

REVIEW ARTICLE

INCIDENCE OF PNEUMOCOCCAL MENINGITIS IN CHILDREN LESS THAN 5 YEARS AGE IN MALAYSIA, SINGAPORE AND THAILAND: REVIEW

Namaitijiang Maimaiti¹, Masoud Lotfizadeh², Zafar Ahmed³, Azam Rahimi⁴, Saad Ali Jadoo³, Syed Aljunid³

¹United Nations University, International Institute for Global Health,

²Department of Community Health, Shahrekord University of Medical Sciences, Iran

³International Centre for Casemix and Clinical Coding (ITCC), UKM Medical Center

⁴Iran social security organization, Shohada Kargar Hospital

ABSTRACT

Streptococcus pneumoniae (pneumococcus) is the most common cause of community-acquired pneumonia, meningitis, and bacteremia in children and adults, including the elderly, and is responsible for high rates of morbidity and mortality worldwide. Aim of this paper to review published articles on incidence of pneumococcal meningitis in children less than 5 years of age in Malaysia, Singapore and Thailand, and compare the incidence of pneumococcal meningitis among the children in the three countries. Literature searches were conducted using google scholar, PubMed, the World Health Organization (WHO) website of the Weekly Epidemiological Record, and the countries' Ministry of Health (MOH) website, and were limited to articles written in English. All relevant publications/abstracts published/presented during the period December 2000 through March 2014. Searches were conducted from April 1, 2014, till July 11, 2014 using various combinations of the following search terms "Pneumococcal diseases" OR "meningococcal" OR "pneumococcal meningitis" OR "meningococcus". A total of five articles and abstracts described the incidence of pneumococcal meningitis among children 5 years old. These five documents include two conference abstracts from Malaysia, one published paper from Singapore and two published papers from Thailand. The Malaysian, Singaporean and Thai pneumococcal meningitis incidence rate was 3.8-8.6, 2.3 and 0.10-1.8 per 100,000 children respectively. Our review confirmed that the incidence rate of pneumococcal meningitis was vary among the countries. The highest incidence rate of pneumococcal meningitis was found in Malaysia followed by Singapore and Thailand.

Key words: *Pneumococcal meningitis, Incidence rate, Malaysia, Singapore, Thailand,*

INTRODUCTION

Streptococcus pneumoniae (pneumococcus) is responsible for high rates of morbidity and mortality among children and adult worldwide¹. Pneumococcal disease is an infection caused by *Streptococcus pneumoniae* bacteria ("pneumococcus"). These bacteria can cause many types of illnesses, including: pneumonia (infection of the lungs), ear infections, sinus infections, meningitis (infection of the covering around the brain and spinal cord), and bacteremia (blood stream infection)². Meningitis is a serious inflammation of the meninges, the membranes (lining) that surround the brain and spinal cord. It can be of bacterial, viral, or fungal origin.

Meningitis is usually the result of a viral or bacterial infection. Viral meningitis, also called aseptic meningitis, is generally less severe and often disappears without specific treatment, while bacterial meningitis can be quite serious and may result in brain damage, hearing loss, or learning disabilities in children. The infection may even cause death. Bacterial meningitis is either monococcal or pneumococcal, depending on the type of bacteria responsible for the infection. Meningitis caused by *Haemophilus influenzae* and related strains (A, B C, Y, and W135) is also called meningococcal meningitis. Similarly, meningitis

due to *Streptococcus pneumoniae* is also called pneumococcal meningitis³. The World Health Organization (WHO) estimated one million children under five years die every year from invasive pneumococcal disease (IPD)⁴.

The incidence of IPD varies by country; it has been reported to be 130-597/100,000 in developing countries^{5, 6, 7, 8}. Meningococcal meningitis is a bacterial form of meningitis, a serious infection of the thin mucosa lining that surrounds the brain and spinal cord⁹. Infection with *Neisseria meningitidis* (the meningococcus) is common, although the majority of infections are transient and asymptomatic¹⁰. The meningococcus can live harmlessly in the nasopharynx of up to 10% of healthy populations¹¹. The factors that determine progression from harmless carriage to invasive disease are poorly understood, but they are influenced by both the virulence of the infecting strain and the susceptibility of the host¹¹.

