Seasonal dynamics of bacterial meningitis: a time-series analysis

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Summary

Background Bacterial meningitis, which is caused mainly by *Neisseria meningitidis*, *Haemophilus influenzae*, and *Streptococcus pneumoniae*, inflicts a substantial burden of disease worldwide. Yet, the temporal dynamics of this disease are poorly characterised and many questions remain about the ecology of the disease. We aimed to comprehensively assess seasonal trends in bacterial meningitis on a global scale.

Methods We developed the first bacterial meningitis global database by compiling monthly incidence data as reported by country-level surveillance systems. Using country-level wavelet analysis, we identified whether a 12 month periodic component (annual seasonality) was detected in time-series that had at least 5 years of data with at least 40 cases reported per year. We estimated the mean timing of disease activity by computing the centre of gravity of the distribution of cases and investigated whether synchrony exists between the three pathogens responsible for most cases of bacterial meningitis.

Findings We used country-level data from 66 countries, including from 47 countries outside the meningitis belt in sub-Saharan Africa. A persistent seasonality was detected in 49 (96%) of the 51 time-series from 38 countries eligible for inclusion in the wavelet analyses. The mean timing of disease activity had a latitudinal trend, with bacterial meningitis seasons peaking during the winter months in countries in both the northern and southern hemispheres. The three pathogens shared similar seasonality, but time-shifts differed slightly by country.

Interpretation Our findings provide key insight into the seasonal dynamics of bacterial meningitis and add to knowledge about the global epidemiology of meningitis and the host, environment, and pathogen characteristics driving these patterns. Comprehensive understanding of global seasonal trends in meningitis could be used to design more effective prevention and control strategies.

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Introduction

Bacterial meningitis causes inflammation of the meninges, which leads to sudden onset of fever, headache, stiff neck, nausea, vomiting, and altered mental status, and can rapidly result in death. *Neisseria meningitidis*, *Streptococcus pneumoniae*, and *Haemophilus influenzae* are the leading causes of bacterial meningitis worldwide.[1] All three pathogens are carried asymptomatically in the human nasopharynx and transmission occurs through respiratory droplets or saliva. Symptoms typically occur within 3–7 days after transmission. The relative contribution of these three pathogens to the incidence of bacterial meningitis differs over time, by location, and by characteristics such as patient age.[2] Although vaccination programmes have been implemented in many countries and have had a considerable impact on disease,[2] more than 1·2 million cases of bacterial meningitis are estimated to occur each year.[3] The case-fatality rate is high for all three pathogens (ranging from 5% to 50%) and neurological sequelae occur in up to 50% of survivors.[3]

Previous work has documented the substantial burden of meningitis worldwide[4–6] and identified prevention of meningitis as a priority.[7,8] However, the temporal dynamics of bacterial meningitis, including the seasonality, interannual variation, and secular trends are poorly characterised in many parts of the world. Thus, many questions remain about the ecology of the disease. Comprehensively assessing the temporal dynamics of bacterial meningitis is the first, key step towards understanding the complex interactions between environmental, demographic, social, immunological, and other factors that might drive these patterns of disease. In this Article, we specifically focus on investigating country-level patterns of the seasonality of bacterial meningitis. Comparing and contrasting the seasonality of infectious diseases across diverse settings can increase understanding of the interactions between host and pathogen biology and ecology; enhance the accuracy of surveillance systems; lead to the development of optimum prevention and control strategies; and improve ability to predict epidemics.[9,10]

Research in context

Evidence before this study

In 2014 we searched the literature to review the existing evidence on seasonality of bacterial meningitis. We searched PubMed for papers including the terms "season*" in Title/Abstract and "bacterial meningitis", "meningococcal meningitis", "pneumococcal meningitis" or "*Haemophilus* meningitis" in MeSH terms, with no language or date restrictions. We found several reports of seasonal trends from single countries, either at the country level or at a sub-country level such as a metropolitan area or a hospital. However, the evidence was sparse and no comprehensive global comparative analysis of the seasonality of bacterial meningitis had been undertaken. We aimed to build upon previous studies that have described the global burden of disease in terms of morbidity and mortality by undertaking an investigation of the country-level, intra-annual variation in incidence with the primary aim of assessing the seasonality of bacterial meningitis worldwide.

