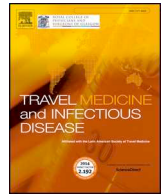




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Clinical respiratory infections and pneumonia during the Hajj pilgrimage: A systematic review

Samir Benkouiten^a, Jaffar A. Al-Tawfiq^{b,c}, Ziad A. Memish^{d,e}, Ali Albarrak^f, Philippe Gautret^{a,*}

^a Aix Marseille Univ, Institut de Recherche pour le Développement (IRD), Assistance Publique-Hôpitaux de Marseille (AP-HM), Service de Santé des Armées (SSA), Microbes Vecteurs Infections Tropicales et Méditerranéennes (VITROME), Institut Hospitalo-Universitaire-Méditerranée Infection (IHU-Méditerranée Infection), Marseille, France

^b Johns Hopkins Aramco Healthcare, Dhahran, Saudi Arabia

^c Indiana University School of Medicine, Indianapolis, IN, USA

^d Ministry of Health, Riyadh, Saudi Arabia

^e College of Medicine, Al Faisal University, Riyadh, Saudi Arabia

^f Department of Internal Medicine, Prince Sultan Military Medical City, Riyadh, Saudi Arabia

ARTICLE INFO

Keywords:

Hajj
Pneumonia
Pneumococcal
Respiratory tract infections
Syndromic surveillance

ABSTRACT

Background: The Islamic Hajj pilgrimage to Mecca is one of the world's largest annual mass gatherings. Inevitable overcrowding during the pilgrims' stay greatly increases the risk of acquiring and spreading infectious diseases, especially respiratory diseases.

Method: The MEDLINE/PubMed and Scopus databases were searched for all relevant papers published prior to February 2018 that evaluated the prevalence of clinical symptoms of respiratory infections, including pneumonia, among Hajj pilgrims, as well as their influenza and pneumococcal vaccination status.

Results: A total of 61 papers were included in the review. Both cohort- and hospital-based studies provide complementary data, and both are therefore necessary to provide a complete picture of the total burden of respiratory diseases during the Hajj. Respiratory symptoms have been common among Hajj pilgrims over the last 15 years. In cohorts of pilgrims, cough ranged from 1.9% to 91.5%. However, the prevalence rates of the most common symptoms (cough, sore throat, and subjective fever) of influenza-like illness (ILI) varied widely across the included studies. These studies have shown variable results, with overall rates of ILI ranging from 8% to 78.2%. These differences might result from differences in study design, study period, and rates of vaccination against seasonal influenza that ranged from 1.1% to 100% among study participants. Moreover, the definition of ILI was inconsistent across studies. In hospitalized Hajj pilgrims, the prevalence of pneumonia, that remains a major concern in critically ill patients, ranged from 0.2% to 54.8%.

Conclusions: Large multinational follow-up studies are recommended for clinic-based syndromic surveillance, in conjunction with microbiological surveillance. Matched cohorts ensure better comparability across studies. However, study design and data collection procedures should be standardized to facilitate reporting and to achieve comparability between studies. Furthermore, the definition of ILI, and of most common symptoms used to define respiratory infections (e.g., upper respiratory tract infection), need to be precisely defined and consistently used. Future studies need to address potential effect of influenza and pneumococcal vaccine in the context of the Hajj pilgrimage.

1. Introduction

The yearly “Hajj” (also known as the pilgrimage to Mecca) in the Kingdom of Saudi Arabia (KSA) is the “Fifth Pillar of Islam” and is mandatory once in a lifetime for all adult Muslim who are physically and financially able. The Hajj is one of the world's largest annual mass gatherings. In 2016, around 1.3 million foreign visitors, from more than

180 countries, gathered in the KSA to complete the Hajj, in addition to over 500,000 domestic Hajj pilgrims [1]. Also, about 5–6 million pilgrims perform the “Umrah” (also known as the lesser pilgrimage) each year.

The Hajj and its rituals are physically demanding for Hajj pilgrims, the majority of whom are elderly [2], with chronic conditions. Although the Hajj rituals only take one week, pilgrims usually stay in the

* Corresponding author. Institut Hospitalo-Universitaire Méditerranée Infection, 19-21 Boulevard Jean Moulin, 13385, Marseille Cedex 05, France.
E-mail address: philippe.gautret@ap-hm.fr (P. Gautret).

<https://doi.org/10.1016/j.tmaid.2018.12.002>

Received 16 August 2018; Received in revised form 1 December 2018; Accepted 3 December 2018

Available online 04 December 2018

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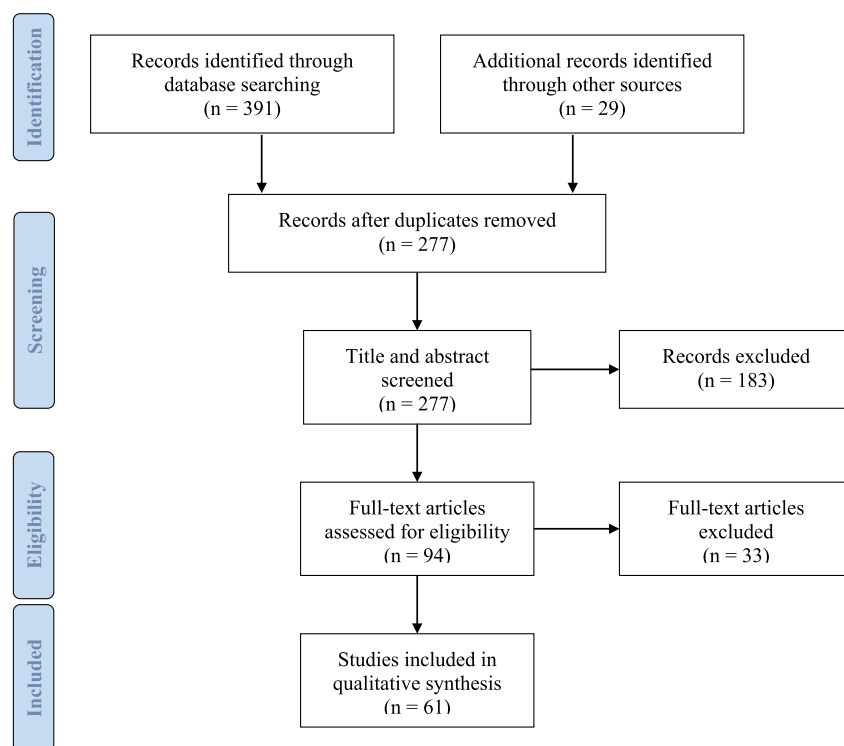


Fig. 1. Flow diagram.

KSA for several weeks throughout the month-long Hajj season, presenting a major public health and infection control concern, and a challenge both for the Saudi authorities, as well as for the national authorities of the countries of origin of the pilgrims. In addition to physical exhaustion, sleep deprivation [3], and heat stress [4], inevitable overcrowding, both in housing and ritual sites, especially in Mina encampment (this is approximately a 3-kilometer square area where pilgrims are accommodated in air-conditioned semi-permanent tents, some with up to 50–100 people) and inside the Sacred Mosque in Mecca (with up to six pilgrims per square meter) [5], greatly increases the risk of acquiring and spreading infectious diseases [6–8], especially respiratory diseases [9,10]. To minimize the spread of infections during the pilgrimage or in the pilgrims' home countries upon their return, vaccination and non-pharmaceutical interventions are thus recommended by national and international public health agencies [11,12].

We carried out a systematic review of cohort and hospital studies that reported the prevalence of clinical symptoms of respiratory infections and pneumonia among pilgrims during the Hajj, and both their influenza and pneumococcal vaccination status, with the aim to provide data allowing the investigation of the impact of this large mass-gathering event on public health policies and services and to identify potential targets for preventive measures.

2. Search strategy and selection criteria

This review was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (<http://www.prismastatement.org>).

The MEDLINE/PubMed and Scopus databases were searched for all relevant papers published prior to February 2018, using the terms:

- #1: Hajj OR hadj OR pilgrim OR pilgrims OR pilgrimage
- #2: Respiratory
- #3: Infection OR infections
- #4: ILI OR URTI OR URTIs OR URI OR URIs OR LRTI OR LRTIs OR

LRI OR LRIs

#5: Pneumonia OR *Streptococcus pneumoniae* OR pneumococcus OR pneumococcal

#6: #1 AND ((#2 AND #3) OR (#4) OR (#5))

In addition, the Saudi epidemiology bulletin (<http://seb.drupalgardens.com/>) was hand searched for additional papers for inclusion. Finally, the reference lists of reviewed articles were searched for additional relevant papers.

For inclusion, the article had to meet the following criteria: (1) Original study involving Hajj pilgrims; (2) detailed description of the study population, including influenza and pneumococcal vaccination status when available; (3) clinical or self-reported respiratory symptoms and diseases. Only articles published in English were included for review. We excluded cohort studies with less than 50 participants and case reports. We also excluded studies conducted among selected groups of individuals suffering from respiratory tract infections, due to lacking denominator data.

The two authors independently performed the searches, screened titles/abstracts for eligibility, selected papers that appeared to be relevant according to the review's inclusion criteria, and reviewed each of the selected manuscripts in full. The data were extracted from the included papers by one reviewer (SB) and collected in the summary table that was included in the review. The extracted data were checked by the two authors (SB and PG) for accuracy. Minor discrepancies were resolved by the authors' discussion.

3. Results

3.1. Included studies

The search strategy initially yielded 391 records, of which 143 were duplicates. Twenty-nine additional papers were identified through manual searches. Of the 277 papers identified 183 records were excluded after screening the title and abstract. Of the 94 full text articles reviewed, 61 were deemed suitable for inclusion in this review

Table 1
Studies conducted among cohorts of Hajj pilgrims.