When disease occurs, its onset is often rapid and life-threatening, and the meningococcus remains one of the major causes of death and disability as a result of invasive bacterial disease¹². Bacterial meningitis occurs globally. Excluding epidemics, the World Health Organization (WHO) estimates that at least 1.2 million cases of bacterial meningitis occur each year out of which 135,000

are fatal¹³. About 500,000 of these meningitis cases are due to the *N. meningitidis*, results in 50,000 deaths and 60,000 disabilities. Of these 250,000 cases, 27,000 deaths¹⁴, 16,000 (6.4%) disabilities of which 10,000 (4%) are due to impaired hearing are from Africa¹⁵. The epidemiology of meningococcal disease in other parts of the developing world, particularly Asia, is not well described^{16,17}.

The incidence rate and the CFR of IPD were different from region to region and country to country¹⁸. We have undertaken a detailed review on incidence of pneumococcal meningitis in Malaysia, Singapore and Thailand to test others researchers' statement that; "the epidemiology of meningococcal disease in other parts of the developing world, particularly Asia, is not well described". We also reviewed how the incidence of pneumococcal meningitis was described in the Southeast Asian countries and determine whether the incidence of pneumococcal meningitis among the children less than 5 years of age significantly different among these countries. Aim of this paper to review published articles on incidence of pneumococcal meningitis in children less than 5 years of age in Malaysia, Singapore and Thailand, and compare the incidence of pneumococcal meningitis among the children in the three countries.

METHODS

We conducted a review of published articles/conference abstracts on incidence of pneumococcal meningitis among children less than 5 years of age in Malaysia, Singapore and Thailand. Literature searches were conducted using google scholar, PubMed, WHO website of the Weekly Epidemiological Record, and the countries' Ministry of Health (MOH) website and were limited to articles written in English. All relevant publications/abstracts published/presented during the period December 2000 through March 2014. Searches were conducted from April 1, 2014, till July 11, 2014 using various combinations of the following search terms 'Pneumococcal diseases' OR 'meningococcal' OR 'pneumococcal meningitis' OR 'meningococcus'.

A team of three individuals independently screened the titles and abstracts of each citation and identified all citations for full review when there was any possibility that the study contained any description of incidence of pneumococcal meningitis. This screening process yielded 14 original publications/abstracts identified by team. We masked the results of all publication selected for full review by obscuring them with a red marker from the tables and text. Our agreement on studies evaluated within the team was good and

all disagreements were solved by consensus which required individuals to discuss the reasoning for their decisions. We included original articles/abstracts that described incidence of pneumococcal meningitis among children less than 5 years of age, with quantitative data. We excluded studies that were not associated with incidence of pneumococcal meningitis among the children under 5 years old, case report and those without quantitative data. Finally, five articles matching these requirements were used for analysis.

On the basis of the literature search a database of contacts of 14 possible informants for incidence of pneumococcal meningitis was identified, only five (37%) reported on incidence of pneumococcal meningitis among children less than 5 years of age in the three countries. The other nine (63%) articles/abstracts reported the incidence of pneumococcal meningitis for adult population or for general population or serotyping study. Only five articles/abstracts containing consistent quantitative data on incidence of pneumococcal meningitis among children less than 5 years in Malaysia, Singapore and Thailand were selected (figure 1).

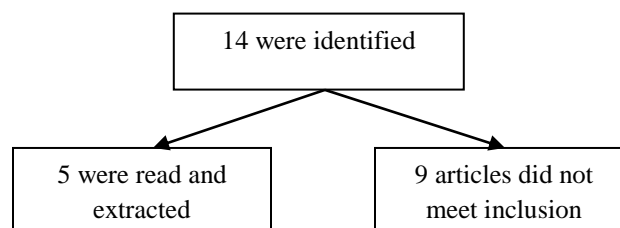


Figure 1. Flow diagram for the process of review of the papers

RESULT

Table 1 presents summary of the five selected studies/abstracts. Two conference abstracts were selected from Malaysia. One of the abstracts reported the incidence rate of pneumococcal meningitis for each age group with multiple study centers and another abstract reported the incidence rate of pneumococcal meningitis for age under 5 years old in only one study center. There were two full text published articles from Malaysia however those articles reported incidence of pneumococcal meningitis for general population there is data available for pediatric population.

One published paper was selected from Singapore, the paper reported the incidence rate of pneumococcal meningitis for age under 5 years old. Two published paper were selected from Thailand, the papers reported the incidence rate of pneumococcal meningitis for age under 5 years old.

