in the villages of rural areas and 47.2% are below poverty line (Census, 2011). The literacy rate is though 64% (NFHS, 2015) generally people are not educated and sensitized regarding the health status of their own and family. They are far-flung from the health accesses ensuring high morbidity and mortality of under five children. In Odisha in remote areas health network is not robust, a mist poor low income households people find difficulty to reach health facility for the treatment of any emergent cases that cause delay in treatment. More ever due to poor health awareness among the mothers in middle and low socio economic class, the early warning signs of acute bacterial meningitis are often missed. In view of the fact that bacterial meningitis one of the most encountered infections among under- five children, the present study envisages in regards to association of etiological agents and study of socio-demographic determinants of the infection.

MATERIALS AND METHODS

This was a cross sectional study undertaken in a pediatric tertiary care hospital cum teaching institution in Cuttack, Odisha, India during April, 2012 to September 2013. Ethical approval was taken from the Institutional Ethics Committee to conduct the study. The purpose of the study was explained to the parent or guardian of the child and informed consent was taken before enrolling them in the study. Suspected meningitis included children of both sexes below 5 years of age with the history of sudden onset of fever more than 38.5°C rectal or more than 38.0°C axillary and the presence of one or more of the following such as neck stiffness, altered consciousness, meningeal sign. Based on the turbidity of CSF and WBC count more than 100 cell/ml or 10-100 cells with glucose less than 40 mg/dl or protein less than 100mg/dl regarded as the probable case and confirmed case of meningitis was defined as the probable cases where as confirmed case of meningitis was defined as all probable case where CSF demonstrated incriminating pathogen either by Latex test, Culture or RT PCR Test.

Epidemiological information of the cases was collected by interviewing the guardians of the children by using a pre-tested Performa, information regarding socio-demographic characteristics of the mother and child and associated factors such as overcrowding, cross ventilation, birth order, birth weight, number of siblings, mother's education, monthly income, domestic hygiene and smoking habit in the family. Overcrowding was assessed based on the number of persons and living rooms.

In the hospital, detailed clinical examination was done. Blood samples and cerebrospinal fluid samples were taken from the patients and analyzed (CDC, 2011). Sterile CSF was placed in suitable transport or holding media and rushed to the hospital laboratory that works 24 hr a day. All CSF samples received at the laboratory were processed immediately. The macroscopic appearance of the CSF was recorded. A total count of CSF cells and differential count were done using a haemocytometer and standard methods. The CSF samples were subjected to centrifugation, the resultant smear was Gram stained and examined microscopically. The procedure used for microbiological analysis was sediment from a centrifuged CSF specimen cultured on specific culture media; the isolated pathogens were identified by specific biochemical tests. The supernant was used for Latex agglutination test and remaining of the sample was stored at -20^0C for real time PCR analysis. The CSF glucose and protein were computed. Statically analysis was performed to scrutinize any significant association that may exist between each of the demographical, clinical development of Bacterial infection.

RESULT

The cross sectional study was undertaken for one year and five months at the pediatric hospital cum teaching institution in year 2012-2013 at Cuttack, Odisha that caters to paediatric cases from six nearby districts with mostly rural and a few urban population. All 634 sick children under five years with presumptive clinical diagnosis of acute bacterial meningitis diagnosed at outpatient department were admitted to the study in the pediatric ward. After detailed clinical examination by the physician,

attempt was made to conduct the guided lumbar puncture to collect 2 ml of CSF and 1 ml of blood intravenously for laboratory analysis. Blood was collected and put into culture where CSF could not collected due to non cooperation of patient or when suspected that CSF was under high pressure to avoid any complications. Based on CSF analysis 634 of suspected meningitis cases only 61 cases were confirmed for diagnosis of bacterial meningitis depending upon isolation of bacterial pathogens in CSF and blood culture, Latex test, Microscopy and RT PCR Test.

Gender wise distributions of suspected meningitis case showed male were 411 (64.83%) and female were 223 (35.17%) where as in probable meningitis case male were 77.38% and female were 22.62%. Out of the total 61 confirmed cases 39 were confirmed by multiplex RT PCR, 14 samples were by latex agglutination (six samples were positive for Hib, seven for *S. pneumoniae* and one for group B Streptococcus) and 13 cases were confirmed by both CSF and blood culture. The isolates are *S.pneumoniae*, Hib, *Pseudomonas aeruginosa*, *Klebseilla pneumoniae*, *E.coli*, *Salmonella typhi* and *Staphylococcus aureus* (Table 2). In Multiplex Real Time PCR 39 cases were confirmed out of which 29 *S. pneumoniae* and 10 cases were positive for Hib (Fig 3). Out of all these pathogens frequency of *S.* pneumoniae was highest. Culture and latex positive samples of *Streptoccus pneumoniae* and Hib were also found positive in RT PCR.

