

**Serious infections caused by
HAEMOPHILUS INFLUENZAE TYPE B
in children aged 2-59 months in Omdurman Children's**

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Abstract:

Haemophilus influenza type b (Hib) is a common cause of serious infections including meningitis, pneumonia and epiglottitis. Isolation of the organism by culture is laborious but a rapid latex test has recently been proved useful for diagnosis. The objectives of this prospective hospital-based study were to (a) determine the incidence of severe Hib disease, namely

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meningitis, epiglottitis and severe pneumonia in children 2-59 months based on the clinical features together with a rapid laboratory test (latex) and (b) report on short term outcome.

During a one-year period, 305 patients admitted to Omdurman Teaching Hospital with suspected Hib disease were enrolled; 117 (39%) were cases of meningitis. Severe pneumonia and epiglottitis comprised 180 (59%) and 8 (3%) cases, respectively. Of 117 cases clinically diagnosed as meningitis, Haemophilus influenzae type b was detected by latex test in 22 (44%) patients; but all blood cultures were negative for Hib. The organism was found to be sensitive to chloramphenicol in 43% of cases. The case fatality rate was 9.1%; hemiplegia and epilepsy each occurred in one of the cases who recovered. The need for introduction of Hib vaccine in the national programme of immunization cannot be overemphasized.

Introduction:

Haemophilus influenzae type b (Hib) primarily inhabits the upper respiratory and trans-pulmonary system⁽¹⁾. Infection leads to epiglottitis, invasive pneumonia and meningitis predominantly in children under five with high morbidity and mortality⁽²⁾. Worldwide, it contributes to 300 000 – 500 000 deaths per year, a third of which occurring in sub-Saharan Africa⁽³⁾. Introduction of Hib vaccine in 1980 to the industrialized countries has resulted in sharp decline of disease burden⁽⁴⁾.

The organism haemophilus influenzae type B, so named because of the false impression that it caused influenza⁽⁵⁾, is a small pleomorphic gram negative bacteria⁽⁶⁾. Based on the antigenic properties of its polysaccharide capsule it is classified into A – F subtypes⁽²⁾, of which type B6 is the commonest serotype and the cause of severe disease⁽⁷⁾. Haemophilus influenzae type b may cause also genitourinary tract infection and sepsis⁽⁸⁾. Isolation of the organism is fastidious, laborious and needs careful sample

taking as well as special culture technique. However, a simple and rapid immunological test (latex agglutination test) that detects the antigen in blood, CSF and urine has been recently proven useful for diagnosis⁽⁹⁾.

The easy way to determine the burden of Hib disease is to use the incidence of Hib meningitis⁽¹⁰⁾. The incidence marker for Hib infection could be reflected from Hib meningitis since it is difficult to identify the micro-organism causing other diseases such as invasive pneumonia and epiglottitis⁽¹¹⁾. Information of the disease burden caused by Hib in developing countries is meager - Sudan is no exception⁽¹²⁾. Preliminary studies conducted during the non-epidemic periods in Sudan indicated that Hib might be the major pathogen that causes meningitis in young children⁽¹³⁾. Hib meningitis is common in Egypt⁽¹⁴⁾ Kingdom of Saudi Arabia⁽¹⁵⁾ while it is less common in European countries e.g. Finland⁽¹⁶⁾, England and Scandinavians⁽¹⁷⁾. The objectives of this prospective hospital-based study were to: (a) determine the incidence of severe Hib disease, namely meningitis, in children 2-59 months based on the clinical features together with using a rapid test (latex) and (b) report on the short term outcome.

Patients and methods:

The study was conducted in Omdurman Teaching Hospital (OTH) during the period August 2003 – July 2004 on a three-day-per-week basis. All children admitted with clinical diagnosis of meningitis, epiglottitis and severe pneumonia were included. The case definition of meningitis is acute onset of fever, refusal of feeding, vomiting, convulsions, bulging fontanelles and neck stiffness plus signs of meningeal irritation i.e. positive Kerning's sign, Brudzinski sign and / or tripod sign^(18,19). Severe pneumonia consisted of acute onset of fever, cough, tachypnea and chest indrawing. Cases of epiglottitis have in addition stridor drooling of saliva and dysphagia. Children who were comatose,

critically ill or whose guardians did not give consent were excluded.