Hajj season	Study population	Study design	Global prevalence of respiratory symptoms (%)	Vaccination coverage (%)	Study	Ref.
2013–2015	847 Chinese pilgrims	Longitudinal survey conducted in returning Hajj pilgrims arriving at Xinjiang and Gansu airports, China	Fever: 1.9% Sore throat or cough: 1.9%	Influenza: 100%	Ma et al., 2017 (BMC Infectious Diseases)	[50]
2014	148 Iranian pilgrims	Follow-up seroepidemiological study among Hajj pilgrims returning to Yazd province, Iran	Cough: 63%	Not specified	Rahimian et al., 2017 (Respiratory Medicine)	[24]
2012–2015	3364 Egyptian pilgrims	A cross-sectional survey among Hajj pilgrims at Cairo Airport, Egypt. Study based on face-to-face interview	ILI ^a : 30.4%	Influenza: 19.7%	Refaei et al., 2017 (Influenza Other Respi. Viruses)	[45]
2013	468 Malaysian pilgrims	Cross-sectional survey conducted in pilgrims recruited at a Hajj course at Universiti Sains Malaysia (USM), Kelantan, Malaysia, at Hajj Building Complex, Malaysia and in Mecca, Saudi Arabia. Study based on post-Hajj self-questionnaires collected on return	ILI ^b : 78.2%	Influenza: 37.4% Pneumococcal: 31.6%	Hashim et al., 2016 (J Travel Med)	[25]
2013	839 African pilgrims	Cross-sectional survey conducted in returning pilgrims recruited at the “Hajj village” special area at Kotoka International Airport, Ghana. Study based on face-to-face interview	Cough: 70.7% Sore throat: 40.9% Elevated temperature: 18.4% Runny nose or sneezing: 18.13% Breathing difficulty: 14.8% ILI ^c : 66.3%	Not specified	Amnan et al., 2015 (Trop Med Int Health)	[17]
2014	270 Indian pilgrims	Cross-sectional survey conducted in pilgrims recruited at departure from Kempegowda International Airport, Bangalore, India. Study based on telephone interview on return	ILI ^d : 46.2% Cough: 80.9% Sore throat: 91.0% Rhinitis: 78.7% Hoarseness: 63.0% Myalgia: 48.3% Subjective fever: 47.3% Cough (average of the 6 weeks of stay): 39.5% Runny nose (average of the 6 weeks of stay): 25.5% Sore throat (average of the 6 weeks of stay): 18.5% Fever (average of the 6 weeks of stay): 7.1% ILI: 61.9%	Influenza: 1.1%	Fatema et al., 2015 (JPMN)	[26]
2012–2014	382 French pilgrims	Longitudinal survey conducted in pilgrims recruited at a specialized Hajj travel agency, Marseille, France. Study based on medical evaluation during travel		Not specified	Gautret et al., 2015 (Travel Med Infect Dis)	[16]
2007	106 Malaysian pilgrims	Longitudinal survey conducted in pilgrims enrolled in the National Pilgrim Management and Fund Board, Malaysia. Study based on follow-up during travel		Influenza: 61.3%	Hasan et al., 2015 (J Immigr Minor Health)	[51]
2013	1676 pilgrims (Paired cohort: 692 pilgrims/Nonpaired cohort: 514 pilgrims at arrival and 470 pilgrims at Mina) from 13 countries (Africa/Asia/USA/Europe)	Cross-sectional survey (unpaired cohort) and longitudinal survey (paired cohort) conducted in pilgrims recruited on arrival at Jeddah airport. Study based on post-Hajj face-to-face interview conducted at Mina		Influenza: 21.9% Pneumococcal: 1.2%	Memish et al., 2015 (Clin Microbiol Infect)	[28]
2011 and 2012	3203 pilgrims (1590 pilgrims at the beginning of the Hajj and 1613 pilgrims at the end of the Hajj) from 18 countries in Africa or Asia	Cross-sectional survey conducted in pilgrims recruited at Mecca for the beginning-Hajj cohort and Mina for the end-Hajj cohort. Study based on face-to-face interview	URTI during Hajj (for the end-Hajj cohort): 29.2%	Influenza or pneumococcal ^d (beginning-Hajj cohort versus end-Hajj cohort): 45.8% versus 76.7%, respectively	Memish et al., 2015 (Clin Microbiol Infect)	[27]

(continued on next page)

Table 1 (continued)

Hajj season	Study population	Study design	Global prevalence of respiratory symptoms (%)	Vaccination coverage (%)	Study	Ref.
2011	164 Australian pilgrims	Cross-sectional survey conducted in pilgrims recruited at Mina encampment. Study based on post-Hajj face-to-face interview	ILI ^a : 63.4% Cough: 46.3% Sore throat: 34.7% Fever: 23.8% Runny nose: 23.8% Sputum: 12.8% Muscle pain: 9.7% Headache: 8.5% Shortness of breath: 2.4% ILI ^b : 11% Sore throat: 59% Cough: 40% Runny nose: 34% ILI ^c : 47.3% Cough: 86.8% Sore throat: 82.9% Rhinorrhea: 72.1% Myalgia: 50.4% Fever: 49.6% Dyspnea: 21.7% ILI ^d : 47.3% Cough: 83.4% Sore throat: 79.7% Rhinorrhea: 68.5% Myalgia: 46.5% Feverishness: 45.4% Dyspnea: 19.6% Runny nose: 51.7% Dry coughs: 51.7% Hoarseness: 47.7% Yellowish-greenish sputum: 42.8% Nose congestion: 38.8% Purulent Post-Nasal Discharge: 35.5% Sore Throat: 34.2% Painful swallowing: 23.8% Throat itch: 28.6% Fever: 26.8% Myalgia: 24.6% Feeling chills: 17.8% Common cold like illness (total): 47.1% ILI ^e (total): 10.7%	Not specified	Barasheed et al., 2014 (Infect Disord Drug Targets)	[20]
2013	1038 pilgrims from Saudi Arabia, Australia and Qatar	Cross-sectional survey conducted in pilgrims recruited at Mina encampment. Study based on post-Hajj face-to-face interview	ILI ^a : 11% Sore throat: 59% Cough: 40% Runny nose: 34% ILI ^b : 47.3% Cough: 86.8% Sore throat: 82.9% Rhinorrhea: 72.1% Myalgia: 50.4% Fever: 49.6% Dyspnea: 21.7% ILI ^c : 47.3% Cough: 83.4% Sore throat: 79.7% Rhinorrhea: 68.5% Myalgia: 46.5% Feverishness: 45.4% Dyspnea: 19.6% Runny nose: 51.7% Dry coughs: 51.7% Hoarseness: 47.7% Yellowish-greenish sputum: 42.8% Nose congestion: 38.8% Purulent Post-Nasal Discharge: 35.5% Sore Throat: 34.2% Painful swallowing: 23.8% Throat itch: 28.6% Fever: 26.8% Myalgia: 24.6% Feeling chills: 17.8% Common cold like illness (total): 47.1% ILI ^e (total): 10.7%	Influenza (Australian versus Qatari versus Saudi pilgrims): 87% versus 80% versus 20%, respectively	Barasheed et al., 2014 (Virol Sin)	[29]
2013	129 French pilgrims	Longitudinal survey conducted in pilgrims recruited at a specialized Hajj travel agency, Marseille, France. Study based on medical evaluation during travel	ILI ^a : 11% Sore throat: 59% Cough: 40% Runny nose: 34% ILI ^b : 47.3% Cough: 86.8% Sore throat: 82.9% Rhinorrhea: 72.1% Myalgia: 50.4% Fever: 49.6% Dyspnea: 21.7% ILI ^c : 47.3% Cough: 83.4% Sore throat: 79.7% Rhinorrhea: 68.5% Myalgia: 46.5% Feverishness: 45.4% Dyspnea: 19.6% Runny nose: 51.7% Dry coughs: 51.7% Hoarseness: 47.7% Yellowish-greenish sputum: 42.8% Nose congestion: 38.8% Purulent Post-Nasal Discharge: 35.5% Sore Throat: 34.2% Painful swallowing: 23.8% Throat itch: 28.6% Fever: 26.8% Myalgia: 24.6% Feeling chills: 17.8% Common cold like illness (total): 47.1% ILI ^e (total): 10.7%	Influenza: None in 2013 and 44.2% in 2012 Pneumococcal: 51.2%	Benkouten et al., 2014 (Emerg Infect Dis) Gautret et al., 2014 (Emerg Infect Dis)	[18,21]
2012	169 French pilgrims	Longitudinal survey conducted in pilgrims recruited at a specialized Hajj travel agency, Marseille, France. Study based on medical evaluation during travel	ILI ^a : 11% Sore throat: 59% Cough: 40% Runny nose: 34% ILI ^b : 47.3% Cough: 86.8% Sore throat: 82.9% Rhinorrhea: 72.1% Myalgia: 50.4% Fever: 49.6% Dyspnea: 21.7% ILI ^c : 47.3% Cough: 83.4% Sore throat: 79.7% Rhinorrhea: 68.5% Myalgia: 46.5% Feverishness: 45.4% Dyspnea: 19.6% Runny nose: 51.7% Dry coughs: 51.7% Hoarseness: 47.7% Yellowish-greenish sputum: 42.8% Nose congestion: 38.8% Purulent Post-Nasal Discharge: 35.5% Sore Throat: 34.2% Painful swallowing: 23.8% Throat itch: 28.6% Fever: 26.8% Myalgia: 24.6% Feeling chills: 17.8% Common cold like illness (total): 47.1% ILI ^e (total): 10.7%	Influenza: 45.6%	Benkouten et al., 2014 (Clin Infect Dis) Benkouten et al., 2013 (Clin Infect Dis) Gautret et al., 2013 (Clin Microbiol Infect)	[19,22,23]
2006	295 Iranian pilgrims	Longitudinal survey conducted in pilgrims recruited at a Hajj caravan. Study based on medical evaluation during travel	ILI ^a : 11% Sore throat: 59% Cough: 40% Runny nose: 34% ILI ^b : 47.3% Cough: 86.8% Sore throat: 82.9% Rhinorrhea: 72.1% Myalgia: 50.4% Fever: 49.6% Dyspnea: 21.7% ILI ^c : 47.3% Cough: 83.4% Sore throat: 79.7% Rhinorrhea: 68.5% Myalgia: 46.5% Feverishness: 45.4% Dyspnea: 19.6% Runny nose: 51.7% Dry coughs: 51.7% Hoarseness: 47.7% Yellowish-greenish sputum: 42.8% Nose congestion: 38.8% Purulent Post-Nasal Discharge: 35.5% Sore Throat: 34.2% Painful swallowing: 23.8% Throat itch: 28.6% Fever: 26.8% Myalgia: 24.6% Feeling chills: 17.8% Common cold like illness (total): 47.1% ILI ^e (total): 10.7%	Influenza and pneumococcal: 63.7% Influenza or pneumococcal: 26.4%	Dabiran et al., 2014 (Health)	[55]
2004–2008	254823 Iranian pilgrims (30037 pilgrims in 2004, 75676 in 2005, 48678 in 2006, 71595 in 2007, and 28837 in 2008)	Longitudinal survey conducted in pilgrims recruited at 1352 Hajj caravans. Study based on medical evaluation during travel	ILI ^a : 11% Sore throat: 59% Cough: 40% Runny nose: 34% ILI ^b : 47.3% Cough: 86.8% Sore throat: 82.9% Rhinorrhea: 72.1% Myalgia: 50.4% Fever: 49.6% Dyspnea: 21.7% ILI ^c : 47.3% Cough: 83.4% Sore throat: 79.7% Rhinorrhea: 68.5% Myalgia: 46.5% Feverishness: 45.4% Dyspnea: 19.6% Runny nose: 51.7% Dry coughs: 51.7% Hoarseness: 47.7% Yellowish-greenish sputum: 42.8% Nose congestion: 38.8% Purulent Post-Nasal Discharge: 35.5% Sore Throat: 34.2% Painful swallowing: 23.8% Throat itch: 28.6% Fever: 26.8% Myalgia: 24.6% Feeling chills: 17.8% Common cold like illness (total): 47.1% ILI ^e (total): 10.7%	Influenza (2004 versus 2005): 75.2% versus 88.3%, respectively Pneumococcal (2004 versus 2005): 2.5% versus 8.9%, respectively	Razavi et al., 2014 (Med J Islam Repub Iran) Razavi et al., 2013 (Med J Islam Repub Iran) Meysamie et al., 2006 (Saudi Med J)	[46–48]
2010	1507 pilgrims	Longitudinal survey conducted in pilgrims recruited at primary health care centers in Riyadh, Saudi Arabia (for the mandatory pre-Hajj meningococcal vaccination). Study based on telephone interview on return	ILI ^a : 11% Sore throat: 59% Cough: 40% Runny nose: 34% ILI ^b : 47.3% Cough: 86.8% Sore throat: 82.9% Rhinorrhea: 72.1% Myalgia: 50.4% Fever: 49.6% Dyspnea: 21.7% ILI ^c : 47.3% Cough: 83.4% Sore throat: 79.7% Rhinorrhea: 68.5% Myalgia: 46.5% Feverishness: 45.4% Dyspnea: 19.6% Runny nose: 51.7% Dry coughs: 51.7% Hoarseness: 47.7% Yellowish-greenish sputum: 42.8% Nose congestion: 38.8% Purulent Post-Nasal Discharge: 35.5% Sore Throat: 34.2% Painful swallowing: 23.8% Throat itch: 28.6% Fever: 26.8% Myalgia: 24.6% Feeling chills: 17.8% Common cold like illness (total): 47.1% ILI ^e (total): 10.7%	Influenza: 94.4%	Al-Jasser et al., 2013 (East Mediterr Health J) Al-Jasser et al., 2012 (Saudi Med J) Al-Jasser et al., 2011 (Saudi Epidemiology Bulletin)	[32,33,36]

