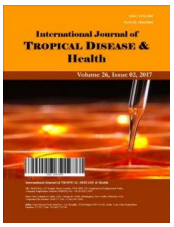

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Meningococcal Meningitis Outbreak (2009) among Children in Maiduguri North-Eastern Nigeria: Epidemiology and Determinants of Outcome

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Authors' contributions

This work was carried out in collaboration between all authors. Authors PS, ART and BM designed the study, wrote the protocol and along with authors MY and INY performed the statistical analysis and wrote the first draft. Authors IHA, AMA and DBA managed the analyses. Author PS also managed the literature searches. All the authors read and approved the final manuscript.

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ABSTRACT

Introduction: Large scale epidemic meningococcal meningitis outbreaks had occurred in the African meningitis belt every 5-12 years for the past century. Children are at high risk yet little attention had been directed toward them.
Methods: This was a prospective cross-sectional study among all the children with clinical suspicion or diagnosis of cerebrospinal meningitis during the meningococcal meningitis outbreak from January to December 2009.

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Results: One hundred and seventeen children were confirmed with meningococcal meningitis with incidence of 10.1%. The results of the unadjusted regression analyses, headache (p=0.046, OR 2.895 95% CI 1.019 – 8.229), duration of symptoms before first antibiotic (p=0.035, OR 3.289 95% CI 1.090 –9.920), dehydration (p=0.002, OR 5.225 95% CI 1.885 – 15.391) and type of antibiotic combination; crystalline penicillin and chloramphenicol (p=0.009, OR 4.043 95% CI 1.426 – 11.463) the only factors that correlate significantly with the death rate. However multivariate (adjusted) logistic regression using only factors with $p < 0.05$ in univariate analysis, only the type of antibiotic combination: Crystalline penicillin/Chloramphenicol and Ceftriaxone/Gentamicin (p=0.030, OR 5.782, 95% CI 1.191 – 28.080) that showed independent association with mortality rate in meningococcal meningitis among children.

Conclusion: Children remained the large population affected with high morbidity and mortality especially in the African meningitis belt. The factors contributing to such effect includes lack of immunization, poor recognition of the disease and lack of policy directed at children wellbeing.

Keywords: Meningococcal meningitis; epidemiology; outbreak; children; outcome.

1. INTRODUCTION

Large scale epidemic meningococcal meningitis outbreaks had occurred in the African meningitis belt every 5-12 years for the past century, resulting in annual incidence as high as 1,000 cases per 100,000 populations during epidemic outbreak such as the ones that occurred in 2003 and 2007 [1,2]. Typical annual incidence in non-epidemic periods ranges from 1-20 cases per 100,000 population and approximately 10% of healthy individuals carry meningococci in their upper respiratory tract [3]. The bacteria spread from person to person by direct physical contact or by airborne droplets that contain viable pathogens [4,5].

The rate of transmission and carriage increases in closed and semi-closed populations like in mass population movement as occur in situation of internally displaced persons (IDP) camps, overcrowded homes, military recruits, school dormitories and household contacts of meningococcal disease [6]. Throat carriage of the pathogens is an age dependent factor; it increases from less than 3% in young children 0-4 years, to a peak carriage (24-33%) in the ages between 15-24 years, and thereafter decline steadily [3-6].

Early clinical recognition of meningococcal meningitis in young age group is very difficult, as the classical manifestations develop later, while less specific features develop early and last for about 4 hours. Despite recent intensive care delivery, mortality range between 10% and 21.4% in children [6-9]. Most importantly, sharing bites of food, a drink, utensils, or any activities where respiratory secretions, throat secretions and saliva are exchanged, as in kissing can definitely spread the disease. The rates of meningococcal disease are highest in young children because of their reduction of protective maternal antibodies and then increasing again for adolescents and young adults [9].

Based on the polysaccharide composition, meningococci are classified into 13 serogroups. Only six of these (A, B, C, W-135, X and Y) are responsible for majority of infections. In endemic situations, serogroup B, is most common in infant's, serogroup C in adolescents and serogroup B and Y in the older adults [10]. In the epidemic of 1996 and 2007 serogroup A was responsible for infections in young children, and little effort was made toward the protection of these vulnerable age group during the epidemic [10,11].

