The hemophilus influenzae typeb health and social care essay

Hemophilus influenzae type b (Hib) is an encapsulated, non-motile and non-spore-forming Gram-negative coccobacillus which causes severe pneumonia, meningitis and other life threatening illnesses1. Hib disease affects almost exclusively (95%) children aged less than 5 yr throughout the world. The World Health Organization (WHO) estimates that Hib is responsible for 8. 13 million cases of serious illnesses, mainly meningitis and approximately 371, 000 deaths worldwide each year in children aged less than 5 yrs2. Uncertainties about Hib disease burden in India have led to delays in introduction of Hib conjugate vaccine. Pneumonia and meningitis comprise the majority of the severe diseases caused by Hib in developing countries. Meningitis is the most severe form of Hib disease, with case fatality rates ranging from 20-25% and rates of severe neurologic sequelae in survivors of 30-40%. Rates of Hib pneumonia in developing countries have been estimated to be 2-5 times higher than rates of Hib meningitis3. Countries using Hib vaccine in national immunization programs have virtually eliminated Hib disease4, 5; however, Hib disease continues to occur in countries that do not use Hib vaccines widely. A large percentage of Indian children are thought to be at a high risk of getting Hib disease due to increasing resistance to antibiotics as well as to limited access to health care facilities. WHO estimate has shown that 72, 000 deaths occurs due to Hib in India in children less than 5 years of age accounting for approximately 4% of all child deaths in India6. Hib vaccine is safe, highly effective and readily available in the market. Hib vaccine has been shown to be > 95% efficacious in diverse populations around the world7. However, the introduction of Hib vaccine is still limited to children of the developed world due to high cost of the vaccine and marked underestimation of the burden of Hib disease. The

objectives of this review were to identify and examine systematically all literature on Hib disease burden from India, and to evaluate critically the quality of these studies. This critical review will highlight the strengths, weaknesses, and limitations of the methodologies used, to draw lessons for surveillance of other bacterial vaccine-preventable diseases, and for surveillance following Hib vaccine introduction.

3. Objectives:

The primary objectives of this systematic review areTo know the burden of invasive Haemophilus influenzae tybe b disease. To determine the need for introduction of Haemophilus influenzae type b conjugate vaccine in the National Immunization Schedule.

4. METHODS:

We conducted a systematic search of the published literature and also tried to acquire information about the unpublished literature from various investigators of the region.

4. 1 Sources of Data:

The searches were current as of January 2013 and we identified articles with information on Hib disease among children < 5 years of age. Our search strategy included the following: (1) Searcing Pubmed, Embase and Cochrane using the search terms " Haemophilus," " Hemophilus," " influenza," " type b," " Hib," as well as the words or roots " meningitis," " pneumonia," " respiratory," " lung infection," " communicable disese," and free words includes " burden," " incidence," " prevalence," " mortality," " communicable diseases," " estimate," " case fatality rate," and India; (2) The reference lists

of the published articles; (3) Reviewing unpublished literature from websites and personal communications. Non English articles were not included. The search details are given in the appendix II. Literature search was done by two authors (KKT, HK). HK helped in obtaining full text articles.

4. 2 Definitions Used:

4. 2. 1 Prevalence is the proportion of children in a population (<5 years of age) who have a Hib disease over a specified period of time. 4. 2. 2 Burden: proportion of children with positive Hib cases/isolates to the total number of isolates from the children under 5 years of age

4. 2. 3 Case Fatality Rate (CFR):

The number of deaths within a designed population of cases to the number of cases due to the disease of interest. If CFRs were not reported by the authors but the relevant data for children less than five years were available, we calculated and recorded the CFRs. If the study did not provide this information, CFR could not be calculated, and this variable was left blank for this study. Standard quality assessment criteria developed based on expert opinion and previous studies, were applied to all studies and included the following: (1) Study authors used a clinical case definition consistent with current WHO standards8, 9; (2) Laboratory methods were explained and considered to be appropriate for the disease outcome measured (used a validated method to identify Hib from one of the otherwise sterile sites of the body like blood, CSF, pleural fluid etc either by culture or by latex agglutination test (LAT)/polymerase chain reaction (PCR) or other technique10; and the study reported on prior antibiotic use.

4. 3 Inclusion Criteria:

Studies - prospective/retrospective with children < 5years of age as /or part of the studied population. Studies with possible data available on Haemophilus influenzae type b isolated from children < 5 years of age. Studies with at least 12 months of surveillance were included in order to overcome the seasonal nature of Hib diseases. Studies conducted only in India. The quality characterization of included studies has been assed and mentioned in Table-1. The inclusion was decided by 3 authors (KKT, NJ, BE) and quality assessment was done by 3 authors (NJ, KKT, BE). Discrepancies if any were resolved by discussion by third author (MS) and the verdict was considered to be final. We excluded case reports, editorials, literature reviews, carriage studies, anti-microbial resistance, and safety and immunogenicity studies. The excluded studies are listed in Table-227-34

4. 4 Data collection and management:

Three authors (KKT, NJ, AK) abstracted data from the included studies in a predesigned table that included study design, setting, no. of suspected cases, no. culture samples taken & positive cultures obtained, and no. positive cultures for Hib. The data from Hospital based studies and population based studies were abstracted separately. To resolve the discrepancies regarding the abstracted data or missing data the authors were contacted and if the discrepancies were not resolved they were not taken up for pooled analysis.

