



Infectious Diseases and Preventive Measures During Hajj Mass Gatherings: A Review of the Literature

Seyed Mansour Razavi,¹ Masoud Mardani,² and Payman Salamati^{3,*}

¹Department of Community Medicine, Tehran University of Medical Sciences, Tehran, Iran

²Infectious Diseases Department, Shahid Beheshti University of Medical Sciences, Tehran, Iran

³Sina Trauma and Surgery Research Center, Tehran University of Medical Sciences, Tehran, Iran

*Corresponding author: Professor of Community Medicine, Sina Trauma and Surgery Research Center, Sina Hospital, Hassan Abad Sq., Imam Khomeini Ave., Tehran, Iran. Tel: +98-2166757001, Fax: +98-2166757009, E-mail: psalamati@tums.ac.ir

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Abstract

Context: Attention and taking care for communicable diseases are very important in mass gatherings. The aim of this study was to illustrate an overview about infectious diseases distribution among pilgrims in Hajj.

Evidence Acquisition: This was a review article, in which the authors used all papers, which were indexed in PubMed and Irandoc from 2000 to 2015. The following key words were searched in the databases: hajj, infectious diseases, emerging and re-emerging diseases, vaccination, and chemoprevention. Three hundred and fifty-four papers were found and their contents were subsequently reviewed after abstract screening.

Results: The results showed that the most frequent diseases in Hajj were respiratory infections. The most frequent causes of respiratory infections were upper respiratory viral infections and bacterial respiratory infections, respectively. In the recent years, emerging and reemerging diseases, such as Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome due to coronaviruses (MERS - CoV), and Ebola have imposed many stresses on the pilgrims and health policy managers.

Conclusions: In this study, the researchers offered some effective recommendations for vaccinations, chemoprophylaxis, and other preventive measures for pilgrims.

Keywords: Preventive Medicine, Travel Medicine, Vaccination, Communicable Diseases

1. Context

Every year, more than two million Muslims travel to Saudi Arabia from all over the world to perform Hajj rituals (1). Pilgrims are at risk of developing diseases, because of special bio-psycho-socio-spiritual circumstances, such as fatigue due to strenuous body movements, stress, getting away from ordinary conditions of life, overcrowding, and changes of climate, water, food and personal habits (2).

Responsible infectious pathogens obtained from pilgrims were rhinoviruses (3), corona viruses (E229 - SARS - MERS) (4), adenoviruses, influenza A (H3N2), B, H1N1, para influenza viruses, enteroviruses, respiratory syncytial viruses, herpes simplex virus (3, 5, 6), arboviruses (7), Phlebovirus (the cause of rift valley fever) (8), hemorrhagic viruses (Ebola) (9), hepatitis A, E, B and C (10), meningococcal infections (11), *Streptococcus* and *Haemophilus influenzae* species (12), *Bordetella pertussis* (13), *Chlamydia pneumoniae*, *Legionella pneumoniae*, *Mycoplasma pneumoniae*, *Enterobacillus* (12), food poisoning agents (14), *Vibrio cholera* (15), *Bru-*

cella (16), respiratory tuberculosis (17), etc.

In this study, by using relevant published articles and ten years of experience in management of pilgrim's health during Hajj, the researchers evaluated the situation of infectious diseases distributions in Hajj and offered effective strategies to deal with these diseases.

2. Evidence Acquisition

This research searched PubMed and Irandoc (an Iranian credible national database) databases, as well as the words of hajj, infectious diseases, emerging and re-emerging diseases, vaccination and chemoprevention as key words. Categories of infectious diseases in 354 papers were found as follows: respiratory infections 134 articles, meningococcal infections 102 articles, vaccination in hajj 99 articles, gastroenteritis six articles, hepatitis six articles, chemoprophylaxis in hajj four articles, brucellosis two articles, and emerging and re-emerging diseases one article.

All the papers were published from 2000 to 2015. The contents of the papers were subsequently reviewed after abstract screening. The main criterion for the quality of the articles was their indexing in above-mentioned databases. The study had been done in accordance with the rules of the ethical review board of Tehran University of Medical Sciences.

