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Carriage of *Neisseria meningitidis* in the Hajj and Umrah mass gatherings

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SUMMARY

Meningococcal disease is a serious public health threat, especially during mass gatherings such as Hajj and Umrah which provide optimal conditions for disease transmission. The disease is caused by *Neisseria meningitidis* and transmitted mainly via asymptomatic carriers. A review of the literature on asymptomatic *N. meningitidis* carriage among Hajj and Umrah pilgrims and their household contacts was performed. Carriage studies reported carriage rates to be higher in Hajj pilgrims compared to Umrah pilgrims and that these events promote acquisition of carriage among pilgrims. With some outliers, most studies found carriage rates among pilgrims to be comparable to those in populations under non-epidemic settings. However, these results should be interpreted with caution, taking into account the limitations within the studies identified. A wide variety of *N. meningitidis* serogroups appear to be circulating among Hajj and Umrah pilgrims, with serogroups W135 and B being most prominent. Current Hajj and Umrah meningococcal disease preventative measures do not necessarily prevent carriage and transmission, which may result in local and international outbreaks among susceptible populations. Monitoring carriage states of visitors and local inhabitants in the Kingdom of Saudi Arabia, as well as the implementation of preventive measures that impact carriage, are warranted to reduce the risk of Hajj and Umrah-related meningococcal disease outbreaks.

1. Introduction

Neisseria meningitidis is one of the leading causes of bacterial meningitis globally and can also cause sepsis, pneumonia, and other localized infections.[1] Invasive meningococcal disease remains a serious public health problem affecting up to 1.2 million people annually and leading to between 50 000 and 135 000 deaths worldwide.[2] Even with appropriate treatment, the case fatality rate is high, and the risk of long-term disabling sequelae of meningococcal infection adds to the disease burden, especially in developing countries.[1] In total, 13 serogroups of *N. meningitidis* have been reported, but only six (A, B, C, W135, X, and Y) cause almost all life-threatening disease worldwide.[3,4]

The Kingdom of Saudi Arabia (KSA) hosts over two million Muslim pilgrims annually from all over the world during the Hajj period and several million pilgrims throughout the year for the Umrah religious mass gatherings in the holy cities of Mecca and Medina. The Hajj pilgrimage is held on every 12th month of the Islamic calendar, while the Umrah pilgrimage may be undertaken at any time of the year. These mass gathering events create conditions of overcrowding that are conducive to human-to-human disease transmission, such as meningococcal disease.[5] Hajj and Umrah have been associated with a number of local and international meningococcal disease outbreaks, including a large serogroup A outbreak in 1987 and major serogroup W135 outbreaks in 2000 and 2001.[6–9] Returning international pilgrims carrying *N. meningitidis* were the vehicle for the exportation of the disease outside KSA and also the introduction of new serogroups into other regions of the world, affecting the global epidemiology of the disease.[3,10,11]

A review of the literature on *N. meningitidis* carriage among Hajj and Umrah pilgrims and their household contacts was performed. The rate of carriage of the organism at these mass gatherings and the serogroups circulating among pilgrims and their contacts is reported here. A PubMed search of the relevant literature (up to 2015) was performed with a combination of the following terms:

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'*Neisseria meningitidis*', 'meningococcal', 'carriage', 'Hajj', 'Umrah', 'pilgrims', and 'pilgrimage'. Reference lists of relevant articles were also hand-searched to identify further material.

2. Asymptomatic carriage of *N. meningitidis*

Asymptomatic carriage of *N. meningitidis* was first described in Europe in 1896[12] and occurs in 8–25% of the human population, with adolescents being the major reservoir.[2] Meningococci are spread from person to person through direct contact with oropharyngeal secretions, and asymptomatic carriers are the primary source of *N. meningitidis* transmission under both epidemic and endemic conditions.[1,13] Although asymptomatic carriage of both pathogenic and non-pathogenic strains is common, few carriers develop invasive disease. For the majority of people, carriage is an immunizing process that results in a systemic, serogroup-specific protective antibody response.[1] Vaccination with the polysaccharide vaccines does not prevent the acquisition of carriage, but there is evidence that conjugate vaccines do impact the carriage state.[1,13–15] For instance, the use of monovalent meningococcal conjugate vaccines in routine universal vaccination programs were associated with reductions in carriage and a consequent herd effect, such as reductions of invasive meningococcal disease in unvaccinated age cohorts.[15]

The prevalence of meningococcal carriage differs within and between countries, varying across age groups, serogroup distribution, and over time. The rate is also influenced by contact with cases and the epidemic/endemic situation. For example, the reported prevalence of meningococcal carriage in the USA is 5–10% under non-epidemic conditions.[16] In comparison, a carriage prevalence of between 3% and 30% has been documented for the African meningitis belt.[17] In closed populations, such as among military recruits, carriage can reach levels of 40–80%.[18]

