Epidemiology of meningitis in Oman, 2000–2005

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وبائيات التهاب السحايا في سلطنة عُمان 2000 - 2005

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الخلاصة: راجع الباحثون الملامح والاتجاهات الوبائية لـ 771 حالة التهاب سحايا حدثت في سلطنة عمان في المدة من كانون الثاني/ يناير 2000 إلى كانون الأول/ ديسمبر 2005، ووجدوا أن 69٪ من الحالات نجم عن الجراثيم، وأن 13٪ منها نجم عن الفيروسات. أما الجراثيم الرئيسية المسببة للمرض فهي المستدمية النزلية (15٪) والعقدية الرئوية (14٪) والنيسيرية السحائية (12٪). ولم يكن من الممكن التعرف على جرثوم مسبب للمرض لدى 56٪ من المرضى الذين كان يشك بإصابتهم بالتهاب السحايا القيحي. وقد كانت ذروة الحدوث لدى الأطفال دون السنتين من العمر. وقد تناقص معدل وقوع التهاب السحايا الناجمة عن المستدمية النزلية من النمط بي بمقدار 96 – 100٪ بعد تنفيذ البرنامج الوطني الموسّع للتمنيع عام 2001؛ أما حدوث الحالات الناجمة عن العقديات الرئوية والنيسيريات السحائية فلازالت ثابتة.

ABSTRACT We reviewed the epidemiologic features and trends for 771 cases of meningitis in Oman from January 2000 to December 2005. We found 69% were bacterial in origin and 13% were viral. Leading bacterial pathogens included *Haemophilus influenzae* (15%), *Streptococcus pneumoniae* (14%) and *Nesseria meningitidis* (12%). For 56% of patients with suspected pyogenic meningitis, no specific bacterial pathogen could be identified. Peak occurrence was in children under 2 years old. The incidence of *H. influenzae* type b decreased by almost 100% after implementation of the national immunization programme in 2001, while the incidence of cases caused by *S. pneumoniae* and *N. meningitidis* remained steady.

Épidémiologie de la méningite à Oman, 2000-2005

RÉSUMÉ Nous avons étudié les caractéristiques et les tendances épidémiologiques de 771 cas de méningite à Oman de janvier 2000 à décembre 2005 et déterminé que 69 % de ces cas étaient d'origine bactérienne et 13 % d'origine virale. Les principaux agents pathogènes bactériens étaient *Haemophilus influenzae* (15 %), *Streptococcus pneumoniae* (14 %) et *Neisseria meningitidis* (12 %). Pour 56 % des patients présentant une suspicion de méningite pyogène, aucun agent pathogène bactérien spécifique n'a pu être identifié. La fréquence maximale s'observait chez les enfants de moins de deux ans. L'incidence des méningites à *H. influenzae* type b a diminué de près de 100 % après la mise en œuvre du programme national de vaccination en 2001, alors que celle des cas dus à *S. pneumoniae* et *N. meningitidis* est restée stable.

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Introduction

Meningitis is a significant cause of morbidity and mortality, especially in children, and remains a common disease worldwide. In 2004, it caused an estimated 173 000 deaths globally, mostly among children in the developing world [*1*]. During the past 2 decades, significant changes have taken place in the epidemiology, in particular, a reduction in the occurrence of *Haemophilus influenzae* type b (Hib) meningitis due to the global availability and expanding use of Hib vaccines [*2–4*].

Oman is a country on the south-east coast of the Arabian Peninsula. The population was about 2 500 000 in 2005 [*5*]. It has one of the most efficient healthcare systems in the Middle East and North Africa region. In Oman, meningitis is a reportable disease, and notification of each case to the Department of Communicable Diseases Surveillance and Control in the Ministry of Health is mandatory within 24 hours. Physicians are provided with official case definitions of meningitis and case reporting guidelines.

During the pre-meningitis vaccination era, the incidence of meningitis in Oman (9.3 cases/100 000 population in 1995) was similar to that of other countries in the region [*6,7*], and *H. influenzae* was the most common causative organism, accounting for 45% of all bacteriologically-proven meningitis cases admitted over a 1-year period in 1990/9 [8]. The Hib vaccine was introduced in Oman in October 2001 as part of the Expanded Programme on Immunization. This monocomponent Hib vaccine was replaced with a pentavalent conjugate vaccine (DTP + Hib + HepB) in July 2003 [*8*].

Since then, the absolute number of cases of meningitis attributable to *H. influenzae* has declined, but the impact of Hib vaccination on the epidemiology of meningitis due to other causes has received little attention. This study describes recent epidemiologic features of meningitis in Oman during the period 2002–2005.

Methods

All recorded information on cases of meningitis reported to the Department of Communicable Diseases Surveillance and Control from January 2000 to December 2005 was examined for basic patient demographic information including age, sex, nationality, travel history, vaccination status against meningitis causes, underlying conditions, microbiologic etiology and clinical outcome.