Added value of this study

We compiled the first global database of monthly bacterial meningitis incidence data as reported by country-level surveillance systems in 66 countries, including 47 countries outside the meningitis belt, and we performed the most comprehensive analysis of global bacterial meningitis seasonality thus far. Our study provides a unique and global perspective on bacterial meningitis seasonality with time-series data from all continents. Our findings confirm previous reports of seasonality in specific contexts and countries and present strong evidence that bacterial meningitis incidence exhibits persistent seasonal patterns across a wide geographic range. In addition, we have shown, for the first time, that the timing of the seasonal peak in bacterial meningitis incidence is correlated to the latitude of the country's most populous city.

Implications of all the available evidence

Characterising bacterial meningitis seasonality is crucial to advancing understanding of the epidemiology, ecology, and transmission dynamics of the disease and is key to designing and implementing optimum prevention and control strategies. Moreover, the latitudinal trend in seasonal timing that we observed provides a basis for developing hypotheses about the potential factors, such as host susceptibility, environment, and pathogen characteristics, driving bacterial meningitis dynamics across various geographic settings. These hypotheses could be investigated through further studies beyond the scope of this analysis. Understanding seasonal patterns of meningitis contributes to ensuring that public health officials can plan and implement the most effective disease mitigation efforts.

Bacterial meningitis is known to peak during the dry season in the African meningitis belt, a group of countries in sub-Saharan Africa that have the highest incidence of bacterial meningitis.[11] Previous epidemiological reports from individual countries outside the meningitis belt show various seasonal patterns of bacterial meningitis. For instance, increased incidences have been observed in May to October in Brazil;[12] December to March in the USA,[13] France,[14] and the UK;[15] and July to September in New Zealand.[16] Here, we compile a global database of reported bacterial meningitis incidence by country to assess whether a significant seasonal signature is detected across diverse geographic settings, to estimate the timing of the meningitis season when seasonality is present, and to determine whether synchrony exists between these three primary causes of bacterial meningitis.

Methods

Database compilation

In our database, we included country-level time-series data from reports of laboratory-confirmed cases of meningitis caused by *H influenzae*, *N meningitidis*, and *S pneumoniae* or reports of suspected or laboratory-confirmed cases of bacterial meningitis (when the pathogen responsible was not specified) that were collected by a national surveillance system serving the general population of an entire country (as opposed to sentinel surveillance or other methods for collecting data from select populations or subnational regions) with weekly or monthly temporal resolution. No age or patient-based restrictions were used.

We obtained data using three strategies. First, we searched public databases using general search terms such as "bacterial meningitis incidence data", "national meningitis surveillance", and "meningitis database", and additional country-specific queries. The databases searched were Google, Google Scholar, PubMed, EuroSurveillance, Global Infectious Diseases and Epidemiology Network (GIDEON), WHO Databases, and Centers for Disease Control and Prevention (CDC) Vital Statistics. Second, we wrote web-crawling Java data-scraping programs to automatically search for links to ministry of health websites, reports, and other databases. The Java scripts were designed to automate the process of locating and exporting data from these websites into Excel spreadsheets. Each result was manually reviewed by AC and evaluated using the inclusion criteria described above. Third, we actively corresponded with public health officials such as ministries of health and authors of papers in which relevant time-series were analysed. Only aggregate and anonymous data were obtained; permission to use the data was acquired from data owners whenever necessary.

We specified that confirmed cases were those confirmed with laboratory-based diagnostic tests, although the specific criteria differed between countries and methods included macroscopic or microscopic