AN AUDIT REPORT ON BACTERIAL MENINGINTIS AMONG CHILDREN ADDMITTED TO MUHIMBILI NATIONAL HOSPITAL, DAR ES SALAAM, TANZANIA

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Abstract

Background: This is a preliminary report of the ongoing paediatric bacterial meningitis surveillance at Muhimbili National Hospital, Dar es Salaam, Tanzania. The World Health Organization (WHO AFRO) introduced this initiative to countries in the African region. The report covers the period beginning October 2001 up to December 2004.
Methodology: All patients suspected to have acute bacterial meningitis were registered and a sample of cerebral spinal fluid (CSF) was taken from each patient and subjected to standard laboratory investigations.
Results: A total of 16350 children were admitted during this period and, out of these, 1529 (9.6%) were suspected to have bacterial meningitis. CSF was collected from 84% of the children suspected of suffering from bacterial meningitis. While Bacteria were isolated from 5.6% of these samples, bacteria isolation rate from turbid CSF(96 samples) was 72.9%. The commonest isolates were *Klebsiella* species (26%), *Streptococcus pneumoniae* (22%), *Haemophilus influenzae* (13%), *Salmonella* species (9.1%) and E. *coli* (6.5%). *N. meningitidis* was not isolated during the three year period. Of all children with suspected bacterial meningitis, 61% were in the first 12 months of life while 3.8% of them were aged 36 months and above. *H. influenzae* was not observed to cause disease after the age of three years while *Streptococcus pneumoniae* continued to cause disease up to the age of 60 months (5years). Whereas *Klebsiela* spp, *S. pneumoniae* and *H. influenzae* contributed to 22.5% death rate each to the total meningitis death burden, *H. influenzae* had the highest microbial agent-specific mortality rate (90%), followed by *E. coli* (80%), and *Salmonella* spp. (66%). About 52.5% of the deaths occurred in the first 5 months of life and the overall disease case mortality rate was 51.9%.
Conclusion: The low bacteria isolation rate could be attributed to the prior use of antibiotics and the use of human blood agar instead of sheep's blood agar for the isolation of *H. influenzae*. The high frequency of *Klebsiella* spp causing meningitis has not been frequently reported in Africa. The results of this study further confirm that there is no consistent pattern of microorganisms causing meningitis in tropical Africa.
Recommendation: The high mortality rate observed in this study supports the need to introduce the *H. influenzae* and *S. pneumoniae* vaccines in our routine immunization schedules. There is a necessity of looking for factors contributing to this high death rate.

Key words: Bacterial Meningintis among Children, Dar es Salaam, Tanzania

Introduction

Bacterial meningitis is one of the top common causes of admissions in the Paediatric Wards of Muhimbili National Hospital(1). Although this condition has not been the leading cause of deaths, the case mortality rate has been, over the years, considerably high. This trend has been observed in other developing countries. Uganda reported a case mortality rate as high as 50% and neurological sequel in 32% of the survivors.(2) In Nigeria, bacterial meningitis contributes to 2.5-5.4% of deaths among the hospitalized children and an unquantified cause of neurological disabilities.(3) The clinical diagnosis of meningitis in younger children is made following a high index of suspicion.

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Typical signs of meningitis are only present in older children. *Haemophillus influenzae*, *Streptococcus pneumoniae* and *N. meningitidis* accounts for up to 95% of causes of meningitis in children beyond the neonatal period in temperate countries.(4,5) There has been previously no consistent pattern of microorganisms causing meningitis in tropical Africa.(6,7,8)

The burden of disease is increasingly concentrated in developing countries where the conjugate vaccines for the three common organisms are inaccessible due to the prevailing poor economical status. The situation is expected to be worse following the increasing trend of microbial resistance to the common antimicrobial agents such as penicillin and chloramphenicol.(9) It is therefore necessary to consistently review the disease so as to highlight possible changes in pattern of microbial agents and their sensitivity to the available drugs.(7)