A pre-coded questionnaire on medical, social and family history was completed after obtaining informed verbal consent. Thorough clinical examination for each child was then conducted. Two milliliters (mls) of venous blood were drawn from all cases for estimation of haemoglobin, blood counts, blood culture and blood sugar. Cerebrospinal fluid (CSF) was withdrawn from cases suspected as meningitis, examined for pressure, macroscopic appearance, cytology, gram stain, sugar, protein and serology. Two mls of CSF were spared for culture in transport media (TIM), then sub cultured in GCII chocolate (GCH) chocolate and chocolate agar incubated for 24 – 72 hours in 10% Co⁽²⁰⁾ atmospheric 37°C then chemical test such as gram stain, catalase oxidase CAPI haemophilus i.e. analytic profile index. Serotyping was done using specific antisera for haemophilus influenza type b and quality control was performed using standard control ⁽²¹⁾.

Simple tabulation of the data was performed using Epiinfo v6b software and the SPSS program was used for analysis with X² of 0.05 level of significance.

Results:

Of a total of 305 patients enrolled in the study, 117 (39%) cases were clinically diagnosed as meningitis; 180 (59%) and 8(3%) were cases of severe pneumonia and epiglottitis, respectively. Of the 117 cases of meningitis, 63 (53.8%) were males and 54 (46.2%) were females. The latex test was positive in 50 (42.7%) cases; these were due to haemophilus influenza type b in 22 (44%) cases, nisseeria meningitis in 18 (36%) and streptococcus pneumonia in 10 (20%) cases. These three organisms had positive CSF cultures in 8 (38.1%), 7 (33.3%) and 6 (28.6%) of the cases, respectively (Table 1). Only three (43%) of the eight

cultures of Hib were sensitive to chloramphenicol. The age distribution of cases caused by haemophilus influenza type b is shown in Tables 2 and all the patients received ceftriaxone for a week. The majority (n=16, 73%) of cases of confirmed Hib meningitis recovered. The complications observed included epilepsy in 2 (9.1%) cases, early cerebral palsy in 1 (4.5%), and one case developed hemiplegia. There were two (9%) reported deaths (Table 3). Table 4 shows no statistically significant difference between the case fatality rate in Hib cases compared to others.

Discussion:

The incidence of severe disease caused by Hib is not easy to document because of the difficulty to isolate the organism from cultures. As shown in this study, none of the cultures from cases of severe pneumonia or epiglottitis were positive (this will be dealt with in a forthcoming publication) while only one third of the Hib meningitis cases proven by latex test had positive CSF cultures. Other factors contributing to low positive cultures include lack of efficient laboratory facilities, reagents and poor specimen transport and handling.

The study showed that Haemophilus influenza type b is the most frequent cause of meningitis in children aged 2 – 59 months during inter-epidemic season. This finding is in agreement with other studies from Sudan (Salih) and with the reports of the hospital records of the Sudan Health Statistics^(21, 12). Moreover, studies done in neighboring countries e.g. Ethiopia, Eritrea and Egypt produced similar results^(22, 23, 14). The peak age for Hib meningitis in this study was observed in children less than one year of age and is comparable to that reported by Salih in Khartoum 20 years ago⁽²³⁾. Although the low sensitivity of the organism to chloramphenicol has long been observed by clinicians and was also reported elsewhere but the numbers tested in this study was too small for making conclusions⁽⁹⁾.

The complications and case fatality rate for Hib meningitis in this study are lower than that reported in previous work done in Sudan⁽²³⁾. This may have many explanations; possibly, the use of better antibiotics, the increase in the level of the health education (awareness) with early reporting, detection and early management as well as better medical care⁽²³⁾.

In conclusion the study shows that Hib meningitis is a public health problem in Sudan, with high case fatality rate. It also reflects the significant burden caused by serious Hib disease that calls for urgent preventive measures. Not to mention the need for introduction of Hib vaccine in the national immunization program.

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Table 1: Cases of meningitis positive by latex test and/or culture

Organism	Latex positive	Culture positive
	N (%)	N (%)
Haemophilus influenza type b	22 (44)	8 (38.1)
Nisseeria meningitis	18 (36)	7 (33.3)
Streptococcus pneumoniae	10 (20)	6 (28.6)
Total	50 (100)	21 (100)

Table 2: Cases of haemophilus influenza type b meningitis according to age (n=22)

Age (months)	Latex positive N (%)	Culture positive N (%)
2 - < 12	9 (40.9)	3 (37.5)
12 - < 24	5 (22.7)	2 (25.0)
24 - < 60	8 (36.4)	3 (37.5)
Total	22 (100.0)	8 (100.0)

Table (3): Outcome of haemophilus influenzae type b meningitis

Outcome	No.	%
Full recovery	16	72.8
Epilepsy	2	9.1
Cerebral palsy	1	4.5
Haemiplegia	1	4.5
Death	2	9.1
Total	22	100 (100.0)

Table 4: The case fatality rates among cases of meningitis (n=117)

