

Impact of the hajj on pneumococcal transmission

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Abstract

Over two million Muslim pilgrims assemble annually in Mecca and Medina, Saudi Arabia, to complete the Hajj. The large number of people in a crowded environment increases the potential for pneumococcal carriage amplification. We evaluated pneumococcal carriage prevalence with four cross-sectional studies conducted at beginning-Hajj (Mecca) and end-Hajj (Mina) during 2011 and 2012. A questionnaire was administered and a nasopharyngeal swab was collected. The swab was tested for pneumococcus, serotype and antibiotic resistance. A total of 3203 subjects (1590 at beginning-Hajj and 1613 at end-Hajj) originating from 18 countries in Africa or Asia were enrolled. The overall pneumococcal carriage prevalence was 6.0%. There was an increase in carriage between beginning-Hajj and end-Hajj cohorts for: overall carriage (4.4% versus 7.5%, prevalence ratio (PR) 1.7, 95% CI 1.3–2.3), and carriage of 23-valent pneumococcal polysaccharide vaccine serotypes (2.3% versus 4.1%, PR 1.8, 95% CI 1.2–2.7), 13-valent pneumococcal conjugate vaccine (PCV) serotypes (1.1% versus 3.6%, PR 3.2, 95% CI 1.9–5.6), 10-valent PCV serotypes (0.6% versus 1.6%, PR 2.6, 95% CI 1.2–5.3), antibiotic non-susceptible isolates (2.5% versus 6.1%, PR 2.5, 95% CI 1.7–3.6) and multiple non-susceptible isolates (0.6% versus 2.2%, PR 3.8, 95% CI 1.8–7.9). Fifty-two different serotypes were identified, most commonly serotypes 3 (17%), 19F (5%) and 34 (5%). These results suggest that the Hajj may increase pneumococcal carriage—particularly conjugate vaccine serotypes and antibiotic non-susceptible strains, although the exact mechanism remains unknown. The Hajj may therefore provide a mechanism for the global distribution of pneumococci.

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Introduction

Streptococcus pneumoniae causes a broad spectrum of illnesses ranging from mild upper respiratory tract infection to severe invasive disease. The World Health Organization has estimated that 1.6 million deaths are caused by pneumococci annually [1].

Pneumococcal infection, or carriage, is a precursor to pneumococcal disease and carriage prevalence may vary greatly across settings from <5% to >50% [2]. Pneumococcal vaccines are widely available and the US CDC recommends that US adults receive vaccination if they are aged ≥ 65 years or aged 19–64 years and at high risk of pneumococcal disease [3]. While 23-valent pneumococcal polysaccharide vaccine (PPV23) does not impact carriage [4], newer 7-, 10- and 13-valent pneumococcal conjugate vaccines (PCV) do; this effect is of such a magnitude that indirect vaccine effects through reduction of carriage and transmission might outweigh direct protection [5].

The Kingdom of Saudi Arabia (KSA) annually hosts more than two million Muslim pilgrims from around 184 countries during the Hajj pilgrimage [6]. The presence of such a large number of pilgrims from across the globe in close contact creates conditions where the potential for transmission of infectious organisms is high [7,8], including those related to severe diseases such as pneumonia. Pneumonia is one of the leading causes of hospitalization and intensive care unit care among pilgrims in Saudi hospitals during Hajj [9,10]. During the 1986 Hajj season, pneumonia was the second most common cause of hospitalization with the highest case fatality ratio among those aged over 50 years [11].

Although limited data are available on the microbiological causes of pneumonia during Hajj, *S. pneumoniae* appears to be a common pathogen isolated from patients with pneumonia and respiratory tract infections [10,12,13]. Among 395 sputum samples collected from Hajjis with respiratory tract infections in 1991 and 1992, *S. pneumoniae* was detected in 4.8% and 12.3% respectively [12], while sputum samples from 64 patients with pneumonia admitted into two tertiary hospitals in Mecca during the 1994 Hajj yielded *S. pneumoniae* in 9.4% of cases [13]. Invasive pneumococcal disease has also been reported in Hajj pilgrims with six of nine cases of acute bacterial meningitis caused by *S. pneumoniae* in 2003 [9].