Materials and Methods

The surveillance is part of the ongoing paediatric bacterial meningitis surveillance activities, which is an initiative of WHO-AFRO that has been adopted by a number of African countries. In Tanzania, the surveillance is done in the Department of Paediatrics and Child Health at Muhimbili National Hospital in Dar es Salaam. The study population comprised of admitted children with signs and symptoms suggestive of acute bacterial meningitis. These signs and symptoms are history of fever during the last 48 hours with two of the following: reduced level of consciousness, stiff neck, bulging fontanel and seizures for children aged from 60 days to 60 months. Children aged less than 60 days were suspected to have meningitis when they presented with the following signs: Fever or low temperature (<35°C), irritability, severe lethargy, bulging fontanelle, stiff neck, high pitched cry, apnoeic episodes and fits as provided in the standard guidelines.

Specimen collection

All children suspected to have meningitis had a lumbar puncture done by a medical officer as soon as the diagnosis was made. One ml. of CSF was collected in each of the two plain sterile bottles for cell counts and for culture and sensitivity. Another 0.5 mls was collected in an oxalate containing bottle for glucose and protein. The bottles were correctly labeled and immediately sent to the laboratory.

Laboratory procedures

Cell counts

Uncentrifuged CSF was thoroughly mixed and a Neubauer counting chamber was used for counting the cells. The CSF was considered to be turbid on macroscopic appearance and when it contained ≥ 100 cells /μL.

Microscopy and Gram Stain

After the CSF was centrifuged, the supernatant was withdrawn and stored at 40^{0}C for *Slidex* antigen testing whenever CSF had pus cells but with no bacterial growth. A drop of the deposit was spread on a glass slide, allowed to dry before staining with the Gram's stain. Another drop of deposit was used for wet preparation and stained with Indian ink.

The deposit was also used for inoculating blood and chocolate agar plates. The plates were incubated at 37^{0}C for 24 to 48 hours in a CO_2 incubator before examining them. The bacteria growing on the plates were identified by use of the standard methods including colony characteristics, Gram staining, sensitivity to Optochin, oxidase test, and requirement for X and V factors, where applicable.

Results

The frequency of suspected meningitis (SMP) was 9.6. There is a decline in the number of suspected meningitis patient with a decline in the number of admissions. The frequence of laboratory confirmed bacterial meningitis was 5.6. The percentage of isolation of bacteria in turbid CSF was 72.9%. The commonest organisms seen in this study were *Klebsiella* spp, *S. peumoniae, H. influeazae* and *E. coli,* in that order. Isolation of *Klebsiella* spp has been increasing while isolation of streptococci has been decreasing over time.

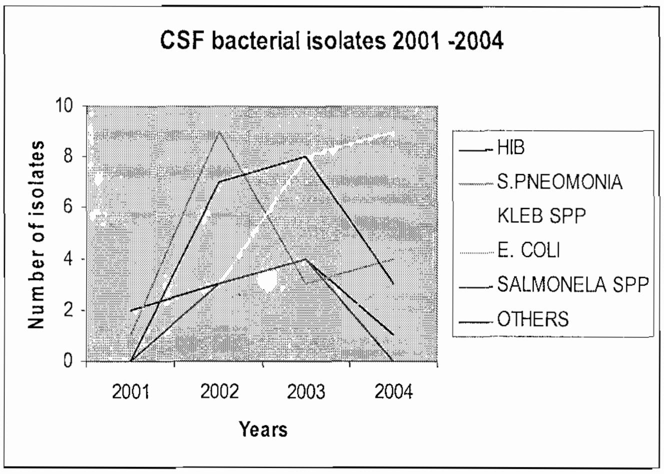
Most children were seen in the fist 36 months of life. Fifty nine percent (59%) of children with meningitis were aged up to six months. *S. peumoniae* was isolated from all age groups but much more common in the first 12 months. *H. influenzae* was not isolated from children older than 36 months. S.aureus was rarely isolated. Overall disease specific mortality rate was 51.9%. Ninety percent of deaths occurred in children aged up to 36 months. Fifty two percent of deaths occurred in babies aged up to six months

Table 1. Indicators for Bacterial Meningitis Surveillance.