In African meningitis belt, which is the region that stretches from Senegal in West-Africa to Ethiopia in the East-Africa is worst affected reoccurring epidemic with young children taking the toll in morbidity as well as high death rate [12]. Efforts to prevent major epidemic outbreaks caused by meningococci have not been successful even with the introduction of a new serogroup A polysaccharide-protein conjugate vaccine (PsA-TT MenAfriVac) seven years ago, in many parts of the meningitis belt, as outbreak have occurred with severe effect on children [4-8]. We decided to prospectively document the clinical features during the outbreak of meningococcal meningitis among children, the epidemiology of the disease, as well as the determinants of treatment outcome.

2. PATIENTS AND METHODS

This is a prospective cross-sectional study conducted on all the children with suspected

meningococcal meningitis infection admitted at emergency paediatric unit (EPU) of the Paediatric Department of University of Maiduguri Teaching Hospital (UMTH) during the meningococcal meningitis outbreak from 1st January to 31st December 2009. The inclusion criteria were 1. All children with clinical suspicion of cerebrospinal meningitis (CSM) are taken, 2. All children of 2 to 15 years are selected 3. All children with fever from the area where outbreak of meningococcal meningitis found.

Exclusion criteria were 1. All children that have unstable cardiopulmonary status depending on oxygen, 2. All children out of the range of age are excluded, 3. Children whose parents do not give their consents were excluded from the study. After meeting the above set criteria patients were recruited into the study as they presented to the emergency paediatric unit (EPU). The researchers were part of the emergency team that were caring for the patients during the meningococcal meningitis outbreak, so each patient that fulfil the criteria were reviewed thoroughly by one of us who was at least a senior registrar. The data obtained from history and clinical examination were; age, sex, place of residence of the affected child, immunization status against meningococcal meningitis, clinical signs, such as pyrexia, meningeal irritation, kernig sign, brudzenski sign and other systemic upset. Also recorded were whether patients had received treatment prior to admission, place where such treatment was offered and the type(s) of treatment offered were recorded by one of the researcher unto a structured proforma. A lumbar tap was performed on all patients that had met the criteria except those that were unstable which was delayed. After cleansing with 70% alcohol followed by 2% povidine iodine, a 1-2ml of cerebrospinal fluid (CSF) was collected in a universal sterile Bijou bottle, the macroscopic appearance of the samples were noted. The specimens were then taken to microbiology and chemical laboratory soon where the samples were processed [12-15]. Patients were then placed either on crystalline penicillin/Chloramphenicol combination or Ceftriaxone/Gentamycin combination. Ethical clearance was obtained from the institution research and ethics committee, and written or verbal was obtained from the parents or caregiver and where appropriate, assent was also obtained from the sick minor. All procedures were carried out in accordance with Helsinki declaration on research involving human subject.

3. RESULTS

Flow chart for patients evaluated for meningococcal meningitis.

During the study period, total of 1120 patients were admitted to Emergency Paediatric Unit (EPU). Of which 117 were confirmed to have meningococcal meningitis disease giving an incidence rate of 10.1%. There were 77 males and 40 females with a male: female ratio of 1.9:1 which has been highlighted in the patients evaluation flow chart above, See Fig. 1.

