



Infectious Diseases and Mass Gatherings

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Abstract

Purpose of Review Mass gatherings (MGs) are characterized by a high concentration of people at a specific time and location. Infectious diseases are of particular concern at MGs. The aim of this review was to summarize findings in the field of infectious diseases with a variety of pathogens associated with international MGs in the last 5 years.

Recent Findings In the context of Hajj, one of the largest religious MGs at Mecca, Saudi Arabia, respiratory tract infections are the leading cause of infectious diseases in pilgrims with a prevalence of 50–93%. The most commonly acquired respiratory viruses were human rhinovirus, followed by human coronaviruses and influenza A virus, in decreasing order. *Haemophilus influenzae*, *Staphylococcus aureus*, and *Streptococcus pneumoniae* were the predominant bacteria. The prevalence of Hajj-related diarrhea ranged from 1.1 to 23.3% and etiologies included *Salmonella spp.*, and *Escherichia coli*, with evidence of acquisition of antimicrobial-resistant bacteria. In other MGs such as Muslim, Christian, and Hindu religious events, sports events, and large-scale open-air festivals, outbreaks have been reported less frequently. The most common outbreaks at these events involved diseases preventable by vaccination, notably measles and influenza. Gastrointestinal infections caused by a variety of pathogens were also recorded.

Summary Because social distancing and contact avoidance are difficult measures to implement in the context of many MGs, individual preventive measures including vaccination, use of face mask, disposable handkerchief and hand hygiene may be recommended. Nevertheless, the effectiveness of these measures has been poorly investigated in the context of MGs.

Keywords Infectious diseases · Outbreaks · Mass gatherings · Hajj · Sport · Festival

Introduction

The WHO defines mass gatherings (MGs) as a “concentration of people at a specific location for a specific purpose over a set period of time which has the potential to strain the planning and response resources of the country or community” [1].

MGs can be either planned or spontaneous and recurrent or sporadic [1]. Planned MGs may include sporting, social, cultural, religious, and political events. Examples include music festivals, the Olympic Games, and the Hajj [2].

Spontaneous MGs, given their nature, are more difficult to plan for and may include events, such as funerals of religious and political figures [1, 2]. MGs may also include the gatherings of displaced populations due to natural disasters, conflicts, and wars [1]. Diverse health risks are associated with MGs, including transmission of infectious disease, non-communicable disease, trauma and injuries (occupational or otherwise), environmental effects (such as, heat-related illnesses, dehydration, hypothermia), illnesses related to the use of drugs and alcohol, and deliberate acts, such as terrorist attacks [1]. Infectious diseases are of particular concern at MGs [3]. In this review, we summarize recent findings in the field of infectious diseases associated with international MGs.

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Results and Discussion

The Hajj (Table 1)

The Hajj, an annual Muslim pilgrimage to Mecca, Saudi Arabia, is one of the largest religious MGs in the world with about two million pilgrims from 185 countries [4]. As part of the Hajj rituals, pilgrims visit various sacred places around the city of Mecca. Most of them also travel to the city of Medina to visit the second holiest site of Islam, the Prophet's mosque containing the tomb of the Prophet Muhammad. The presence of a large number of pilgrims from different countries of the world and overcrowded condition considerably increases the risk of occurrence of infectious diseases, particularly respiratory and gastrointestinal diseases [5]. Furthermore, a vast majority of pilgrims are elderly people with a high prevalence of chronic diseases. In the past, Hajj-related cholera has been a public health problem and the main cause of morbidity and mortality among pilgrims, leading to major epidemics and international spread. Due to improved sanitary conditions in Saudi Arabia in general and at religious sites, large-scale cholera outbreaks have not been recorded during the last decades [6, 7]. Similarly,

Table 1 Hajj and large-scale open-air festivals—key points

Hajj—key points

- Event: annual Muslim pilgrimage
- Place: Mecca, Saudi Arabia
- Population size: 2 million from 185 countries (high proportion of elderly pilgrims with co-morbidities)
- Prevalence of respiratory symptoms in overall population of pilgrims: 50–93%
- Pneumonia among the leading cause of admission in Saudi hospitals during the Hajj
- Acquisition of respiratory pathogens: 13.5–34.1% rhinovirus, 12.4–14.6% non-MERS coronavirus, 1.9–7.8% influenza A virus, 7.1–36.6% *Streptococcus pneumoniae*, 11.4% *Haemophilus influenzae*, 7.5% *Staphylococcus aureus*
- No case of MERS-CoV, *Bordetella pertussis*, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae* observed in pilgrims in recent years
- Antibiotic consumption in overall population of pilgrims: 45–61.8%
- Prevalence of diarrhea: 1.1–23.3%
- Hajj-associated diarrhea mostly due to bacteria including: *Salmonella spp.* and *Escherichia coli*.
- Evidence for acquisition of antimicrobial-resistant bacteria

