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TITLE:

**Mass Gathering events and transmission of RTIs -updates pre and post COVID-19
lockdown**

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Purpose of review: This article reviews the epidemiology and transmission of respiratory tract infections during mass gathering events before and during the COVID-19 pandemic.

Recent findings: Respiratory tract infections (RTIs) of viral aetiology such as influenza, rhinovirus, and coronaviruses (229E, HKU1, OC43) are common in mass gathering events (MGEs). No cases of MERS-CoV have yet been identified in pilgrims during Hajj despite the fact that MERS-CoV continues to circulate in the Middle East. Due to the COVID-19 pandemic, organizers of mass gathering religious and sporting events have implemented risk-based infection control measures and lockdowns that limited transmission of RTIs.

Summary: Large scale RTI outbreaks at MGEs are uncommon due to more robust public health planning, prevention, risk assessment and improved health infrastructures in host countries during the COVID-19 pandemic.

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Key points:

Respiratory tract infections (RTIs) of viral aetiology such as influenza, rhinovirus, and coronaviruses (229E, HKU1, OC43) are common in mass gathering events.

No cases of MERS-CoV have yet been identified in pilgrims during Hajj despite the fact that MERS-CoV continues to circulate in the Middle East.

Due to the COVID-19 pandemic, organizers of mass gathering religious and sporting events have introduced risk-based infection control measures that limited transmission of RTIs.

INTRODUCTION

Emergence of the novel coronavirus (SARS-CoV-2) in Wuhan, China in late 2019, with rapid spread to all continents through international travel, reflected in inadequacies of the current global public health systems [1]. On 30 January 2020, the outbreak was declared by the WHO as a Public Health Emergency of International Concern and the new CoV disease was named as COVID-19 on 11 Feb 2020. On 11 March 2020, the WHO announced the scale of the global outbreak of COVID-19 as having reached a status of pandemic [2]. Mass gathering events (MGEs) provide ideal conditions for transmission of respiratory tract infections (RTIs) between attendees and globalization after their return to home countries. High profile international sporting events such as FIFA World Cups or the Olympics and international religious events such as the Hajj count as MGEs. However, lower profile conferences and other events can also meet WHO's definition of a mass gathering if the number of people it brings together is so large that it has the potential to strain the planning and response resources of the health system in the community where it takes place [3]. The COVID-19 pandemic has posed enormous and unprecedented health, economic, and social challenges to many countries due to implementation of non-pharmaceutical interventions (NPIs) including universal masking, hand hygiene, and social distancing measures aiming at containing or mitigating the spread of the virus in the local community/country. This article reviews the epidemiology and transmission of RTIs during MGEs before and during the COVID-19 pandemic.

EPIDEMIOLOGY

Before COVID-19

MGEs attract people from different parts of the world and enhance the risk of spread of RTIs. RTIs are common in pilgrims attending the Hajj, which is the world's largest recurring annual pilgrimage. A cross-sectional study was conducted in 2013 of 839 adult African Hajj pilgrims

returning to Accra in Ghana, West Africa, to assess the prevalence of respiratory symptom and infections due to Middle East respiratory syndrome coronavirus (MERS-CoV), human rhinovirus (HRV), respiratory syncytial virus (RSV) and influenza A virus (Flu A). Altogether 651 (77.6%) pilgrims reported respiratory symptoms. Altogether 179 (21.3%) of all pilgrims tested positive for at least one of the viruses other than MERS-CoV in, with 22.4% detection in symptomatic vs. 17.6% detection in asymptomatic pilgrims. MERS-CoV was not detected but common respiratory viruses were prevalent, with positive findings for HRV in 141 individuals (16.8%), RSV in 43 individuals (5.1%) and Flu A in 11 individuals (1.3%). Results were positive for more than one virus in 16 (1.9%) individuals, including 14 (1.7%) RSV/HRV co-infections and 2 (0.2%) Flu A/HRV co-infections. Overall 146 (22.4%) of the symptomatic returnees vs 33 (17.6%) of the asymptomatic pilgrims tested positive for at least one respiratory virus in their samples. Thus the prevalence of viral RTIs among Hajj pilgrims in both symptomatic and asymptomatic subjects was high although MERS-CoV was not detected in the tested population [4].