Out of these 61 laboratory confirmed cases of bacterial meningitis during the study period, 56 (74.7%) were males and 19 (24.3%) were females (Table 1). Around 40 infants less than one year of age had highest incidence of bacterial meningitis (53.3%) followed by children less than 2 years of age (15 cases) and rest (6 cases) were between 2 to 5 years age. When the data is analyzed by paired sample T test showed confirmed case of meningitis is positively correlated with the sex and the difference is statistically significant ($p<0.001$). The most marked seasonal variation was observed with a high incidence in the winter season (November to February) followed by summer (March to June).

When the cases were split according to the time of presentation the highest incidence was observed in the month of December (Fig 1).

The most common outcome of the treatment was complete recovery which was observed in 45(74%) out of 61 cases (Fig 3). During the study period 10 deaths were recorded due to bacterial meningitis, thus giving a case fatality rate (CFR) of 13.3%. These fatal cases were then further analyzed by breakup into the various age groups. Most of the fatal cases were in infants or young children and due to *Streptococcus pneumoniae*. When age specific CFRs were studied, infants had the highest CFR of 41.6%. This was followed by the children between the age groups of 1 to 2 years. A higher CFR of 30% was observed in these age groups. A gender-wise breakdown of the fatal cases showed that more deaths were recorded in males then females. Results show that 8 out of 56 male patients died due to bacterial meningitis during the study period 2 deaths in a total of 49 females that presented during the same period.

The distribution of selected socio-demographic characteristics among parents who participated in this study show that the highest proportion of the parents 41 (39.4%) were within the age group of 26-30 years whereas there were only 2(1.9%) below 20 years. According to the distribution of different income group to the bacterial meningitis case the low socioeconomic group as the high percentage of affected children with $p<0.0001$ and the OR ratio was found to be 8.82 suggesting socio economic level was a relative risk factor of the disease (Table 3). The health seeking behavior was also a major contributing factor for the acute bacterial meningitis development. In the present study it was recorded that 63.4 % of sick children were availed heath care facility after 48 hrs of onset of illness and sometimes this gap between the onset of illness and admission to the said referral hospital were more than 5 days (9.9%). Nutritional status of children explains the higher infection rate among the malnourished children. Among the total suspected case (N =634) though the percentage of malnourished cases was only 26.9% and the incidence of the diseases is 27.9% where as in normal children the incidence is only 4.1%.

Overcrowding of house with more than 3 persons in single room with inadequate cross ventilation and more number of sibling had direct effect on occurrence of the disease observed in the investigation having $p < 0.001$. Mother's education had direct impact on the infection rate. In case of the illiterate mother the number of meningitis case was higher almost half of the total no of cases where as a decline trend was observed with the level of education (Table 3).

DISCUSSION

The study is a hospital based study and conducted in a referral tertiary health care centre. So the true prevalence and incidence of bacterial meningitis are difficult to define in populace due to the fact that most of the cases treated with broad spectrum antibiotics before reaching the hospital yielding in less no of culture isolates. The study showed a marked male predominance (male to female ratio of 1.7:1) in both suspected and confirmed cases of meningitis. Throughout the various age groups the trend of male predominance also tends to persist. Various large scale studies conducted worldwide show a higher incidence in males. Several studies conducted in India also revealed the male predominance which corroborated with our present investigation [8]. Lower proportion of female children in the study points towards poor health seeking behavior and utilization rates of parents towards female child in India [9]. Bacterial meningitis is generally a disease of childhood. In this study the most commonly affected age group was found to be the infants. Data showed that almost half of the cases (53.3%) were less than 1 year age group. But as per hospital based study in India in children aged 1 month to 5 years suffering from acute bacterial meningitis, 77.7% were below the age of 1 year [4]. The higher rate of meningitis in early age children may be because of the underdeveloped immune system. During the study period 10 deaths were recorded due to bacterial meningitis, thus giving a case fatality rate (CFR) of 13.3% and when age specific CFRs were studied, infants had the highest CFR of 41.6%. Different study conducted in India and other developed countries reported the case fatality rate as 16 to 30% [4]. The cases of bacterial meningitis mainly occurred in winter and spring season [10; 11] which is corroborated with the

present scenario where the most marked seasonal variation was observed with a high incidence in the winter followed by summer.