3. Results

3.1. Respiratory Infections

3.1.1. Ordinary Viral Respiratory Infections

Balkhy et al. conducted a study on 500 pilgrims with upper respiratory tract symptoms. The pilgrims were screened for viruses, including influenza A and B, parainfluenza, adenoviruses, Respiratory Syncytial Virus (RSV), Herpes Simplex Virus (HSV), and enteroviruses in this study. Fifty-four patients (10.8%) were throat viral culture positive. Of these cases, 27 patients (50%) had influenza B, 13 cases (24.1%) were infected by HSV, seven cases (12.9%) had been infected with RSV, four patients (7.4%) by parainfluenza viruses, and three cases (5.6%) had infected by influenza A virus. No enteroviruses or adenoviruses were detected. Only 22 cases (4.7%) of the pilgrims had received the influenza vaccine. Furthermore, according to the results of this study, Balkhy et al. estimated that, annually 24000 pilgrims will develop the flu in Hajj (5).

Alborzi et al., in one study conducted on 135 females and 120 males, screened the upper respiratory tract for viruses at the time of return of the pilgrims from the Hajj in Shiraz (a city in southern Iran). Viral pathogens were identified in 83 patients (32.5%) and the frequencies of viruses were as follows: flu virus in 25 (9.8%), parainfluenza virus in 19 (7.4%), rhinovirus in 15 (5.9%), adenovirus in 14 (5.4%), enterovirus in five (2%), RSV in four (1.6%), and co infection with two viruses in one patient (0.4%) (3).

Razavi et al., evaluated 32 370 Iranian pilgrims in one study. They calculated that about 70% of the under studied population had had Influenza Like Illness (ILI) (18).

The frequencies of the responsible viruses in Razavi et al.'s study were reported as follow: adenoviruses 38 (36.2%), rhinoviruses 31 (30%), and influenza type B virus 21 (20%) (12).

According to Razavi et al.'s study, the percentages of Common Cold-Like Syndrome (CCLS) and Influenza Like Illness (ILL) in Hajj, were 47% and 10.7%, respectively (19).

3.1.2. Bacterial Respiratory Infections

Most of the upper respiratory problems were due to infections and among infectious pathogens, in addition to

viruses, bacterial infections are also involved in the development of respiratory diseases. Bacterial infections may be primary or secondary infections, followed by respiratory viral infections.

Razavi et al. discussed about the frequencies and trend of primary or secondary respiratory illnesses during five consecutive years in Hajj. On the basis of this study, the percentages of secondary infections were as follows: exudative pharyngitis (7.76), bronchitis, sinusitis, sino-bronchitis (10%), pneumonia (0.45%), asthma, and super imposed COPD infections (1.9%) (19).

Razavi et al., in another study, reported the frequency of some bacteria in the respiratory tract of the pilgrims with respiratory problems as follows:

Enteric bacilli 19.4%, Chlamydia pneumonia 15.8%, Haemophilus 9.1%, and Streptococcus A, C, and G 8.5% (12).

The risk of pneumonia is high among Hajj pilgrims. Ridda et al. found that *Streptococcus pneumoniae* was present in about 10% of respiratory tract samples of symptomatic pilgrims; with about 20% resistance to penicillin (20).

Every year many pilgrims from different countries with a high incidence of Tuberculosis (TB) travel to Saudi Arabia to perform the Hajj. Some risk factors, such as overcrowding, physical exhaustion, attendance of elderly pilgrims, and co-morbid conditions make them susceptible to infection, or reactivation of latent TB.

In the year 2009, Makkah had the greatest number of TB cases (1648), and the highest TB incidence rate (26 per 100000) compared to all other Saudi Arabia provinces (21).

Spread of Multiple - Drug Resistant (MDR) TB and Extensively Drug - Resistant (ExDR) TB cases are real problems around the world (22) and it will become more important under conditions of population density in Hajj.

Wilder - Smith et al. reported that Tuberculosis is a common infection among hospitalized pilgrims in Hajj. They conducted a prospective study on 357 paired samples to assess the risk of this infection among pilgrims. They measured the immune response to TB antigens using QuantiFERON TB assay, prior to departure and repeated the test, three months after return from the Hajj pilgrimage. According to this study, 149 pilgrims were negative for TB before the journey and 15 (10%) had a significant raised immune response against TB antigens. The authors suggested that pilgrims may be at high risk of acquiring TB infection during Hajj. Therefore, preventive measures should be considered for pilgrims (17).

Al-Orainey et al., suggested that pilgrims, who travel to Saudi Arabia from countries with high prevalence of TB, should be screened with chest x-ray, and those, who travel from countries with low incidence of TB, should be

assessed with Quanti - FERON TB assay before and after the journey (23).

Another bacterial respiratory infection is Pertussis. Wilder Smith et al. conducted a prospective seroepidemiological study on 358 adult pilgrims and reported that 1.4% of the pilgrims had acquired pertussis infection (13).

