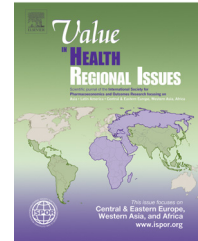




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CLINICAL OUTCOMES STUDIES

Clinical Burden of Invasive Pneumococcal Disease in Selected Developing Countries

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ABSTRACT

Objective: To measure the clinical burden of invasive pneumococcal disease (IPD) in selected developing countries. **Methods:** This is an extensive literature review of published articles on IPD in selected developing countries from East Asia, South Asia, Middle East, sub-Saharan Africa, and Latin America. We reviewed all the articles retrieved from the knowledge bases that were published between the years 2000 and 2010. **Results:** After applying the inclusion, exclusion, and quality criteria, the comprehensive review of the literature yielded 10 articles with data for pneumococcal meningitis, septicemia/bacteremia, and pneumonia. These selected articles were from 10 developing countries from five different regions. Out of the 10 selected articles, 8 have a detailed discussion on IPD, one of them has a detailed discussion on bacteremia and meningitis, and another one has discussed pneumococcal bacteremia. Out of these 10 articles, only

5 articles discussed the case-fatality ratio (CFR). In our article review, the incidence of IPD ranged from less than 5/100,000 to 416/100,000 population and the CFR ranged from 12.2% to 80% in the developing countries. **Conclusions:** The review demonstrated that the clinical burden of IPD was high in the developing countries. The incidence of IPD and CFR varies from region to region and from country to country. The IPD burden was highest in sub-Saharan African countries followed by South Asian countries. The CFR was low in high-income countries than in low-income countries.

Keywords: clinical burden, developing countries, East Asia, IPD, Latin America, Middle East, South Asia, sub-Saharan Africa.

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Introduction

Streptococcus pneumoniae is a major public health problem causing meningitis, bacteremia, pneumonia, and acute otitis media [1,2]. *S. pneumoniae* is the most common cause of pneumonia worldwide, causing approximately 36% of all childhood pneumonias. *S. pneumoniae* can cause potentially life-threatening lung infections including severe pneumonia, which hinders the movement of oxygen into the bloodstream, potentially resulting in death from respiratory failure [3]. Invasive pneumococcal infections often prove rapidly fatal, even where good medical treatment is readily available. In developed countries, up to 20% of people who contract pneumococcal meningitis die; however, in the developing world, mortality is closer to 50%, even among hospitalized patients [4]. In one study from Gambia, 48% of children who contracted pneumococcal meningitis and reached hospital did not survive [5]. The World Health Organization (WHO) estimated that 1.6 million people die from pneumococcal disease every year [6], with 0.7 million to 1 million being children younger than 5 years [7]. The pneumococcal disease burden among adults is also

high, with an estimated 600,000 to 800,000 adult deaths each year from pneumococcal pneumonia, meningitis, and sepsis [8]. The vast majority of its victims come from the world's poorest countries, and half of them are children younger than 5 years. It is extraordinary, in view of these facts, that pneumococcal disease remains a relatively unknown disease and does not have a higher place on the agenda of the international community [3]. Compared with other diseases affecting the developing world, determining the incidence of pneumococcal disease is relatively difficult [9]. This is due to a number of factors including the difficulties involved in stringent laboratory testing and sample collection and the unavailability of quality surveillance data in developing countries. This lack of epidemiological evidence has likely contributed to a gross underappreciation of the economic, clinical, and human burdens imposed by pneumococcal disease and hindered public health planning and decision making in developing countries [3]. Most of the researchers have done the review of invasive pneumococcal disease (IPD) for patients belonging to a particular age group, for example, pediatric age group, and limited to a single region. We extended our review of

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IPD to all age groups on the basis of availability of data and extended to five different regions in the world. The developing countries are defined as a nation with a low living standard, underdeveloped industrial base, and low human development index relative to other countries [10]. This will help us better understand the disease burden in all the age groups in selected developing countries in different parts of the world. We measured the clinical burden of IPD in selected developing countries by geographical and economical point of view. Clinical burden is a burden that differs from genetic burden mainly in the added component of morbidity; a trait that is either clinically or genetically lethal may be grossly disabling [11].