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Table 1 (continued)

Hajj season	Study population	Study design	Global prevalence of respiratory symptoms (%)	Vaccination coverage (%)	Study	Ref.
2009	274 French pilgrims	Longitudinal survey conducted in pilgrims recruited at a travel medicine clinic of a university hospital, France (for the mandatory pre-Hajj meningococcal vaccination). Study based on telephone interview on return	ILI ^a : 8.0% Cough: 48.5% Sore throat: 36.1% Rhinorrhoea: 23.7% Sputum: 13.5% Subjective fever: 10.9% Myalgia: 9.5% Shortness of breath: 2.9% Voice failure: 2.9%	Influenza: 97.4% Influenza A(H1N1): 5.8% Pneumococcal: 31.4%	Gautret et al., 2013 (Travel Med Infect Dis) Gautret et al., 2011 (J Travel Med)	[31,37]
2006	338 Iranian Pilgrims	Longitudinal survey conducted in pilgrims recruited at a Hajj and pilgrimage organization at Chaharmahal va Bakhtiari Province, Iran. Study based on post-Hajj face-to-face interview	Cough: 70.0% Hoarseness: 53.6% Sore throat: 49.7% Coryza: 43.8% Wheezing: 43.5% Myalgia: 30.8% Dyspnea: 17.8% AFRI ^b : 9%	Not specified	Imani et al., 2013 (International Journal of Travel Medicine & Global Health)	[52]
2012	541 Australian pilgrims	Cross-sectional survey conducted in pilgrims recruited at Mina encampment. Study based on post-Hajj face-to-face interview	Cough: 30.1% Sneezing: 25.8% Sore throat: 15.6% Fever: 13.4% Congestion: 8.6% Breathing problems: 2.1% "Bronchitis" ^{ph} : 1.1% ILI ^a : 9.7% ILI ^b : 37.8%	Not specified	Rashid et al., 2013 (Med J Aust)	[30]
2009	186 US pilgrims	Longitudinal survey conducted in pilgrims recruited at pretravel clinic for Hajj travelers in Minnesota, US, and Arab Community Center for Economic and Social Services at multiple settings, including mosques, community health clinics, and the Detroit Wayne County International Airport, in Michigan, US. Study based on post-Hajj face-to-face and telephone interview	Cough: 30.1% Sneezing: 25.8% Sore throat: 15.6% Fever: 13.4% Congestion: 8.6% Breathing problems: 2.1% "Bronchitis" ^{ph} : 1.1% ILI ^a : 9.7% ILI ^b : 37.8%	Influenza: 63.0% Influenza A(H1N1): 38.7%	Balaban et al., 2012 (J Travel Med)	[34]
2010	1659 Afghan pilgrims	Longitudinal survey conducted in pilgrims recruited at four transit areas located next to the Kandahar, Balkh, Hirat and Kabul airports, Afghanistan. Study based on post-Hajj telephone interview	Fever: 11.1% Cough: 48.2% Sore throat: 46.2% Nasal symptoms: 60.6% Myalgia: 31.8% Cough: 72.2%	Not specified	Saeed et al., 2012 (J Epidemiol Glob Health)	[35]
2009	305 Iranian pilgrims	Cross-sectional survey conducted in returning pilgrims recruited Shiraz Airport, Iran	Fever: 11.1% Cough: 48.2% Sore throat: 46.2% Nasal symptoms: 60.6% Myalgia: 31.8% Cough: 72.2%	Influenza: 97.7%	Ziyaeyan et al., 2012 (Influenza Other Respir Viruses)	[53]
2010	1717 pilgrims	Cross-sectional survey conducted in returning pilgrims recruited at King Abdulaziz International Airport, Jeddah	ILI ^a : 40.1 Cough: 91.5% Runny nose: 79.3% Fever: 59.2%	Influenza: 52.4%	Maslami et al., 2011 (Saudi Epidemiology Bulletin)	[54]
2007	387 Malaysian pilgrims	Cross-sectional survey conducted in returning pilgrims recruited at transit centers at Jeddah and Medina	Cough: 90.1% Runny nose: 78.2% Fever: 58.4%	Influenza: 72.9%	Deris et al., 2010 (J Trop Biomed)	[14,15]
2007	394 Malaysian pilgrims	Cross-sectional survey conducted in returning pilgrims recruited at transit centers at Jeddah and Medina	Sore throat: 57.1% Cough: 90.1% Runny nose: 78.2% Fever: 58.4%	Not specified	Deris et al., 2009 (Saudi Med J)	[73]
2006	580 French pilgrims	Longitudinal survey conducted in pilgrims recruited at a travel medicine clinic of a university hospital, France (for the mandatory pre-Hajj meningococcal vaccination). Study based on telephone interview on return	Sore throat: 56.3% Cough: 60.6% Fever: 16.6%	Influenza: 34.3%	Gautret et al., 2009 (Clin Microbiol Infect)	[49]

(continued on next page)

Table 1 (continued)

Hajj season	Study population	Study design	Global prevalence of respiratory symptoms (%)	Vaccination coverage (%)	Study	Ref.
2004	170 Iranian pilgrims	Longitudinal survey conducted in pilgrims recruited to departure from Iran (details not provided). Study based on medical follow-up at Mina encampment	Common cold ^d : 57.0% ILI ^e : 10.9%	Not specified	Razavi et al., 2007 (JCID)	[38]
2002	1027 domestic pilgrims	Longitudinal survey conducted in pilgrims recruited at primary health care centers in Riyadh, Saudi Arabia (for the mandatory pre-Hajj meningococcal vaccination). Study based on telephone interview on return	ARI ^f : 39.8%	Not specified	Choudhry et al., 2006 (East Mediterr Health J)	[39]
2004	995 pilgrims from Riyadh	Longitudinal survey conducted in pilgrims recruited from randomly selected Hajj groups in Riyadh, Saudi Arabia. Study based on post-Hajj telephone interview	ARI ^g : 25.6%	Not specified	Abdin et al., 2005 (Saudi Epidemiology Bulletin)	[40]
2003–2004	51100 Iranian pilgrims (32370 pilgrims in 2003 and 18730 pilgrims in 2004)	Longitudinal survey conducted in pilgrims recruited at 180 Hajj caravans in 2003/110 caravans in 2004. Study based on medical evaluation during travel	ILI ^h in 2003: 70.1% ILI ^h in 2004: 35.8%	Influenza (2003 versus 2004): 10.7% versus 75.2%, respectively	Razavi et al., 2005 (Acta Medica Iranica) Razavi et al., 2004 (Acta Medica Iranica)	[41,42]
2003	115 UK pilgrims	Longitudinal survey conducted in pilgrims recruited at East London Mosque, London, UK. Study based on medical evaluation after travel	Respiratory symptoms: 80.9%	Influenza: 26.1%	El Bashir et al., 2004 (Emerg Infect Dis)	[56]
2003	1027 pilgrims from Riyadh	Longitudinal survey conducted in pilgrims recruited at 10 randomly selected primary health care centers in Riyadh, Saudi Arabia (for the mandatory pre-Hajj meningococcal vaccination). Study based on telephone interview on return	ARI ⁱ : 39.8%	Influenza: 10.5%	Al-Mudameigh et al., 2003 (Saudi Epidemiology Bulletin)	[43]
1999	412 domestic and international pilgrims	Cross-sectional survey conducted in pilgrims recruited at Mina. Study based on post-Hajj self-administered questionnaires	Rummy nose: 18.0% Cough: 14.0% Sore-throat: 12.0% ILI ^j : 47.9% Documented fever $\geq 38.8^\circ\text{C}$: 29.8% URTI ^k : 72.2%	Not specified	Fatani et al., 2001 (Saudi Epidemiology Bulletin)	[13]
1999	2070 Pakistani pilgrims	Longitudinal survey conducted in pilgrims recruited in organized groups in Pakistan. Study based on medical evaluation during travel		Influenza: 54%	Qureshi et al., 2000 (Vaccine)	[44]

^a ILI was defined according to the presence measured fever of $\geq 38^\circ\text{C}$, and cough; with onset within the last 10 days.