Large-scale open-air festivals—key points

- Events: music festivals and other cultural festivals in various places in the world.
- Population size: variable but usually less than 400,000 participants (mostly young participants)
- Outbreaks of respiratory tract infections and gastrointestinal infections are regularly reported including notably measles and mumps, influenza, diarrhea due to bacterial and viral infections.

invasive meningococcal disease has been a Hajj-related public health concern with its last outbreaks (serogroup W-135) in the 2000s. However, with the strengthening of prevention through mandatory vaccination, no case of meningococcal disease has been reported in Mecca since 2006 [8, 9].

While gastrointestinal diseases and diarrhea have changed towards a lower prevalence, respiratory tract infections (RTIs) now account for the vast majority of health problems during the Hajj [4, 5]. The inevitable overcrowding conditions at the Grand Mosque in Mecca and the accommodation in tents in Mina with an average of 50 to 100 people per tent are likely responsible for the high rate of respiratory infections among Hajj pilgrims [5].

Respiratory Infections at the Hajj

Over the last 5 years, a significant number of publications from different countries based on both syndromic surveillance and PCR-based investigation of respiratory pathogen carriage were made available. Studies were conducted in out- and in-patients at health structures in Saudi Arabia or on return in pilgrim's country of origin and in cohorts of pilgrims regardless of symptoms [10–34] (Table 2).

RTIs are among the leading causes of admission to hospitals in Mina, Mecca, and Medina during the Hajj period (Table 2). Most cases are upper respiratory tract infections [10–16], but severe respiratory tract infections [17] and pneumonia are not uncommon among pilgrims [18, 19, 20•]. Respiratory diseases were the second cause of mortality in Indonesian pilgrims during the Hajj (following cardiovascular diseases) [35]. Among pathogens detected by PCR methods in ill pilgrims, the most common viruses were human rhinovirus (HRV), followed by human coronaviruses (HCoV) and influenza A virus (IAV). *Haemophilus influenzae*, *Staphylococcus aureus*, and *Streptococcus pneumoniae* were the predominant bacteria isolated by culture [36, 37].

Cross-sectional and longitudinal cohort studies have recorded 53–93.4% prevalence of RTI symptoms among Hajj pilgrims [21–23, 26•, 28, 32, 34•]. The rate of ILI varied from 1.9 to 78.2% [21, 22, 26•, 27, 28, 30–33]. Cohort surveys allow evaluating the acquisition rate of respiratory pathogens regardless of symptoms. The most commonly acquired viruses were human rhinovirus (HRV) (13.5–34.1%), followed by human coronavirus E229 (HCoV-E229) (2.0–14.6%) and influenza virus (IAV) (1.9–20.0%) [21, 22, 27, 28, 30, 31•, 33]. The most commonly acquired bacteria were *S. pneumoniae* (7.1 to 36.6%) and *S. aureus* (7.5 to 22.8%) and *H. influenzae* (11.4%) [25, 28, 29, 31•, 34•]. *Bordetella pertussis*, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae* have not been detected in pilgrims in recent studies [13, 28, 31•]. Middle East Respiratory Syndrome Coronavirus (MERS-CoV) that emerged in the Arabian Peninsula in 2012 is associated with severe acute respiratory infection with high

