



HAL
open science

Antibiotic use for respiratory infections among Hajj pilgrims: A cohort survey and review of the literature

Van-Thuan Hoang, Thi-Thu-Thuy Nguyen, Khadidja Belhouchat, Mohammed Meftah, Doudou Sow, Samir Benkouiten, Thi-Loi Dao, Tran Duc Anh Ly, Tassadit Drali, Saber Yezli, et al.

► To cite this version:

Van-Thuan Hoang, Thi-Thu-Thuy Nguyen, Khadidja Belhouchat, Mohammed Meftah, Doudou Sow, et al.. Antibiotic use for respiratory infections among Hajj pilgrims: A cohort survey and review of the literature. *Travel Medicine and Infectious Disease*, Elsevier, 2019, 30, pp.39-45. 10.1016/j.tmaid.2019.06.007 . hal-02280019

HAL Id: hal-02280019

<https://hal-amu.archives-ouvertes.fr/hal-02280019>

Submitted on 20 Jul 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution-NonCommercial 4.0 International License

Antibiotic use for respiratory infections among Hajj pilgrims: a cohort survey and review of the literature

Van-Thuan Hoang^{1,2,3}, Thi-Thu-Thuy Nguyen^{2,4}, Khadidja Belhouchat^{1,2}, Mohammed Meftah^{1,2}, Doudou Sow^{1,2,5}, Samir Benkouiten^{1,2}, Thi-Loi Dao^{1,2,3}, Tran Duc Anh Ly^{1,2}, Tassadit Drali^{1,2}, Saber Yezli⁶, Badriah Alotaibi⁶, Didier Raoult^{2,7}, Philippe Parola^{1,2}, Vincent Pommier de Santi^{1,2,8}, Philippe Gautret^{1,2*}

¹Aix-Marseille Université, Institut de Recherche pour le Développement, Assistance Publique – Hôpitaux de Marseille, Service de Santé des Armées, Vecteurs – Infections Tropicales et Méditerranéennes (VITROME), Marseille, France

²Institut Hospitalo-Universitaire (IHU)-Méditerranée Infection, Marseille, France

³Thai Binh University of Medicine and Pharmacy, Thai Binh, Viet Nam

⁴Université Claude Bernard Lyon 1, France

⁵Service de Parasitologie-Mycologie, Faculté de médecine, Université Cheikh Anta Diop, Dakar, Senegal

⁶The Global Centre for Mass Gatherings Medicine, Ministry of Health, Riyadh, Saudi Arabia

⁷Aix Marseille Université, Microbes Evolution Phylogénie et Infection (MEPHI) , Marseille, France

⁸French Military Center for Epidemiology and Public Health Marseille, France

*Corresponding author:

Philippe Gautret

VITROME, Institut Hospitalo-Universitaire Méditerranée Infection, 19-21 Boulevard Jean Moulin
13385 Marseille Cedex 05, France. Phone: + 33 (0) 4 13 73 24 01. Fax: + 33 (0) 4 13 73 24 02. E-
mail address: philippe.gautret@club-internet.fr

Abstract

Background: To evaluate the occurrence and determinants associated with antibiotic use for respiratory tract infections (RTIs) among Hajj pilgrims.

Methods: Prospective cohort surveys were conducted among French pilgrims from 2012 to 2017. We also conducted a systematic review about available evidence for antibiotic consumption in relation with RTIs during the Hajj.

Results: 783 pilgrims were included in the survey. During the Hajj, 85.3% presented respiratory symptoms and 47.6% used antibiotics. Pilgrims with productive cough or fever were three times and twice as likely to have used antibiotics. Dry cough, sore throat and voice failure were also associated with increased antibiotic use. 26.3% of pilgrims presented symptoms compatible with a lower tract respiratory infection. According to the French recommendations, only 39.6% of pilgrims who used an antibiotic actually had an indication for it. Antibiotic intake was associated with an increased frequency of persistent symptoms post-Hajj (aRR = 1.31, 95%CI [1.04-1.66]).

The review included 14 articles. The use of antibiotic for respiratory tract infections during the Hajj varied from 7% to 58.5%. In 9 studies, the antibiotic consumption rate was > 30%.

Conclusion: Respiratory tract infections are common during the Hajj, leading to high prevalence of inappropriate antibiotic intake.

Key words: Hajj; pilgrims; antibiotic; respiratory tract infections; recommendation; determinants.

Text

Introduction

The Muslim Hajj pilgrimage in Saudi Arabia, is among the largest annual religious mass gatherings on earth. Each year, it welcomes more than 2 million pilgrims from more than 180 countries, a third of whom come from outside Saudi Arabia. The Hajj takes place in three main places in the Mecca area, which are the Grand Mosque in the Holy city of Mecca, the Mina valley and the plain of Arafat (about 5 and 18 kilometers from Mecca respectively) [1]. A large proportion of pilgrims are elderly people, many with chronic diseases [2]. Furthermore, the presence of many pilgrims from different countries around the world and overcrowding considerably increase the risk to contract infectious diseases, particularly respiratory and gastrointestinal infections, resulting in a considerable demand for antibiotic use [3, 4]. The predominance of bacterial pathogens in Hajj-related gastrointestinal infections poses a major public health risk due to the potential emergence and transmission of antimicrobial resistant bacteria [5]. Antibiotic resistant gastro-intestinal and respiratory organisms have been frequently isolated from Hajj pilgrims [6-11]. Although a prescription has been required in order to receive antibiotics in Saudi Arabia for more than 30 years [12], many pilgrims use antibiotic without a prescription [13]. To date, few studies on the appropriateness of antibiotic use among pilgrims were conducted. The objective of this study is to assess the prevalence of antibiotic use during Hajj over a period from 2012 to 2017 among French pilgrims and to study the demographic and clinical determinants associated with antibiotic use during this event. We also conducted a systematic review on available evidence for antibiotic consumption in relation to respiratory tract infections (RTIs) during the Hajj.