4. 5 Data analysis:

Data analysis was done using Comprehensive Meta Analysis (CMA) V2 by 3 authors (KKT, NJ, and AK). The similar studies were pooled together. Sub group analysis for determining the Hib burden in India was done in children <5 years of age.

5. RESULTS:

A total of approximately 12790 articles in multiple languages have yielded by our initial searches. After a review of the titles and abstracts of these articles for relevance, we identified a total of 16 studies (Table-1) that presented the hospital based data on Hib disease in India, including 4 surveillance studies (3 multicentre surveillance studies). Of the 16 studies identified 14 studies are prospective studies and 2 studies are retrospective studies. No population based studies were identified from India.

5. 1 Prospective studies: 11-24

5. 1. 1 Invasive Hib disease:

We based our estimates of invasive Hib disease burden and case-fatality ratios on data from the literature review. As there are several estimates from India, we generated a summary value using a random-effects meta-analysis. We included 14 studies which had the data about invasive Haemophilus influenzae disease in children <5 years of age (Table-3)10-21. All the studies were hospital based and the meta analysis using randon-effects detected Hib disease in 10. 7% (95% CI, 6-18. 4) (Fig-1) of children less than 5 years of age and about 32. 6% (95% CI, 26. 6-39. 2) (Fig-2) of all invasive bacterial disease are due to H. Influenzae.

5. 1. 2 Pneumonia:

Using random-effects meta-analysis, we developed a summary estimate of the proportion of all-cause pneumonia cases caused by Hib. Of the 14 included studies from India, 5 studies gave the definite data about Hib pneumonia (Table-4). The meta-analysis using random-effects showed that 3% (95% CI, 0. 40-17. 6) (Figure-3) of all cases of pneumonia are due to Hib pneumonia and about 10. 2% (95% CI, 3. 20-27. 7) (Figure-4) of all bacterial causes of pneumonia is Hib.

5. 1. 3 Meningitis:

Most reported estimates of Hib meningitis incidence come from hospital-based surveillance studies. Ten studies gave the definite data about Hib meningitis (Table-5). The pooled analysis using the random-effects showed that 14% (95% CI, 9. 30-20. 4) (Figure-5) of all cases of meningitis are due to Hib meningitis and 9 studies described about 35% (95% CI, 26. 90-44. 20) (Figure-6) of all bacterial causes of meningitis is Hib. 5. 2 Retrospective studies23, 24: The review included 2 retrospective hospital based studies from India (Table-6)23, 24 and the pooled analysis showed the prevalence of Hib meningitis is 25% (95% CI, 22. 0-28. 20) (Figure-7) of all cause meningitis and 35% (95% CI, 17. 80-57. 30) (Figure-8) prevalence of all bacterial causes of meningitis is Hib.

5. 3 Case fatality Ratio:

There were 5 studies which commented on Hib disease mortality and mostly these studies report mortality in meningitis. The total CFR was about 15% (95% CI, 10. 30-21. 30) due to invasive Hib disease (Figure-9) and 17. 3%

(11. 9-24. 7) due to Hib meningitis alone (Figure-10). Only 5. 3% (95% CI, 0. 70-29. 40) of CFR was due to Hib pneumonia (Figure-11). The studies included in this review have mortality data due to meningitis. So it is difficult to comment on mortality due to invasive Hib disease.

6. DISCUSSION:

The present systematic review in India show that H. Influenzae type b is detected in 10. 7% of all hospitalization due to bacterial infections in children <5 years of age and is therefore one of the major cause of concern causing morbidity and mortality as seen from the hospital perspective. There is no study available on population based surveillance on Hib disease from India. In India, 97. 5% of all H. influenzae isolates from cases of invasive disease were serotype b. Pooling of Indian studies detected the etiology of Hib disease is 32. 6% of all invasive bacterial disease in children <5 years of age. These figures may be an underestimate of the current situation as the studies discuss only hospitalized cases and the milder forms go unreported.`H. influenzae is major bacterial cause for severe pneumonia and also for bacterial meningitis in children. About 75% of studies the studies reviewed from India show the estimates of meningitis due to Hib, indicating meningitis is the most severe form of invasive disease caused by Hib in children <5 years of age. About 35% of confirmed bacterial meningitis was caused by Hib. This proportion of bacterial meningitis caused by Hib is less than reported from the United States and European countries before the introduction of Hib vaccine in the the immunization schedule35, 36 and Bangladesh37, 38 but similar to reports from Srilanka 39 and Thailand40, 41. A recent study from Pakistan42 detected 19% of Hib meningitis cases from a

