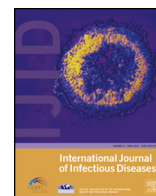




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## Proportion of adult community-acquired pneumonia cases attributable to *Streptococcus pneumoniae* among Hajj pilgrims in 2016



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### ABSTRACT

**Background:** The Hajj mass gathering is a risk for pneumococcal disease. This study was performed to evaluate the proportion of adult community-acquired pneumonia (CAP) cases attributable to *Streptococcus pneumoniae* among Hajj pilgrims in 2016. To add sensitivity to etiological attribution, a urine antigen test was used in addition to culture-based methods.

**Methods:** Adult subjects hospitalized with X-ray-confirmed CAP were enrolled prospectively from all general hospitals designated to treat Hajj pilgrims in the holy cities of Mecca and Medina. Patients were treated according to local standard of care and administered the BinaxNow *S. pneumoniae* urine antigen test.

**Results:** From August 23 to September 23, 2016, a total of 266 patients with CAP were enrolled in the study, 70.6% of whom were admitted to hospitals in Mecca; 53% of the cases were admitted after the peak of Hajj. Patients originated from 43 countries. Their mean age was 65.3 years and the male to female ratio was 2:1. Just over 36% of the cases had diabetes, 10% declared that they were smokers, and 45.4% of cases were treated in the intensive care unit (ICU). The overall case-fatality rate was 10.1%, but was higher among those treated in the ICU and in those with invasive disease. The proportion of CAP cases positive for *S. pneumoniae*, based on culture or urine antigen test, was 18.0% (95% confidence interval 13.9–23.1%).

**Conclusions:** CAP during Hajj has an important clinical impact. A proportion of CAP cases among Hajj pilgrims were attributable to *S. pneumoniae*, a pathogen for which vaccines are available. Additional studies to determine the serotypes causing pneumococcal disease could further inform vaccine policy for Hajj pilgrims.

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### Introduction

The Hajj religious mass gathering hosted by the Kingdom of Saudi Arabia (KSA) is attended by millions of Muslims annually from all over the globe (Yezli et al., 2017). The event can facilitate the acquisition and transmission of infectious agents, including those responsible for respiratory tract infection, and has been

linked to both local and international outbreaks of diseases (Ahmed et al., 2006; Memish et al., 2015a,b; Yezli et al., 2016a). Examples include meningococcal disease and influenza (Salmon-Rousseau et al., 2016; Yezli et al., 2016a). Experience from Hajj shows that the implementation of appropriate prevention measures such as vaccination can significantly reduce the incidence of disease and outbreaks associated with this mass gathering. Of note is the prevention of meningococcal disease outbreaks since 2001, after the introduction of compulsory vaccination with the quadrivalent meningococcal vaccine and targeted chemoprophylaxis (Yezli et al., 2016b).

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*Streptococcus pneumoniae* is a common cause of pneumonia and an important cause of morbidity and mortality worldwide (Feldman and Anderson, 2016; Varon et al., 2010). Hajj presents many risk factors for pneumococcal disease acquisition and transmission. Many pilgrims are elderly with pre-existing underlying health conditions and worship under crowded conditions that promote respiratory disease transmission and infection (Al-Tawfiq and Memish, 2016). Crowding in particular has been associated with pneumococcal disease outbreaks (Banerjee et al., 2005; Mercat et al., 1991). The acquisition and transmission of *S. pneumoniae* is well documented during Hajj, independent of clinical status (Memish et al., 2016, 2015a), and the organism is a leading cause of pneumonia-related hospitalizations and intensive care unit (ICU) admissions during the event (Al-Tawfiq and Memish, 2016; Memish et al., 2014).

Vaccines against pneumococcal disease are available and are recommended for those at risk (such as the elderly and those with underlying health conditions) in many countries, including countries in the Gulf states such as Bahrain, Kuwait, Oman, Qatar, and the United Arab Emirates (Feldman et al., 2013; Tomczyk et al., 2014). The Saudi Thoracic Society has also recently published guidelines on pneumococcal vaccination for Hajj pilgrims (Alharbi et al., 2016). However, there is no official KSA recommendation for vaccination for Hajj pilgrims (Saudi Ministry of Health, 2017).