Two studies performed in Saudi Arabia to screen symptomatic pilgrims for RTIs showed a range of microbial etiologies. In the first [5] 132 nasopharyngeal samples were collected from pilgrims presenting with acute respiratory symptoms at the healthcare facilities in the holy sites during the 5 days of the 2014 Hajj season. No MERS-CoV cases were detected in any of the samples. In 50.8% of the cases where viruses were detected, 64.2% of the cases were caused by a single-virus infection while 35.8% were due to the co-infections with up to 4 viruses. The most common respiratory virus was Flu A, followed by non-MERS human coronaviruses, HRV, and Flu B. In the second study [6] during the five days of Hajj, 126 nasopharyngeal swabs from 185 patients (68.11%) tested positive for one or more respiratory viruses by PCR. Among the 126 pilgrims there were 93/126 (74%) with a single virus infection, 33/126 (26%) with coinfection with more than one virus (up to four viruses). Human rhinovirus (HRV) was

the most common (42%), followed by 27 (21.43%) cases of influenza A (H1N1), and 23 (18.25%) cases of influenza A other than H1N1. Twenty-five cases of CoV-229E (19.84%) were detected more than other coronavirus members (5 CoV-OC43 (3.97%), 4 CoV-HKU1 (3.17%), and 1 CoV-NL63 (0.79%). RSV and influenza B 4 (3.17%) for each, and Parechovirus 1 (0.79%). Whether identification of viral nucleic acid represents nasopharyngeal carriage or specific causal etiology of RTI remains to be defined.

Thus it is common for respiratory viruses other than MERS-CoV causing acute respiratory symptoms among pilgrims. The observed high prevalence of influenza viruses highlights the importance of more effective surveillance during the Hajj and requirements of stringent vaccination for all pilgrims [5].

Petersen et al reviewed literature on the prevalence of viral and bacterial infectious diseases with special focus on the Hajj. The prevalence of bacterial and viral infections was found to increase, due to the acquisition of HRV, coronaviruses (229E, HKU1, OC43), flu A H1N1, *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Staphylococcus aureus* during Hajj. No cases of MERS-CoV have yet been identified in pilgrims during Hajj despite the fact that MERS-CoV continues to circulate in the Middle East. RTIs are a major cause of morbidity in pilgrims attending MGEs. The management of severe RTIs consists of investigation and empirical coverage for the most likely pathogens based on syndromic surveillance data from the hosting country and /or other relevant exposure history during MGEs. Pneumococcal and Pertussis vaccines are recommended for Hajj pilgrims [7].

During COVID-19

MGEs are associated with the transmission of COVID-19. Between 6 and 10 March 2020, several MGEs related to the *Falles* festival were held in Borriana, a municipality in the province of Castellon in Spain. A study was conducted to estimate the incidence of COVID-19 and its

association with these MGEs, and to understand the potential risk factors of its occurrence. Between May and June 2020, a retrospective population-based cohort study was carried out by the Public Health Center of Castello´ and the Hospital de la Plana in Vila-real on a representative sample of 1663 people with potential exposure at 6 MGEs. A questionnaire survey was carried out to obtain information about attendance at MGEs and COVID-19 disease. In addition, a serologic survey of antibodies against SARS-CoV-2 was conducted. Altogether 1338 subjects participated in the questionnaire survey (80.5%), and 997 of whom undertook the serologic survey. Altogether 570 cases were observed with an attack rate (AR) of 42.6% with an average age of 36 years, 62.3% being female, while 536 cases were confirmed by laboratory tests, and 514 cases were positive with SARS-CoV-2 total antibodies. Considering MGE exposure, AR was 39.2% (496/1264). A dose-response relationship was found between MGE attendance and COVID-19, (adjusted relative risk [aRR] = 4.11, 95% confidence interval [CI]3.25–5.19). Two MGEs with a dinner and dance in the same building had higher risks. The risk factors associated with the incidence were older age, obesity, and upper and middle class versus lower class while current smoking was protective. The study suggests the significance of MGEs in the COVID-19 transmission that could explain the subsequent outbreak in Borriana [8].

About 30,000 Hasidic and Orthodox Jews travel to Uman, Ukraine, annually during the Jewish New Year to pray at the burial place of the founder of the Breslov Hasidic movement. Many pilgrims come from the north-eastern USA. The global health implications of this MGE were reflected in 2019 when measles outbreaks occurred in the USA and Israel, linked to the pilgrimage. The pilgrimage was cancelled in 2020 as part of the COVID-19 travel restrictions imposed by Ukraine. To prepare for the 2021 event, the National Public Health Institute, the Public Health Center of Ukraine, organized mitigation measures for pilgrims arriving in Uman, and the CDC COVID-19 International Task Force assisted with mitigation measures for

pilgrims coming from the USA. Joint efforts were implemented to support COVID-19 mitigation measures before, during, and after this mass gathering. Predeparture measures included COVID-19 hotline, video and poster education promoting safe celebration, distribution of CDC fact sheets, and negative PCR 72 hrs before entry to Ukraine. Measures in Uman included provision of rapid antigen test kits, hand sanitizer and disposable face masks, limiting capacity in the dining halls and at individual dining tables was limited to 50%, and COVID-19 mitigation banners and posters were available on site of the MGE. The US government imposed COVID-19 mitigation measures for international travelers arriving in the USA, including mask mandates on all US airlines. All air passengers, including US citizens and fully vaccinated persons, were required to have a negative COVID-19 test result within 3 days before date of travel or documentation of COVID-19 recovery in the previous 3 months. COVID-19 incidence rates in Brooklyn, New York, USA, associated with the MGE in Uman, Ukraine, during September 2021 were less than 190/100,000 persons [9].