Table 2 Respiratory tract infections at the Hajj

Date of study	Clinical setting Place of study	Clinical findings	Number of pilgrims/cases	Pathogens isolated	Comments/highlights	References
2010	Retrospective survey of medical data registered by Iranian caravan physicians at Mecca, Medina, Arafat, and Mina, Saudi Arabia	RTIs 61.82%, cough 24%, rhinorrhea 19% <i>n</i> , sore throat 18%	107,074 ill Iranian pilgrims		RTIs were the most diagnosed diseases	[10]
2013–2015	Survey conducted among ill returning pilgrims presenting to hospitals in the Midlands South West and North England, UK		202 UK pilgrims with RTI	14.4% HRV, 13.9% IAV, 6.4% IBV, 5.0% PIV virus		[11]
2013–2016	In-patient of a survey admitted to the Kurmitola General Hospital isolation unit, Dhaka, Bangladesh		81 Bengali pilgrims hospitalized with RTIs	12.3% IAV, 10% IBV, 2.8% ADV, 2.8% MPV, 2.8% PIV		[12]
2014	Survey conducted among ill returning pilgrims consulting at 12 hospitals in Jordan	76% cough, 50% sore throat, 41% fever, 37% rhinorrhea, 16% dyspnea	125 Jordan pilgrims with RTIs	47% HRV/EX, 12.8% HCoV and 3% IAV		[13]
2014	Cross-sectional study conducted at primary health care services of the Al Noor Specialized Hospital in Medina, Saudi Arabia	66.8% acute rhinosinusitis	343 ill hospitalized pilgrims with RTI	93 (41.2%) bacterial rhinosinusitis, including 49.5% <i>S. aureus</i> , 15% <i>K. pneumoniae</i> , 8.6% <i>E. coli</i> , 4.3% <i>S. pneumoniae</i> and 3.2% <i>H. influenzae</i>		[14]
2014–2015	Cross-sectional survey conducted in returning Hajj and Umrah pilgrims with current respiratory symptoms or fever arriving from Mecca and landing at Srinagar Airport, India. Study based on face-to-face interview	89.7% cough, 86.3% rhinorrhea, 66.2% sore throat, 49.8% fever	300 Indian pilgrims	11% influenza virus		[15]
2016	Cross-sectional study conducted at an Indian medical mission in Mecca, Medina and Jeddah, Saudi Arabia	930 ill pilgrims needed secondary care, of whom 585 (62.9%) were hospitalized.	374,475 ill Indian pilgrims		Infectious diseases were most commonly due to overwhelming respiratory infections (49.4%)	[16]
2013–2016	Cross-sectional survey conducted in pilgrims admitted to Iranian hospitals on returning from the Hajj		3840 Iranian pilgrims hospitalized with severe acute respiratory infections	13% influenza virus		[17]
2004–2013	Retrospective cohort study conducted at Al-Ansar general hospital, Medina, Saudi Arabia	59.2% productive cough, 30.1% dry cough, 44.7% dyspnea, 26.8% sore throat. 31% admitted in ICU.	1059 hospitalized pilgrims with pneumonia (23% of total hospital admissions)	Organisms isolated from sputum cultures: 36.1% <i>S. aureus</i> , 29% <i>K. pneumoniae</i> , 24.3% <i>H. influenzae</i> , 6.5% community-acquired MRSA, 3.1% <i>P. aeruginosa</i> , 1% <i>S. pneumoniae</i> 14.9% multiple pathogen	The mortality rate was 2.4% in the ward and 21.45% in the ICU	[18]
2013	Cross-sectional study conducted at 15 healthcare facilities of Mecca and Medina, Saudi Arabia		38 pilgrims hospitalized with bilateral pneumonia	57.7% HRV, 23.1% IAV, 19.2% HCoV, 57.7% <i>H. influenzae</i> , 53.8% <i>S. pneumoniae</i>		[19]
2016	Prospective survey conducted in 13 hospitals in Mecca and Medina, Saudi Arabia	91% cough, 87.2% difficulty breathing, 32.3% chest	266 hospitalized pilgrims with confirmed	19% <i>S. pneumoniae</i> identified by culture		[20]

Table 2 (continued)