Methods

Prospective cohort

Participants and study design

Pilgrims from Marseille, France participating in the Hajj from 2012 to 2017 were recruited at a specialized travel agency organizing trips to Mecca. Potential adult participants were invited to participate in the study. They were recruited and followed-up by a medical bilingual (Arabic and French) doctor who traveled with the group. The participants were interviewed using a standardized pre-Hajj questionnaire that collected information on demographic characteristics and medical conditions before departing from France. A post-Hajj questionnaire that collected clinical data and information on the use of antibiotics was completed two days before the pilgrims' return to France. Influenza-like illness (ILI) was defined in the current study as the presence of subjective fever, sore throat and cough [14]. Possible pulmonary involvement requiring antibiotic therapy was suspected based on the presence of the following symptoms: productive cough without nasal or throat symptoms; febrile productive cough; dyspnea or febrile dyspnea, according to expert consensus statements [15, 16]. Streptococcal pharyngitis was suspected based on the presence of fever and sore throat without cough or runny nose [17]. The protocol was approved by the Aix-Marseille University institutional review board (July 23rd, 2013; reference no. 2013-A00961-44). The study was performed according to the good clinical practices recommended by the Declaration of Helsinki and its amendments. All participants provided a written consent.

Statistical analysis

Statistical analysis was conducted using STATA software version 11.1 (Copyright 2009 StataCorp LP, <http://www.stata.com>). Differences in the proportions were tested by Pearson's chi-square or Fisher's exact tests when appropriate. Unadjusted associations between multiple factors and prevalence of antibiotics use for respiratory symptoms were examined by univariate analysis. The results were presented by percentages and risk ratio (RR) with 95% confidence interval (95%CI).

Results with a p value ≤ 0.05 were considered statistically significant. Only the variables with a prevalence $\geq 5.0\%$ were considered for statistical analysis. Variables with p values < 0.2 in the univariate analysis were included in the multivariate analysis. Log-binomial regression was used to calculate adjusted risk ratios regarding antibiotic consumption [18].

Review of antibiotic use during the Hajj

Search strategy and selection criteria

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and MetaAnalyses (PRISMA) guidelines (<http://www.prisma-statement.org>). The following databases were investigated in an attempt to identify all relevant studies published on: PubMed (<http://www.ncbi.nlm.nih.gov/pubmed>) and Google Scholar (<http://scholar.google.fr/>). The most recent search was conducted on November 12, 2018. The topic search terms used for searching the databases were the following:

#1: “Hajj” OR “pilgrims”

#2: “antibiotic” OR “antibacterial” OR “antimicrobial” OR “treatment”

#3: #1 AND #2

Only articles published in English were included. For inclusion, articles had to fulfil three criteria: (1) be related to Hajj, (2) be conducted among group of pilgrims independently to the presence of symptoms and (3) report the use of antibiotic. Studies that recruited only sick pilgrims from hospitals or outpatient departments, case reports and reviews were excluded. Reference lists of selected articles were screened to identify studies that might have been missing from the research.

Two researchers (GP and HVT) independently performed the screening of the abstracts. Any discordant result was discussed in a consensus meeting. After screening the abstracts, the full texts

of the articles were assessed for eligibility by the same two researchers and selected or rejected for inclusion in the systematic review.

Data collection process

The following data (if available) were extracted from each article: year, countries of origin of pilgrims, study design, sample size of attendees, prevalence of symptoms and ratio of antibiotic use.

Data synthesis and analysis

As a result of the nature of the studies and the heterogeneity in patient populations, a formal meta-analysis was not possible. Therefore, the study results were summarized to describe the main outcomes of interest (i.e. the prevalence of antibiotic use). When possible, percentages not presented in the articles were calculated from the available data.

Results

Cohort survey during the Hajj 2012-2017

Characteristics of study participants

A total of 783 of the 803 pilgrims contacted (97.5%) agreed to participate in our study and completed the questionnaire required before the trip. Of them, 754 (96.3%) also responded to the post-Hajj questionnaire. 328 pilgrims were male (41.9%) with a gender ratio of 1:1.4. The median age was 62 years of age (interquartile = (54-68), min = 21, max = 96 years). Hypertension (28.0%) and diabetes (29.4 %) were the most common comorbidities (Table 1).

Clinical features and antibiotic intake during the Hajj

Figure 1 shows the prevalence of respiratory symptoms and antibiotic use among pilgrims during the Hajj. Most frequent symptoms were cough (77.8%, 587/754), rhinitis (57.3%, 432/754) and sore

throat (65.1%, 491/754). 26.1% (197/754) of pilgrims had ILI and 26.3% (198/754) had a possible pulmonary involvement. Only 2 pilgrims presented with symptoms of possible streptococcal pharyngitis and both used antibiotics. At total, 3 patients were hospitalized. Two days prior to leave Saudi Arabia, 46.6% (351/754) of pilgrims were still symptomatic. A total of 47.6% (359/754) of pilgrims took antibiotics during their pilgrimage, representing 55.6% of ill pilgrims. Beta-lactams were the most commonly used antibiotic (35.0%), followed by macrolides (11.4%), cephalosporines (2.3%), quinolones (1.5%) and sulfonamides (0.1%).