Nisseria Meningitidis is one of the important bacteria in Hajj, which causes Meningococcal infections. Although meningococcal diseases may manifest in different forms, because, the main origin of the carrier state is throat, we have classified these diseases in respiratory categories.

In an outbreak of meningococcal meningitis among Sudan's pilgrims in Hajj, 196 patients had clinical symptoms and signs of meningitis. In this outbreak, 18.9% had positive culture for *Neisseria meningitidis*. The rate of *N. meningitidis* types were as follows: Type A in 29 (78.4%) patients, type C in three (8.1%), and type W135 was found in five (15.5%) cases (11).

Ceyhan et al., in a cohort study in Turkey, assessed the acquisition of meningococcal carriage in Hajj pilgrims, who had received meningococcal ACWY vaccine after their return to their country in 2010. They illustrated that acquisition of meningococcal carriage, will predominantly occur by serogroup W-135 in pilgrims attending the Hajj (24).

Wu et al. reported three cases of ciprofloxacin - resistant *Neisseria meningitidis* during conduction of a pharyngeal - carriage survey in America. The cases were due to the same serogroup B strain. The authors suggested that acquiring resistance occurred via gene transfer with commensal *Neisseria lactamica* (25).

An international outbreak occurred with W135 *Neisseria meningitidis* among Singaporean pilgrims returning from Hajj 2001 and their close contacts. During this time, in Singapore, this strain was a new emerging problem. After this event, the administration of quadrivalent meningococcal vaccine was introduced (26).

3.2. The Other Infections

Food poisoning/gastroenteritis is a very important health problem in the Kingdom of Saudi Arabia (KSA, especially during the summer months and Hajj season). *Salmonella* species, *Escherichia coli* (*E. coli*) and Norwalk-like viruses are the most important pathogens in this problem. Meat and chicken are the main sources in these conditions (14).

Razavi et al., in a five-year study conducted on 254823 Iranian pilgrims, found that the mean percentage of non-invasive gastroenteritis was reported 2.5% and the rate for invasive gastroenteritis was 0.17% (19).

The last cases of cholera in Hajj were reported in 1989 (15).

Every year, a few million heads of sheep and goats are transported to Saudi Arabia for sacrifice during Hajj from different countries, such as Africa, India, and Australia. Brucellosis due to *Brucella melitensis* is a zoonotic disease, which remains endemic in Saudi Arabia. Uncontrolled importation of animals and poor screening for the disease can cause endemicity of brucellosis in this country. The incidence of human brucellosis was reported about 40 cases per 100000 in 2002, according to a national report of this country (16).

A five-year serological survey for brucellosis antibodies on 14000 serum samples from native domestic animals and imported livestock was reported. The highest incidence of brucellosis (11.6%) was seen in small ruminants, followed by imported animals (2.6%) and lower (1.5%) incidence was found in local livestock sacrificed and very low (1.1%) among other groups during the same Hajj season (27).

In Arafat and Mina (deserts around Mecca), each 100 or more pilgrims spend a few days together in large tents. They share common toilet facilities and if they do not observe health principles, they can be exposed to oral fecal infections, like hepatitis A and E. On the other hand, at the end of the journey, the pilgrims have to shave their hairs by themselves or by street barbers, and re-use of their razors may expose them to hepatitis B or C. Improvement of health education about the risk of these diseases and appropriate immunizations can play an important role in prevention of these diseases (10).

3.3. Emerged and Re-Emerged Diseases

According to Wilde Smith et al., *Neisseria meningitidis* type W135 is an emerging problem, and paying attention to is essential in Hajj (26). This serogroup of NM, emerged in Hajj of 2000 and caused widespread epidemic meningococcal disease, especially among African nations (28).

Emerging of Rift Valley Fever (RVF) is also potentially important in Hajj pilgrimage (10). Rift Valley Fever is a vector - borne virus, which caused a hemorrhagic fever outbreak in the Kingdom of Saudi Arabia (KSA) and Yemen in the year 2000 (8).

Ashshi et al. assessed 1600 pilgrims regarding influenza type A and influenza H1N1pdm09 in Hajj 2010. They analyzed oropharyngeal swabs by real-time Polymerase Chain Reaction (PCR) for these viruses. On the basis of this study, a total of 120 pilgrims (7.5%) had a positive test for influenza A and nine were positive for H1N1pdm09 (16).

The emergence of Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) coronaviruses are also special issues in Hajj rituals, which have caused widespread fear among the population. It seems that both SARS and MERS have an animal origin (4).

