

## Emergence of drug resistant bacteria at the Hajj: A systematic review



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### ABSTRACT

**Background:** Hajj is the annual mass gathering of Muslims, and is a reservoir and potential source of bacterial transmission. The emergence of bacterial transmission, including multi-drug resistance (MDR) bacteria, during Hajj has not been systematically assessed.

**Methods:** Articles in Pubmed, Scopus, and Google scholar were identified using controlled words relating to antibiotic resistance (AR) at the Hajj from January 2002 to January 2017. Eligible studies were identified by two researchers. AR patterns of bacteria were obtained for each study.

**Results:** We included 31 publications involving pilgrims, Hajj workers or local patients attending hospitals in Mecca, Mina, and the Medina area. Most of these publications provided antibiotic susceptibility results. Ten of them used the PCR approach to identify AR genes. MRSA carriage was reported in pilgrims and food handlers at a rate of 20%. Low rates of vancomycin-resistant gram-positive bacteria were reported in pilgrims and patients. The prevalence of third-generation cephalosporin-resistant bacteria was common in the Hajj region. Across all studies, carbapenem-resistant bacteria were detected in fewer than 10% of *E.coli* isolates tested but up to 100% in *K. pneumoniae* and *A. baumannii*. Colistin-resistant *Salmonella enterica*, including *mcr-1* colistin-resistant *E.coli* and *K.pneumoniae* were only detected in the pilgrim cohorts.

**Conclusion:** This study provides an overview of the prevalence of MDR bacteria at the Hajj. Pilgrims are at high risk of AR bacterial transmission and may carry and transfer these bacteria when returning to their home countries. Thus, pilgrims should be instructed by health care practitioners about hygiene practices aiming at reducing traveler's diarrhea and limited use of antibiotics during travel in order to reduce the risk of MDR bacterial transmission.

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## 1. Introduction

Hajj (pilgrimage to Mecca) is the largest annual mass gathering of Muslims with more than two million participants every year from more than 184 countries gathering in Saudi Arabia. During their journey, pilgrims visit the Holy Mosque in Mecca, stay in a tented camp in Mina and usually travel to Medina [1]. This mass gathering has a high potential for an outbreak due to the transmission of infectious diseases among pilgrims via person-to-person

contact, contaminated foods or water, and the environment [1]. During the Hajj season, pilgrims are required to follow time-sensitive religious rituals at specific times at different places simultaneously for a week. This intensely crowded situation has the potential for outbreaks of meningococcal disease [2], for the transmission of tuberculosis [3] other bacterial and viral respiratory tract infections [4] and for diarrheal diseases [5]. Additionally, many pilgrims travel to the Hajj in a group, sharing transport and accommodation including airlines and buses, food, tents, and toilets for a week, which constitutes an additional risk for transmission of communicable diseases. Nowadays, the global spread of antibiotic-resistant (AR) bacteria, such as extended spectrum

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beta-lactamase Enterobacteriaceae (ESBL-E), through international travelers is common [4,5]. The acquisition of carbapenem-resistant bacteria has also been described in travelers, including NDM-1 in travelers returning to the UK from India or KPC-producing bacteria in travelers returning to France from the United States [6]. AR bacteria are prevalent in Saudi Arabia [7–11]. Hajj pilgrims therefore have the potential to disseminate or acquire AR bacteria during their stay in Saudi Arabia and to spread these bacteria when returning to their home country. Here, we review the available literature on the prevalence of major gram-positive and gram-negative AR bacteria isolated in pilgrims or other populations living in the area where pilgrims stay, including Mecca, Mina, and Medina.

## 2. Methods

We performed a systematic review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (<http://www.prismastatement.org>). The electronic literature search was conducted in three electronic databases, Pubmed, Scopus, and Google Scholar, for articles about the emergence of antibiotic resistant bacteria during the Hajj. Searches were specified only in Hajj areas including Mecca, Mina, and Medina. Papers published from January 2002 to January 2017 and written in English were included. MeSH terms included “Gram positive bacteria”, “Streptococcus”, “Staphylococcus”, “Enterococcus”, “Gram negative bacteria”, “Acinetobacter”, “Enterobacteriaceae”, “Campylobacter”, “Escherichia”, “Klebsiella”, “Neisseria”, “Pseudomonas”, “Salmonella”, “Shigella”, “Yersinia”, “methicillin”, “MRSA”, “vancomycin”, “VRSA”, “VRE”, “carbapenem”, “Extended spectrum”, “ESBL”, “colistin”, “drug resistant”, “colonization”, “susceptibility”, “Hajj”, “pilgrims”, “Makkah”, “Mecca”, “Mina”, “Madinah”, and “Medina” (see Appendix). The search results were imported into the Mendeley references manager and de-duplicated. The articles were independently screened based on titles and abstracts by two researchers (Leangapichart and Gautret) and any discord was discussed between the two researchers. In addition, the Saudi epidemiology bulletin (<http://fep.edu.sa/Bulletin.html>) was hand searched for additional papers for inclusion. Studies were eligible for inclusion if they reported on phenotypic and/or genetic antibiotic resistance patterns and provided prevalence data. We excluded case reports. Reference lists of selected papers were screened to retrieve additional relevant studies. The following data were extracted from each study: year of study, geographical area, study setting, demographics, bacterial species investigated, and antibiotic resistance patterns. Prevalence of bacteria resistant to a given antibiotic was calculated from the number of AR bacteria divided by the total number of isolates tested.