Appropriate evidence-based policies regarding vaccination for pilgrims require a better understanding of the clinical burden of the disease associated with the event (Al-Tawfiq and Memish, 2016). The evidence currently available for the burden of Hajj-associated pneumococcal disease is suggestive, but limited by the insensitivity of bacterial cultures as a means of diagnosing the full burden of invasive or non-invasive pneumococcal pneumonia (Bartlett, 2011). The addition of urine antigen testing for adult pneumonia patients is expected to add sensitivity to the etiological attribution, without inappropriately minimizing specificity (Mandell et al., 2003). The sensitivity and specificity of this test in the diagnosis of community-acquired pneumonia (CAP) due to *S. pneumoniae* have been reported to be in the range of 77%–97% and

67%–100%, respectively (Gutierrez et al., 2003; Klugman et al., 2008; Molinos et al., 2015; Song et al., 2013).

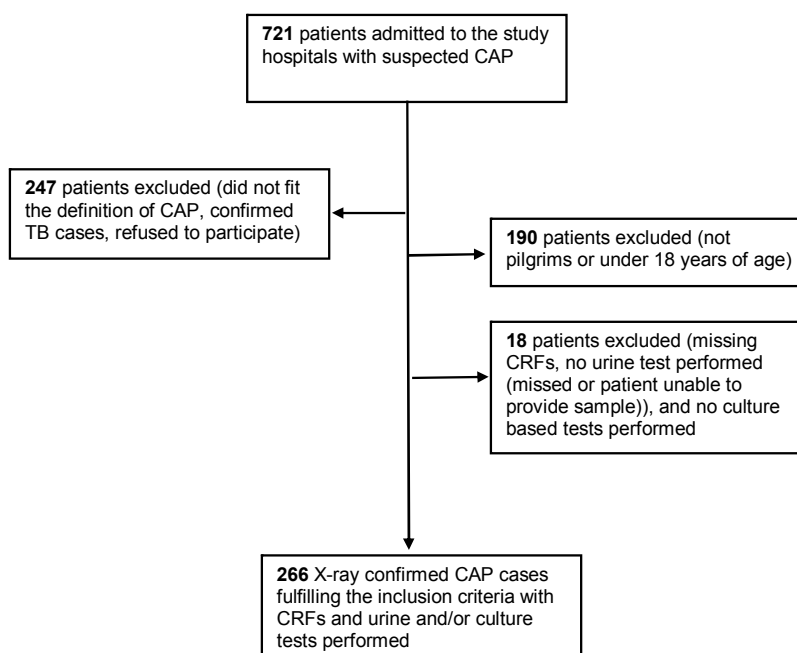
The aim of this study was to evaluate the proportion of hospitalized, X-ray-confirmed CAP attributable to *S. pneumoniae* among adult Hajj pilgrims in 2016, using the urine antigen test as well as standard culture-based tests, in order to determine the clinical burden of disease associated with Hajj and inform vaccination policy-making.

## Materials and methods

### Setting and study population

This was a prospective case-series study conducted in hospitals in the holy cities of Mecca and Medina, KSA. The study was conducted over a 1-month period from August 23 to September 23, 2016 (20 Dull Qida to 20 Dull Hija 1437H in the Islamic calendar) around the date of the Hajj peak of September 9. The study was therefore able to capture three time periods: pre-Hajj (August 23 to September 8), Hajj (September 9 to September 14), and post-Hajj (September 15 to September 23). Patients were enrolled from all general hospitals (excluding specialty hospitals such as obstetrics and gynecology hospitals and pediatric hospitals) designated to treat Hajj pilgrims. These included four general hospitals and seven temporary (holy sites) hospitals in Mecca and four general hospitals in Medina.

The study population comprised adult pilgrim patients aged  $\geq 18$  years old diagnosed with X-ray-confirmed CAP. For this protocol, CAP was defined in accordance with the US Food and Drug Administration (FDA) (US Food and Drug Administration, 2014) as an acute infection of the pulmonary parenchyma associated with symptoms such as fever or hypothermia, chills, rigors, cough, chest pain, or dyspnea, accompanied by the presence of a new lobar or multilobar infiltrate on a chest radiograph within 72 h of hospital admission. Patients with known or suspected active tuberculosis (TB; defined as smear-positive after three acid-fast bacilli tests), those  $< 18$  years old, non-Hajj pilgrims, and



CAP, community-acquired pneumonia; TB, tuberculosis; CRF, case report form

**Figure 1.** Patient enrollment flowchart.

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