The Middle East Respiratory Syndrome coronavirus (MERS - CoV) emerged in the year 2012 on the Arabian Peninsula and caused a severe respiratory disease with considerable confirmed cases. No MERS - CoV was detected among African pilgrims after return from Hajj to their home in Annan et al.'s study. Annan et al., in a cross sectional study conducted on 839 adult African Hajj pilgrims at returning time to their country (Ghana) in 2013, assessed the prevalence of respiratory problems. In this study, 651 pilgrims (77.6%) had respiratory symptoms. The frequencies of these problems were as follows, MERS - CoV in 179 (21.3%), human rhinovirus (HRV) in 141 individuals (16.8%), RSV in 43 individuals (5.1%), and Influenza type A in 11 individuals (1.3%) (29).

MERS - CoV was also reported by Lu et al. (30). Benkoutien et al., in one study, conducted on 129 French pilgrims obtained nasal and throat swab specimens, before and after Hajj in 2013. The frequencies of detected viruses were as follow: rhinovirus (14%), coronavirus E229 (12.4%), and influenza A (H3N2) virus (6.2%). None of the participants were positive for MERS - CoV (1).

Reemergence of Alkhurma (an endemic disease in Saudi Arabia) is also important and should be considered. Alkhurma haemorrhagic fever is an Arboviral disease, which emerged in Saudi Arabia in the 1990s. It must be differentiated from other similar arboviral haemorrhagic fevers, like dengue haemorrhagic fever (7).

In addition to the above - mentioned diseases, health managers in Hajj should be prepared to deal with a possible outbreak of diseases, such as Ebola hemorrhagic fever, yellow fever, and poliomyelitis (9).

3.4. Prevention

3.4.1. Vaccination

Husain et al. studied meningococcal carrier state on 177 participants. They took throat swabs from the pilgrims one week after returning from Hajj. Overall, 163 (92%) of the pilgrims were vaccinated with meningococcal ACWY vaccine and 97 (83%) of them had received one dose of ciprofloxacin before leaving Saudi Arabia. None of them were carriers after return. Therefore, they concluded that meningococcal vaccination before arriving in Saudi Arabia and administration of ciprofloxacin for prophylaxis, before leaving this country will be effective in preventing throat colonization with *Neisseria meningitidis* (31).

Memish et al., in a case series study, conducted on 796 serum samples of various Hajj pilgrims, evaluated four meningococcal serogroups (A, C, W, and Y). They found that 98.2% of pilgrims had received quadrivalent meningococcal vaccine in the last three years before arrival to Kingdom of Saudi Arabia and concluded that the majority of pil-

grims were vaccinated and protected against serogroups A, C, W, and Y of meningococcal infections (32).

Furthermore, Memish et al., in a Case series study on Saudi citizens, foreign pilgrims, and immigrants showed that following the introduction of the ACWY vaccine in Hajj 2002, the incidence of Invasive Meningococcal Disease (IMD) decreased (33).

In another cohort study conducted on 5235 nasopharyngeal samples of adult pilgrims from 22 countries, the authors showed that all of the understudied pilgrims were vaccinated against meningococcal infections, and quadrivalent vaccine had been used for 93% of them (34).

Robert Read et al., reported that a quadrivalent glycoconjugate vaccine reduced pharyngeal meningococcal carrier state in university students aged 18 to 24 years old in the UK. They concluded that it might affect transmission of the disease when widely used (35).

Influenza is a common disease and administration of vaccine is recommended for prevention of this disease in over the 50 - year - old individuals.

In Razavi et al.'s study, conducted on 32370 Iranian pilgrims, a total of 3465 pilgrims (10.7%) were vaccinated against influenza before departure. The incidence of ILI among vaccinated pilgrims against influenza was about 56% and among those not vaccinated was 72% ($P < 0.001$), with Odds Ratio (OD) of 0.50; thus, the efficacy of the influenza vaccine in this study was 50% (18).

In another study, Dabiran et al. suggested that high-risk groups should be vaccinated with combination of flu and pneumovax-23 vaccines in Hajj. The rate of high-risk groups was estimated as 25.6% of Iranian pilgrims. These individuals were afflicted with diseases, such as diabetes, cardiovascular diseases, hypertension, asthma, and COPD, and a number of pilgrims older than 65 years old had underlying disabilities (2, 36).

To deal with pertussis - induced problems, researchers recommend that acellular pertussis vaccine for the pilgrims should be administered before Hajj (13). In addition, hepatitis A and B, typhoid, and Polio vaccines are also recommended (37).