## 3. Results

### 3.1. Study selection

A total of 275 papers resulted from the initial search. After de-duplication, 185 studies were screened based on abstract content and 148 were excluded. Subsequently, 37 full-text articles were assessed for eligibility and 31 were included in the qualitative synthesis of the systematic review with the first publication in July 2002 (Fig. 1). Most of the publications provided antibiotic susceptibility results. Eleven of them used the PCR approach to identify AR genes. The main findings are presented in Tables 1 and 2.

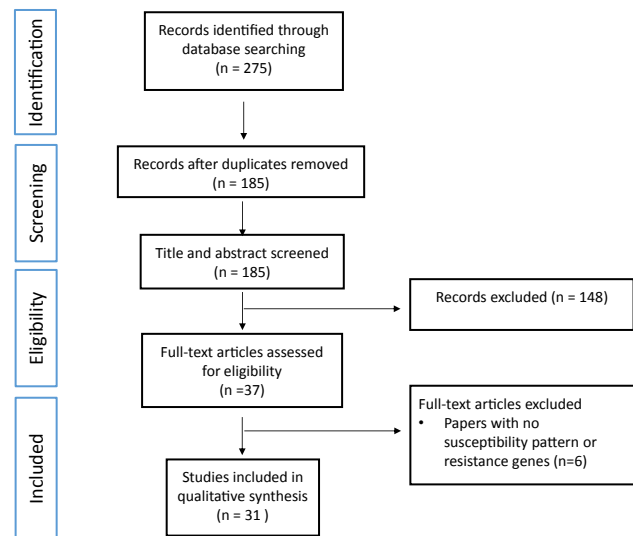


Fig. 1. Study selection. Flow diagram of identification and selection process included in systematic review.

### 3.2. Studies conducted in pilgrims and Hajj workers (Table 1)

A total of 14 publications were retrieved [12–25]. Studies were conducted during the Hajj season from 2000 through 2015. Most studies were conducted in Mecca and Medina, and one study was conducted in the Mina area. Study designs included cross-sectional surveys enrolling ill pilgrims attending health care structures in Saudi Arabia and food handlers and kitchen workers from Mecca. Other studies were prospective-cohort studies and were conducted in group of pilgrims before and after participating in the Hajj or the Umrah. The number of individuals in each study varied from 80 to 374. Participants originated from different continents and countries (the Gulf region, Europe, Asia, Africa, America), with the majority from Saudi Arabia and France. Participants were selected through travel agencies, food facilities in Mecca and various Saudi health care structures. Studies conducted involving ill pilgrims included patients suffering from skin infections [12], respiratory tract infections [23] and urinary tract infections [25]. In two studies, the syndromic classification of infectious diseases was not documented [14,24]. Most samples were collected using nasal swabs (for respiratory pathogens), and rectal swabs (for intestinal pathogens). Clinical infections in ill pilgrims were documented in five studies while nine studies reported on asymptomatic bacterial carriage in pilgrims and Hajj workers (5 respiratory carriage studies and 4 digestive carriage studies). Only one study analyzed risk factors for CTX-M acquisition by PCR detection in French pilgrims, during 2013–2014 Hajj. Shortness of breath, diarrhea, and  $\beta$ -lactam use were significantly associated with high CTX-M acquisition. By contrast, the use of macrolide was associated with low CTX-M acquisition.

#### 3.2.1. Studies investigating MRSA colonization and resistant *Streptococcus pneumoniae*

Several studies addressed oxacillin or methicillin-resistant *Staphylococcus aureus* (MRSA) carriage, starting from the 2000 Hajj.

**3.2.1.1. Ill pilgrims consulting hospitals during the Hajj.** The proportion of MRSA in positive isolates reported in patients varied according to the type of infection, reaching 2% in pilgrims suffering from pyoderma in 2000 [12], 7% in patients suffering from various types of infection in 2004, 28% in pilgrims suffering from sinusitis in

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