Determinants associated with antibiotic consumption during the Hajj and impact of antibiotics on respiratory symptoms

Table 2 shows results of univariate and multivariate analysis about determinants associated with antibiotic consumption. Pilgrims suffering from productive cough or fever were three times and twice as likely, respectively, to have used antibiotics than others (aRR = 2.97, 95%CI [2.28-3.88], $p < 0.0001$ and aRR = 2.01, 95%CI [1.53-2.63], $p < 0.0001$ respectively). Dry cough, sore throat and voice failure were also associated with increased antibiotic use. Of note, antibiotic intake was not significantly increased in individuals with a possible pulmonary involvement compared to others (18.7% versus 28.9% respectively) (Table 2).

With regard to the persistence of respiratory symptoms post-Hajj, no socio-demographic factors and no chronic conditions was associated. Antibiotic intake was associated with increased frequency of symptom persistence (aRR = 1.31, 95%CI [1.04-1.66], $p = 0.02$) (Table 3). This increase was only observed in pilgrims with symptoms of LRTI (RR = 1.86, 95%CI [1.32-2.61], $p = 0.0002$) but not in those with symptoms of URTI (RR = 0.93, 95%CI [0.75-1.15], $p = 0.50$) (data not shown).

Review on antibiotic consumption at the Hajj

A total of 157 articles were identified in the database search and 5 additional articles were found through the manual search. After screening the titles and abstracts, 14 articles were eventually retained for full-text assessment. All 14 articles were included in the qualitative synthesis of the systematic review (supplementary figure 1). Studies were conducted during the Hajj seasons from 1999 to 2016 and included a total of 7774 pilgrims originating from various countries, including Pakistan, Malaysia, Ireland, US, Singapore, UK, Iran, Australia and India. Most studies were conducted based on a prospective cohort follow-up design and some used a cross-sectional survey design. RTIs were common among pilgrims and hospitalization rates were low. The use of antibiotic for RTIs during the Hajj varied by nationality, from 7% in a Singaporean survey in 2001 to 58.5% among Iranian pilgrims in 2012. In 9 studies out of 14, the antibiotic consumption prevalence was >30% [13, 19-31] (Table 4).

Discussion

Our study confirms that RTIs are common during the Hajj with a high proportion of antibiotic use of 47.6%. The multivariate analysis showed that upper respiratory tract infection (URTI) symptoms (dry cough, sore throat and voice failure), productive cough and fever were independent factors associated with increased antibiotic use. In this study, only 26.3% of pilgrims reported clinical symptoms, suggesting a lower respiratory tract infection (LRTI) that may require antibiotic use according to the French recommendations [15]. The antibiotic consumption, however, was lower in patients with a possible pulmonary involvement compared to others presenting with symptoms of URTI. According to the French recommendations [15], only 142/359 (39.6%) of pilgrims who have used an antibiotic had an indication for their use. By contrast, 57/198 (28.8%) pilgrims with a possible LRTI did not receive antibiotic although they had an indication for them. Furthermore, pilgrims who took antibiotics during their stay were significantly more likely to present with

persisting symptoms of LRTI, post-Hajj. A possible explanation for this finding is that the sicker patients were more likely to take antibiotics and also more likely to have persistent symptoms. Alternatively, antibiotics may have altered either the underlying flora or the immune responses in ways that impeded recovery.

The high prevalence of antibiotic use at the Hajj is not observed among French pilgrims only. Our review shows that a high proportion of pilgrims of different nationality used antibiotics during their pilgrimage because of RTIs. In a survey conducted among 1162 pilgrims from 13 different countries in 2013, at the Jeddah airport, 62% ILI was observed after the Hajj and 45.5% received antibiotic [29]. Most RTI cases during the Hajj are URTIs, while pneumonia is uncommon among pilgrims [19-21, 32]. Most URTIs are due to viruses with no formal need for antibiotic treatment [33]. Antibiotic resistance of bacteria in Saudi Arabia has recently emerged for several reasons, including self-prescribing of antibiotics by patients, irrational or over-prescription by medical staffs, sub-therapeutic doses of antimicrobial agents and poor case management by unsuitable combinations and, non-compliance with prescribed treatments by patients. In one study conducted at one hospital in Jeddah, 59.3% *Klebsiella pneumoniae* respiratory isolates were resistant to ampicillin and piperacillin [34]. In another study, conducted at one hospital in Taif, 30.5% gram-negative bacteria isolates had an extended spectrum β -lactamases phenotype [35]. Recent publications have shown that antibiotic-resistant bacteria acquisition at the Hajj is frequent [36]. Among French pilgrim cohorts sampled in 2013 and 2014 a significant acquisition of extended spectrum β -lactamases-, carbapenemase-producing bacteria or *mcr-1*-positive isolates was reported [8-11]. It is therefore likely that antibiotics used by French pilgrims in the present study, might have been at least partially ineffective in treating LRTI symptoms.

The assessment of the bacterial origin of RTI in pilgrims would necessitate taking a sputum sample before starting treatment for identification and sensitivity testing, since antibiotic intake prior to

pneumonia diagnosis can impair the detection of the causative agent [37]. However, most of ill pilgrims are seen in outpatient clinics or by medical missions. In this context, paraclinical diagnosis such as radiology and the culture of respiratory pathogens is difficult and the prescription of antibiotics is often based on the clinical evaluation of the patient. Therefore, antibiotic prescription should be restricted to patients presenting with symptoms of LRTI. Access to antibiotic without prescription is another cause of high prevalence of antibiotic use during the Hajj. A recent knowledge, attitude and practice survey showed that 66.6% pilgrims accessed antibiotics without prescription through a pharmacist. Over 87% of them used non-prescribed antibiotics. A proportion of 79.2% used multiple sources to access antibiotics. Only 12.7% of respondents indicated that in the event of illness, they would visit a clinic and only take the medications prescribed by a doctor. A proportion of 26.5% used antibiotics prescribed to them by a doctor for a previous illness and 10% antibiotics prescribed by doctors for their relatives [38].