^b Influenza-like illness (ILI) was defined according to the presence of the triad of cough, subjective fever and sore throat.

^c ILI was defined as subjective (or proven) fever plus one respiratory symptom (e.g. dry or productive cough, runny nose, sore throat, shortness of breath).

^d ILI was defined as subjective (or proven) fever and at least one respiratory symptom such as cough, sore throat and rhinorrhea.

^e ILI was defined as symptoms and signs such as: sudden headache, dry cough, high grade fever, myalgia, coryza, malaise and loss of appetite with an abnormal general appearance.

^f Upper respiratory tract infections (URTI) was defined as any person who reported having developed at least one of the constitutional symptoms (fever, headache, myalgia) and one of the local symptoms (running nose, sneezing, throat pain, cough with/without sputum) after reaching Mecca for the Hajj or within 2 weeks from return to Riyadh.

^g Acute febrile respiratory infection (AFRI) was defined as the presence of subjective fever plus at least one respiratory symptom (cough, sore throat, runny nose or breathlessness).

^h Two travelers who reported “bronchitis” as a symptom were also included.

ⁱ ILI was defined as fever plus sore throat and/or coughing.

^j Common cold was defined as sore throat with coryzal symptoms, and low grade fever.

^k ILI was defined as fever $> 38.5^\circ\text{C}$, myalgia, low back pain, coryzal symptoms and cough.

^l Acute respiratory infection (ARI) was defined as one of the constitutional symptoms (fever, headache, myalgia) along with one of the local symptoms (running nose, sneezing, throat pain, cough with/without sputum, difficulty breathing).

^m ARI was defined as any person suffering from at least one of the constitutional symptoms (fever, headache, myalgia) along with one of the local symptoms (runny nose, sneezing, throat pain, cough with/without sputum, difficulty in breathing) developing after reaching Makkah for the Hajj.

ⁿ ILI was defined as cough and fever $> 38^\circ\text{C}$ with or without the coryzal symptoms and myalgia.

^o ARI was defined as any person suffering from at least one of the constitutional symptoms (fever, headache, myalgia) along with one of the local symptoms (runny nose, sneezing, throat pain, cough with/without sputum, difficulty in breathing) developing after reaching Mecca for the Hajj.

^p ILI was defined as sore throat with either temperature $\geq 38.8^\circ\text{C}$ or cough.

^q Cough or sore throat or rhinorrhea or muscle ache or headache.

according to the inclusion/exclusion criteria. The results of the search strategy are shown in Fig. 1.

3.2. Cohort studies addressing the prevalence of respiratory tract infections among Hajj pilgrims

A total of 45 publications were identified. These studies were conducted among cohorts of pilgrims from the 1999 through the 2015 Hajj seasons. The results of these studies are presented in Table 1. Various study designs were used, including cross-sectional studies, case-control studies, and prospective cohort studies with follow-up of pilgrims, before, during and after the Hajj. Participants were from different countries and continents (Africa, North America, Asia, Europe, as well as from Australia), with the majority from Iran, and they were recruited from different settings, including travel medicine clinics, vaccination centers, Hajj travel agencies, international airports and transit zones, Mecca's city and Mina encampments. Their numbers varied widely in these studies, ranging from 106 to 107,074.

Respiratory symptoms were common during the Hajj. Overall, the prevalence of cough ranged from 1.9% in domestic and international pilgrims in 1999 [13] to 91.5% in Malaysian pilgrims in 2007 [14,15] (Table 3). More recent studies, conducted in different populations of pilgrims during the 2011–2014 Hajj seasons, reported prevalence of cough ranging from 46.3% to 86.8% [16–24]. These studies also reported a comparable prevalence of sore throat ranging from 34.7% to 91% among pilgrims [16–23].

In addition, many of these studies have investigated the epidemiology of respiratory tract infections among pilgrims by estimating the common prevalence of upper respiratory tract infection (URTI), acute respiratory infection (ARI) or influenza-like illness (ILI), which were inconsistently defined across studies by a combination of general symptoms (e.g. cough, sore throat and fever). Overall prevalence of ILI varied in these studies from 8% to 78.2% [14–16,18–23,25–45] (Table 3). In large studies conducted among Iranian pilgrims between 2003 and 2005, the prevalence of ILI was, respectively, 70.1% and 35.8% in 2003 and 2004 [41,42], but 19.6% in 2005 [46]. In another large 5-year (2004–2008) follow-up study conducted among 254823 Iranian pilgrims, only 10.7% of pilgrims complained of ILI during the Hajj [47,48]. However, the ILI syndromic case definition used in the 2003–2004 study (ILI was defined as cough and fever of more than 38 °C with or without the coryzal symptoms and myalgia) [41,42] was different with that used in the 2004–2008 study (ILI was defined as symptoms and signs such as sudden headache, dry cough, high grade fever, myalgia, coryza, malaise and loss of appetite with an abnormal general appearance) [47,48]. Also, it is unclear from the 2005 study [46] if the definition used was consistent with those used in the two previous studies [41,42,47,48]. In a recent large study, conducted among 3364 Egyptian pilgrims between 2012 and 2015, the prevalence of ILI was 30.4% (ILI was defined according to the World Health Organization definition as the presence of measured fever of ≥ 38 °C, and cough; with onset within the last 10 days) [45]. Other studies of different sizes (from 129 to 468) and design were conducted from 2007 through 2014 among different populations of pilgrims using a common ILI definition (the association of cough, sore throat, and subjective fever). These studies have shown variable results, with overall rates of ILI ranging from 8% to 78.2% [14–16,18,19,21–23,25,26,31,35,37]. Thus, during the 2013 Hajj season, while the highest prevalence of ILI was observed among Malaysian pilgrims, with a prevalence estimated at 78.2% [25], a lower prevalence was observed among French pilgrims (47.3%) [18,21].

Coverage of seasonal influenza vaccination among pilgrims was evaluated in many studies, which have yielded varying results, with reported rates of influenza vaccination ranged from 1.1% to 100% [14,15,18,21–23,25,26,28,29,31–34,36,37,41–51,53–56]. A variation over time in influenza vaccination coverage was observed, as

exemplified by a rate of 10.5% observed in a survey of pilgrims from Riyadh in 2003 [43], but 94.4% in a similar survey in 2010 [32,33,36]. During the 2013 Hajj season, influenza vaccination rates also varied according to pilgrims' country of origin [29], with 20% observed among Saudi pilgrims, 80% among Qatari pilgrims, and 87% among Australian pilgrims, while a study involving French pilgrims interestingly reported that none of them had received the 2013 influenza vaccine before departing for the Hajj because the vaccine was not available at this time [18,21]. The majority of the studies reported influenza vaccination coverage among pilgrims, but only 13 [18,19,21–23,25,27,28,31,46–48,55] reported their pneumococcal vaccination status, with rates ranging from 1.2% among a multinational cohort of 1676 pilgrims from 13 countries (from Africa, Asia, USA and Europe) in 2013 [28] to 51.2% among a small study of 129 French pilgrims in 2013 [18,21].

3.3. Hospital-based studies addressing the prevalence of respiratory tract infections among ill Hajj pilgrims

Of the 61 publications that were included in this review, 16 specifically addressed ill Hajj pilgrims at health care facilities from 1993 through 2014 Hajj seasons. Medical facilities included primary health care centers (PHCCs) and different specialized wards in tertiary care hospitals, including ear, nose and throat (ENT) departments, intensive care units, emergency units, infectious disease units and unspecified medical units. Pilgrim participants were included either as inpatients or outpatients. The results of these studies are summarized in Table 2.

Overall, the prevalence of upper respiratory tract infections (URTI) ranged from 1.4% to 42.1% (Table 3). This prevalence was 1.4% among 141 Pakistani pilgrims who attended the King Abdul Aziz hospital in Medina during the 1992 Hajj [57] and 42.1% among 3087 Saudi and non-Saudi patients (47.5% of them were pilgrims) who attended the ENT clinic at Al-Noor Specialist Hospital in Mecca during the 2009 Hajj [58]. Pharyngitis was also frequently reported among ill pilgrims. Thus, in this study of 3087 pilgrims during the 2009 Hajj, the overall prevalence of pharyngitis was 45.7% [58]. More recently, in 2008, the prevalence of pharyngitis in a large cohort of 4136 outpatients patients from 82 nationalities who attended 13 randomly selected Mina PHCCs (94.9% of whom were pilgrims) was found to be 23.7% [59,60], and 61% in a study of 1047 Saudi and non-Saudi patients (2.3% of them were inpatients) [61]. However, in this second study of 1047 patients, only 34.5% were pilgrims. On the contrary, lower prevalence rates of bronchitis were reported during the Hajj (1.4%–9.6%) [59–63]. A recent retrospective cross-sectional multicenter study of 185 Turkish inpatients (87.5% were pilgrims) who returned to Turkey from the Arabian Peninsula countries between 2012 and 2014 reported a slightly higher prevalence of acute tracheobronchitis (13.6%) [64]. In addition, in this study, pneumonia was among the most common clinical diagnosis among the hospitalized Hajj patients and represented about half of diagnoses [64]. As pneumonia remains a major concern in critically ill patients, most of them reported the prevalence of pneumonia among pilgrims [57,59,60,62–71], with reported rates ranging from 0.2% in 2008 in 13 randomly selected Mina primary health care centers [59,60] to 54.8% in 2004 in two ICU in Mecca [68] (Table 3). The prevalence of pneumonia was not reported in 3 papers [58,61,72]. Pneumonia was the second most common admitting diagnosis (22%) in a study of 140 patients admitted to the ICUs in four hospitals in Mina during the 2004 Hajj [68]. This result is further confirmed by a recent study of 452 critically ill Hajj patients, of over 40 nationalities, admitted to 15 hospitals in 2009 and 2010. In this study, pneumonia was defined as the primary cause of critical illness (27.2%) of all ICUs admissions during the Hajj [65]. Also, in another prospective study of pilgrims admitted in two major ICUs in Mecca for the 2004 Hajj season, community acquired pneumonia (CAP) was the commonest source of sepsis, 54.8% [66].

