Full Length Research Paper

Characteristics of morbidity and mortality in children less than 5 years of age with acute bacterial meningitis in Omdurman, Sudan

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Bacterial meningitis is still a common disease in Sudan. The disease has the potential to cause serious morbidity and mortality, especially within the paediatric age group. In this study, 58 children proven to have bacterial meningitis by PCR in Omdurman teaching hospital from 2004-2005 were assessed, managed and followed up in an attempt to point out the characteristics associated with morbidity and mortality. It was observed that cases with mortality were mainly in the less than 1 year age group (33.3% of the cases), more than half of the cases (53.3%) received breastfeeding for less than 1 year, more than of half of the cases had at least a parent who is a smoker. Males formed more than 60% of the cases. It has been observed that most cases with morbidity and mortality were associated with late presentation, presentation with coma, onset of convulsions, hypotension and petechial rash. Most of the survivors received 3rd generation cephalosporins, 64% of the cases were sensitive to long acting benzyl penicillin, 58% were sensitive to chloramphenicol. Bacterial meningitis incidence and occurrence needs to be reduced in Sudan. Appropriate vaccination and prophylaxis methods exist and could yield excellent results in the future if implemented correctly. The use of third generation cephalosporin as empiric treatment whenever lumbar puncture is not possible is the advised management.

Keywords: Haemophilus influenzae type b, meningitis, Neisseria meningitides, Risk factors, Streptococcal pneumoniae meningitis, Sudan.

INTRODUCTION

Although a vaccine against the common causes of bacterial meningitis do exist (Hemophilus influenzae type b, Streptococcus pneumonia and Nesseria meningitides) (Dickinson and Perez, 2005; Iriso et al., 2008; Sheldon and Marvin, 1988) still, many around the world do suffer both its morbidity and mortality (Mantese et al., 2002). In developing countries, where expensive and advanced diagnostic facilities are not available, the load of the

morbidity and mortality are expectedly high (Mantese et al., 2002; Mani et al., 2007; El Bashir et al., 2003; Yagob et al., 2004). Even in developed countries, (Berg et al., 1996) which have extensive vaccination programs, (Nakhla et al., 2003) bacterial meningitis is still considered a serious illness with damaging outcomes especially in children which could lead to detrimental morbidity and even mortality (Mantese et al., 2002; Mani et al., 2007; Ahmed et al., 1996; Brefani et al., 2006). The objective of this study is to assess the burden of acute bacterial meningitis by determining the risk factors and determining the prognostic factors and try to look for any advances in case management.

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MATERIAL AND METHODS

This is an observational case findings hospital-based study over 1 year period in Omdurman hospital with sampling of every patient that presented to the accident and emergency department and clinics with signs of meningitis for 3 days a week between April 2008 – April 2009. Number of cases that were assessed and had cerebrospinal fluid samples taken from was 117 patients, of which 58 were found to be positive. Parents/ guardians consent was taken for all patients and confidentiality during data collection, analysis and publishing was strictly protected.

The paediatrics hospital of Omdurman Teaching hospital is located in the western sector of the capital of Sudan, Khartoum. It has a catchment area of 5 million populations, 240 beds. Out of 350 paediatric patients visiting the emergency room an average of 18-25 patients get admitted daily. 117 cases were assessed for bacterial meningitis over that year. From them 58 cases with signs and symptoms of meningitis, cerebrospinal fluid (CSF) 7ml was taken for purpose of polymerase chain reaction (PCR). A minimum of 50µl of CSF of microscopy negative samples and 10µl of microscopy-positive samples were used for extraction of DNA. The deoxyribonucleic acid (DNA) was prepared using the QIAamp mini kit (QIAGEN, Hilden, Germany) according to the instructions of the manufacturer. Total DNA was eluted in 50µl of AE buffer (QIAGEN) and stored at 20°C until amplification by the PCR machine. The amplification mixture of the N. meningitides PCR consisted of 2 l of 10µl reaction mix (LightCycler Fast-Start master DNA, SYBR green; Roche Diagnostics, Germany), 4mM MgCl2, 0.5µM concentrations of each primer, and 2µl of template DNA in a final volume of 20µl. Samples were amplified as follows: an initial denaturation step at 95°C for 10 min and 40 cycles of denaturation at 95°C for 0 s, annealing at 54°C for 10 s, and elongation at 72°Cfor 20 s. The temperature transition rate was 20°C/s. The Mx3000P QPCR System (STRATAGENE, USA) was used. Simple tabulation of the data was performed using Epinfo V6b software and the SPSS program version 16.0 was used for analysis with Chi squared test with 0.05 level of significance.