3.4.2. Chemoprophylaxis

Balkhi et al., in their report recommended that the influenza vaccine and antiviral drugs (e.g. oseltamivir) for prophylaxis should be considered as a priority for those attending the Hajj pilgrimage (5).

Alborzi et al. studied meningococcal carriage before and after hajj among two groups of Iranian pilgrims. The first group, consisted of 674 randomly selected Iranian pilgrims, and the second group included 123 pilgrims, who had received 500 mg of ciprofloxacin 24 hours before returning from Hajj. In this study, in the first group, the

prevalence of carriage was unchanged and in the second group, that had received ciprofloxacin, the carrier state became zero (38).

3.4.3. The Other Ways of Prevention

Wang et al. suggested that use of standard facemasks in preventing viral respiratory tract infections at mass gatherings will be useful and effective (39).

Middle East is a known area of the world, in which zoonosis is prevalent. In this area, consumption of raw dairy products, such as raw camel milk, may be associated with zoonotic infections, such as Brucellosis. Therefore, it is recommended that pilgrims should avoid consumption of unpasteurized dairy products, especially raw camel milk (40).

4. Discussion

The most common problem in Hajj rituals is respiratory illness. What remains to be elucidated is the main cause of this illness.

Razavi et al. in a cross-sectional study evaluated 130 Iranian volunteer pilgrims (two paired and 260 serum samples) for the levels of serum immunoglobulin A, M, G, and E, gamma interferon Interleukin (IL)-4, Nitro Blue Tetrazolium test (NBT) before and after the Hajj ritual. They concluded that significant increase of IgM and gamma interferon after travel, as well as, decreased NBT function can represent infectious processes of respiratory illnesses, while no significant changes in IgE and IL-4 refuse allergic causes of these problems. Therefore, the probability of interfering infections as the cause of respiratory illnesses in Hajj is more than allergies (41).

Another important question is whether vaccination against influenza prevents respiratory infections.

The effectiveness of this vaccine among Hajj pilgrims was not confirmed in some studies (42).

This indicates that research should also consider other organisms as the etiologic pathogens of respiratory problems, such as adenoviruses, respiratory syncytial viruses, Streptococcus, Hemophilus species, gram-negative bacilli, Legionella pneumophila, and Chlamydia (43, 44).

Dabiran et al., in one study, suggested that high-risk groups should be vaccinated with combination of flu and pneumovax-23 vaccines in Hajj (45).

According to Ridda's report, the most prevalent pneumococcal serotypes are 23F, 6B, 19F, 18C, 4, 14, and 19A, and 90% of these serotypes will be covered by 23-valent pneumococcal polysaccharide vaccine. Therefore, the pneumococcal vaccine can be used in Hajj, at least for high risk

groups, yet, since all pneumonia that occur during hajj are not Pneumococcal pneumonia, researchers should also consider the other preventive measures, such as reducing environmental pollutions, smoking cessation, and vaccinations by flu and pertussis vaccines (20).

Regarding the control of diarrheal infections in Hajj, fortunately, at present, facilities for fighting against food poisoning and diarrheal diseases are more accessible to health authorities. Exemplary successful Iranian experiences in the control of diarrheal diseases in Hajj, are setting up a central kitchen and exclusive use of the bottled water during the journey. In addition, it seems that mechanization of the altars (the places of sacrificing animals in rituals) in Mecca, were effective measures to control diarrheal diseases and zoonosis, such as brucellosis. However, despite obvious changes, further investigations are still required.

The current researchers recommend the establishment of a mass gathering department within health service system of all countries, which send pilgrims to Hajj, as an appropriate method to monitor the pilgrims' status before the journey and track primary and secondary cases after coming back to their country (45). For preventing gastrointestinal problems, hand hygiene practice (e.g. hand washing) is strictly recommended. Furthermore, proper training and health education of the public in general, especially food handlers, are needed.

The final important point is that because of the presence of vast variety of infectious agents, those, who are responsible for the security of Hajj pilgrims or other mass gatherings, must place the bio-terroristic actions under strict care.

The current study had a few limitations. The researchers only searched PubMed and Irandoc databases from 2000 to 2015. The authors suggest further research on this topic, reviewing other databases for different periods of time.

In conclusion, the authors emphasize on medical examinations and health screening of the pilgrims before the journey, vaccinations, chemoprophylaxis, protective and preventive measures, and also education before and during the rites.

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Footnote

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