Table 2
Studies conducted among ill Hajj pilgrims at health care facilities.

Hajj season	Study population	Recruitment	Proportion of ill patients with respiratory symptoms globally (%)	Proportion of ill patients with pneumonia (%)	Study	Ref.
2012–2014	185 Turkish patients (87.5% were pilgrims) returning to Turkey from the Arabian Peninsula countries	15 referral Turkish centers with infectious diseases departments (inpatients)	URTI ^a : 33.1% Acute tracheobronchitis ^b : 13.6% Acute exacerbation of COPD ^c : 8.9%	50.3%	Erdem et al., 2016 (Eur J Clin Microbiol Infect Dis)	[64]
2008	4136 patients (94.9% were pilgrims) from 82 nationalities	13 randomly selected Mina primary health care centers (outpatients)	Common cold: 20.6% Pharyngitis: 23.7% Bronchitis: 9.6% Tonsillitis: 4.2%	0.2%	Alzahrani et al., 2012 (J Infect Public Health) Alzahrani et al., 2009 (Saudi Epidemiology Bulletin)	[59,60]
2009–2010	452 pilgrims from over 40 nationalities	Intensive care unit of 15 hospitals in Mecca, Mina, Arafat, and Medina (inpatients)	Not specified	27.2%	Mandourah et al., 2012 (BMC Infect Dis)	[65]
2009	3087 Saudi and non-Saudi patients (47.5% were pilgrims)	Ear, nose, and throat clinic at Al-Noor Specialist Hospital, Mecca (mostly outpatients)	Pharyngitis: 45.7% URTI ^d : 42.1%	Not specified	Alherabi et al., 2011 (Saudi Med J)	[58]
2008	1047 Saudi and non-Saudi patients (34.5% were pilgrims)	Ear, nose, and throat clinic at Al-Noor Specialist Hospital, Mecca (mostly outpatients)	Pharyngitis: 61.0% URTI ^d : 18.6% Tonsillitis: 5.5% Otitis media: 2.2%	Not specified	Alherabi et al., 2009 (Saudi Med J)	[61]
2004	165 pilgrims	Two intensive care units (King Faisal Hospital and King Abdul Aziz Hospital) in Mecca (inpatients with sepsis)	Not specified	54.8%	Baharoon et al., 2009 (Travel Med Infect Dis)	[66]
2007	2411 patients	Emergency room of Al-Anssar Hospital and 4 primary health care centers in Medina (in and outpatients)	Not specified	1%	Al-Quwaidhi et al., 2008 (Saudi Epidemiology Bulletin)	[67]
2007	248 pilgrims	Two randomly selected Mina hospitals (Mina al Tawarri & Mina El-Jesser) (outpatients)	Cough: 28.2% Dyspnea: 27.4% Fever: 25.0% Running nose: 16.5% Chest pain: 15.3%	Not specified	Khamis et al., 2008 (J Egypt Public Health Assoc)	[72]
2004	140 patients (97.9% were pilgrims)	Intensive care units in Mina and Arafat hospitals (inpatients)	Respiratory failure: 5.0% Upper airway obstruction: 0.7%	22.1%	Madani et al., 2007 (Ann Saudi Med)	[68]
2005	689 pilgrims from 49 countries	Tertiary care hospital in Mina (inpatient medical departments)	Dyspnea: 38.3% Chest pain: 24.8% Cough: 22.1% Fever: 19.2%	26.0%	Khan et al., 2006 (Saudi Med J)	[69]
2003	575 patients (97.4% were pilgrims)	Seven hospitals in Mina and Arafat (inpatient medical wards)	URTI ^d : 4.7% Acute bronchitis: 1.7%	29.4%	Madani et al., 2006 (Ann Saudi Med)	[62]
2002	160 patients	Two hospitals in Arafat and two hospitals in Mina (in patient medical wards)	URTI ^d : 3.1% Dyspnea: 53.0% Cough: 49.0% Fever: 47.0% Chest pain: 12.5% Sore-throat: 6.8% Common cold: 6.0%	39.4%	Al-Ghamdi et al., 2003 (Saudi Med J)	[70]
1993	7676 pilgrims	Emergency Department of Al-Noor Hospital in Mecca (in and outpatients)	URTI ^d : 4.4% Bronchitis: 3.7% Headache: 1.6% Cough: 1.2%	2.0%	Al-Harbi et al., 2000 (J Family Community Med)	[63]
1993	773 pilgrims	King Abdul Aziz hospital in Medina (inpatient medical wards)	URTI ^d : 7.1%	45.8%	Yousuf et al., 1995 (Ann Saudi Med)	[71]
1992	141 Pakistani pilgrims	King Abdul Aziz hospital in Medina (inpatient medical wards)	URTI ^d : 1.4% Acute bronchitis: 1.4%	29.1%	Yousuf et al., 1993 (PJMR)	[57]

^a Upper respiratory tract infection (URTI) was defined as an acute infection that includes tonsillitis, pharyngitis, laryngitis, sinusitis, otitis media, and the common cold.

^b Acute tracheobronchitis was defined as a patient with dry cough and/or low-grade of fever ($< 38^{\circ}\text{C}$), sub-sternal pain, and fatigue in the absence of opacities on chest X-ray.

^c Acute exacerbation of chronic obstructive pulmonary disease (COPD) was defined as an association with increased frequency and severity of coughing and/or shortness of breath and wheezing, increased amount of sputum production, and/or a change in appearance of sputum in a patient with COPD.

^d Was not defined.

Table 3
Prevalence of cough, influenza-like illness, upper respiratory tract infection and pneumonia reported in the included studies.

Symptoms	Prevalence (%)	Range (%)
Cough (in cohorts of Hajj pilgrims)	1.9	1.9–91.5
	14.0	
	30.1	
	39.5	
	40.0	
	46.3	
	48.2	
	48.5	
	51.7	
	60.6	
	63.0	
	70.0	
	70.7	
	72.2	
	80.9	
	83.4	
	86.8	
Cough (in ill Hajj pilgrims at health care facilities)	1.2	1.2–49
	22.1	
	28.2	
	49.0	
ILI ^a (in cohorts of Hajj pilgrims)	8.0	8.0–78.2
	9.7	
	11.0	
	10.7	
	10.9	
	30.4	
	35.8	
	37.8	
	40.1	
	46.2	
	47.3	
	47.3	
	47.9	
	61.9	
	63.4	
	66.3	
	URTI ^b (in cohorts of Hajj pilgrims)	
53.1		
72.2		
72.2		
URTI ^b (in ill Hajj pilgrims at health care facilities)	1.4	1.4–42.1
	4.4	
	4.7	
	7.1	
	18.6	
	33.1	
	42.1	
	42.1	
Pneumonia (in ill Hajj pilgrims at health care facilities)	0.2	0.2–54.8
	1.0	
	2.0	
	22.1	
	26.0	
	27.2	
	29.1	
	29.4	
	39.4	
	45.8	
	50.3	
54.8		

^a Influenza-like illness.

^b Upper respiratory tract infection.

4. Discussion

The purpose of this review was to provide syndromic surveillance data that may be useful, in conjunction with microbiological data that will be presented in further papers, for the surveillance of respiratory infections and pneumonia during the Hajj. Despite the fact that some of the included studies in our review were performed among small numbers of pilgrims and cannot be extrapolated, it is clear from this work that respiratory symptoms have been common among Hajj pilgrims over the last 15 years, as evidenced by the high prevalence of cough (over 90%) among Malaysian pilgrims during the 2007 Hajj [73]. Cough is a common symptom among pilgrims [16,74] and likely results from crowded conditions during the Hajj. This close contact among such individuals may increase the risk of the transmission of respiratory pathogens, and therefore may contribute to respiratory disease outbreaks. Climatic conditions and air pollution in Mecca and surrounding holy sites during the Hajj [75] may also play a role. Recent follow-up studies thus evidenced a significant acquisition of respiratory viruses, particularly rhinovirus, influenza virus, and coronaviruses other than Middle East Respiratory Syndrome Coronavirus (MERS-CoV), and of bacteria, including *Streptococcus pneumoniae*, *Hemophilus influenzae*, *Staphylococcus aureus* and *Klebsiella pneumoniae* by Hajj pilgrims upon their return from the Hajj [76,77]. Respiratory diseases are the most common diseases observed among pilgrims attending Mina primary health care centers [59] and a major cause of hospital admission during the Hajj [70], with pneumonia a leading cause of admission to intensive care units [62,68], where they are responsible for about half of the cases of sepsis [66]. Unfortunately, while numerous articles on Hajj pilgrims were retrieved from our literature search, relatively few recent articles specifically addressed ill pilgrims in the context of hospital settings. The use of cohort studies allows investigators to evaluate the actual incidence of clinical events in Hajj pilgrims since it provides a denominator, but may not identify and capture the prevalence of some underlying conditions and of severe forms of respiratory tract infections, which are more likely to be evidenced in hospital patient populations. Conversely, hospital studies use data that may be biased, frequently lacking denominator values, and so probably overestimating the occurrence of severe illness. Moreover, a hospital-based study will, by definition, not capture some minor illness cases that do not require hospitalization.