Table 1. Incidence of pneumococcal meningitis

Country	Year of published	Study duration	Age group	Incidence rate/100,000 population	Source
Malaysia	2012	2008-2009	<5 years old	3.8	¹⁹
	2007	2004-2006	<5 years old	8.6*	²⁰
Singapore	2011	1997-2004	<5 years old	2.3	²¹
Thailand	2010, 2011	2008	<5 years old	0.10	^{22, 23}
	2004, 2011	2000-2001	<5 years old	1.8	²⁴

*=The study was carried out at single center study

DISCUSSION

Pneumococcal infection is a major cause of morbidity and mortality worldwide. In 2005, WHO estimated that 1.6 million deaths were caused by this agent annually; this estimate included the deaths of 0.7-1 million children aged under 5 years. Most of these deaths occurred in poor countries and included a disproportionate number of children under the age of 2 years²⁵. Bacterial meningitis, caused by *Streptococcus pneumoniae*, is a rare but severe disease in infants and young children²⁶. Between 1980 and 2005, the worldwide incidence of pneumococcal meningitis was 17 per 100,000 children aged below 5 years, while the European incidence was lower with 6 per 100,000 children²⁷. In Austria, incidence equaled the European incidence rate of 6 per 100,000 children aged below 5 years between 2001 and 2003²⁸. The Malaysian, Singaporean and Thai incidence rate 3.8-8.6, 2.3 and 0.10-1.8 per 100,000 children respectively, the countries' incidence rate was lower than worldwide and European incidence rate. One of the study from Malaysia reported the incidence rate 8.6 per 100,000 children in 2004-2006, the study was conducted only at single study center, and another study reported that the incidence rate 3.8 per 100,000 children in 2010, this study was carried out at multiple study centers. The incidence rate of pneumococcal meningitis varied in the 2 Malaysian studies, and it may be due to the year the study was conducted in and the study centers. The incidence rate of pneumococcal meningitis in Thailand varies widely between the Ministry of Health Thailand (MOH) report and the published, the MOH reported the incidence rate of the disease was 0.10 per 100,000 population whereas researchers reported the incidence rate of the disease was 1.8 per 100,000 children. However, there is no published article, data, conference abstract from Indonesia. Mézner addressed that the real

disease burden due to *Streptococcus pneumoniae* infections are under recognized worldwide both by the general public and by the medical community in general²⁶. Limited data are available on rates of carriage and disease in Asia. The vast majority of data is not population-based, and focuses on invasive isolates²⁹. Our search only database for English publications, there was a possibility of publication bias and lack of a broad information base given the absence of articles from other languages. With these limitations, our investigation may not provide a true picture of incidence of pneumococcal meningitis among children less than 5 years of age in the three countries. However, given what we know from this study and for the purpose of improving pneumococcal meningitis control in countries and region, we call for more researchers to do research on this disease among children with subsequent publication of results.

CONCLUSION:

Our review confirmed that the incidence rate of pneumococcal meningitis varies between the countries. The highest incidence rate of pneumococcal meningitis was found in Malaysia followed by Singapore and Thailand. The incidence rate of the disease was very different in Thailand between the report by Thai government and report by researchers.

References

1. Lynch 3rd JP, Zhanell GG. *Streptococcus pneumoniae*: epidemiology, risk factors, and strategies for prevention. *Semin Respir Crit Care Med* 2009; 30:189-209.
2. CDC, Pneumococcal Disease (*Streptococcus pneumoniae*) <http://wwwnc.cdc.gov/travel/diseases/>