In a study conducted during the Grand Magal de Touba, in Senegal, in 2017, 41.8% pilgrims reported respiratory symptoms and only 2.7% received antibiotics [39]. We are not aware about studies documenting the antibiotic intake among participant to other mass gatherings. Such studies would be of interest.

Our study was based on questionnaires and has some limitations including notably the lack of data about clinical examination of participants, the lack of radiological and microbiological documentation of RTIs and the lack of duration of antibiotic treatment. Also we did not differentiated self-prescription of antibiotics and antibiotics prescription by the accompanying doctor.

Conclusion

RTIs are common during the Hajj and antibiotic use is frequent in this context. It is therefore necessary to follow the recommendations for antibiotic use based on clinical symptoms in pilgrims in order to raise rational consumption of antibiotics during Hajj. A pilgrim education strategy on Hajj-related pathologies and indications of antibiotics and the promotion of influenza and pneumococcal vaccination is needed. In particular, it is important to organize information sessions before travel to Mecca, or to use documents (flyers) or information online. In addition, it is important to control the delivery of antibiotics in the countries of origin of pilgrims and to enforce the legislations of KSA government [38]. Rapid identification tests for respiratory pathogens could help medical staff in charge of pilgrims to rationalize their prescriptions for antibiotics.

Funding

This study was supported by the Institut Hospitalo-Universitaire (IHU) Méditerranée Infection, the National Research Agency under the program « Investissements d'avenir », reference ANR-10-IAHU-03, the Région Provence Alpes Côte d'Azur and European funding FEDER PRIM1.

Conflict of Interest

Van-Thuan Hoang, Thi-Thu-Thuy Nguyen, Khadidja Belhouchat, Mohammed Meftah, Doudou Sow, Samir Benkouiten, Thi-Loi Dao, Tran Duc Anh Ly, Tassadit Drali, Saber Yezli, Badriah Alotaibi, Didier Raoult, Philippe Parola, Vincent Pommier de Santi, Philippe Gautret declare that they have no conflict of interest

References

- [1]. Gatrads AR, Sheikh Z. Hajj: journey of a lifetime. *BMJ* 2005;330:133-7. <https://doi.org/10.1136/bmj.331.7514.442>.
- [2]. Memish ZA, Zumla A, Alhakeem RF. Hajj: infectious disease surveillance and control. *Lancet* 2014;383:2073–82. [https://doi.org/10.1016/S0140-6736\(14\)60381-0](https://doi.org/10.1016/S0140-6736(14)60381-0).
- [3]. Abubakar I, Gautret P, Brunette GW, Blumberg L, Johnson D, Pomerol G, et al. Global perspectives for prevention of infectious diseases associated with mass gatherings. *Lancet Infect Dis* 2012;12:66-74. [https://doi.org/10.1016/S1473-3099\(11\)70246-8](https://doi.org/10.1016/S1473-3099(11)70246-8).
- [4]. Al-Tawfiq JA, Memish ZA. Mass gatherings and infectious diseases: prevention, detection, and control. *Infect Dis Clin North Am.* 2012;26:725-37. <https://doi.org/10.1016/j.idc.2012.05.005>.
- [5]. Abd El Ghany M, Alsomali M, Almasri M, Padron Regalado E, Naeem R, Tukestani A, et al. Enteric Infections Circulating during Hajj Seasons, 2011-2013. *Emerg Infect Dis.* 2017;23:1640-9. <https://doi.org/10.3201/eid2310.161642>.
- [6]. Asghar AH. Frequency and antimicrobial susceptibility patterns of bacterial pathogens isolated from septicemic patients in Makkah hospitals. *Saudi Med J* 2006;27:361-7.
- [7]. Asghar AH, Faidah HS. Frequency and antimicrobial susceptibility of gram negative bacteria isolated from 2 hospitals in Makkah, Saudi Arabia. *Saudi Med J* 2009;30:1017-23.
- [8]. Leangapichart T, Tissot-Dupont H, Raoult D, Memish ZA, Rolain JM, Gautret P. Risk factors for acquisition of CTX-M genes in pilgrims during Hajj 2013 and 2014. *J Antimicrob Chemother.* 2017;72:2627–35. <https://doi.org/10.1093/jac/dkx155>.
- [9]. Leangapichart T, Dia NM, Olaitan AO, Gautret P, Brouqui P, Rolain J-M. Acquisition of extended-spectrum b-lactamases by *Escherichia coli* and *Klebsiella pneumoniae* in gut microbiota

of pilgrims during the hajj pilgrimage of 2013. *Antimicrob Agents Chemother.* 2016;60:3222–6. <https://doi.org/10.1128/AAC.02396-15>.

[10]. Leangapichart T, Gautret P, Griffiths K, Belhouchat K, Memish Z, Raoult D, et al. Acquisition of a high diversity of bacteria during the Hajj pilgrimage, including *Acinetobacter baumannii* with blaOXA-72 and *Escherichia coli* with blaNDM-5 carbapenemase genes. *Antimicrob Agents Chemother.* 2016;60:5942–8. <https://doi.org/10.1128/AAC.00669-16>.