The prevalence rates of cough, sore throat and subjective fever varied widely across the included studies. These differences may result from differences in study design that may lead to potential biases (for example bias related to the method of data collection, using either self-report questionnaires or telephone interview), study period (with regards to the seasonality of respiratory viral infections), and rates of vaccination against seasonal influenza among study participants which may widely vary from one study to another, as described in this review. Thus, all data regarding the pilgrims, including demographic data, medical history, clinical data and information on vaccination status and compliance with non-pharmaceutical preventive measures, should be carefully collected by using standardized questionnaires. In addition, in the context of syndromic surveillance for respiratory pathogens, data regarding the pilgrim's symptoms should be collected prospectively during face-to-face interviews by trained medical investigators who travel with the pilgrims. One important result of this review is the finding of a lack of consistency ILI syndromic case definitions across included studies. Thus, in a 2003 study (that did not fulfill the inclusion criteria for this review) [78], of 1310 Malaysian pilgrims who had a clinic visit for upper respiratory tract symptoms at five clinics during

the 2000 Hajj, with the aim of determining influenza vaccine effectiveness against clinically defined ILI, 63% had ILI (defined as sore throat in combination with either temperature $\geq 38^\circ\text{C}$ or cough) and 14% had influenza by the CDC definition (defined as measured fever [$\geq 100^\circ\text{F}$ (37.8°C)] and a cough and/or a sore throat). Only one of the studies reported here used the CDC definition of ILI or the WHO definition (an acute respiratory infection with measured fever of $\geq 38^\circ\text{C}$ and cough, with onset within the last 10 days) [45]. In his paper, Rashid et al. demonstrated the low sensitivity of the CDC criteria and proposed therefore the use of the triad of 'cough, sore throat and subjective fever' to clinically define ILI at the Hajj or other mass gatherings, since this new simple clinical case definition is more specific and sensitive than the CDC definition [79]. This definition was used over the last years by French [16,18,19,21–23,31,37], Malaysian [14,15,25], Indian [26] and Afghan [35] investigators leading cohort studies among Hajj pilgrims, thus allowing more reliable comparisons of findings between studies (Table 1).

Respiratory diseases are a major concern during the Hajj. Non-pharmaceutical interventions (e.g., hand hygiene, wearing face masks, social distancing) are known to reduce the spread of respiratory viruses from person to person and are therefore recommended to pilgrims by public health agencies. Although hand hygiene compliance is high among pilgrims, face mask use and social distancing remain difficult challenges. Data about the effectiveness of these measures for preventing acute respiratory infections at the Hajj are limited, and results are contradictory, highlighting the need for future large-scale studies [80].

In addition to non-pharmaceutical interventions, vaccination against influenza is recommended for all Hajj pilgrims by the Ministry of Health of Saudi Arabia [11,12]. Differences in study design and heterogeneity in the ILI definition across studies make it difficult to compare findings from different studies and inhibits the drawing of conclusions regarding the potential effects of this vaccination on related clinical symptoms of influenza disease. However, recent papers by Alqahtani et al. and Alfelali et al. found the influenza vaccine to be effective, respectively, against both laboratory-confirmed influenza [81] and clinical influenza [82]. As influenza vaccination is generally considered effective in reducing influenza-related infections, the Scientific Committee for Influenza and Pneumococcal Vaccination guidelines (SCIPV) thus recommends, in its recent guidelines, an influenza vaccination for all people, especially those at high risk, at least 2 weeks before the Hajj [83]. It also recommends, for the next Hajj seasons that will take place from June to September, the administration (prior to the Hajj) of the Southern Hemisphere influenza vaccine for pilgrims from the Southern Hemisphere (where influenza positivity rates are higher during this period). Furthermore, as the influenza vaccine is not expected to be available for pilgrims from the Northern Hemisphere before these next Hajj seasons, the SCIPV also recommends the administration of the Southern Hemisphere influenza vaccine for those pilgrims from the opposite hemisphere before the Hajj [83]. Because of the mismatching between circulating and vaccine strains that has frequently occurred since 2003 [84], Alfelali et al. recommends, when the composition of influenza vaccines differs and whenever logistically feasible, taking into consideration the dual vaccination of Hajj pilgrims with both the Southern and Northern Hemispheres' vaccines. However, such strategy is impaired by the frequent unavailability of the Southern Hemisphere influenza vaccine in the Northern Hemisphere. The issue of influenza vaccine availability to match Southern and Northern hemispheres was discussed by the Saudi Ministry of Health in consultation with the WHO and it was recommended to use the available hemisphere strain as long as there is a match in circulating strains [85]. Despite the risk of acquisition of *S. pneumoniae* during the Hajj, there is currently no consistent guideline on the use of pneumococcal vaccine for Hajj pilgrims across pilgrim countries of origin [86,87]. Thus, and because many of the Hajj pilgrims are elderly and have chronic illnesses and underlying risk conditions for which pneumococcal vaccination is

recommended [86], the SCIPV also recommended, in its 2016 pneumococcal vaccination guidelines, pneumococcal vaccination of the at-risk population at the appropriate time before the Hajj, using the 2 types of pneumococcal vaccines that are currently available: the 23-valent polysaccharide pneumococcal vaccine (PPSV23) and the 13-valent conjugate vaccine (PCV13) [88]. However, it did not recommend providing a pneumococcal vaccine routinely to healthy persons aged less than 50 years, because of lack of evidence. In addition, it has been well demonstrated that the conjugate vaccine against *S. pneumoniae* targets the most virulent serotypes associated with Invasive Pneumococcal Diseases (IPD) that are also associated with antibiotic resistance [89]. These arguments reinforce the need for compliance with current recommendations for vaccinating at-risk Hajj pilgrims against IPD and influenza [89].

Respiratory tract infections, including influenza, continue to be a major concern during the Hajj. Both cohort- and hospital-based studies provide complementary data and potentially useful information, and both are therefore necessary to provide a complete picture of the total burden of respiratory diseases during this mass gathering. Large multinational follow-up studies are thus recommended for clinic-based syndromic surveillance, in conjunction with microbiological surveillance. Matched cohorts ensure better comparability across studies, particularly in terms of origin of pilgrims and possible travelling conditions. However, the study design and data collection procedures should be standardized, to facilitate reporting and to achieve comparability between studies. Furthermore, the definition of ILI, and of most common symptoms used to define respiratory infections (e.g., URTI), needs to be precisely defined and consistently used. Future studies need to address the potential effects of influenza and pneumococcal vaccine in the context of the Hajj pilgrimage. Moreover, because of the mismatching between circulating and vaccine strains that has frequently occurred since 2003 [84], Alfelali et al. recommends, when the composition of influenza vaccines differs and whenever logistically feasible, taking into consideration the dual vaccination of Hajj pilgrims with both the southern and northern hemispheres' vaccines. However, such strategy is impaired by the frequent unavailability of the southern hemisphere influenza vaccine in the northern hemisphere. Despite the risk of acquisition of *S. pneumoniae* during the Hajj, there is currently no consistent guideline on the use of pneumococcal vaccine for Hajj pilgrims across pilgrim countries of origin [86,87]. Thus, and because many of the Hajj pilgrims are elderly and have chronic illnesses and underlying risk conditions for which pneumococcal vaccination is recommended [86], the SCIPV also recommended, in its 2016 pneumococcal vaccination guidelines, pneumococcal vaccination of the at-risk population at the appropriate time before the Hajj, using the 2 types of pneumococcal vaccines that are currently available: the 23-valent polysaccharide pneumococcal vaccine (PPSV23) and the 13-valent conjugate vaccine (PCV13) [88]. Also, it did not recommend providing a pneumococcal vaccine routinely to healthy persons aged less than 50 years, because of lack of evidence.

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Funding

None.

Conflicts of interest

The authors have no conflicts of interest to declare.

Acknowledgments

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.tmaid.2018.12.002>.