- pneumococcal-disease-streptococcus-pneumoniae
3. Children's Health. <http://www.healthofchildren.com/M/Meningitis.html>
4. World Health Organization (WHO). Pneumococcal conjugate vaccine for childhood immunization - WHO position paper. *WklyEpidemiol Rec* 2007; 82: 93-104.
5. O'Dempsey TJD, McArdle TF, Morris J, *et al.* A study of risk factors for pneumococcal disease among children in a rural area of West Africa. *Int J Epidemiol*1996; 25: 885-93.
6. Karstaedt AS, Khoosal M, Crewe-Brown HH. Pneumococcal bacteremia during a decade in children in Soweto, South Africa. *Pediatr Infect Dis* 2000; 19: 454-7.
7. Brent AJ, Ahmed I, Ndiritu M, *et al.* Incidence of clinically significant bacteraemia in children who present to hospital in Kenya: community-based observational study. *Lancet* 2006; 367: 482-8.
8. Roca A, Sigauque B, Quinto L, *et al.* Invasive pneumococcal disease in children <5 years of age in rural Mozambique. *Trop Med Int Health* 2006; 11: 1422-31.
9. World Health Organization. <http://www.who.int/mediacentre/factsheets/fs141/en/>
10. Stephens DS. Uncloaking the meningococcus: dynamics of carriage and disease. *The Lancet* 1999;353, 941-942.
11. Yardi D, Gaikwad S &Deodhar L. Incidence, mortality and bacteriological profile of septicemia in pediatric patients. *Indian Journal of Paediatrics*1984,51, 173-176.
12. Rosenstein NE, Perkins BA, Stephens DS, Popovic T &Hughes JM. Meningococcal disease. *New England Journal of Medicine*, 2001, 344, 1378-1388.
13. <http://www.who.int/topics/meningitis/en/>
14. TikhomirovE, Santamaria M, Esteves K. Meningococcal disease: public health burden and control. *World Health Stat. Q.* 1997,50: 170-177
15. Hodgson A, Smith T, Gagneux S, Akumah I, Adjuik M, Pluschke G, Binka F, Genton B. Survival and sequelae of meningococcal meningitis in Ghana. *Int. J. Epidemiol.* 2001,30: 1440-1446.
16. Manchanda V, Gupta S &Bhalla P, Meningococcal disease: history, epidemiology, pathogenesis, clinical manifestations, diagnosis, antimicrobial susceptibility and prevention. *Indian Journal of Medical Microbiology*, 2006, 24, 7-9.
17. Harrison LH, Trotter CL & Ramsay ME. Global epidemiology of meningococcal disease. *Vaccine*, 2009, 27, B51-B63.
18. Namaitijiang Maimaiti, Zaleha Md Isa, Zafar Ahmed, Syed Aljunid," Clinical burden of invasive pneumococcal disease in selected developing countries", *Journal of Value Health Regional Issues* Volume 2, Issue 2, September-October 2013, Pages 259-263.
19. Syed Aljunid, NamaitijiangMaimaiti, Zafar Ahmed, Amrizal Muhammad Nur, ZalehaMd Isa, Economic Burden of Pneumococcal Disease in Malaysia. 14th Asia Pacific Congress of Pediatrics (APCP) & 4th Asia Pacific Nursing Conference (APNC) 7th - 12th September 2012, Borneo Convention Centre Kuching (BCKC) in Kuching, Sarawak state, Malaysia
20. Suhaimi M, Asmiati AH, Soo TL. Pneumococcal meningitis in children aged 2-60 months at Queen Elizabeth (QE) Hospital, Sabah, Malaysia: before and after the introduction of Hemophilus influenza type b vaccination [abstract 0345].In: 5th World Congress of the World Society for Pediatric Infectious Diseases.2007. Available at: <http://www.kenes.com/wspid2007/program/session1.asp?SessionId.P10&SSessionDate=11/19/2007>. Accessed 30 July 2008.
21. Karen Richards Tyoa, Melissa M. Rosena, Wu Zenga, Mabel Yapb, Keng Ho Pweeb, Li Wei Angb, Donald S. Sheparda. Cost-effectiveness of conjugate pneumococcal vaccination in Singapore:Comparing

- estimates for 7-valent, 10-valent, and 13-valent vaccines. *Vaccine* 29, 2011, 6686- 6694
22. Thai Department of Disease Control, Ministry of Public Health. Surveillance Reports 2007 and 2008 (<http://epid.moph.go.th/>). Accessed 17 March 2010.
23. A. VYSE1, J.M. WOLTER, J. CHEN, T. NG AND M. SORIANO-GABARRO. Meningococcal disease in Asia: an under-recognized public health burden. *Epidemiol. Infect.* (2011), 139, 967-985. f Cambridge University Press 2011 doi:10.1017/S0950268811000574
24. Rerks-Ngarm S, et al. Prospective population-based incidence of *Haemophilus influenzae* type b meningitis in Thailand. *Vaccine* 2004; 22: 975-983.
25. <http://www.who.int/ith/diseases/pneumococcal/en/>
26. D. S. Klobassa& B. Zoehrer& M. Paulke-Korinek& U. Gruber-Sedlmayr& K. Pfurtscheller& V. Strenger& A et al. The burden of pneumococcal meningitis in Austrian children between 2001 and 2008. *Eur J Pediatr* ,2014,173:871-878.
27. O'Brien KL, Wolfson LJ, Watt JP et al. Burden of disease caused by *Streptococcus pneumoniae* in children younger than 5 years: global estimates. *Lancet*, 2009, 374:893-902.
28. Rendi-Wagner P, Georgopoulos A, Kundi Met al. Prospective surveillance of incidence, serotypes and antimicrobial susceptibility of invasive *Streptococcus pneumoniae* among hospitalized children in Austria. *J Antimicrob Chemother*, 2004, 53:826-831.
29. Mészner Z. Pneumococcal disease prevention from early infancy to old age. *OrvHetil.* 2014 Feb 16;155(7):243-7. doi: 10.1556/OH.2014.29753.