prospective surveillance which is lower than the reported prevalence (35%) rates from India. The low prevalence rates in Pakistan42 study was due to prior intake of antibiotics (cephalosporins) before hospitalization. Hib was the predominant organism (10. 7%) isolated as the sole pathogen followed by S. pneumonia (9. 2%), S. aureus (2. 5%), Klebsiella (2. 1%), S. typhi (2. 1%), E. coli (2%), N. meningitidis etc. The reports of Hib cases identified by culture of blood and CSF specimens that are positive for Hib antigens suggest that Hib organisms cause disease but are not detected by culture. This may be due to number of factors, including prior antibiotic treatment before hospitalization, storage and transport of specimens before laboratory analysis or technical problems in microbiology laboratory may result in the under estimate of Hib organism. About 60% of studies included in the present review have shown prior antibiotic treatment before hospitalization, indicating less number of positive isolates on blood and CSF culture. The IBIS17 study group showed the proportion of H. influenzae isolates that had antimicrobial resistance was fairly high for ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole, and erythromycin. However, a third-generation cephalosporin did not show any resistance to Hib. These data on antimicrobial resistance confirm the findings of retrospective reports from single hospitals43 and suggest that strains of Hib with antimicrobial resistance are widespread in India. A large percentage of children in India is thought to be at high risk of getting Hib disease due to increasing resistance to third generation antibiotics as well as to limited access to health care facilities. The CFR rate of Hib meningitis in India was 17. 4% among children aged <5 years, while all invasive Hib disease had a CFR of 15%. Studies from other developing regions have reported Hib meningitis mortality rates ranging from 5% to 55% 44. Watt

and collegues2 estimated the burden of invasive Hib disease in India in 2000 to be about 2. 4 million cases with 72, 000 deaths/1, 00, 000 in children aged <5 accounting for approximately 4% of all child deaths in India. The global burden of H. Influenzae disease is significantly high and is almost entirely vaccine preventable. Elaborate use of Hib vaccine could decrease pneumonia and meningitis, and reduce childhood mortality2. Indian data show that Hib disease is a prominent preventable cause of death and hospitalization of children in India and the government should consider the introduction of Hib vaccination in the national immunization programme. The increase in the level of antibiotic resistance in Hib, which mandate use of expensive antibiotics, provides an additional reason to consider prevention by means of vaccination43. After licensure, Hib vaccines were immediately introduced in North America and western Europe, but gradually in developing countries45 because of high cost, concerns about program viability, limited vaccine supply, and ambiguity about Hib disease burden 2. Hib vaccine has virtually eradicated Hib disease in all industrialized and developing countries where it has been introduced (Uganda46, Kenya47, Malawi48 and Gambia7); however, burden of Hib disease continues to arise in countries, like India that do not use Hib vaccines extensively3. In the latest policy report on Hib vaccine, WHO supported the inclusion of Hib conjugate vaccines in national immunization programs without waiting for local Hib disease-burden data49. The impact of intensified immunization accomplishment will be particularly significant in the developing world like India where limited medical resources increase the burden of Hib disease49. The WHO and GAVI have been working to expand supplies of Hib vaccines, reduce vaccine cost, and assist especially low-income countries with vaccine introduction2. Hib vaccine is

safe, highly efficacious and freely available in the market. Hib vaccine has been shown to be > 95% effective in distinct populations around the world7. A case-control study in Bangladesh, which showed that three doses of Hib conjugate vaccine reduced rates of laboratory-confirmed meningitis by 90% and radiologically confirmed pneumonia by 16–32%50Indian studies reported that there were no significant adverse reactions associated with Hib vaccination and that the vaccines are highly immunogenic51, 52. The seroconversion rate after vaccination, as defined by anti-PRP antibody concentration > 0. 15 µg, was 100% in all Indian studies52. Furthermore, combination vaccines have proven highly immunogenic. Hib vaccination fits into the India's national immunization programme. The earliest age when vaccination can be given is 6 weeks, with a minimum gap of 4 weeks between each dose, i. e., recommended ages for vaccination (6, 10 and 14 weeks) which corresponds with the schedule for oral polio, DPT and hepatitis B vaccines and then a booster dose at 18–24 mo of age which also corresponds with the Universal Immunization Programme (UIP) schedule for booster dose of DPT and Oral Polio. The National Technical Advisory Group on Immunization (NTAGI)6 in the July 2008 meeting not only endorsed this but also recommended to the Government of India that Hib vaccine should be introduced in all states as early as feasible. The vaccine can be given in combination with DPT and Hepatitis B, therefore not requiring a separate injection. The adoption of Hib vaccine in the national immunization schedule is clear. This will help India in combating a large but preventable burden of Hib disease, and achieving the Millennium Development Goal 4 of reducing under-5 child mortality.