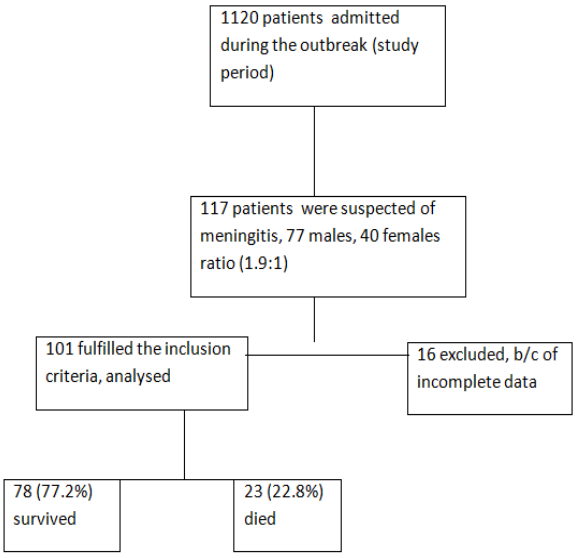

Fig. 1. Flow chart of patient's evaluations and recruitment

Of the 117 cases, 16 cases were not included in the statistical analysis because of incomplete data at the time of data entry, so 101 patients were eventually analysed and the serogroup responsible for the outbreak was serogroup A. Also during the one year period of the study, there were two peak in the epidemic outbreak, first was between March-May and the second was September-October with drop in the month of July and finally the outbreak halted by the end of December 2009, See Fig. 1. None of the patients with confirmed cases of meningitis were vaccinated against meningococcal meningitis within the two years prior to the epidemic outbreak. Meningococcal meningitis was higher among males (69.3%), as against females (30.7%), children of mothers with no formal education (86.1%), among children from urban slum (63.4%) and under-five children (53.5%). These observations however were not statistical significance (Table 1). The common clinical features were fever 98 cases (97.0%), pyrexia temperature >37.5°C 93 cases (92.1%), nuchal rigidity 83 cases (82.2%), meningeal irritation 83 cases (82.2%), Kernig sign 75 cases (74.3%), Brudzinski sign 69 cases (68.3%), neck pain/retraction 64 cases (63.4%), vomiting 55 cases (54.5%), headache 51 cases (50.5%) and coma was found in 7 cases (06.9%), see Table 2.

The association of each variable with recovery rate or death rate from bacterial meningitis was first assessed using univariate (unadjusted) regression analysis. The degree of association was expressed as an odds ratio. The sensitivity of the selection of variables for the multivariate (adjusted) logistic regression model was established using a cut-off point of $p < 0.10$ in univariate analysis with consideration for the socio-demographic variables including the sex, age, and mother's level of formal education . The statistical significance of the results obtained was assessed using estimated odds ratios at 95 % confidence interval.

The variables initially tested using univariate regression analyses were categorized into four distinct groups as shown by Tables 1 – 4. These distinct groups covers some selected socio-demographic factors and clinical features as well as disease history of bacterial meningitis and they includes: socio-demographic factors, clinical features, Central Nervous System signs and pre-admission intervention taken by patients (anti-malaria, anti-biotics given or not and place of such treatment). The entire variables tested include age, sex, residential area, Mother's level of formal education. time elapsed until the first dose of antibiotics in the emergency unit (duration of symptoms in days), fever, headache, neck pain, convulsion, vomiting, irrational behaviour, body rash, number of symptoms, pyrexia grade, pallor, hydration status, weight, petechie, mental state(conscious or comatose), bulging AF, meningeal irritation, Brudzinski sign, Kernick sign, number of combined CNS sign(≤ 2 or ≥ 3). Some clinical signs such as vomiting, convulsions, dyspnoea, fever, headache and coma were considered in isolation because they have been most commonly identified as factors determining prognosis in previous studies.

Table 1. Univariate analysis of patient's epidemiologic characteristics

Variables	Responses	Frequency	% death	p-value	OR	95% C.I
Sex	Male	70	25.7	0.178	2.25	0.690-7.327
	Female	31	13.3	Ref		
Age (yrs)	1<5	54	24.1	0.253	2.537	0.514-12.528
	5-10	28	25.0	0.258	2.607	0.487-14.608
	10>15	19	11.1	Ref		
Residence	USLP	64	28.1	0.180	2.935	0.609-14.146
	ULD	15	15.4	0.773	1.364	0.166-11.223
	UHD	17	11.8	Ref		
	Rural	05	0.0		NC	
Maternal education	No formal education	87	23.0	0.310	2.985	0.360-24.755
	Formal education	14	9.1	Ref		

UHD=Urban high density population, ULD=Urban low density population, USLP=Urban slump, NC=Not computed, Ref=Reference