References

- [1] The General Authority for Statistics in the Kingdom of Saudi Arabia. 2016 <http://www.stats.gov.sa/>, Accessed date: 18 October 2016.
- [2] Ahmed QA, Ebrahim S, Memish ZA. From hajj services to mass gathering medicine: Saudi arabia formalizes a novel discipline. *Trav Med Infect Dis* 2018. pii: S1477-8939(18)30217-5.
- [3] Gatrad AR, Sheikh A. Hajj: journey of a lifetime. *BMJ* 2005;330(7483): 133–7. Erratum in: *BMJ* 2005;331(7514):442.
- [4] Abdou AEA. *Atmos Clim Sci* 2014;4(3):457–81.
- [5] Alnabulsi H, Drury J. Social identification moderates the effect of crowd density on safety at the Hajj. *Proc Natl Acad Sci U S A* 2014;111(25):9091–6.
- [6] Memish ZA, Zumla A, Alhakeem RF, Assiri A, Turkestani A, Al Harby KD, Alyemmi M, Dhafar K, Gautret P, Barbeschi M, McCloskey B, Heymann D, Al Rabeeah AA, Al-Tawfiq JA. Hajj: infectious disease surveillance and control. *Lancet* 2014;383(9934):2073–82.
- [7] Abubakar I, Gautret P, Brunette GW, Blumberg L, Johnson D, Poumerol G, Memish ZA, Barbeschi M, Khan AS. Global perspectives for prevention of infectious diseases associated with mass gatherings. *Lancet Infect Dis* 2012;12(1):66–74. Erratum in: *Lancet Infect Dis* 2012;12(3):175.
- [8] Ahmed QA, Arabi YM, Memish ZA. Health risks at the hajj. *Lancet* 2006;367(9515):1008–15.
- [9] Al-Tawfiq JA, Zumla A, Memish ZA. Respiratory tract infections during the annual Hajj: potential risks and mitigation strategies. *Curr Opin Pulm Med* 2013;19(3):192–7.
- [10] Alzeer AH. Respiratory tract infection during Hajj. *Ann Thorac Med* 2009;4(2):50–3.
- [11] Algarni H, Memish ZA, Assiri AM. Health conditions for travellers to Saudi arabia for the pilgrimage to Mecca (hajj) - 2015. *J Epidemiol Glob Health* 2016;6(1):7–9.
- [12] Health conditions for travellers to Saudi arabia for the pilgrimage to Mecca (hajj), 2016. *Wkly Epidemiol Rec* 2016;91(26–27):331–5.
- [13] Fatani A, Sehli A, Al-Rabeah AM, Nooh RM. Health status of non-organized Hajjees (Muftaresheen) during 1420H, hajj season. *Saudi Epidemiol Bull* 2001;8:9–10.
- [14] Deris ZZ, Hasan H, Sulaiman SA, Wahab MS, Naing NN, Othman NH. The prevalence of acute respiratory symptoms and role of protective measures among Malaysian hajj pilgrims. *J Trav Med* 2010;17(2):82–8.
- [15] Deris ZZ, Hasan H, Ab Wahab MS, Sulaiman SA, Naing NN, Othman NH. The association between pre-morbid conditions and respiratory tract manifestations amongst Malaysian Hajj pilgrims. *Trop Biomed* 2010;27(2):294–300.
- [16] Gautret P, Benkouiten S, Griffiths K, Sridhar S. The inevitable Hajj cough: surveillance data in French pilgrims, 2012–2014. *Trav Med Infect Dis* 2015;13(6):485–9.
- [17] Annan A, Owusu M, Marfo KS, Larbi R, Sarpong FN, Adu-Sarkodie Y, Amankwa J, Fiafemeti S, Drosten C, Owusu-Dabo E, Eckerle I. High prevalence of common respiratory viruses and no evidence of Middle East respiratory syndrome coronavirus in Hajj pilgrims returning to Ghana, 2013. *Trop Med Int Health* 2015;20(6):807–12.
- [18] Benkouiten S, Charrel R, Belhouchat K, Drali T, Nougairède A, Salez N, Memish ZA, Al Masri M, Fournier PE, Raoult D, Brouqui P, Parola P, Gautret P. Respiratory viruses and bacteria among pilgrims during the 2013 Hajj. *Emerg Infect Dis* 2014;20(11):1821–7.
- [19] Benkouiten S, Gautret P, Belhouchat K, Drali T, Salez N, Memish ZA, Al Masri M, Fournier PE, Brouqui P. Acquisition of *Streptococcus pneumoniae* carriage in pilgrims during the 2012 Hajj. *Clin Infect Dis* 2014;58(4):e106–9.
- [20] Barasheed O, Almasri N, Badahdah AM, Heron L, Taylor J, McPhee K, Ridda I, Haworth E, Dwyer DE, Rashid H, Booy R, Hajj Research Team. Pilot randomised controlled trial to test effectiveness of facemasks in preventing influenza-like illness transmission among Australian hajj pilgrims in 2011. *Infect Disord - Drug Targets* 2014;14(2):110–6.
- [21] Gautret P, Charrel R, Benkouiten S, Belhouchat K, Nougairède A, Drali T, Salez N, Memish ZA, Al Masri M, Lagier JC, Million M, Raoult D, Brouqui P, Parola P. Lack of MERS coronavirus but prevalence of influenza virus in French pilgrims after 2013 Hajj. *Emerg Infect Dis* 2014;20(4):728–30.
- [22] Benkouiten S, Charrel R, Belhouchat K, Drali T, Salez N, Nougairède A, Zandotti C, Memish ZA, al Masri M, Gaillard C, Parola P, Brouqui P, Gautret P. Circulation of respiratory viruses among pilgrims during the 2012 Hajj pilgrimage. *Clin Infect Dis* 2013;57(7):992–1000.
- [23] Gautret P, Charrel R, Belhouchat K, Drali T, Benkouiten S, Nougairède A, Zandotti C, Memish ZA, al Masri M, Gaillard C, Brouqui P, Parola P. Lack of nasal carriage of novel corona virus (HCoV-EMC) in French Hajj pilgrims returning from the Hajj 2012, despite a high rate of respiratory symptoms. *Clin Microbiol Infect* 2013;19(7):E315–7.
- [24] Rahimian M, Hosseini M. Serological study of Bordetella Pertussis, Mycoplasma Pneumonia and Chlamydia Pneumonia in Iranian hajj pilgrims with prolonged cough illnesses: a follow-up study. *Respir Med* 2017;132:122–31.
- [25] Hashim S, Ayub ZN, Mohamed Z, Hasan H, Harun A, Ismail N, Rahman ZA, Suraiya S, Naing NN, Aziz AA. The prevalence and preventive measures of the respiratory illness among Malaysian pilgrims in 2013 Hajj season. *J Trav Med* 2016;23(2):tav019.
- [26] Fatema J, Manjunatha S, Abrar ul Huq M, Kruthika N. Influenza like illness (ILI): prevalence and preventive practices among Indian Haj pilgrims of Karnataka. *IJPMN* 2015;2(2):23–8.
- [27] Memish ZA, Assiri A, Almasri M, Alhakeem RF, Turkestani A, Al Rabeeah AA, Akkad N, Yezli S, Klugman KP, O'Brien KL, van der Linden M, Gessner BD. Impact of the Hajj on pneumococcal transmission. *Clin Microbiol Infect* 2015;21(1):77.e11–8.
- [28] Memish ZA, Assiri A, Turkestani A, Yezli S, Al Masri M, Charrel R, Drali T, Gaudart J, Edouard S, Parola P, Gautret P. Mass gathering and globalization of respiratory pathogens during the 2013 Hajj. *Clin Microbiol Infect* 2015;21(6):571.e1–8.
- [29] Barasheed O, Rashid H, Alfelali M, Tashani M, Azeem M, Bokhary H, Kalantan N, Samkari J, Heron L, Kok J, Taylor J, El Bashir H, Memish ZA, Haworth E, Holmes EC, Dwyer DE, Asghar A, Booy R, Hajj Research Team. Viral respiratory infections among Hajj pilgrims in 2013. *Viol Sin* 2014;29(6):364–71.
- [30] Rashid H, Barasheed O, Booy R. Acute febrile respiratory infection symptoms in Australian Hajjis at risk of exposure to Middle East respiratory syndrome coronavirus. *Med J Aust* 2013;199(7):453.
- [31] Gautret P, Parola P, Brouqui P. Relative risk for influenza like illness in French Hajj pilgrims compared to non-Hajj attending controls during the 2009 influenza pandemic. *Trav Med Infect Dis* 2013;11(2):95–7.
- [32] Al-Jasser FS, Kabbash IA, Almazroa MA, Memish ZA. Patterns of diseases and preventive measures among domestic hajjis from Central, Saudi Arabia [complete republication]. *East Mediterr Health J* 2013;19(Suppl 2):S34–41.
- [33] Al-Jasser FS, Kabbash IA, Almazroa MA, Memish ZA. Patterns of diseases and preventive measures among domestic hajjis from Central, Saudi Arabia. *Saudi Med J* 2012;33(8):879–86.
- [34] Balaban V, Stauffer WM, Hammad A, Afgarshe M, Abd-Alla M, Ahmed Q, Memish ZA, Saba J, Harton E, Palumbo G, Marano N. Protective practices and respiratory illness among US travelers to the 2009 Hajj. *J Trav Med* 2012;19(3):163–8.
- [35] Saeed KM, Mofleh J, Rasooly MH, Aman MI. Occurrence of acute respiratory infection, diarrhea and jaundice among Afghan pilgrims, 2010. *J Epidemiol Glob Health* 2012;2(4):215–20.
- [36] Al-Jasser FS, Al-Zahrani A, Kabbash I. Pattern of diseases and preventive measures among domestic Hajjis from Riyadh, 1431 H. *Saudi Epidemiol Bull* 2011;18:45–7.
- [37] Gautret P, Vu Hai V, Sani S, Doutchi M, Parola P, Brouqui P. Protective measures against acute respiratory symptoms in French pilgrims participating in the Hajj of 2009. *J Trav Med* 2011;18(1):53–5.
- [38] Razavi SM, Ziaee H, Mokhtari Azad T, Hamkar R, Doroodi T, Mir Salehian A, Nakhjavan F, Nejat F, Sadeghipoor H, Masoud A, Kordbacheh P, Zeini F, Saf Ara M, Mirafshar M, Bamdad K, Bazarjani F. Surveying respiratory infections among Iranian Hajj pilgrims. *ICJID* 2007;2(2):67–70.
- [39] Choudhry AJ, Al-Mudaimigh KS, Turkistani AM, Al-Hamdan NA. Hajj-associated acute respiratory infection among hajjis from Riyadh. *East Mediterr Health J* 2006;12(3–4):300–9.
- [40] Abdin EZ, Choudhry AJ, Al-Naji A. Effect of the use of face mask on hajj related acute respiratory infection among Hajjis from Riyadh, a health promotion intervention study. *Saudi Epidemiol Bull* 2005;12:27–8.
- [41] Razavi M, Sadeghi-Hassanabadi M, Salamati P. The comparison of influenza vaccine efficacy on respiratory diseases among Iranian pilgrims in the 2003 and 2004 seasons. *Acta Med Iran* 2005;43(4):279–81.
- [42] Razavi SM, Dabiran S, Ziaee H. The incidence of influenza like illness and determination of the efficacy of Flu vaccine in Iranian pilgrims during Hajj pilgrimage. *Acta Med Iran* 2004;42(6):397–401.
- [43] Al-Mudaimigh K, AlNaji A, AlEnezi M, Choudhry AJ, Turkistani AM. Incidence of hajj-related acute respiratory infection among hajjis from Riyadh, 1423 H. *Saudi Epidemiol Bull* 2003;10:25–6.
- [44] 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(26):2956–62.
- [45] Refaey S, Amin MM, Roguski K, Azziz-Baumgartner E, Uyeke TM, Labib M, Kandeel A. Cross-sectional survey and surveillance for influenza viruses and MERS-CoV among Egyptian pilgrims returning from Hajj during 2012–2015. *Influenza Other Respir Viruses* 2017;11(1):57–60.
- [46] Meysamie A, Ardakani HZ, Razavi SM, Doroodi T. Comparison of mortality and morbidity rates among Iranian pilgrims in Hajj 2004 and 2005. *Saudi Med J* 2006;27(7):1049–53.
- [47] Razavi SM, Mohazzab Torabi S, Salamati P. Treatment and prevention of acute respiratory infections among Iranian hajj pilgrims: a 5-year follow up study and review of the literature. *Med J Islam Repub Iran* 2014;28:31.
- [48] Razavi SM, Sabouri-Kashani A, Ziaee-Ardakani H, Tabatabaei A, Karbaksh M, Sadeghipour H, Mortazavi-Tabatabaei SA, Salamati P. Trend of diseases among