Date of study	Clinical setting Place of study	Clinical findings	Number of pilgrims/cases	Pathogens isolated	Comments/highlights	References
2004–2009	Longitudinal survey conducted in pilgrims recruited at 1352 Hajj caravans. Study based on medical evaluation during travel	pain 83.1% fever, 79.4% tachypnea 71.2% RTIs, 10.7% ILI, 0.5% pneumonia	community-acquired pneumonia 254,823 Iranian pilgrims	357 samples tested were positive for respiratory bacteria with 15.8% <i>C. pneumoniae</i> , 6.6% <i>L. pneumophila</i> , 8.5% <i>streptococcus</i> , 9.1% <i>haemophilus</i> 105 pairs of pharyngeal samples tested were positive for respiratory virus with 36.2% ADV, 30% HRV, 20% IVB, 1.9% RSV		[21, 22]
2009	Longitudinal survey conducted in pilgrims recruited at primary healthcare centers in Riyadh, Saudi Arabia (for the mandatory pre-Hajj meningococcal vaccination). Study based on telephone interview on return	53% RTIs	1507 pilgrims		RTIs were leading cause of consultation (97% of ill pilgrims)	[23]
2010	Cross-sectional study conducted at Jeddah airport		1600 pilgrims	7.5% IAV		[24]
2012	Longitudinal survey conducted in pilgrims recruited at a specialized Hajj travel agency, Marseille, France. Study based on medical evaluation during travel		169 French pilgrims	The overall acquisition of nasal <i>S. aureus</i> carriage was 22.8%		[25]
2012–2014	Longitudinal survey conducted in pilgrims recruited at a specialized Hajj travel agency, Marseille, France. Study based on medical evaluation during travel	80.9% cough, 46.2% ILI, 91% sore throat, 78.7% rhinorrhea, 63.0% voice failure, 21.0% dyspnea	382 French pilgrims		The prevalence of cough was significantly higher among females than men. Pilgrims with chronic respiratory disease showed a slightly increased prevalence of cough.	[26]
2012–2015	Cross-sectional study conducted at Cairo International Airport, Egypt	30.4% reported symptoms consistent with ILI 14.5% laboratory-confirmed influenza	3364 Egyptian pilgrims	14.5% influenza including, 3.5% H1N1, 5.6% H3N2, 5.4% IBV		[27]
2013	Longitudinal survey conducted in pilgrims recruited at a specialized Hajj travel agency, Marseille, France. Study based on medical evaluation during travel	Cough 86.8% Sore throat 82.9%, ILI 47.3%	129 French pilgrims	HRV, HCoV-E229 and IAV prevalence was 13.5%, 12.4% and 7.8%, respectively. Of note, 36.6% of pilgrims acquired <i>S. pneumoniae</i> after the Hajj		[28]
2013	Prospective cohort study conducted among pilgrims recruited at King Abdul Aziz International airport Jeddah and Mina, Saudi Arabia		1175 pilgrims	The carriage rate of <i>S. pneumoniae</i> was 1.8% pre- and 7.1% post-Hajj		[29]

Table 2 (continued)

Date of study	Clinical setting Place of study	Clinical findings	Number of pilgrims/cases	Pathogens isolated	Comments/highlights	References
2013	Cross-sectional survey conducted in pilgrims recruited at Mina encampment. Study based on post-Hajj face-to-face interview	63.4% ILI, 46.3% cough, 34.7% sore throat, 23.8% rhinorrhea	164 Australian pilgrims	25% HRV, 4% IAV, 2% HCoV		[30]
2013	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	62% ILI	1676 pilgrims	The acquisition rates of HRV, human coronavirus E229 (HCoV-E229) and IAV was 34.1%, 14.6%, and 1.9%, respectively and acquisition rates of <i>S. pneumoniae</i> , <i>H. influenzae</i> and <i>S. aureus</i> were 12%, 11.4%, and 7.5%, respectively		[31]
2013	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	93.4% respiratory symptoms 78.2% ILI 2.1% hospitalization	468 Malaysian pilgrims		Most of pilgrims acquired the infection intensely at Arafat (81.2%)	[32]
2013–2015	Longitudinal survey conducted in returning Hajj pilgrims arriving at Xinjiang and Gansu airports, China	ILI, 1.9%	847 Chinese pilgrims	4.0% IAV, 1.7% IBV, 0.5% MPV, 0.2% RSV		[33]
2016	Prospective multisite cohort study conducted in pilgrims recruited in 4 cities of India	76% pilgrims had at least one respiratory symptoms, cough 60.6%, sore throat 25.0%	807 Indian pilgrims	28% were positive for <i>S. pneumoniae</i> by culture methods (65% were symptomatic) and 65.9% were positive by qPCR (59% were symptomatic)	None of the participants reported receiving the pneumococcal vaccine	[34]

RTIs respiratory tract infections, ILI influenza-like illness, ICU intensive care unit, *S. aureus* *Staphylococcus aureus*, *S. pneumoniae* *Streptococcus pneumoniae*, *K. pneumoniae* *Klebsiella pneumoniae*, *H. influenzae* *Haemophilus influenzae*, *P. aeruginosa* *Pseudomonas aeruginosa*, *C. pneumoniae* *Chlamydia pneumoniae*, *L. pneumophila* *Legionella pneumophila*, *E. coli* *Escherichia coli*, *MRSA* methicillin-resistant *staphylococcus aureus*, *HRV* human rhinovirus, *EV* enterovirus, *HCoV* human coronavirus, *IAV* influenza A virus, *IBV* influenza B virus, *PIV* parainfluenza virus, *RSV* respiratory syncytial virus, *ADV* adenovirus, *MPV* metapneumovirus

mortality rates. Numerous studies were conducted in returning pilgrims with the aim of detecting MERS-CoV infections and all resulted negative [11–13, 15, 17, 24, 27, 28, 30, 33, 38–46].