3. Carriage of *N. meningitidis* at the Hajj and Umrah mass gatherings

There are several risk factors associated with meningococcal carriage. These include crowded conditions (e.g., military barracks, dormitories, events), travel to endemic areas, personal behaviors (e.g. kissing, coughing, smoking), and respiratory viruses and Mycoplasma.[6,13,19] In this context, mass gatherings such as the Hajj and Umrah are very relevant. These events are characterized by heavily overcrowded conditions of a pilgrim population originating from diverse geographical areas. These pilgrims all live for extended periods of time in close proximity to each other, with shared facilities, and perform exhausting religious rites. These are optimal conditions for meningococcal exposure and colonization of susceptible individuals and carrier-to-carrier acquisition of strains, as well as increased rate of new carrier acquisition.[6] It is not surprising that a very high prevalence of asymptomatic *N. meningitidis* carriage has been reported at such events, with a rate of up to 86% documented for Mecca pilgrims in 1992.[7]

Local data show that the carriage rate of *N. meningitidis* among the population is higher in cities hosting the Hajj and Umrah mass gatherings compared to other regions of KSA. Two such studies, one performed by Ashoor and Turkestani[20] and the other by Kholeidi et al.,[21] both outside the Hajj pilgrimage season, showed the carriage rate among locals from Mecca to be higher than that in those from Medina (the second most holy city for Muslims) and also higher than that among local inhabitants from the city of Riyadh, where there is no contact with pilgrims; rates were 1.1%, 0.1%, and 0%, respectively. Another study conducted during the 2001 pilgrimage found the carriage rate among the local population of Jeddah and Mecca to be 4.7%.[22] Serogroup W135 accounted for 40% of the meningococci isolated, while only 6.5% were serogroup A and 13% were serogroup B. This is not surprising given that serogroup W135 was the outbreak strain in the 2000 and 2001 Hajj seasons.[6,23]

3.1. *Rate of* N. meningitidis *carriage among Hajj pilgrims*

A number of *N. meningitidis* carriage studies have been conducted on Hajj pilgrims (Table 1). Most of these studies have reported an overall carriage rate of 5–10%, which is comparable to those found in populations in non-epidemic settings.[16] However, there are some outliers. For example, studies among pilgrims from the USA in 2001[24] and Singapore in 2002[25] found significantly lower carriage rates of only 1.9% and 1.7%, respectively. More recently, Benkouiten and colleagues did not detect *N. meningitidis* carriage among 298 French pilgrims sampled before and after the 2013 Hajj,[26] while Ceyhan et al. reported a high (18.7%) overall carriage rate among Turkish pilgrims attending the 2010 Hajj.[27] Several studies have also documented the effect of Hajj on the acquisition of carriage (Table 1), the majority of which found that the pilgrimage increased *N. meningitidis* carriage. However a number of studies have found carriage rates among pilgrims post-Hajj to be lower than those pre-Hajj, even among the same cohorts of pilgrims.[25,28,29]

The above findings however need to be put into context considering a number of important factors. First, most of these carriage studies were conducted in small cohorts of country-specific pilgrim populations.

Second, given the demographics of Hajj pilgrims, carriage studies during the event were conducted on a mostly adult population. The *N. meningitidis* carriage rate differs with age, with a rate of <3% in children younger than 4 years, increasing to 24–37% in the age group 15–24 years, and decreasing to <10% in older age groups.[13]

Third, most of these carriage studies were conducted during, or soon after, the 2000 and 2001 international Hajj-related meningococcal disease outbreaks. Hence, they were performed at a time when a number of meningococcal disease prevention measures had been introduced, both in Saudi Arabia and internationally, to prevent future outbreaks. Of note is the introduction of compulsory meningococcal vaccination with the quadrivalent (A/C/W/Y) vaccine by 2002 for all pilgrims before attending Hajj.[6] The Saudi recommendations do not yet specify which vaccine technology should be used. Although licensed since 2005, the quadrivalent conjugate meningococcal vaccine is still not used universally by all countries participating in Hajj.[30] In most of the Hajj carriage studies the majority of pilgrims, if not all of them, received meningococcal vaccination (Table 1). Vaccination using the polysaccharide quadrivalent vaccine does not prevent carriage, nor does it eradicate existing meningococcal carriage.[1,27] The effect of the polysaccharide vaccines on colonization and the transmission of the organisms are transient or negligible.[13] However, vaccination protects pilgrims from invasive disease and has been linked to a significant reduction in cases of disease during Hajj.[8] The effect of vaccinating the entire Hajj population led to a reduction in invasive disease, which would have impacted carriage rates.[31,32]

Fourth, antibiotic use among pilgrims was found to vary between studies, ranging from 13% to 59% (Table 1). This factor is partially relevant for studies reporting carriage rates in pilgrims post-Hajj. Antibiotic use is common during Hajj and can lead to a reduction or elimination of *N. meningitidis* carriage. In one study, a single dose of ciprofloxacin (500 mg) given to a cohort of Iranian pilgrims 24 h before leaving Hajj reduced the carriage rate from 8.1% before Hajj to 0% post-Hajj.[29] In another study, *N. meningitidis* carriage was not detected post-Hajj among 177 Kuwaiti pilgrims, 83% of whom received one dose of ciprofloxacin before leaving Hajj.[33]