Indicator	Number of patients under each Year of study				
	2001	2002	2003	2004	Grand total
Number of patients	1324	6427	4720	3879	16350
No. of SMP	121	542	535	331	1529
% of SMP	9.1	8.7	11.3	8.6	9.6
LP Done	106	344	474	322	1246
%LP Done	87.6	63.5	88.6	97.3	84.3
No. Purulent CSF	5	41	38	12	96
% Purulent CSF	4.7	11.9	8.0	3.7	7.7
Purulent CSF with growth	3	26	21	20	70
% Purulent CSF with growth	66.7	63.4	55.3	166.7	72.9
% Isolates	2.8	7.6	4.4	6.2	5.6

Table 2. Bacterial isolates over the period of surveillance $1^{ST.}$ October, 2001- 31^{st}.December, 2004.

Bacterial isolates	Year of surveillance				Total isolates
	2001	2002	2003	2004	
HIB spps	2	3	4	1	10 (13.0%)
S. pneumoniae	1	9	3	4	17 (22.0%)
Kleb. Spps.	0	3	8	9	20 (26.0%)
E.coli	0	1	1	3	5 (6.5%)
Salmon. Spps	0	3	4	0	7 (9.1%)
Others	0	7	8	3	18 (23.4%)
Total	3	26	28	20	77



Other organisms include: Unspecified *Streptococcus* species, Colifoms, *Streptococcus pyogenes*, *Acenobacter* species, *Staphylococcus albus*, and unspecified Gram-negative rods.

Figure1. CSF bacterial isolates 2001 - 2004

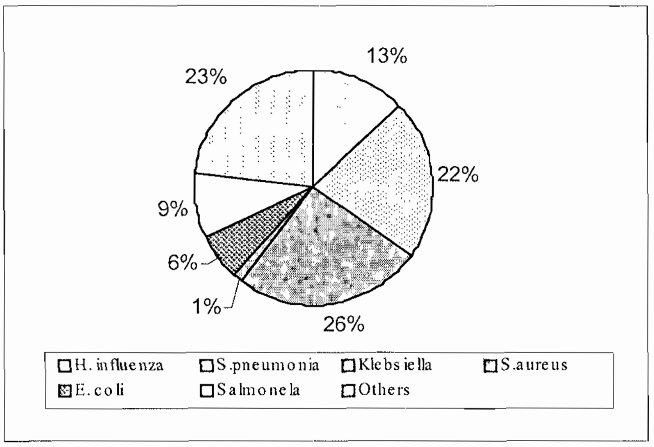
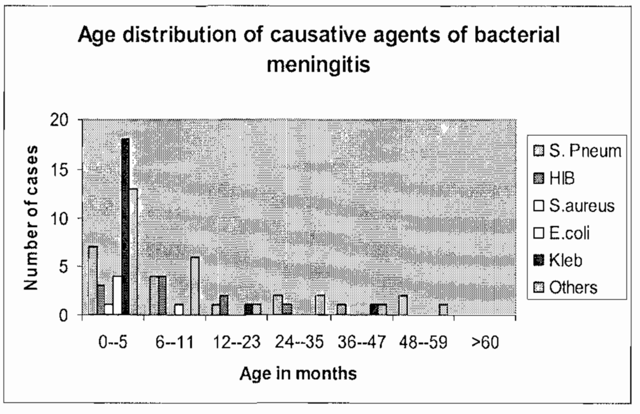


Figure 2. Proportion of microbial causing Paediatric Meningitis

Table 3: Age distribution of cases by causative agents of bacterial meningitis:

Age in months	Type of the organism						
	S. Pneum	HIB	S.aureus	E.coli	Kleb	Others	Total
0-5	7	3	1	4	18	13	46
6-11	4	4	0	1	0	6	15
12-23	1	2	0	0	1	1	5
24-35	2	1	0	0	0	2	5
36-47	1	0	0	0	1	1	3
48-59	2	0	0	0	0	1	3
≥60	0	0	0	0	0	0	0
Total	18	10	1	1	20	25	77



The most lethal organisms were *H. influenzae*, *E. coli*, *Salmonella* spp, *Klebsiella* spp and *S. pneumoniae*, in that order. *H.influenzae*, *S. pneumoniae* and *Klebsiella* spp singly contributed to 22.5% of the deaths.