Tuberculosis (TB) transmission is another concern at the Hajj, but there are no large-scale, specific studies to determine its prevalence among pilgrims [47]. A prospective cross-sectional study was conducted in Mecca, during the Hajj period in September 2015. One thousand one hundred sixty-four pilgrims with cough were selected from five countries in Africa and South Asia that are endemic for TB and 1.4% had active previously undiagnosed TB [48•]. During the Hajj in 2015, 44 cases of TB among pilgrims and non-pilgrims were diagnosed in Mecca hospitals [48•].

Gastrointestinal Diseases at the Hajj

A review on diarrhea at the Hajj published in 2015 showed a prevalence of diarrhea ranging from 1.1 to 23.3% in 14 cohort studies including 262,999 pilgrims from various countries between 2002 and 2013 [49•]. Five percent of pilgrims from Riyadh developed diarrheal symptoms during the 2009 Hajj [23]. Twenty-one percent of Iranian female pilgrims suffered from gastroenteritis during the 2011 Hajj [50]. In 2013, 23.3% pilgrims from Marseille, France, had diarrhea during the Hajj [51] while a 13.7% prevalence was recorded in 2016 [52]. In the latter study, *Escherichia coli* was the predominant pathogen isolated from pilgrims by PCR. Enteropathogenic *E. coli*, enteroaggregative *E. coli*, and Shiga-like toxin-producing *E. coli* were acquired by 29.9%, 10.2%, and 6.5% pilgrims, respectively [52]. Among persons infected during the 2011–2013 Hajj and hospitalized in Saudi hospitals, the pathogens responsible for enteric infection were mostly bacteria, with a prevalence of *Salmonella spp.* of 11.4%, while that of diarrhea associated *E. coli* ranged between 1.3 and 8.8% according to pathotypes [53]. Two cases of *Tropheryma whipplei* were recorded in a cohort of French pilgrims during the 2013 Hajj [51].

Antibiotic Consumption During the Hajj

The frequency of infectious diseases during the Hajj results in a significant demand for antibiotic use. The rate of antibiotic use among pilgrims varied according to their nationality and year with 61.8% in Malay pilgrims in 2013 [32], 53.8% in French pilgrims in 2012 [25], 45–48.3% in Indian pilgrims in 2016 [16, 34•], and 58.5% in Iranian pilgrims in 2012 [54]. A prospective study conducted among 218 pilgrims from Marseille, France, during the periods of Hajj in 2013–2014 showed that 54.8% of the population used antibiotics because of respiratory diseases and 5.4% because of diarrhea [55]. Although the dispensing of antibiotics without a prescription has been banned in Saudi Arabia for more than 30 years [56], 27% of Australian pilgrims used antibiotics either delivered in

Saudi Arabia without prescription or purchased in Australia before traveling [57].

Hajj and Antimicrobial-Resistant Bacteria

The predominance of bacterial pathogens in Hajj-related gastrointestinal infections poses a major risk to public health through the potential emergence and transmission of antimicrobial-resistant bacteria [53]. Methicillin-resistant *S. aureus* had been isolated in 28% of pilgrims with acute sinusitis in 2014 [14] and 63% of pilgrims with community-acquired infections hospitalized during the Hajj in 2015 [58•]. One study addressed the carriage of resistant *S. pneumoniae* in a multinational cohort of pilgrims and showed that 23% of isolates were resistant to multiple antibiotics (resistant to three or more classes of antibiotics) [29]. Extended spectrum beta-lactamase Enterobacteriaceae are also common among hospitalized pilgrims. During the 2014–2015 Hajj, 47% of pilgrims attending hospitals for urinary tract infections showed blaCTX-M genes in *E. coli* isolates [59].