The European Soccer Championship (EURO) is a popular global sport event. EURO2020 generated a growing media and population interest across the month period, that peaked with large spontaneous celebrations across the country upon winning the tournament. A retrospective study in Italy analysed data from the national surveillance system (indicator based) and from event-based surveillance to assess how the epidemiology of SARS-CoV-2 changed in June–July 2021 and to describe cases and clusters linked with EURO2020. Widespread increases in transmission and case numbers, mainly among younger males, were documented in Italy but none were linked with stadium attendance. Vaccination coverage against SARS-CoV-2 was lower among cases linked to EURO2020 than among the general population. Transmission increased across the country, mainly due to gatherings outside the stadium, where, conversely, strict infection control measures were enforced [including indoor or outdoor mask wearing, physical distancing, limiting live attendance at 25% of total stadium

capacity, established access verification and managed spectator flows, and all spectators >6 yrs old were required to have negative SARS-CoV-2 test performed within the previous 48 hours, vaccination (at least one dose), prior SARS-CoV-2 infection ended within the previous 6 months]. However informal 'side' gatherings were dispersed across the entire country and difficult to control due to increased interpersonal contacts and non-compliance with physical distancing and mask wearing. Targeted communication and control strategies to limit the impact of informal gatherings occurring outside official sites of MGEs should be further developed [10].

Mass indoor gatherings were banned in early 2020 to prevent the spread of SARS-CoV-2. A study was conducted in France to assess, under controlled conditions, whether infection rates among attendees at a large, indoor gathering event would be similar to those in non-attendees, given implementation of a comprehensive prevention strategy including antigen-screening within 3 days, medical mask wearing, and optimised ventilation. The non-inferiority, prospective, open-label, randomised, controlled SPRING trial was done on attendees at a live indoor concert held in the Accor Arena on May 29, 2021 in Paris, France. Participants, aged 18–45 years, recruited via a dedicated website, had no comorbidities, COVID-19 symptoms, or recent case contact, and had had a negative rapid antigen diagnostic test within 3 days before the concert. Participants were randomly allocated in a 2:1 ratio to the experimental group (attendees) or to the control group (non-attendees). The primary outcome measure was the number of patients who were SARS-CoV-2-positive by RT-PCR test on self-collected saliva 7 days post-gathering in the per-protocol population (non-inferiority margin <0.35%). Between May 11 and 25, 2021, 18 845 individuals registered on the dedicated website, and 10 953 were randomly selected for a pre-enrolment on-site visit. Among 6968 who kept the appointment and were screened, 6678 participants were randomly assigned (4451 were assigned to be attendees and 2227 to be non-attendees; median age 28 years; 59% women); 88% (3917) of

attendees and 87% (1947) of non-attendees complied with follow-up requirements. The day 7 RT-PCR was positive for 8 of the 3917 attendees (observed incidence, 0.20%; 95% CI 0.09–0.40) and three of the 1947 non-attendees (0.15%; 0.03–0.45; absolute difference, 95% CI –0.26% to 0.28%), findings that met the non-inferiority criterion for the primary endpoint. Participation in a large, indoor, live gathering without physical distancing was not associated with increased SARS-CoV-2–transmission risk, provided a comprehensive preventive intervention was implemented [11].

CONCLUSION:

The annual Hajj to Saudi Arabia attracts millions of pilgrims from around the world. Influenza, rhinovirus and parainfluenza were the most common viruses detected among pilgrims. Coronaviruses other than MERS-CoV were also detected among pilgrims. The acquisition of MERS-CoV remains very limited and systematic screening of pilgrims showed no infections [12]. Due to the COVID-19 pandemic, organizers of MG religious and sporting events introduced risk-based infection control measures that limited transmission of RTIs. The 2020 and 2021 Hajj were conducted with limited numbers of pilgrims compared to the annual millions of pilgrims. The Tokyo 2020 Olympic and Paralympic Games were cancelled and postponed to 2021. The success of the COVID-19 countermeasures at the 2021 Hajj and 2021 Tokyo Olympics was based on implementing good public health and social distancing measures alongside a comprehensive testing strategy [13]. Concerns about the spread of infectious diseases at MG are often focussed on crowding, lack of sanitation and the mixing of population groups from different places. International sporting events pose a challenge to the control of communicable disease transmission. Despite this, large scale RTI outbreaks at sporting events have been rare in recent decades, particularly since the rise of more robust

public health planning, prevention, risk assessment and improved health infrastructures in host countries [14]. However, large scale controlled studies are required to generate accurate evidence base of the impact of individual public health interventions.

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• *of special interest*

•• *of outstanding interest*

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