- Iranian pilgrims during five consecutive years based on a Syndromic Surveillance System in Hajj. *Med J Islam Repub Iran* 2013;27(4):179–85.
- [49] Gautret P, Yong W, Soula G, Gaudart J, Delmont J, Dia A, Parola P, Brouqui P. Incidence of Hajj-associated febrile cough episodes among French pilgrims: a prospective cohort study on the influence of statin use and risk factors. *Clin Microbiol Infect* 2009;15(4):335–40.
- [50] Ma X, Liu F, Liu L, Zhang L, Lu M, Abudukadeer A, Wang L, Tian F, Zhen W, Yang P, Hu K. No MERS-CoV but positive influenza viruses in returning Hajj pilgrims, China, 2013–2015. *BMC Infect Dis* 2017;17(1):715.
- [51] Hasan H, Deris ZZ, Sulaiman SA, Abdul Wahab MS, Naing NN, Ab Rahman Z, Othman NH. Effect of influenza vaccination on acute respiratory symptoms in Malaysian hajj pilgrims. *J Immigr Minor Health* 2015;17(4):1114–9.
- [52] Imani R, Hafizi Esfahani M, Ale Rasul M, Taheri S. Time to revisit presumptions on the essentiality of influenza vaccination for hajj pilgrims: a prospective cohort study international. *J Trav Med Global Health* 2013;1(1):18–22.
- [53] Ziyaeyan M, Alborzi A, Jamalidoust M, Moeini M, Pouladfar GR, Pourabbas B, Namayandeh M, Moghadami M, Bagheri-Lankarani K, Mokhtari-Azad T. Pandemic 2009 influenza A (H1N1) infection among 2009 Hajj Pilgrims from Southern Iran: a real-time RT-PCR-based study. *Influenza Other Respir Viruses* 2012;6(6):e80–4.
- [54] Maslamani Y, Choudhry AJ. Health related experiences among international pilgrims departing through King Abdul Aziz international airport, Jeddah, Saudi Arabia, Hajj 1431 H (2010). *Saudi Epidemiol Bull* 2011;18:42–4.
- [55] Dabiran S, Razavi S, Kashani A, Karbakhsh M, Naser-Hodjati H, Peyafarin F. Effects of flu vaccine, solely or accompanied by pneumovax-23 vaccine on clinical consequences of the respiratory diseases among Iranian pilgrims in Hajj. *Health* 2004;6:123–7.
- [56] El Bashir H, Haworth E, Zambon M, Shafi S, Zuckerman J, Booy R. Influenza among U.K. pilgrims to hajj, 2003. *Emerg Infect Dis* 2004;10(10):1882–3.
- [57] Yousuf M, Zafar F, Maqbool M. Medical problems of Pakistani pilgrims in Saudi Arabia. *Pakistan J Med Res* 1993;32:172–5.
- [58] Alherabi AZ. Impact of pH1N1 influenza A infections on the otolaryngology, head and neck clinic during hajj, 2009. *Saudi Med J* 2011;32(9):933–8.
- [59] Alzahrani AG, Choudhry AJ, Al Mazroa MA, Turkistani AH, Nouman GS, Memish ZA. Pattern of diseases among visitors to Mina health centers during the Hajj season, 1429 H (2008 G). *J Infect Public Health* 2012;5(1):22–34.
- [60] Alzahrani AG, Choudhry AJ, Al-Hayani O, Nageeb M. Pattern of diseases among visitors to Mina health centers during the Hajj season, 1429 H (2008 G). *Saudi Epidemiol Bull* 2009;16(23):19.
- [61] Alherabi AZ. Road map of an ear, nose, and throat clinic during the 2008 hajj in makkah, Saudi arabia. *Saudi Med J* 2009;30(12):1584–9.
- [62] Madani TA, Ghabrah TM, Al-Hedaithy MA, Alhazmi MA, Alazraqi TA, Albarrak AM, Ishaq AH. Causes of hospitalization of pilgrims in the Hajj season of the Islamic year 1423 (2003). *Ann Saudi Med* 2006;26(5):346–51.
- [63] Al-Harbi MA. Pattern of surgical and medical diseases among pilgrims attending Al-noor hospital makkah. *J Family Community Med* 2000;7(1):21–4.
- [64] Erdem H, Ak O, Elaldi N, Demirdal T, Hargreaves S, Nemli SA, Cag Y, Ulug M, Naz H, Gunal O, Sirmatel F, Sipahi OR, Alpat SN, Ertem-Tuncer G, Sozen H, Evlice O, Meric-Koc M, Dogru A, Koksaldi-Motor V, Tekin R, Ozdemir D, Ozturk-Engin D, Savasci U, Karagoz E, Cekli Y, Inan A. Infections in travellers returning to Turkey from the Arabian peninsula: a retrospective cross-sectional multicenter study. *Eur J Clin Microbiol Infect Dis* 2016;35(6):903–10.
- [65] Mandourah Y, Al-Radi A, Ocheltree AH, Ocheltree SR, Fowler RA. Clinical and temporal patterns of severe pneumonia causing critical illness during Hajj. *BMC Infect Dis* 2012;12:117.
- [66] Baharoon S, Al-Jahdali H, Al Hashmi J, Memish ZA, Ahmed QA. Severe sepsis and septic shock at the Hajj: etiologies and outcomes. *Trav Med Infect Dis* 2009;7(4):247–52.
- [67] Al-Quwaidhi A, Choudhry AJ, Al-Hayani O. Pattern of diseases among visitors of health care facilities in Madinah during Hajj season, 1428 H (2007 G). *Saudi Epidemiol Bull* 2008;15(29):25–6.
- [68] Madani TA, Ghabrah TM, Albarrak AM, Alhazmi MA, Alazraqi TA, Althaqafi AO, Ishaq A. Causes of admission to intensive care units in the Hajj period of the Islamic year 1424 (2004). *Ann Saudi Med* 2007;27(2):101–5.
- [69] Khan NA, Ishag AM, Ahmad MS, El-Sayed FM, Bachal ZA, Abbas TG. Pattern of medical diseases and determinants of prognosis of hospitalization during 2005 Muslim pilgrimage Hajj in a tertiary care hospital. A prospective cohort study. *Saudi Med J* 2006;27(9):1373–80.
- [70] Al-Ghamdi SM, Akbar HO, Qari YA, Fathaldin OA, Al-Rashed RS. Pattern of admission to hospitals during muslim pilgrimage (Hajj). *Saudi Med J* 2003;24(10):1073–6.
- [71] Yousuf M, Al-Saudi DA, Sheikh RA, Lone MS. Pattern of medical problems among Haj pilgrims admitted to king Abdul Aziz hospital, Madinah Al-Munawarah. *Ann Saudi Med* 1995;15(6):619–21.
- [72] Khamis NK. Epidemiological pattern of diseases and risk behaviors of pilgrims attending mina hospitals, hajj 1427 h (2007 g). *J Egypt Publ Health Assoc* 2008;83(1–2):15–33.
- [73] Deris ZZ, Hasan H, Sulaiman SA, Wahab MS, Naing NN, Othman NH. Preference of treatment facilities among Malaysian Hajj pilgrims for acute respiratory symptoms. *Saudi Med J* 2009;30(8):1103–4.
- [74] Shafi S, Booy R, Haworth E, Rashid H, Memish ZA. Hajj: health lessons for mass gatherings. *J Infect Public Health* 2008;1(1):27–32.
- [75] Simpson IJ, Aburizaiza OS, Siddique A, Barletta B, Blake NJ, Gartner A, Khwaja H, Meinardi S, Zeb J, Blake DR. Air quality in Mecca and surrounding holy places in Saudi Arabia during Hajj: initial survey. *Environ Sci Technol* 2014;48(15):8529–37.
- [76] Gautret P, Benkouiten S, Al-Tawfiq JA, Memish ZA. Hajj-associated viral respiratory infections: a systematic review. *Trav Med Infect Dis* 2016;14(2):92–109.
- [77] Gautret P, Benkouiten S. Circulation of respiratory pathogens at mass gatherings, with special focus on the Hajj pilgrimage. In: Kon K, Rai M, editors. *The microbiology of respiratory system infections*. first ed. 2016. p. 81–93.
- [78] Mustafa AN, Gessner BD, Ismail R, Yusoff AF, Abdullah N, Ishak I, Abdullah N, Merican MI. A case-control study of influenza vaccine effectiveness among Malaysian pilgrims attending the Haj in Saudi Arabia. *Int J Infect Dis* 2003;7(3):210–4.
- [79] Rashid H, Shafi S, El Bashir H, Haworth E, Memish ZA, Ali KA, Booy R. Influenza and the Hajj: defining influenza-like illness clinically. *Int J Infect Dis* 2008;12(1):102–3.
- [80] Benkouiten S, Brouqui P, Gautret P. Non-pharmaceutical interventions for the prevention of respiratory tract infections during Hajj pilgrimage. *Trav Med Infect Dis* 2014;12(5):429–42.
- [81] Alqahtani AS, Rashid H, Heywood AE. Vaccinations against respiratory tract infections at Hajj. *Clin Microbiol Infect* 2015;21(2):115–27.
- [82] Alfelali M, Barasheed O, Tashani M, Azeem MI, El Bashir H, Memish ZA, Heron L, Khandaker G, Booy R, Rashid H, Hajj Research Team. Changes in the prevalence of influenza-like illness and influenza vaccine uptake among Hajj pilgrims: a 10-year retrospective analysis of data. *Vaccine* 2015;33(22):2562–9.
- [83] Zeitouni MO, Al Barrak AM, Al-Moamary MS, Alharbi NS, Idrees MM, Al Shimemeri AA, Al-Hajjaj MS. The Saudi Thoracic Society guidelines for influenza vaccinations. *Ann Thorac Med* 2015;10(4):223–30.
- [84] Alfelali M, Khandaker G, Booy R, Rashid H. Mismatching between circulating strains and vaccine strains of influenza: effect on Hajj pilgrims from both hemispheres. *Hum Vaccines Immunother* 2016;12(3):709–15.
- [85] Al-Tawfiq JA, Gautret P, Memish ZA. Expected immunizations and health protection for Hajj and Umrah 2018 - an overview. *Trav Med Infect Dis* 2017;19:2–7.
- [86] Al-Tawfiq JA, Memish ZA. Prevention of pneumococcal infections during mass gathering. *Hum Vaccines Immunother* 2016;12(2):326–30.
- [87] Ridda I, King C, Rashid H. Pneumococcal infections at Hajj: current knowledge gaps. *Infect Disord - Drug Targets* 2014;14(3):177–84.
- [88] Alharbi NS, Al-Barrak AM, Al-Moamary MS, Zeitouni MO, Idrees MM, Al-Ghobain MO, Al-Shimemeri AA, Al-Hajjaj MS. The Saudi Thoracic Society pneumococcal vaccination guidelines-2016. *Ann Thorac Med* 2016;11(2):93–102.
- [89] Leangapichart T, Rolain JM, Memish ZA, Al-Tawfiq JA, Gautret P. Emergence of drug resistant bacteria at the Hajj: a systematic review. *Trav Med Infect Dis* 2017;18:3–17.