Figure 3. Age distribution of causative agents of bacterial meningitis

Table 4. Association between agents causing meningitis and mortality.

Type of organism	No. of patients	% of total	No. of deaths	% of total deaths	Organism specific mortality rate (%)
H. influenzae	10	12.9	9	22.5	90.0
S. pneumoniae	17	22.0	9	22.5	41.0
Klebsiella spp	20	25.9	9	22.5	47.6
S. aureus	1	1.2	0	0.0	0.0
E. coli	5	6.4	3	7.5	80.0
Salmonella spp	7	9.0	4	10.0	66.6
Others	18	23.3	6	15.0	33.3
Total	**77**	**100.0**	**40**	**100.0**	

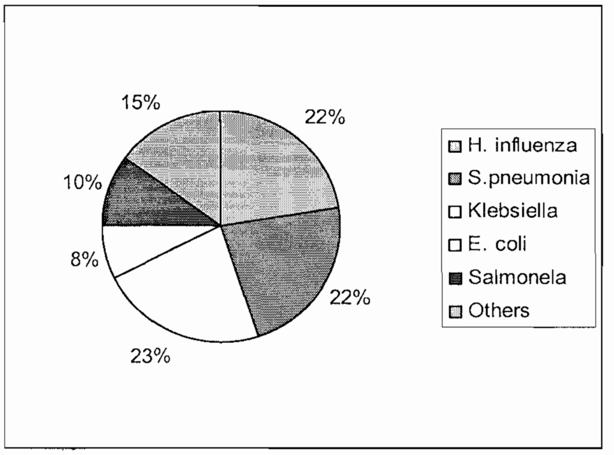


Figure 4. Microbial specific mortality rates

Table 5. Deaths distribution by age of the patient and the causative agent.

Age in months	Types of organisms						Total	
	S. pneumoniae	HIB	S. aureus	E. coli	Kleb	Others	N	%
0--5	5	1	0	2	8	5	21	52.5
6--11	1	3	0	0	0	1	5	12.5
12--23	0	4	0	1	1	0	6	15.0
24--35	1	1	0	0	0	2	4	10.0
36--47	1	0	0	0	0	1	2	5.0
48--59	1	0	0	0	0	1	2	5.0
≥60	0	0	0	0	0	0	0	0.0
Total	9	9	0	3	9	10	40	100.0

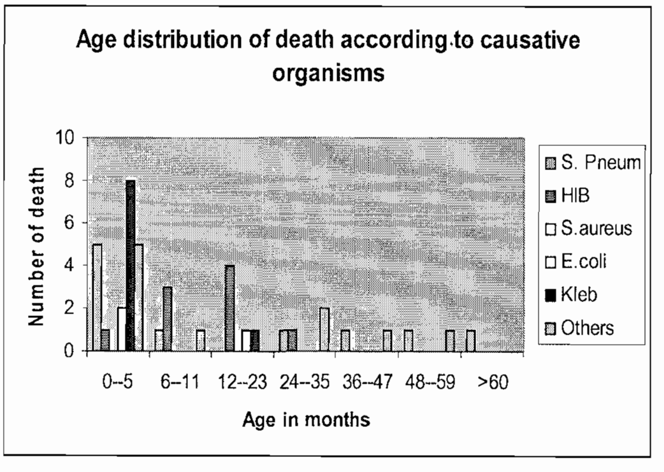


Figure 5. Age distribution of death according to causative organisms

Discussion

The number of hospital admissions declined during the period of surveillance most likely due to ongoing strengthening of municipal hospitals that refer patients to MNH. The decline in admissions might have contributed in the decline in the number of suspected cases of meningitis noted in this report (Table 1 and 2). The frequency of suspected cases of meningitis is likely to vary depending on the case definition used.