While substantial work has been performed on transmission during the Hajj of *Neisseria meningitidis* group A [14–16], influenza [17–19] and respiratory diseases as a whole [20–22], limited data are available for pneumococcal disease. In addition, although the dominant invasive pneumococcal serotypes in KSA among adults and children are 4, 3, 19F, 9V, 6A, 19A, 14 and 23F (accounting for 75% of all serotypes) [23], the current serotype distribution among Hajj pilgrims is unknown.

If the Hajj increases pneumococcal carriage, several potential consequences may follow. First, pilgrims may experience more acute infections due to contact with more invasive clones. Second, transmission of more invasive serotypes or antibiotic-resistant clones may lead to more disease or disease that is more difficult to treat in pilgrims' countries of origin after the Hajj. Finally, the mix of pneumococcal serotypes at the Hajj may facilitate serotype replacement in countries that have implemented routine infant vaccination with PCV. The first step in determining the plausibility of these outcomes is to document whether pneumococcal carriage prevalence increases during the Hajj and if so, with which serotypes and clones.

A recent small cohort survey of 169 French pilgrims performing the 2012 Hajj demonstrated the acquisition of *S. pneumoniae* nasal carriage among returning pilgrims [24]. The authors of the study called for large-scale studies to confirm the result of their small-scale preliminary investigation, to detect specific serotypes and to better understand the epidemiology of

S. pneumoniae carriage during mass gathering events. We aimed to perform such a study by evaluating pneumococcal nasopharyngeal carriage prevalence among a large cohort of pilgrims at the beginning and end of Hajj during two Hajj seasons. We also determined the serotype, genotype and antimicrobial susceptibility profiles of identified *S. pneumoniae* isolates.

Materials and methods

Study design

The Hajj progresses through a series of stages, commencing in Mecca and ending in Mina, KSA. We conducted four prospective, cross-sectional, carriage studies with cohorts tested in Mecca (beginning-Hajj) and Mina (end-Hajj) during each of the 2011 and 2012 Hajj seasons. This design was selected because of the difficulty in following individual subjects throughout the Hajj period.

Study population

During the 2011 and 2012 Hajj seasons, we screened 3203 pilgrims (1590 at the beginning of the Hajj and 1613 at the end of the Hajj). The study population consisted of a convenience sample of pilgrims 18 years of age and older originating from 18 countries in Africa or Asia (see [Supporting information, Table S1](#)). Among represented countries, only Ethiopia had introduced a PCV into routine infant immunization programmes and coverage was estimated at 12% (website: http://apps.who.int/immunization_monitoring/globalsummary, last accessed 5 June 2014). A study population of 3200 was designed to provide 80% power to detect a prevalence ratio of 1.4 at the 95% confidence level in the end-Hajj compared to the beginning-Hajj cohorts, given a beginning of Hajj pneumococcal carriage prevalence of 2%.

A standardized data collection form was used to obtain information from the beginning-Hajj cohort regarding the participants' age, gender, country of origin, formal education, smoking habits, medical conditions and vaccination history. A similar form was used for the end-Hajj cohort except that it also included data related to the Hajj such as clinical illness during the event, medication use and housing conditions, from the end-Hajj cohort.

The exclusion criteria were pilgrims under 18 years of age and those who refused to participate and give consent.

Sample collection and processing

A nasopharyngeal sample was collected from all participants by trained physicians using a dacron polyester-tipped nasopharyngeal swab. For the beginning-Hajj cohort, the nasopharyngeal swab was collected within 2 days of arrival in Mecca, while for the end-Hajj cohort collection was at anytime after arrival in

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