RESULTS

All samples of CSF fluid taken from the patients looked turbid and were under tension. They were all tested using latex agglutination. Latex was positive in 50 (42.7%) cases, out of which 22 (44%), 18 (36%) and 10 (20%) cases were due to Hemophilus influenzae type b, Streptococcus pneumonia and Nesseria meningitides (Hib, SPM and N.M), respectively. There was no significant difference in the sero-positivity between the

three groups (p<0.73) as shown in Table 2. Out of 106 CSF samples tested using polymerase chain reaction (PCR), 58 (54.74%) were positive for bacterial meningitis; of which 37 (50.92%), 11 (10.37%) and 10 (9.43%) were due to N.M, Hib and SPM respectively. The difference in positivity between the groups is highly significant (p<0.001). Regarding the study population, 60 % of cases were male, 40% female, 80% of the patients were of low socioeconomic class and 60 % had a parent who smokes tobacco. Case fatality was 15 patients (25.86%), 6 of which (40%) due to N. meningitidis, 7 (46.7%) were due to Hemophilus influenzae type b and 2 (13.3%) due to Streptococcus pneumoniae infection. 20% of the patients with morbidity and mortality were sicklers. Most of the morbidity and mortality occur in children less than 1 year which we have 5 (33.3%) cases with minimal complications occurring in the 3-4 years age group 1(6.7%). 8 of the cases with complications had (53.3%) ceased receiving breast feeding in less than 12 weeks. Morbidity and mortality of Hemophilus influenzae and N. meningitidis are more or less the same about 50% of the cases where only about 2 cases occur in Streptococcus pneumoniae.

In descending order, the presentations related to morbidity and mortality found were convulsions, hypotension, age less than1y, coma, long duration of symptom before presentation and petechial rash with 46% 40% 33.3% 26% 20% 6% respectively. 89% of those with morbidity and mortality risk responded well to 3rd generation cephalosporins, 50% to chloramphenicol and 68% to long acting benzyl penicillin.

DISCUSSION

The study showed that of 58 patients with positive antigen PCR tests, 37 were N. meningitidis positive, 11 patients were Hemophilus influenzae positive and 10 were Streptococcus pneumoniae. HI meningitis was found to have an increased incidence in the < 1 year age groups (Dickinson and Perez, 2005). This is iterated in the 1st Saudi attempt at defining the profile of meningitis (Nakhla et al., 2003). It was also found that male to female ratio was 1.38 to 1. This is evident in most literature, similar or even larger ratios have appeared in many papers and no evidence is clear regarding the reason (Dickinson and Perez, 2005; Yagob et al., 2004). This is possibly related to the social context where male children spend more time outdoors or to any other factor, it is a definite topic for additional research.

What was of interest in this study is that of the 58 cases that tested positive for bacterial meningitis 15 patients showed signs of co-morbidity.

The median age for the whole study group was 15 months at presentation, whereas for the group that had further morbidity or mortality it was about 18 months, that

Table 1: Patients characteristics

Characteristic	Frequency	Percentage
1- Sex		
Male	9	60%
Female	6	40%
Total	**15**	**100%**
2- Age group (months)		
2 – 12	5	33.3
13 – 24	3	20
25 – 36	4	26.7
37 – 48	1	6.7
49 – 60	2	13.3
Total	15	100%
3- Outcome		
With co-morbidity	15	25.9%
Recovered well	43	74.1%
Total	58	100%
4- Type of morbidity		
Recovered completely	43	74.1%
Epilepsy	4	6.9%
Cerebral palsy	2	3.4%
Hemiplegia	1	1.7%
Hydrocephalus	1	1.7%
Deafness	2	3.4%
Blindness	1	1.7%
Death	4	6.9%
Total	58	100%
5- Risk factors		
5.1. Breastfeeding:		
Months of breast feeding		
0 – 6	2	13.3%
7 – 12	8	44.4%
13 – 18	4	26.7%
19 – 24	1	6.7%
Total	**15**	**100%**
5.2. Indicator for prognosis:		
Long duration of symptoms	3	20%
Coma	4	26%
Age less than 1 year	5	33.3%
Petechial rash	1	6%
Hypotension	6	40%
Convulsion	7	46%
5.3. Smoking:		
Smoking father	8	53.3%
Smoking mother	1	6.7%
Others	0	0%
No smoking	6	40.0%
5.4. Socioeconomic status		
Poor	12	80.0%
Average	3	20.0%
Good	0	0%
Total	**15**	**100.0%**
5.5. Sickle cell anaemia		
Sickler	3	20.0%
No sickler	12	80.0%
Total	**15**	**100.0%**
5.6. Other risk factors		
Care outside home	1	6.7%
History of Otitis Media	1	6.7%
Other sibling at elementary school	8	53.3%
Total	**10**	**66.7%**