[11]. Leangapichart T, Gautret P, Brouqui P, Memish ZA, Raoult D, Rolain J-M. Acquisition of mcr-1 plasmid-mediated colistin resistance in *Escherichia coli* and *Klebsiella pneumoniae* during Hajj 2013 and 2014. *Antimicrob Agents Chemother.* 2016;60:6998–9. <https://doi.org/10.1128/AAC.01486-16>.

[12]. Bawazir SA: Prescribing pattern at community pharmacies in Saudi Arabia. *International Pharmacy Journal* 1992;6:222-4.

[13]. Azeem M, Tashani M, Barasheed O. Knowledge, Attitude and Practice (KAP) Survey Concerning Antimicrobial Use among Australian Hajj Pilgrims. *Infectious Disorders – Drug Targets* 2014;14; 125-32. <https://doi.org/10.2174/1871526514666140713161757>.

[14]. Rashid H, Shafi S, El Bashir H, Haworth E, Memish ZA, Ali KA, et al. Influenza and the Hajj: defining influenza-like illness clinically. *Int J Infect Dis.* 2008;12:102-3. <https://doi.org/10.1016/j.ijid.2007.03.009>.

[15]. Agence française de sécurité sanitaire des produits de santé. Antibiothérapie par voie générale en pratique courante dans les infections respiratoires basses, http://www.infectiologie.com/UserFiles/File/medias/_documents/consensus/2005-infVRB-recos-afssaps.pdf; 2005 [accessed 8 November 2018].

- [16]. Hill AT, Gold PM, El Solh AA, Metlay JP, Ireland B, Irwin RS, et al. Adult Outpatients With Acute Cough Due to Suspected Pneumonia or Influenza: CHEST Guideline and Expert Panel Report. *Chest*. 2019;155:155-67. <https://doi.org/10.1016/j.chest.2018.09.016>.
- [17]. Choby BA. Diagnosis and treatment of streptococcal pharyngitis. *Am Fam Physician*. 2009;79:383-90.
- [18]. McNutt LA, Wu C, Xue X, Hafner JP. Estimating the relative risk in cohort studies and clinical trials of common outcomes. *Am J Epidemiol*. 2003;157:940-3. <https://doi.org/10.1093/aje/kwg074>
- [19]. Qureshi H, Gessner BD, Leboulleux D, Hasan H, Alam SE, Moulton LH. The incidence of vaccine preventable influenza-like illness and medication use among Pakistani pilgrims to the Hajj in Saudi Arabia. *Vaccine* 2000;18:2956-62. [https://doi.org/10.1016/S0264-410X\(00\)00116-X](https://doi.org/10.1016/S0264-410X(00)00116-X).
- [20]. Raja Ali R.A, O'Halloran J, Flaherty G. An Analysis of the Pattern of Travel-Related Morbidity Reported by Hajj Pilgrims: An Irish Perspective. Northern Conference on Travel Medicine Programme and Abstracts, Conference Center Hamburg (CCH) May 26 - 29, 2010.
- [21]. Hashim S, Ayub ZN, Mohamed Z, Hasan H, Harun A, Ismail N, et al. The prevalence and preventive measures of the respiratory illness among Malaysian pilgrims in 2013 Hajj season. *J Travel Med* 2016;5:1-7. <https://doi.org/10.1093/jtm/tav019>.
- [22]. Dull PM, Abdelwahab J, Sacchi CT, Becker M, Noble CA, Barnett GA, et al. *Neisseria meningitidis* serogroup W-135 carriage among US travelers to the 2001 Hajj. *J Infect Dis* 2005;191:33-9. <https://doi.org/10.1086/425927>.

- [23]. Wilder-Smith A, Barkham TM, Earnest A, Paton NI. Acquisition of W135 meningococcal carriage in Hajj pilgrims and transmission to household contacts: prospective study. *BMJ*. 2002;325:365-6. <https://doi.org/10.1136/bmj.325.7360.365>.
- [24.] Wilder-Smith A, Paton NI, Barkham TM, Earnest A. Meningococcal carriage in Umra pilgrims returning from Saudi Arabia. *J Travel Med*. 2003;10:147-9. <https://doi.org/10.2310/7060.2003.35751>.
- [25]. Wilder-Smith A, Barkham TM, Chew SK, Paton NI. Absence of *Neisseria meningitidis* W-135 electrophoretic Type 37 during the Hajj, 2002. *Emerg Infect Dis* 2003;9:734-7. <https://doi.org/10.3201/eid0906.020725>.
- [26]. El Bashir H, Coen PG, Haworth E, Taylor S, Mifsud A, El Baki A, et al. Meningococcal W135 carriage; enhanced surveillance amongst east London Muslim pilgrims and their household contacts before and after attending the 2002 Hajj. *Travel Med Infect Dis* 2004;2:13-5. <https://doi.org/10.1016/j.tmaid.2004.01.006>.
- [27]. Alborzi A, Oskoe S, Pourabbas B, Alborzi S, Astaneh B, Gooya MM, et al. Meningococcal carrier rate before and after hajj pilgrimage: effect of single dose ciprofloxacin on carriage. *East. Mediterr. Health J* 2008;14:277-82.
- [28]. Metanat M, Sharifi-Mood B, Sanei-Moghaddam S, Rad NS. Pharyngeal carriage rate of *Neisseria meningitidis* before and after the Hajj pilgrimage, in Zahedan (southeastern Iran), 2012. *Turk J Med Sci* 2015;45:1317-20. <https://doi.org/10.3906/sag-1405-7>.
- [29]. Memish ZA, Assiri A, Turkestani A, Yezli S, Al Masri M, Charrel R, et al. Mass gathering and globalization of respiratory pathogens during the 2013 Hajj. *Clin Microbiol Infect*. 2015;21:571.e1-8. <https://doi.org/10.1016/j.cmi.2015.02.008>.