LAT test detected bacterial antigens in 23% cases of bacterial meningitis, with the most common organism being *S. pneumoniae* followed by Hib. This finding was similar to that in other studies, where LAT was positive in 15.4% cases of bacterial meningitis [12]. Isolation rate of *Streptococcus pneumoniae* and Hib were less in the study. This may be because of fastidious nature of the organisms, vaccine implementation against these organisms or antibiotic treatment prior to lumber puncture. The CSF becomes sterilized within 4 hours of parenteral antibiotic treatment in case of pneumococcal meningitis [13]. Real time PCR analysis found more sensitive than Latex test and culture where the positivity rate is 59%. Latex detects bacterial capsular antigens for the identification of the isolates while culture identification is dependent on the recovery of a viable isolate from a specimen [14]. In contrast, rt-PCR targets specific genes and does not require a viable pathogen [15]. The RT-PCR method offers several other advantages, including the provision of results within hours, high throughput, and high sensitivity and specificity [15].

The risk factors associated with developing such an infection using chi square test with P-value of <0.01 showed that there was statically significant association with household income, mother education, overcrowding, smoking and ventilation. According to the socioeconomic status, the prevalence of bacterial meningitis was more in low socioeconomic groups compared to other groups. This difference is statistically significant (χ= P< 0.001). Overcrowding has the direct influence on the prevalence bacterial meningitis it was higher in children living in overcrowding houses having more, number of sibling and inadequate ventilation. It was also reported that house crowding encouraged the development of meningitis due to most of the detected pathogens are air transmission and the smoking in these houses aggravated the infection by diminishing the capacity of epithelial cells covering of the

respiratory tract for prevention of acquiring infection in addition to the prevalence of healthy carriers of pathogens [16;17]. Mother's education plays a vital role on bacterial meningitis infection rate. It was observed children from mothers who had no education or primary education only, had a higher chance of developing infection than children from more educated mothers (secondary education and above). The comparison of incidence of the disease among the three group was statistically significant with $p<0.003$. This is probably because children spend more time with their mothers, and mothers' educational level will determine the quality of care and many social and environmental factors that the child will be exposed to.

CONCLUSION

High prevalence of acute bacterial meningitis in our population with high CFR in young children even in tertiary care facility indicates late arrival of cases with prior irregular treatment and particularly in bulk drop of poor nutritional status of children where immunity is optimal. Hence it is important to ensure early detection and appropriate treatment by establishing adequate peripheral health facility, enhancing mother's health education and awareness to recognize early health indicators of sickness in children, provision of transport facility in remote areas for early case detection by local doctors.

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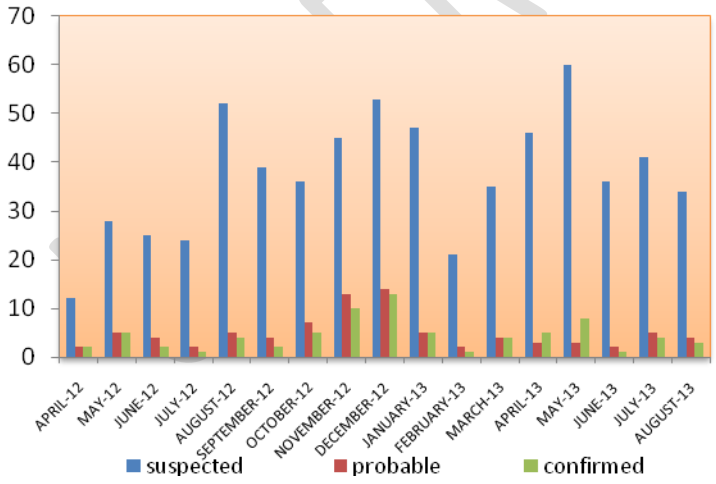

Fig. 1- Seasonal variation of meningitis

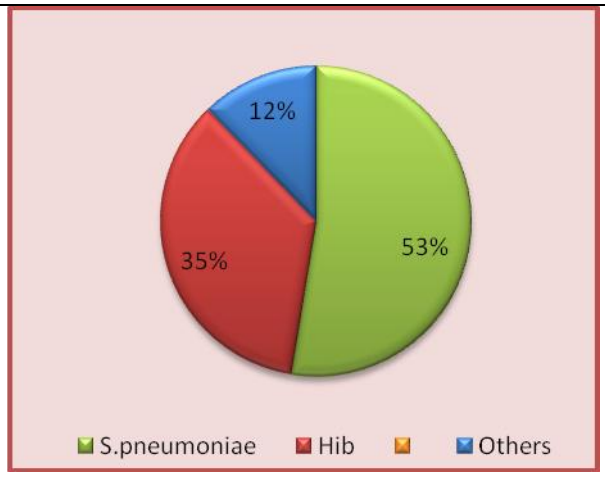

Fig. 2- Etiological agent of Bacterial meningitis

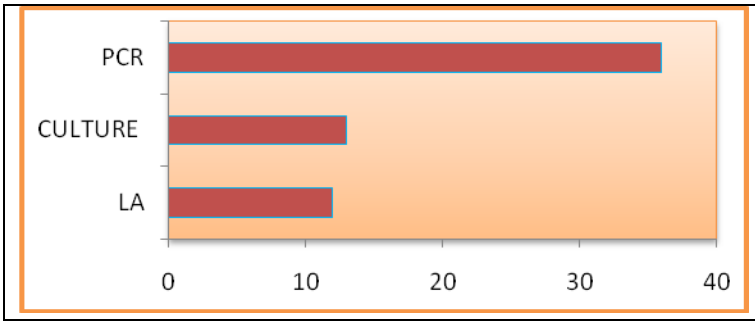

Fig 3: Confirmed meningitis case by different techniques.