The following clinical and microbiologic case definitions of meningitis were used in this study:

- a diagnosis of *meningitis* was based upon clinical assessment, with features including fever and ≥ 1 of the following: severe headache, nausea and vomiting, neck stiffness and pain, photophobia, and altered mental status (in children < 2 years of age, a case with sudden onset of fever ≥ 38.5 °C, and irritability or bulging fontanelles was clinically defined as *meningitis*);
- *confirmed bacterial meningitis* was defined by a positive Gram stain of cerebrospinal fluid (CSF), or antemortem or postmortem culture isolation of a relevant microorganism from CSF or blood, or by detection of bacterial antigens in CSF;
- meningitis was presumed to be bacterial in origin (*suspected bacterial meningitis*) based upon clinical features and if ≥ 1 of the following features were seen in CSF examination: turbidity; neutrophilic pleocytosis [> 500 white blood cells (WBCs)/mm^3], hypoglycorrachia (< 50 mg/dL); and a positive Gram stain;

- *suspected viral meningitis* was diagnosed presumptively on clinical grounds and by exclusion of bacterial meningitis, and the presence of ≥ 1 of the following: normal CSF glucose or mild increase (50 mg/dL) in CSF protein; moderate increase in CSF WBCs (< 500/mm^3) and lymphocyte predominance (50%); an epidemiologic link to a confirmed case;
- *confirmed viral meningitis* was defined as a suspected case with laboratory confirmation (e.g. virus culture isolation or positive CSF polymerase chain reaction).

We chose to determine the epidemiology of true bacterial meningitis, and thus cases of infection caused by *Mycobacterium tuberculosis* were excluded from the study.

Results

During the study period, 771 cases of meningitis were reported in Oman, of which 69% (536) were bacterial and 13% (99) viral in origin. Clinical diagnosis of meningitis was made in 136 (18%) cases, but in each of these instances no specific microbial etiology could be determined.

Among the bacterial causes of meningitis, *H. influenzae* was the most frequent causative agent, occurring in 82 (15%) cases (mostly in children), followed *by Streptococcus pneumoniae* in 73 (14%) cases, and *Neisseria meningitidis* in 65 (12%) cases. Eleven (2%) cases of group B streptococcal meningitis occurred in neonates, and there was 1 case each of meningitis due to *Escherichia coli*, *Klebsiella pneumoniae*, and *Staphylococcus aureus*. In 302 cases (56%), meningitis was presumptively attributed to bacterial pathogens without final determination of the causative organism.

Most (71 of 82) cases of meningitis due to *H. influenzae* type b occurred in children under 2 years of age, and were reported before 2003. The incidence of meningitis due to Hib began to decrease significantly after implementation of the national immunization programme in October 2001 (Table 1), and this trend continued during the study period. The incidence of meningitis due to *S. pneumoniae* remained steady through the study period (Table 1). Cases of viral meningitis were mainly seen in children, teenagers and young adults attending school.

Meningitis affected people from 16 nationalities although 91% of cases occurred among Omani nationals (non-Omani expatriates constitute around 15%–20% of the population in Oman).

Information on vaccination status against Hib was available for the study cohort but was lacking for pneumococcal and meningococcal vaccines.

Apart from patients with diabetes mellitus, none of our cohort was immunocompromised. Travel-related infection was only reported for 1 case of meningococcal meningitis in a hajj pilgrim to Mecca. Fever, neck stiffness, seizure, vomiting, and bulging fontanelle were the most frequent presenting features.

The incidence of meningeal infection of all types in Oman ranged from 8.4/100 000 population in 2000 to 3.0/100 000 in 2005, with an overall downward trend by year (Table 1). The age group 0–5 years had the highest proportion of meningitis (44.6%), with the largest number of cases (n = 369) occurring in children under 2 years old. The incidence of meningitis was greater in males (65%) than in females (35%). Meningitis cases were observed throughout the year without any seasonal variation. The case-fatality rate was 2.2% (17 of 771), and all the reported deaths (17 of 536, or 3%) were due to bacterial causes (documented or presumptive). Mortality rate was high (47%) in children below the age of 10 years.

Table 1 **Distribution of meningitis cases in Oman (2000–2005) according to causative organism**

Year	Total cases	*Haemiphilus influenzae*	*Neisseria meningitidis*	*Streptococcus pneumoniae*
2000	202	21	28	10
2001	137	27	15	11
2002	156	26	6	9
2003	111	7	11	12
2004	89	0	4	14
2005	76	1	1	12

Lumbar puncture was refused by 87 (11%) of the patients with a diagnosis on admission of suspected meningitis. Patients who did not undergo spinal tap were all young children, and in most of these cases the parents refused to consent to lumbar puncture.

Discussion

The overall incidence of meningitis cases in Oman has been declining over the past 6 years. Annual incidence fell from 8.4/100 000 population in 2000 to 3/100 000 population in 2005. This decrease can be potentially attributable to multiple factors, including the introduction of vaccines against *H. influenzae* type b and *N. meningitidis*, improvements in living conditions, better availability of health care facilities, earlier detection of meningitis and improved prevention and control strategies by the Ministry of Health for all types of meningitis. We do not believe that this decrease in incidence was due to reporting bias since there were no modifications in case reporting or surveillance during the study period.