- [30]. Azeem MI, Tashani M, Badahdah AM, Heron L, Pedersen K, Jeoffreys N, et al. Surveillance of Australian Hajj pilgrims for carriage of potentially pathogenic bacteria: Data from two pilot studies. *World J Clin Cases* 2017;16;5:102-11. <https://doi.org/0.12998/wjcc.v5.i3.102>.
- [31]. Ganaie F, Nagaraj G, Govindan V, Basha R, Hussain M, Ashraf N, et al. Impact of Hajj on the *S. pneumoniae* carriage among Indian pilgrims during 2016 - a longitudinal molecular surveillance study. *Travel Med Infect Dis* 2018;23:64-71. <https://doi.org/10.1016/j.tmaid.2018.04.002>.
- [32]. Mustafa AN, Gessner BD, Ismail R, Yusoff AF, Abdullah N, Ishak I, et al. A case-control study of influenza vaccine effectiveness among Malaysian pilgrims attending the Haj in Saudi Arabia. *Int. J. Infect. Dis* 2003;7;210-4. [https://doi.org/10.1016/S1201-9712\(03\)90054-3](https://doi.org/10.1016/S1201-9712(03)90054-3).
- [33]. Cars T, Eriksson I, Granath A, Wettermark B, Hellman J, Norman C, et al. Antibiotic use and bacterial complications following upper respiratory tract infections: a population-based study. *BMJ Open*. 2017;7:e016221. <https://doi.org/10.1136/bmjopen-2017-016221>.
- [34]. Alam MZ, Alam Q, Jiman-Fatani AA, Shukri HA, Haque A. A surveillance study on the prevalence and antimicrobial resistance pattern among different groups of bacteria isolated from Western province of Saudi Arabia. *Biomedical Research*. 2017;28:898-906.
- [35]. Al-Garni SM, Ghonaim MM, Ahmed MMM, Al-Ghamdi AS, Ganai FA. Risk factors and molecular features of extended-spectrum beta-lactamase producing bacteria at southwest of Saudi Arabia. *Saudi Med J*. 2018;39:1186-94. <https://doi.org/10.15537/smj.2018.12.23273>.
- [36]. Leangapichart T, Rolain JM, Memish ZA, Al-Tawfiq JA, Gautret P. Emergence of drug resistant bacteria at the Hajj: A systematic review. *Travel Med Infect Dis*. 2017;18:3-17. <https://doi.org/10.1016/j.tmaid.2017.06.008>.

[37]. Falguera M, Pifarre R, Martin A, Sheikh A, Moreno A. Etiology and outcome of community-acquired pneumonia in patients with diabetes mellitus. *Chest*. 2005;128:3233-9. <https://doi.org/10.1378/chest.128.5.3233>.

[38]. Yezli S, Yassin Y, Mushi A, Maashi F, Aljabri N, Mohamed G, et al. Knowledge, attitude and practice (KAP) survey regarding antibiotic use among pilgrims attending the 2015 Hajj mass gathering. *Travel Med Infect Dis*. 2019;28:52-8. pii: S1477-8939(18)30272-2. <https://doi.org/10.1016/j.tmaid.2018.08.004>.

[39]. Hoang VT, Goumballa N, Dao TL, Ly TDA, Ninove L, Ranque S, et al. Respiratory and gastrointestinal infections at the 2017 Grand Magal de Touba, Senegal: A prospective cohort survey. *Travel Med Infect Dis*. 2019. pii: S1477-8939(19)30069-9. <https://doi.org/10.1016/j.tmaid.2019.04.010>.

Table 1: Characteristics of the study population, Hajj pilgrims (N=783)

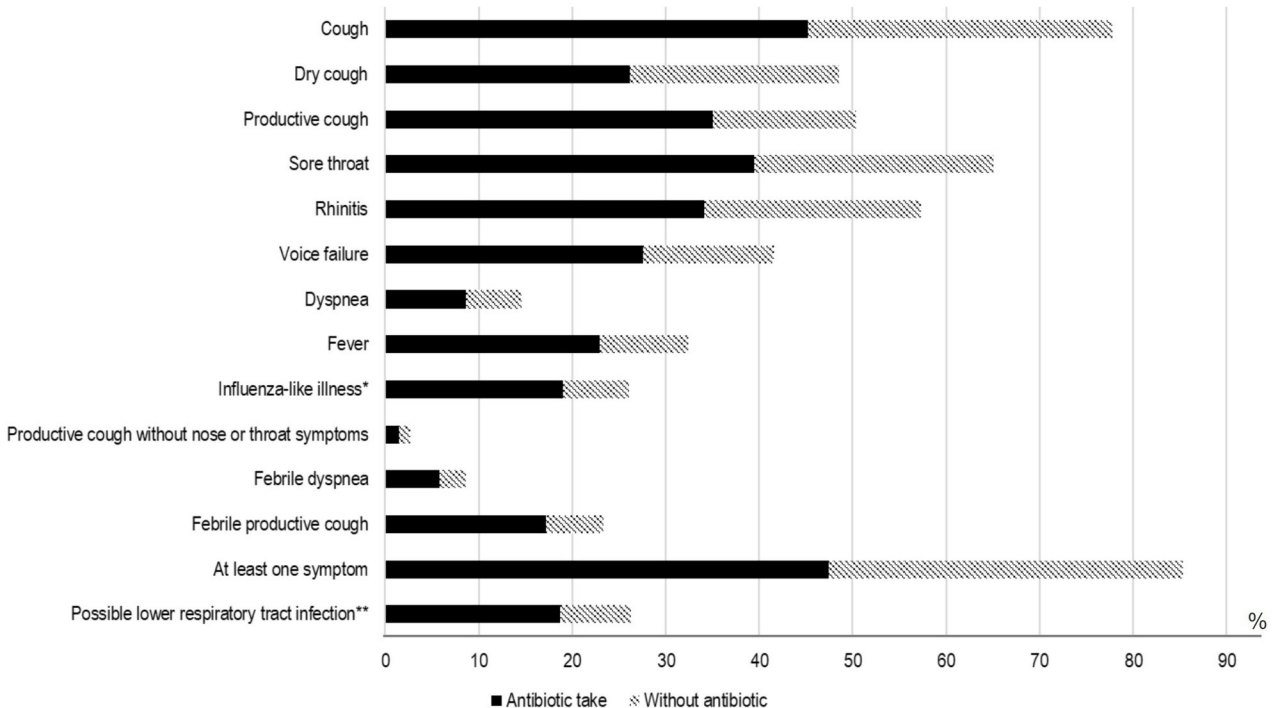
Table 2: Associated factor to antibiotic consumption during the Hajj (N=754)