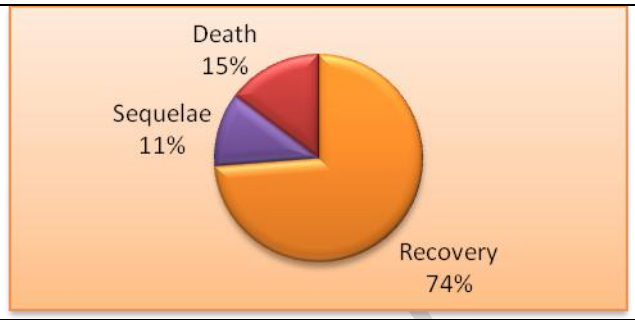

Fig 4. Outcome of Bacterial meningitis

Table 1: Demographic profile of bacterial meningitis cases admitted

	Level	Suspected case (N=634)		Probable case (N=107)		Confirmed case (N=61)	
		N	Percentage	N	Percentage	N	Percentage
Variables	0 - 1	355	55.99	57	53.27	35	57.3
	1- 2	136	21.45	26	24.30	11	18
Age (years)	2 - 3	66	10.41	13	12.15	8	13.1
	3 - 4	41	6.47	7	6.54	6	9.8
	4 -5	36	5.68	4	3.74	1	1.6
Gender							
Male	411		64.83	78	60.75	48	78.68
Female	223		35.17	29	17.76	13	21.32

Table 2. Laboratory confirmation of bacterial meningitis pathogens.

Organism	LATEX	Culture		RT PCR	Total	Percentage
		CSF	Blood			
S.pneumoniae	7	1	1	29	35	57.3
Hib	6	2	0	10	16	26.11
N.meningitis	0	0	0	0	0	-
S. aureus	0	0	2	0	2	0.3
S. typhi	0	1		0	1	0.1
P.aeruginosa	0	0	2	0	2	0.3
K.pneumoniae	0	0	2	0	2	0.3
E.coli	0	0	2	0	2	0.3
Group B	1	0	0	0	1	0.1

Streptococcus						
	14	13		39	61	
Percentage	23.0	21.3		69.3		

Table 3 Confirmation of bacterial meningitis pathogens in different techniques

Test	*S.pneumoniae* (N=35)		*Hib* (N=16)	
	n	%	n	%
LATEX	**7**	**20**	**6**	**37.5**
Culture	**2**	**5.8**	**2**	**12.5**
PCR	**29**	**82.8**	**10**	**62.5**
More than one test				
LATEX and culture	**2**	**5.8**	**2**	**12.5**
Culture and RT PCR	**2**	**5.8**	**2**	**12.5**
Latex and RT PCR	**7**	**20**		
Culture, RT PCR and Latex	**2**	**5.8**	**2**	**12.5**

Table 4: The demographic characteristics and the risk factors associated with developing of bacterial meningitis

Variable	Total no of cases	Meningitis cases	Percent	P value	OR
Family income					
High	113	2	1.76		
Moderate	196	8	4		
Low	325	51	15.7	<0.0001	8.82
Over crowding of House					
<3	241	12	4.9		
>3	393	49	12.4	<0.01	0.37
No of sibling					
0	72	1	1.3	<0.00001	

1	148	8	5.4		
2	243	16	6.5		
>2	171	36	21		
Gender					
Male	411	48	11.6		
Female	223	13	5.8	<0.0289	2.14
Mother Education					
Illiterate	196	31	15.8		
Elementary	371	28	7.5		
Higher secondary/ University	67	2	3	<0.003	0.18
Smoking					
Smoking	224	49	21.8	<0.0001	9.52
Non Smoking	410	12	2.9		
Ventilation					
Adequate	436	15	3.4		0.12
Non Adequate	198	46	23.2	<0.0001	
Admission to hospital					
Within 24 hrs	232	3	1.3		11.18
More than 24 hrs	402	58	14.4	<0.0001	
Nutritional Status					
Malnourished	171	40	27.9	<0.0001	0.16
Normal	463	21	4.3		