Table 2. Clinical features of patients with meningococcal meningitis

Features	Responses	Frequency	%death	p-value	OR	95% C.I
Fever	Yes	99	50.0	0.365	0.273	0.016-4.546
	No	02	21.4	Ref		
Headache	Yes	57	31.4	0.046	2.895	1.019-8.229
	No	44	13.6	Ref		
Neck pain	Yes	64	26.6	0.263	1.881	0.622-5.686
	No	37	16.1	Ref		
Convulsion	Yes	39	14.7	0.278	0.540	0.178-1.644
	No	62	24.2	Ref		
Vomiting	Yes	55	21.8	Ref		
	No	46	22.7	0.914	1.054	0.407-2.731
Irrational beh	Yes	08	28.6	0.665	1.400	0.263-8.095
	No	93	21.5	Ref		
Body rashes	Yes	04	0.0	0.999	NC	
	No	97	22.7			
No of symptoms	≤2	25	8.0	Ref		
	3-4	66	27.3	0.063	4.312	0.922-20.179
	≥5	10	22.0	0.275	3.281	0.389-27.781
Duration of symptoms	<3	42	11.9	Ref		
	3-4	52	30.8	0.035	3.289	1.099-9.920
	>4	07	0.0	0.999	NC	
Pyrexia	37.5≤38.0	22	4.5	Ref		
	38.0-39.0	53	22,6	0.091	6.146	0.748-50.530
	>39.0	26	27.3	0.068	7.875	0.860-72.122
Pallor	Yes	26	9.1	Ref		
	No	75	21.3	0.358	2.712	0.323-22.757
Hydration status	Good	65	10.8	Ref		
	Dehydrated	36	39.40	0.002	5.386	1.885-15.391
Weight	Normal	51	21.6	0.126	5.225	0.628-43.474
	U/weight	20	5.0	Ref		
Petechiae	Yes	11	42.0	0.174	3.000	0.616-14.617
	No	90	20.0	Ref		

Table 3. Central nervous system (CNS) signs regression analysis

Features	Responses	Frequency	%Death	p-value	OR	95% C.I
Mental state	Conscious	93	23.9	0.999	NC	
	Unconscious	08	0			
Bulging AF	Yes	15	23.1	0.145	4.200	0.610-28.918
	No	86	6.7	Ref		
Meningeal irrit	Yes	84	22.3	0.716	1.286	0.332-4.991
	No	17	18.8	Ref		
Brudzinski's sign	Yes	70	24.6	0.38.4	1.635	0.541-4.937
	No	31	16.7	Ref		
Kernig's sign	Yes	75	26.7	0.554	7.637	0.963-60.537
	No	26	4.5	Ref		
Comb. cns signs	≤2	25	8.0	Ref		
	≥3	76	26.7	0.067	4.182	0.903-19.368

AF=Anterior fontanalle

The results of the unadjusted regression analyses as shown by Table 1 through 4 identified presence of headache (p=0.046, OR 2.895 95% CI 1.019 – 8.229), Duration of symptoms of 3 – 4 days before first antibiotic (p=0.035, OR 3.289 95% CI 1.090 – 9.920), dehydration (p=0.002, OR 5.225 95% CI 1.885 – 15.391) and type of initial antibiotics given before presentation to hospital (p=0.009, OR 4.043 95% CI 1.426 – 11.463) were the factors that correlated significantly with unfavourable outcome (death). Others factors do not show significant association with the mortality rate. Findings from univariate analysis, children who presented with headache are about 2.9 times more likely to die from the bacterial meningitis than those without headache. Patient who had symptom of 3-4 days before their first antibiotic are about 3.3 times more likely to die than those who presented with symptoms of less than 3 days duration. Children who presented with some form of dehydration were about 5.2 times more likely to die than children without dehydration. It also revealed that patients who were treated with crystalline penicillin and/or Chloramphenicol were about 4 times more likely to die from bacterial meningitis than children treated with combination of Ceftriaxone and gentamicin.

Table 4. Intervention before evaluation at emergency paediatric unit (EPU)

Variables	Responses	Frequency	% death	p-value	OR	95% C.I
Anti-malaria	Yes	29	17.2	Ref		
	No	72	24.3	0.445	0.650	0.215-1.966
Antibiotics	Yes	53	11.3	Ref		
	No	48	34.0	0.009	4.043	1.426-11.463
Place of treatment	Chemist	13	0.00	0.999	NC	
	Pharmacy	25	20.0	0.719	1.625	0.115-22.981
	Priv fac	18	28.6	0.389	2.600	0.284-23.814
	GH/PHC	45	13.3	Ref		