Table 3: Associated factors to persistence of respiratory symptoms at return from the Hajj (uni- and multi-variate analysis (N = 646 ill pilgrims))

Table 4: Review of literature on antibiotic consumption during the Hajj

Figure 1: Antibiotic consumption according to respiratory tract infections during the Hajj 2012-2017 (N=783)

Supplementary figure 1. Flow diagram of the search strategy.



*ILI: cough, sore throat and fever, **Possible lower respiratory tract infection: productive cough without nasal or throat symptoms; febrile productive cough; dyspnea or febrile dyspnea

Table 1: Characteristics of the study population, Hajj pilgrims (N=783)

Variables		n	%
Pilgrimage years	2012	169	21.6
	2013	129	16.5
	2014	98	12.5
	2015	119	15.2
	2016	117	14.9
	2017	151	19.3
Gender	Male	328	41.9
	Female	455	58.1
Age	Median	62	
	Interquartile	54 - 68	
	Min-max	21 - 96	
Comorbidities	Diabetes mellitus	216	28.0
	Hypertension	227	29.4
	Chronic respiratory disease	75	9.7
	Chronic heart disease	56	7.3
	Chronic kidney disease	7	0.9
	Immunodeficiency	3	0.4
Duration of stay in KSA (mean \pm SD) (days)		22.9 \pm 1.7	

KSA; Kingdom of Saudi Arabia

Table 2: Associated factor to antibiotic consumption during the Hajj (N=754)

Variables	Univariate analysis				Multivariate analysis	
	ATB use = Yes	ATB use = No	RR	P-value	aRR	P-value
	n (%)	n (%)	[95%CI]		[95%CI]	
Socio-demographic characteristics						
Gender	Male	123 (38.8)	194 (61.2)	0.72	<10 ⁻⁴	
	Female	236 (54.0)	201 (46.0)	[0.61-0.84]		
Age*	≥ 60 years	200 (46.1)	234 (53.9)	0.93	0.35	
	<60 years	157 (49.5)	160 (50.5)	[0.80-1.08]		
Comorbidities						
Diabetes mellitus*	Yes	96 (45.5)	115 (54.5)	0.94	0.46	
	No	262 (48.5)	278 (51.5)	[0.79-1.11]		
Hypertension*	Yes	100 (45.2)	121 (54.8)	0.93	0.39	
	No	258 (48.7)	272 (51.3)	[0.78-1.10]		
Chronic respiratory disease*	Yes	41 (56.2)	32 (43.8)	1.20	0.13	
	No	317 (46.8)	361 (53.2)	[0.97-1.49]		
Chronic heart disease*	Yes	30 (54.5)	25 (45.5)	1.16	0.29	
	No	328 (47.1)	368 (52.9)	[0.90-1.49]		
Respiratory symptoms						
Cough	Yes	341 (58.1)	246 (41.9)	5.34	<10 ⁻⁴	
	No	18 (10.8)	149 (89.2)	[3.47-8.38]		
Dry cough	Yes	198 (54.1)	168 (45.9)	1.30	5.10 ⁻⁴	1.56
	No	161 (41.5)	227 (58.5)	[1.12-1.52]		[1.23-2.00]
Productive cough	Yes	264 (69.5)	116 (30.5)	2.74	<10 ⁻⁴	2.97
	No	95 (25.4)	279 (74.6)	[2.27-3.29]		

Dyspnea	Yes	65 (59.1)	45 (40.9)	1.29	0.01		
	No	294 (45.7)	350 (54.3)	[1.08-1.54]			
Sore throat	Yes	298 (60.7)	193 (39.3)	2.62	<10 ⁻⁴	1.52	10 ⁻³
	No	61 (23.2)	202 (76.8)	[2.08-3.30]			
Voice failure	Yes	208 (66.2)	106 (33.8)	1.93	<10 ⁻⁴	1.41	0.01
	No	151 (34.3)	289 (65.7)	[1.66-2.46]			
Rhinitis	Yes	257 (59.5)	175 (40.5)	1.88	<10 ⁻⁴		
	No	102 (31.7)	220 (68.3)	[1.57-2.24]			
Fever	Yes	173 (70.9)	71 (29.1)	1.94	<10 ⁻⁴	2.01	<10 ⁻⁴
	No	186 (36.5)	324 (63.5)	[1.69-2.24]			
ILI	Yes	143 (72.6)	54 (27.4)	1.87	<10 ⁻⁴		
	No	216 (38.8)	341 (61.2)	[1.63-2.14]			