Methods

We conducted a detailed review of published articles on IPD. Literature searches were conducted by using the PubMed database, Google scholar, and The Lancet, and were limited to articles written in English. We selected 10 developing countries from five regions, namely, East Asia (Malaysia and Thailand), South Asia (Bangladesh and Nepal), Middle East (Saudi Arabia and Qatar), sub-Saharan Africa (The Gambia and Mozambique), and Latin America (Cuba and Peru). The World Bank categorizes the countries by income into five different categories: low-income economics, lower-middle-income economics, upper-middle-income economics, high-income economics, and high-income Organisation for Economic Co-operation and Development members [12]. The main criterion for the selection of these countries from the designated regions was that they should belong to same economic status (as defined by the World Bank) and preferably be neighbors. When selected countries did not have an equivalent neighbor, we selected the next nearest country in the region with the same economic status.

The search term combinations used to search the knowledge base included pneumococcal pneumonia, epidemiology, incidence rate, clinical burden AND pneumococcal meningitis, epidemiology, incidence rate, clinical burden AND pneumococcal septicemia, epidemiology, incidence rate, and clinical burden. We started with reviewing the abstracts of these articles published between the year 2000 and 2010 to find out which of the studies met our inclusion criteria and then reviewed only those full-length articles that complied with our inclusion criteria. The knowledge base searches were conducted from March 1, 2011, till July 31, 2011. We included only published articles and articles that described the clinical burden of pneumococcal disease with

the quantitative data of the selected developing countries in the different regions. If there was more than one article in each country, the most comparable study or the study with a high quality of methodology was reviewed. We excluded case reports, reports, and special populations, such as reports for patients with HIV/AIDS. We also excluded articles published before 2000 and after 2010, or articles from developed countries. We accepted each author’s definition and methods except for the exclusion criteria mentioned.

Two individuals (Namaitijiang Maimaiti and Zafar Ahmed [NM and ZA]) independently screened the titles and abstracts of each citation retrieved from the search term and identified the articles for full review. The decision to review an article in detail was based on the content of the abstract and whether the article described the clinical burden of pneumococcal disease. If the reviewed article included both clinical and economic burdens of pneumococcal disease, we still included this article in our study, but reviewed only the clinical burden of disease for our study.

Initially, the search process using the search term yielded 51 articles. Finally, 22 articles remained to be reviewed in detail. If more than one article from the same country was identified that described the clinical burden of pneumococcal disease, we selected the article with the later publication date with same quality or better quality methods compared with previous studies. The detailed review of the selected 22 articles was carried out by MN and ZA in a team, and finally they selected 10 articles that fulfilled all the selection criteria. Out of these 10 selected articles, 8 were full-text original publications and 2 were review articles, and the 10 articles selected were then used for our analysis. We gathered information such as study design (retrospective/prospective study), study period, study location (urban/rural), study population and age of sample, incidence rate, and case-fatality ratio (CFR) (Fig. 1).

Results

The list of the selected articles from 10 developing countries belonging to five different regions is presented in Table 1.

Among the 10 articles selected, 8 articles had a detailed discussion on IPD, 1 discussed meningitis, and 1 discussed pneumococcal bacteremia. Out of the 10 articles selected, only 5 articles described the CFR (Table 2). The studies included in this review were carried out in a variety of settings. Seven studies were carried out in an urban seating; two studies were carried out in rural areas, whereas only one study was carried out in both urban and rural settings.

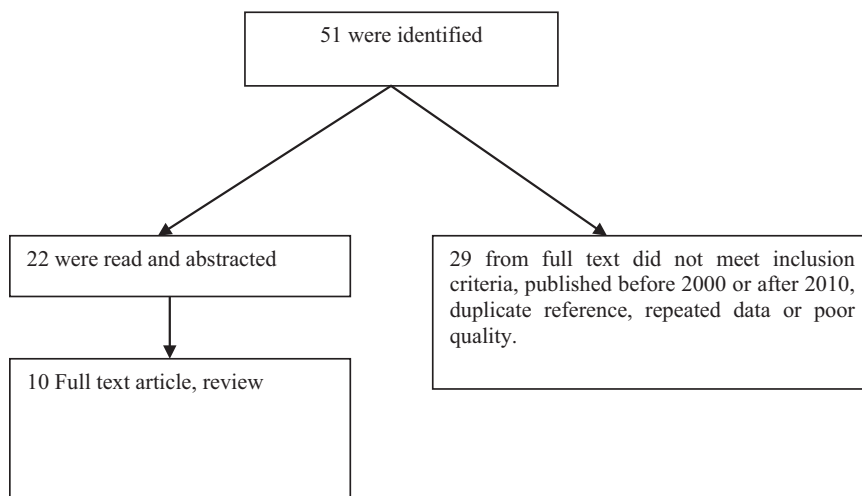


Fig. 1 – Flow diagram for the process of review of the literature. *HI, high income; LI, low income; UMI, upper-middle income.

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