The reported prevalence of suspected case of meningitis of 9.5% is much higher than that of 1.04% reported in Ghana [12] and1.3% in Kenya.[13] A high index of suspicion is needed in order to identify all those children who need to be treated for meningitis to avoid unnecessary complications following inadequate therapy. The prevalence of laboratory culture confirmed meningitis was 5.6%. However turbid CSF's were not frequently found and appeared at a frequency of 4.7% to 11.9%. Although this might be attributed to inaccurate counting, it might also be in keeping with the low bacteria isolation rate of 5.6% that was encountered in this study. When markedly abnormal, results of CSF total protein, glucose concentration, and percent neutrophils have value for diagnosing acute bacterial meningitis even among children with low white blood cell (WBC) counts in CSF.[14] In some children bacteria are occasionally isolated from CSF that contains few WBC counts. The bacteria isolation rate in turbid CSF was 63.45-72.9%. The use of human blood agar for isolating *H. influenzae* and antibiotics prior to admission might have contributed to the low bacterial isolation rate. Although this was not specifically looked for in this surveillance, Muhimbili National Hospital serves an area where IMCI guidelines are widely used. In the guidelines, it is recommended to give antibiotics to all patients with severe febrile illness before referral.

An explanation for not isolating *Neisseria meningitidis* in the whole 3-year period of this surveillance is difficult to come by. *N. meningitidis* was isolated from 14.5% of cases in a study done at Kenyata National Hospital involving 92 patients (52 adults and 40 children).[8] Another study in Uganda reported 5.4% isolation rate of *N. meningitides*.[2] It appears that in East Africa this organism might not be a frequent cause of meningitis as is the case in West Africa.[2,6,7,12] Unlike in these previous studies in West Africa and East Africa, Klebsiella spp have been found to be an important cause of meningitis in this study, contributing up to 27.7% of cases replacing *E. coli*. This is similar to the results of a study done at Al-Thawrah Hospital in Yemen where the predominant organism in CSF were *Klebsiella* spp(33.33%) followed by *Haemophilius influenzae* (23.8%) and *Streptococcal pneumoniae* (14.28%).[15]

From the results shown in Table 4 and Figure 2, acute bacterial meningitis appears to be a problem in the first three years of life. These results are quite similar to what has earlier been reported in Africa.

In developing countries where vaccination is not being implemented, there have been worsening morbidity and mortality statistics.[7] The case fatality rate of 51.9% noted in this report is much higher than that previously reported in Ghana and Kenya of 22% and 30.1%, respectively.[12,13] Our observation of *H influenzae* being associated with the highest mortality rate of 90% is not in agreement with findings in Ethiopia where *S. pneumoniae* was responsible for 41% of deaths while *H. influenzae* was responsible for 37% of deaths.[16] In both Ghana and Ethiopia study *S. pneumoniae* was associated with the highest mortality.[12,16] In Ghana most deaths occurred in the fist 24 hours and late referral and therefore delayed therapy was considered to have contributed to these deaths. In these previous studies the high mortality rate has also been attributed to an increasing resistance of bacteria to penicillin and chloramphenical. Tanzania like many other poor resource countries is still using chloramphenical as first line initial therapy for meningitis in children. In another study done in a rural area in Tanzania, no resistance to antibiotics was demonstrated in spite of a high mortality rate. In this previous study, poor laboratory testing, long doctor/patient delays and /or poor drug administration were considered to be contributing factors.[17] Therefore the high mortality rate found in this study might not be attributed to drug resistance alone, further studies are necessary to determine other underlying factors.

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