During the 2013 and 2014 Hajj seasons, studies were conducted using rectal samples obtained before and after the Hajj in cohorts of French pilgrims to assess the carriage of the blaCTX-M gene. Acquisition rates of 31.0–34.8% were observed [55, 60]. There was also a significant increase in the number of pilgrims harboring *E. coli* resistant to ceftriaxone and ticarcillin-clavulanic acid [60].

The prevalence of C3G-resistance was observed in 90.6% *Acinetobacter baumannii* isolates in a cohort of French pilgrims in 2014 [61] and in 76.2% of isolates obtained from hospitalized pilgrims suffering from community-acquired infections in 2015 [58•]. Two French pilgrims carried *S. enterica*, resistant to ceftriaxone, gentamycin, and colistin after the 2013 Hajj [62]. Mrc-1 resistance gene screening from rectal swabs was conducted in French pilgrims in 2013–2014 and found an acquisition rate of 9.0% after Hajj [63].

Risk factors for the spread of antibiotic-resistant bacteria at the Hajj include international travel, misuse of antibiotics, and availability of over-the-counter antibiotics [64]. However, gastrointestinal diseases and diarrhea continue to occur in pilgrims, outbreaks of food poisoning are reported, and the acquisition of multi-resistant bacteria is emerging. The ongoing monitoring of these diseases is part of the public health response regarding the Hajj [49•, 55].

Meningococcal Carriage at the Hajj

Currently, meningococcal vaccination (A, C, Y, W-135) is mandatory for all pilgrims, national and international, as well as local residents of holy cities and workers in contact with pilgrims; however, polysaccharide vaccine which does not prevent meningococcal carriage is still in use in many countries. Mandatory oral ciprofloxacin prophylaxis is provided

upon arrival to all the pilgrims coming from the “meningitis belt” of sub-Saharan Africa [8, 9, 65, 66]. A cross-sectional study among pilgrims arrived at King Abdul Aziz International Airport, in Jeddah for the Hajj in 2012 showed antibody titers under the level of protection against serogroups A, C, W, and Y of only 0.1%, 0.4%, 17.4%, and 9.4%, respectively. Most of them (98.2%) had received meningococcal vaccination in the three previous years [67]. In a prospective cohort study conducted in Turkish Hajj pilgrims during 2010, the carriage prevalence of *Neisseria meningitidis*, assessed by culture method, was 13% before and 27.0% after the Hajj with the majority being serogroup W-135 [68]. In a prospective culture-based cohort study conducted among Iranian pilgrims in 2012, 1.4% acquired *N. meningitidis* at the Hajj [54]. A prospective study conducted in 2014 among international pilgrims at King Abdul Aziz International Airport showed 3.0% *N. meningitidis* carriage by culture method upon arrival and 0.9% upon departure, with the majority of typable isolates being serogroup B [69]. Outbreaks of the disease including those due to serogroups not included in the required vaccines, such as serogroups B and X, are therefore possible at the Hajj. Despite the wide use of polysaccharide vaccine, it does not prevent the carriage of serogroup W-135 and subsequent transmission to unvaccinated individuals by returning pilgrims.

Others Religious Meetings

The Grand Magal of Touba, the largest Muslim pilgrimage in Senegal, has specific features. Besides its setting in a tropical environment, its population is characterized by a large range of age groups since most pilgrims travel with their family, including young children. A preliminary survey in 2015 has showed a high rate of febrile systemic illnesses and malaria (4.9%), diarrheal diseases (4.5%), and RTIs (5.2%) among ill pilgrims consulting at health care structures during the pilgrimage. The overall hospitalization rate was 3.4% including gynecological cases (16.2%) and confirmed malaria (14.5%) [70••].

The Kumbh Mela in India is the largest MG in the world with about 100 million visitors. It posed an exciting challenge to the provision of healthcare services. Increased population density, reduced sanitation, and exposure to environmental pollutants open the way for easy transmission of pathogens [71]. During Kumbh Mela in 2013, 412,703 patients consulted at hospitals. Respiratory infections accounted for 70% of illnesses and diarrheal diseases for 5%. In total, 4429 (1.1%) were hospitalized. Gastrointestinal disease risk, including cholera, is high because of potential contamination of water and food. In addition, vaccination against cholera is no longer considered adequate or even feasible in this context [72].

The Ashura MG at Karbala is an increasingly popular religious event in Iraq with about three to four million Muslims from within and outside Iraq. In 2010, a cross-sectional study conducted in three public hospitals at Karbala city showed that

about 80% of the 18,415 consultations were at emergency rooms. Febrile illness was recorded seven times more frequently during this event compared to previous events, in relation to an eight-fold increase in the population in the area during the event [73].