* patients may have more than one of the factors together

Table 2: Table of drug sensitivities among the pathogens during culture

Drugs	Sensitivity	Resistant	Total
3rd generation Cephalosporins	89 %	11%	100%
Chloramphicol	52%	48%	100%
Benzyl penicillin	64%	36%	100%

Table 3: Number of cases in each type of meningitis according to latex agglutination and PCR

Lab test Organism	Latex		PCR		P. value
	Positive	Negative	Positive	Negative	
Niesseria meningitides (NM)	18	99	37	69	0.001
Haemophilus influenzae (Hib)	22	95	11	95	0.13
Streptococcal pneumoniae meningitis (SPM)	10	107	10	96	0.0997
Total	50	67	58	56	
P. value	0.073		0.001		

M m m* by the author in a previous paper Acta Paed vol 99 dec 2010 supp 462 p69.

said it is postulated that if neonates were introduced into the study that number would have dropped significantly. The disease incidence was found to increase in children who have not completed their breastfeeding or those who had breastfeeding interrupted before completion of 1 year. This is supported by the paper of the International Epidemiological association of 1999 "protective effect of breastfeeding" by Sven-Arne Silfverdal, Lennart Bodin and Per Olcen (Sven-Arne et al., 1999)**.** The paper insists that breastfeeding has a definitive preventive effect, more precisely as was researched in the paper, Haemophilus influenzae infection which was found to be epidemiological among Sudanesse patients. This was mentioned in 'Haemophilus type B meninigitis in Saudi children under 5 years old, (Nakhla et al., 2003) and 'Endemic bacterial meningitis in Sudanesse children (Salih, 1990). In this research Hemophilus influenzae meningitis seemed to be associated with children in the less than 1 year age group. Of the most serious prognostic factors that were classified by the World Health Organization (WHO) prognostic scale (hypotension, tachycardia, tachpnoea, capillary refill time, paediatric coma scale < 8, no neck stuffiness and petchiae/purpura) for meningitis only hypotension and petechial rash were recorded in cases with increased morbidity and mortality. The prognostic scale produced by the WHO mentioned and praised by the paper 'Epidemiological, Clinical and Prognostic Profile of Acute Bacterial meningitis among children in Alexandria' (Abdel-Farrah, 2005) is actually of certain importance but it did not actually concord with the results mentioned above.

Sudan has prevalent sickle cell anaemia which is known for its effects on splenic functions and it has been associated with septicaemia and even meningitis. In the 15 patients that had increased risk factors and co-morbidities 20% of that population were sicklers. This number is definitely pertinent but its significance is still to be researched (Robinson, 1966).

It found that within the 15 patients who had further morbidity and mortality, 80% were of low socioeconomic status, this is evident in most data even the one mentioned above (Salih, 1990). This has been attributed to decreased living space and overcrowding leading to easier dispersion of pathogens within the household context, in addition to lower levels of hygiene, inadequate nutrition and even a lower threshold for seeking medical care. Another risk factor that was found to be high in the same patient group was that 60% of these patients had a parent that smokes, yet this remains expected, evidently since tobacco and nicotine have been linked to many side effects, one of which is decreased immunity (Sopori, 2007).

The disease still carries serious outcomes for the patients, many outcomes were noticed in this paper, yet the paper did indeed fail to document them, but still 'coma, epilepsy and hypotension' were among the most common. A paper like the 'Outcome of bacterial meningitis in children' (Baraff 1993) needs to be conducted for Sudan.

A seasonal winter association was also noticed in the study, though the study 'Haemophilus type B. meninigitis in Saudi children under 5 years old (Nakhla et al., 2003) claimed a bi modal pattern of seasonal distribution. A study conducted in Alexandria followed the same pattern but it was also related to a streptococcal infestation in that period (Abdel-Farrah, 2005). An actual paper focusing on the topic needs to be done.

Third generation cephalosporins were the most effective treatment as documented by many papers since resistance is low by the three most common causes of acute bacterial meningitis, in this paper, only 11% of the pathogens were resistant to it (El Bashir et al., 2003;

Baraff, 1993).

CONCLUSION

The study showed that of the 58 patients with positive PCR, 37 were N. meningitidis positive, 11 patients were Hemophilus influenzae positive and 10 were Streptococcus pneumoniae. HI meningitis was found to have an increased incidence in the < 1 year age groups. It was also found that male to female ratio was 1.38 to 1. The disease incidence was found to increase in children who have not completed their breastfeeding or those who had breastfeeding interrupted before completion of 1 year. Other studies also demonstrated that breastfeeding has a definitive preventive effect. Haemophilus influenzae infection which was found to be the most prominent amongst Sudanese patients. Third generation cephalosporins were the most effective treatment. If lumber puncture is difficult on ill patient, empirical third generation cephalosporin is recommended. More papers need to be done to establish further the tendencies of this devastating disease among the Sudanese population.

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