GH=General hospital, PHC=Primary health care, Priv fac=Private facility

Table 5. Multivariate analysis of factors determining mortality

Factors	Responses	Frequency	% death	p-value	OR	95% C.I
Sex	Male	70	25.7	0.086	0.213	0.037-1.247
	Female	31	13.3	ref		
Age (yrs)	1>5	54	24.1	0.893	0.857	0.090-8.134
	5-10	28	25.0	0.964	0.948	0.093-9.688
	10<15	19	11.1	ref		
Mat. Educ	No form edu	87	23.0	0.563	0.440	0.027-7.118
	Form edu	14	9.1	ref		
Headache	Yes	57	31.4	0.680	0.631	0.071-5.620
	No	44	13.6	ref		
No of CF	≤2	26	8.0	ref		
	3-4	66	27.3	0.493	2.233	0.225-22-198
	≥5	09	22.0	0.768	1.631	0.063-42.208
D of CF	<3	42	11.9	ref		
	3-4	52	30.8	0.308	2.177	0.488-9.703
	>4	07	0.0	NC		
Pyrexia	37.5-<38.0	22	4.5	ref		
	38.0-39.0	53	22.6	0.471	2.613	0.190-35.685
	>39.0	26	27.3	0.260	5.013	0.303-82.852
CNS signs	≤2	25	8.0	ref		
	≥3	76	26.7	0.900	1.114	0.206-6.033
Hyd status	Well hydrat	65	10.8	ref		
	Dehydrated	36	39.4	0.056	4.129	0.966-17.651
Treatment	Cryst+Chlor	47	34.0	0.030	5.782	0.191-28.080
	CEF+GEN	54	11.3	ref		

**CF=Clinical features, CNS=Central nervous system, D=Duration in days, Hyd=Hydration status, Mat edu=Maternal educational status, CEF=Ceftriaxone, GEN=Gentamicin, Cryst=Crystalline penicillin, Chlo=Chloramphenicol*

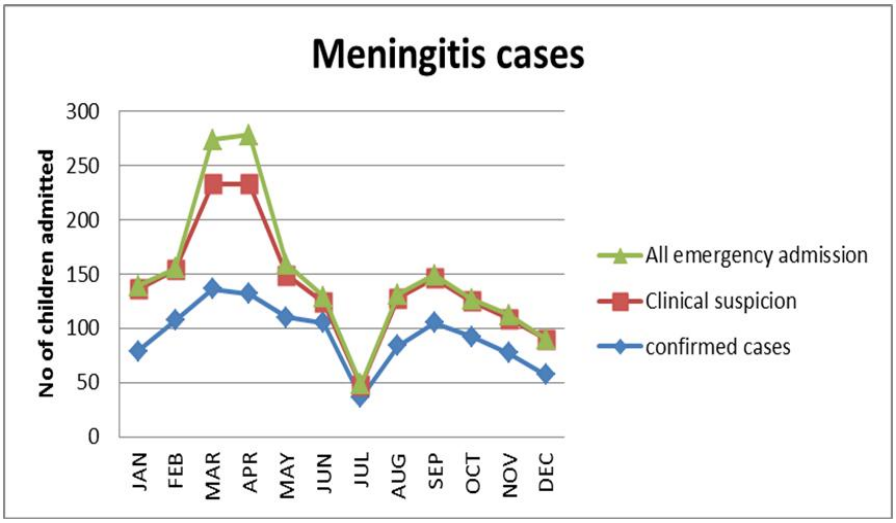

Fig. 2. Shows all emergency admission, suspected and confirmed cases of meningitis

However, on multivariate (adjusted) logistic regression using only factors with $p < 0.01$ in univariate analysis, clinical and socio-demographic features, only the type of antibiotic combination (Crystalline penicillin and Chloramphenicol) (p=0.030, OR 5.782, 95% CI 1.191 – 28.080) showed independent association with unfavourable outcome (death) in meningococcal meningitis among children, see Table 5. They were 5.8 times more likely to die from bacterial meningitis than children treated with combination of Ceftriaxone and gentamicin. Overall 77.2% of children with meningococcal meningitis survived, while 21.8% died.

4. DISCUSSION

Epidemic meningococcal meningitis usually starts at onset of dry season and ends at the starts of the raining season [16]. It is believed that, during the hot dry season with high ambient temperature and low humidity, respiratory mucosal damage and a lowered immunity predispose to colonization by meningococcal organisms in the airway [17]. Meningococcal Epidemic infections outbreak usually stops /aborts with the onset of rain. This was contrary to our finding as the outbreak had persist throughout the year, this was similar to report by Alhaji et al. [12] who also found all year round occurrence. As stated earlier in the introduction, vaccination had not been conducted in the region for over two years before the epidemic outbreak of the disease; probably this may have contributed to the lingering of the occurrence for the whole year round. Most of the reported cases of meningococcal meningitis outbreak had concentrated on its burden as it affects adult, neglecting children who are worst affected. In this study children were affected with associated high mortality, this was similar to work by Rabasa et al. [9] who reported meningococcal outbreak affecting children during similar outbreak a decade ago. Like in previous study our finding revealed that male were affected more than the female population. The incidence rate of 10.1% of children was significantly lower than the report by Emma et al. [18] who reported incidence rate 25%-36% of children population in similar developing countries like Nigeria.