Other notable events include the Moulay Abdellah Amghar Moussem, an 8-day annual gathering in Morocco, that documented an increase of gastrointestinal diseases from 11 to 14% between 2009 and 2010 [74]. During the 2010 anniversary of the death (Urs) of Baba Farid, an annual MG in Pakpattan, Pakistan, 58% of 5918 people seen at 15 healthcare facilities were affected by communicable diseases, including 26% gastrointestinal illnesses and 21% RTIs [75]. Also in 2010, a cross-sectional study of 700,000 attendees to the 5-day Eid Al Adha holiday, Aqaba (one of the largest Muslim MGs in Jordan), identified 23% and 33% increases in emergency department attendance and hospital admissions, respectively; however, no food poisoning outbreaks were reported [76]. Unlike the syndromic surveillance data mentioned above that lacked reliable identification of the responsible pathogen, *S. enterica* serotype typhimurium was determined to cause 64 cases of gastrointestinal illness among 9000 participants in a Christian religious festival in Hamilton County, Ohio; the outbreak was associated with the consumption of pulled pork prepared in a private house and sold at the festival [77].

Large-Scale Open-Air Festivals (Table 1)

Although numerous gastrointestinal and respiratory outbreaks have been documented at large-scale open-air festivals, particularly music festivals, with thousands of participants, these events are probably neglected, in terms of public health attention, as well as surveillance and prevention of infectious disease strategies, compared to other categories of MGs [78]. Since this review was published, several outbreaks were reported in the context of festivals.

Between July 10 and 24, 2013, during the annual independence celebrations in Kiribati, the Kiribati Syndromic Surveillance System reported an increase in children presenting with severe diarrhea due to Rotavirus. In total, 1118 cases of gastroenteritis were reported and 6 (0.5%) died among 103 (9.2%) hospitalized. Most of them (93.4%) were younger than 5 years of age [79].

An outbreak of measles with 44 cases identified at an international dog show occurred in November 2014 in Slovenia, where measles virus had not been circulating for many years. Twenty-three persons were infected there and 21 were presumable secondary and tertiary cases. Most cases (39) were adults. Five were unvaccinated children [80]. Also, a multi-state measles outbreak that caught global attention occurred at the Disney theme parks in California, USA [81].

The 23rd World Scout Jamboree (WSJ) in Yamaguchi, Japan, from July 28 to August 8, 2015, was a MG attended

by more than 33,000 participants from 155 countries. The event is designed for scouts aged 14 to 17 years to live together, experience diverse cultures, and take part in recreational activities. In this event, six cases of invasive meningococcal disease related to the WSJ were reported, affecting 19.5 per 100,000 WSJ attendees, far exceeding the annual incidence rate in Japan in 2014 (0.03 per 100,000 population) [82•].

Finally, an outbreak of measles (52 cases) was reported at music and art festivals in England and Wales between June and October 2016. Almost half of the cases occurred in participants aged 15 to 19 years. Several people who contracted measles at a festival later attended another festival when they were contagious, resulting in multiple, interconnected outbreaks. Only one confirmed case was fully vaccinated. Forty-two were not vaccinated. Nine cases were not fully vaccinated, or their immunization status was unknown [83].

Sport Events (Table 3)

A review of outbreaks at large sport events including the Summer and Winter Olympics, FIFA world cup and the EURO football cup from 1984 through 2015 found little evidence for infectious outbreaks with the exception of 36 cases of influenza among participants to the Winter Olympiad in Salt Lake City in 2002 and a small outbreak of gastrointestinal disease affecting a single team during the pre-race sailing competition in Brazil in 2015, prior to the 2016 Olympics [84••].

An epidemic of measles occurred during the XXI Olympic Winter Games that were held in February 12–28, 2010, in Vancouver, Canada, with 82 cases [85]. Another epidemic of measles was noted during the 16th edition of the Italia Super Cup, international junior football tournament in Rimini, Italy, from June 2nd to 5th, 2011. Most ill individuals had not been vaccinated [86].

During the London 2012 Olympic and Paralympic Games, no major public health incidents occurred. Only a few outbreaks of gastrointestinal and respiratory infections were recorded during this period. No food-borne illness was directly linked to a Games venue, despite the tendency for those reporting them to label them as such [87]. During this event, 289 Olympic visitors were followed for sexually transmitted infections (STI), 47 new STI diagnoses were made including 15 non-specific genital infection, eight chlamydia, and eight

genital warts (first episode) diagnoses. There were no new HIV or syphilis diagnoses [88].