Possible lower respiratory tract infections

Productive cough without nasal or throat symptoms	Yes	11 (55.0)	9 (45.0)	1.16	0.50		
	No	348 (47.4)	386 (52.6)	[0.77-1.74]			
Febrile dyspnea	Yes	44 (67.7)	21 (32.2)	1.48	7.10 ⁻⁴		
	No	315 (45.7)	374 (54.3)	[1.23-1.78]			
Febrile productive cough	Yes	130 (73.9)	46 (26.1)	1.86	<10 ⁻⁴		
	No	229 (39.6)	349 (60.4)	[1.63-2.13]			

RR: risk ratio, aRR: adjusted relative risk, ATB: antibiotic

**: N = 751, data missing for 3 subjects*

Table 3: Associated factors to persistence of respiratory symptoms at return from the Hajj (uni- and multi-variate analysis (N = 646 ill pilgrims))

Variables		Persistence of respiratory symptoms			
		n (%)	RR [95%CI]	P-value	aRR [95%CI]
Socio-demographic characteristics					
Gender	Male	148 (46.7)	1.01	0.92	
	Female	202 (46.3)	[0.86-1.18]		
Age*	≥ 60 years	214 (56.6)	1.10	0.18	
	<60 years	136 (51.3)	[0.95-1.28]		
Comorbidities					
Diabetes mellitus*	Yes	95 (52.2)	0.95	0.51	
	No	254 (55.1)	[0.81-1.14]		
Hypertension*	Yes	114 (58.8)	1.12	0.13	
	No	235 (52.3)	[0.97-1.30]		
Chronic respiratory disease*	Yes	41 (59.4)	1.11	0.36	
	No	308 (53.7)	[0.90-1.37]		
Chronic heart disease*	Yes	29 (58.0)	1.07	0.58	
	No	320 (54.0)	[0.84-1.38]		
Antibiotic consumption					
Antibiotic intake	Yes	209 (58.4)	1.18	0.02	1.31 [1.04-1.66]
	No	142 (49.3)	[1.02-1.37]		

Beta-lactamine	Yes	158 (59.8)	1.18	0.02
	No	193 (50.5)	[1.03-1.36]	
Macrolide	Yes	47 (54.7)	1.01	0.95
	No	304 (54.3)	[0.82-1.24]	

RR: risk ratio, aRR: adjusted relative risk

**: data of 3 subjects missing*

Table 4: Review of literature on antibiotic consumption during the Hajj

Pilgrim age year	Study design	Number of pilgrims	Prevalence of respiratory symptoms	Prevalence of antibiotic intake	Reference
2013	Cross-sectional study conducted among Australian Hajj pilgrims in Mina and Mecca, Saudi Arabia	1162	Not documented	34.9%. The reason for antibiotic use was: RTIs in 83.9% cases	14
1999	Prospective cohort study conducted among Pakistani Hajj pilgrims enrolled in Pakistan before the Hajj based on identification numbers attributed by the Pakistani government	2070	ILI (sore throat and cough or temperature $\geq 38^{\circ}\text{C}$) 47.9% URTI (cough or sore throat or rhinitis or myalgia or headache) 72.2% Hospitalization 0.3%	26.6%	19
2008	Prospective cohort study conducted among Irish Hajj pilgrims recruited at a travel clinic.	167	Sore throat or cough or ILI 79% per-Hajj and 15% post-Hajj Hospitalization 1.2% with 1 case of pneumonia and 1 case of tonsillitis.	31%	20

2013	Cross-sectional study conducted among Malaysian Hajj pilgrims on returning to Malaysia	246	RTIs 93.4%, ILI (cough and fever and sore throat) 78.2% hospitalization 1.9%	57.7% population studied (61.8% symptomatic pilgrims)	21
2001	Prospective cohort study conducted among American Hajj pilgrims enrolled at JFK International Airport, New York on departing to Jeddah, Saudi Arabia.	844	Sore throat 53%, fever 21.2% and cough 59.2%	44.8%	22
2001	Prospective cohort study conducted among Singaporean Hajj pilgrims recruited at a vaccination center in Singapore	171	Cough 56%, sore throat 44%	41%	23, 24
2001	Prospective cohort study conducted among Singaporean Umrah pilgrims recruited at a vaccination center in Singapore	160	Cough 13%, sore throat 8%	7%	24
2002	Prospective cohort study conducted among Singaporean Hajj pilgrims recruited at a vaccination center in Singapore	193	Cough 70%	52.9%	25
2002	Prospective cohort study conducted among English Hajj pilgrims recruited at a London	174	Not documented	21% among pilgrims with RTIs.	26

	Mosque				
2003	Prospective cohort study conducted among Iranian Hajj pilgrims recruited at health centers before travel to Mecca.	797		58.2% (because of RTIs)	27
2012	Cross-sectional study conducted among returning Iranian Hajj pilgrims	422	Not documented	58.5%	28
2013	Cross-sectional survey conducted among Hajj pilgrims from 13 countries at Jeddah airport	468	ILI 62%	45.5%	29
2014	Prospective cohort survey conducted among Australian Hajj pilgrims recruited on returning to Australia	93	Not documented	17.2%	30
2016	Prospective multisite cohort study conducted among Indian pilgrims recruited from 4 cities in India	807	76% pilgrims had at least one respiratory symptom	29.4%	31

ILI: influenza like illness, URTI: upper respiratory tract infection, RTI: respiratory tract infection