In the early phase 4–6 h of onset of meningococcal infection in children manifestation is protean with non-specific symptoms such as fever, poor feeding or decreased appetite, nausea, vomiting, and irritability [19]. This symptoms usually mimic several non-meningococcal infections including viral illnesses so that parents resort to chemist for treatment thus further prolonging home stay, this might be the reason responsible for the delay in presenting to hospital in time as revealed in this study [6,15].

In this study the findings revealed that factors like those patients that presented with headache were at risk death than those without headache, longer of duration of symptoms before presenting to health facility and delay in starting antibiotics treatment was associated with risk of death than those started early and prompt. Also the types of antibiotics regimen, patients who were treated

with chloramphenicol/crystalline penicillin were at risk of death compare to those treated with ceftriaxone. Those patients who were dehydrated at presentation to hospital had poor outcome than those that were not dehydrated at presentation. This was in agreement with finding by Thompson et al. [20] who also reported that those that delayed greater than 3 days before presentation to health facility as well as those who received medications from drug vendors due to false assurance to the patients increased the risk of death. In standard literature, it is said that oily chloramphenicol depot injection and or additional crystalline penicillin course for 7-10 days was associated with 70% cure rate [21], in this study, those patients who received chloramphenicol/crystalline penicillin combination had an increased risk of unfavourable outcome than those patients who received ceftriaxone and gentamycin combination had quick and full recovery with lesser number of mortality.

Prompt care of patient's hydration status as well as other ancillary care also had effect to the patient's outcome; this was similar to the finding by Stephens et al. [10] and Welch and co-worker; who asserted that correction of hypovolaemia, hypoglycaemia and use of some inotropic agent decreased death rates [22]. In this study several factors such as delay in presentation to health facility, receiving treatment from other sources other than the hospital, children with dehydration and treatment with chloramphenicol/crystalline penicillin combination were associated with increased risk of death. At the same time treatment with ceftriaxone /gentamycin was associated quick recovery and reduction in mortality rate as well as reduction in duration of hospital stay which was demonstrated by Thomson et al. [8].

The overall mortality rate of 21.8% was similar to that reported by other workers in Maiduguri and Azare towns from the same region a decade ago [9,12] and from another African study where mortality rate 5-15% was reported [23]. It is therefore pertinent for healthcare professional working in the tropics, the African meningitis belt, to be familiar with the pattern of recurrence of meningococcal meningitis outbreak and to vaccinate as much as possible periodically against the serotypes such as serotypes A, B, C, and W-135. This may halt cyclical recurrent outbreak so as to avert the high morbidity and mortality associated with it especially among children.

5. CONCLUSION

Meningococcal meningitis has remained a public health menace worldwide and worse in the tropics especially in the region of African meningitis belt. Children have remained the large population affected with high morbidity and mortality and yet less attention are attached to them thereby taking toll on these vulnerable group patients. In this study which looked at an outbreak as it affect children <15 years, the meningococcal organism responsible for the infection was serogroup A, and all the children affected did not receive the appropriate vaccine (MenAfricVac) 2 years prior to the outbreak. This was largely due lapses in the vaccine administration/management by the health care professional saddled with this responsibility. On this note we recommend vaccination of the children/population at risk should be enforced and monitored on regular bases so to break the cycle of the epidemics and the unwanted morbidity and mortality associated with it.

6. LIMITATION

The research work financing was expensive, so we could not afford to do another lumber tap for collection of repeat sample to ascertain the clearing of the cerebrospinal fluid. Also the study was during an outbreak of meningococcal meningitis and there was pressure on the limited bed space and therefore long time follow up was not feasible.

CONSENT

As per international standard or universal standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or universal standard, written approval of Ethics committee has been collected and preserved by the authors.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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