During Euro 2012 European Football, according to national data from Ukraine, 1299 cases of acute gastroenteritis occurred in host cities, but daily notifications remained consistently below the epidemic threshold determined by Ukraine. Similarly, 109 measles cases were reported in the host cities during the tournament, only one of which occurred in a foreign visitor. This number represented about 10% of the new cases reported throughout Ukraine during the same period [89].

During the European Youth Olympic Festival in Utrecht, the Netherlands, in 2013, a prospective cohort study was conducted among 2272 participants from 49 countries. Forty-six cases of diseases were reported. Infection was the most commonly reported cause of illness (56.5% overall) with 43.5% patients reporting gastrointestinal symptoms and 26.1% respiratory symptoms [90].

Among the 2788 athletes in the Sochi 2014 Olympic Winter Games, a total of 249 illnesses were reported, resulting in an incidence of 8.9 illnesses per 100 athletes (95% CI 7.8 to 10.0). Most ill athletes suffered from respiratory symptoms (63.9%), followed by gastrointestinal symptoms (11%) with 58% caused by infections [91]. Only three cases of dengue fever were confirmed at the 2014 FIFA World Cup [92].

A recent multinational *Salmonella* outbreak was reported at an international youth ice hockey competition in Riga, Latvia in 2015 [93].

Among 11,274 athletes from 207 countries participating to the Rio de Janeiro 2016 Olympic Summer Games, 613 illnesses were reported, resulting in 5.4 illnesses per 100 athletes. Two hundred two individuals (47%) presented with respiratory symptoms and ($n = 131$; 21%) gastrointestinal symptoms with 56% ($n = 346$) due to infections [94]. Dengue case count was negligible and no case of Zika virus was detected [95, 96].

More recently, the Pyeong Ghang 2018 Winter Olympiad may have been hindered by a norovirus outbreak days before the event commenced. This outbreak affected mainly security staff for the games rather than athletes or visitors [97].

Conclusion

This review has some limitations. It was limited to articles written in English, which may have been a source of bias. There was a significant heterogeneity in the studies in relation to the populations studied, the clinical criteria for syndromic surveillance and the diagnostic methods applied.

Infectious diseases at MGs are dominated by respiratory tract and gastrointestinal infections. Meningitis outbreaks were also reported in some instances. Inter-human transmission of airborne diseases is favored by the temporal and spatial concentration of people. Because social distancing and contact

Table 3 Sport events—key points

- Events: Summer and Winter Olympics, FIFA world cup, EURO football cup
- Population size: variable 1–6 million attendees at largest events
- Outbreaks of respiratory tract infections have been reported, notably measles and influenza
- Gastrointestinal infections and diarrhea due to *Salmonella spp.* and norovirus have been recorded.

avoidance are difficult measures to implement in the context of many MGs, individual preventive measures such as cough etiquette, the use of face mask and disposable handkerchiefs and hand hygiene may be recommended. Nevertheless, the effectiveness of these measures has been poorly investigated in the context of MGs. Most available data come from Hajj studies and results are contradictory [98].

Non-compliance with hygiene rules and inadequate sanitation are responsible for fecal–oral transmission of gastrointestinal infections. Public health measures aiming at provision of safe water and food supplies with rigorous quality control are likely the best way to limit the occurrence of gastrointestinal outbreaks at MGs. Planned organization by highly specialized teams of staff is a key element.

It should be noted that many MG-associated diseases are vaccine-preventable, including influenza, measles, mumps, meningococcal, and pneumococcal disease. Mandatory vaccination against meningitis has proven effective in the context of the Hajj. Measles and mumps and meningococcal vaccination status should certainly be verified and updated if needed in young people attending MGs. Influenza and pneumococcal vaccination should be recommended in at-risk individuals participating to MGs. This particularly applies to elderly people participating to religious MGs.

Finally, because of the evidence of circulation of resistant bacteria, at least in the Hajj context, rationalization of antibiotic consumption should be promoted.

Unfortunately, official recommendations for prevention at MGs are lacking, with the exception of the Hajj [99].

Compliance with Ethical Standards

Conflict of Interest Philippe Gautret and Van-Thuan Hoang declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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