The 3 leading causes of meningitis were *H. influenzae* (15%), *S. pneumoniae* (14%) and *N. meningitidis* (12%). However, the incidence of meningitis due to *H. influenzae* has become rare since the introduction of the conjugate Hib vaccination in Oman in late 2001. In 2001, there were 27 cases, but this fell to only 1 case during the period 2003–2005. Similar epidemiology has been reported worldwide, including the neighbouring countries of Qatar, Saudi Arabia, and the United Arab Emirates, where the incidence of all forms of invasive Hib disease has been dramatically reduced as a result of systematic and mandatory immunization of all children [*9–11*]. Since 2004, there has been only a single case of Hib meningitis reported in Oman, thus demonstrating the remarkable success of the national immunization programme. The incidence of meningitis due to other pathogens like *S. pneumoniae* and *N. meningitidis* remained steady during the study period, and similar findings have been reported from other countries which experienced a dramatic drop in the incidence of *H. influenzae* meningitis [*12,13*].

In our study, the occurrence of cases of meningitis of undetermined etiology, as well as the failure to isolate a causative microorganism in over half the cases of suspected bacterial meningitis, reflects laboratory deficiencies, incomplete reporting and the common cultural phenomenon of refusal of lumbar puncture. This limitation on clinical management ultimately affects the etiological diagnosis, treatment and accuracy of surveillance data. Furthermore, for those patients who do undergo lumbar puncture, failure to isolate a causative agent

is most often related to antibiotic treatment received prior to the procedure. The etiological diagnosis of meningitis can be enhanced by using more sophisticated techniques like antigen detection (especially useful when a patient with bacterial infection is partially-treated with antibiotics before examination of CSF) and nucleic acid amplification [*14,15*], and these tests could be routinely incorporated into standard laboratory practice and made available at all the reference laboratories in Oman.

The male predominance seen in our study (male:female ratio 1.8:1) is similar to several previous reports but it may not reflect true disease incidence. Instead, it may indicate the greater potential contact exposure of men to community cases of meningitis in particular, and gender-based health care attitudes and practices in general, in this traditional Muslim society [*16,17*].

The case-fatality rate (2.2%) is consistent with published data [*18,19*]; mortality is greatest, up to 20%, for *S. pneumoniae*, and 3%–7% for meningitis caused by *H. influenzae* and *N. meningitidis*. Mortality was highest among children below the age of 10 years, and acute bacterial meningitis in childhood is known to be associated with significant mortality, complications and long-term neurological sequelae [*20,21*].

Our study had several potential limitations. We analysed only notified cases of meningitis, the true incidence of the disease in the community may have been under-reported. Furthermore, cases of infection presumed to be bacterial in origin might have been misdiagnosed cases of tuberculous meningitis, paraventricular brain abscess, drug-induced meningitis, or primary amoebic meningo-encephalitis caused by *Naegleria fowleri*. Unfortunately, detailed information on antibiotic use before presentation was lacking, and cases of presumed viral meningitis could have represented cases of partially-treated bacterial meningitis.

A final limitation of this retrospective study was an inability to fully determine the morbidity of meningitis due to complications such as hydrocephalus, cerebral oedema, sensorineural hearing loss, visual impairment and failure to thrive because patient-specific clinical outcomes were generally unavailable. Accurate and regular recording of clinical outcomes and long-term patient follow-up, especially for cases involving young children, would be extremely valuable.

In summary, we have demonstrated a decreasing incidence of meningitis in Oman over the study years, 2001–2005. Bacterial meningitis caused by *H. influenzae* dropped remarkably after the introduction of the Hib vaccine nationally in 2001, while the proportion of meningitis cases due to other etiologies remained steady during the study period. The large number of cases of meningitis for which a specific microbial cause could not be determined, including those presumed to be bacterial in etiology, indicates that improved methods of bacterial detection and reporting are needed to further help reduce the incidence, morbidity and mortality in Oman.

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Corrections

1. **A new role for Women Health Volunteers in urban Islamic Republic of Iran H. Behdjat, S.B. Rifkin, E. Tarin and M.R. Sheikh. *Eastern Mediterranean Health Journal*, 2009, 15(5):1164–73.**

In the list of authors, M.R. Sheikh[4] should read: M.R. Sheikh[3]. The affiliation is: World Health Organization, Tehran, Islamic Republic of Iran.

2. **Asthma and other allergic diseases in 13-14-year-old schoolchildren in Urmia: an ISAAC study. M.H. Rahimi Rad, M.E. Hejazi, R. Behrouzian. *Eastern Mediterranean Health Journal*, 2007, 13(5):1005–16.**

In this paper, as the study was not registered in ISAAC, this should not be included in the title. The title should therefore read: "Asthma and other allergic diseases in 13–14-year-old schoolchildren in Urmia, Iran".

In addition, the first paragraph under the heading "Questionnaires" should read: "We used translated Persian versions of the ISAAC questionnaires. They had already been translated according to ISAAC recommendation and used in the Iranian branch of the ISAAC study in Tehran and Rasht and the results published by ISAAC steering committee report [*4,5*]."