Organisms	No. of cases	No. of death	Case fatality rate (%)
<i>Haemophilus influenzae</i>	22	2	9.1
<i>Nisseria meningitidi</i>	18	1	5.6
<i>Streptococcus pneumoniae</i>	10	0	0.0
No organisms	67	2	3.0
Total	117	5	4.2

$$X^2 = 21.84.$$

$$P = 0.600$$

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Figure 2: Clinical Presentation in Severe Pneumonia

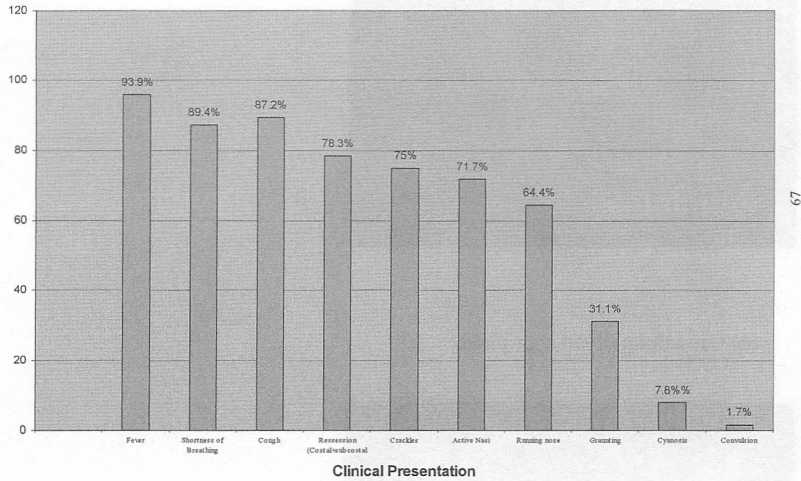
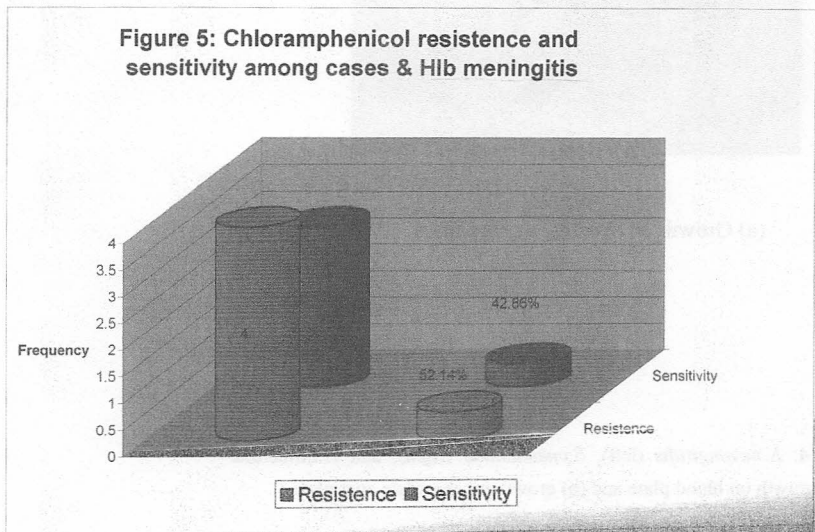
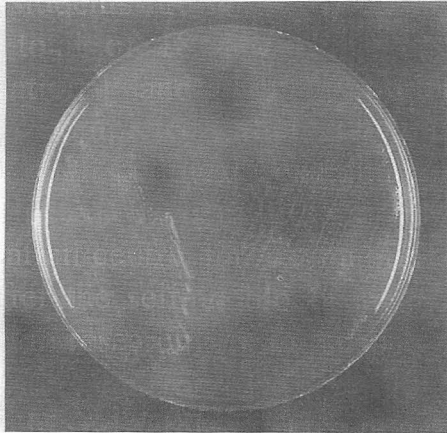
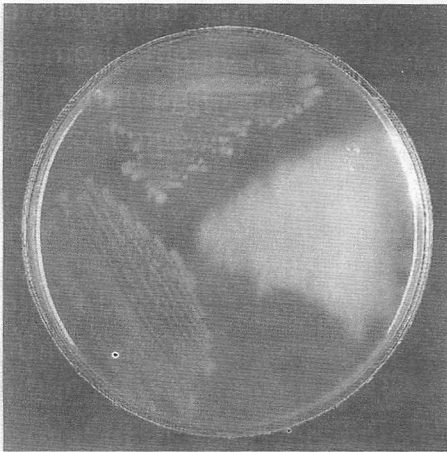


Figure 5: Chloramphenicol resistance and sensitivity among cases & Hib meningitis





(a) Growth on blood agar plate.



(a) Growth on chocolate agar plate.

Figure 14: *N.meningitidis* (left), *S.pneumoniae* (right), and *H.influenzae*
(top) (a) growth on blood plate and (b) growth on chocolate agar plate.