International Journal of Infectious Diseases xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Meningococcal carriage in high-risk settings: A systematic review

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ARTICLE INFO

Article history:
Received 29 March 2018
Received in revised form 29 May 2018
Accepted 30 May 2018
Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keywords:
Neisseria meningitidis
Meningococcal
Carriage
University
Hajj
Military

ABSTRACT

Background: Historically, semi-closed populations have had high rates of meningococcal carriage and have experienced recurrent outbreaks. As such, these high-risk groups are recommended for targeted vaccination in many countries.
Methods: A systematic review of eight databases and Google Scholar forward citations was conducted to characterize serogroup-specific meningococcal carriage in university students, military personnel, and Hajj pilgrims from 2007 to 2016.
Results: A total of 7014 records were identified and 22 studies were included. Overall carriage ranged from 0.0% to 27.4% in Hajj pilgrims, from 1.5% to 71.1% in university students, and from 4.2% to 15.2% in military personnel. Among serogroups A, B, C, W, X, and Y, serogroup B was most prevalent in Hajj pilgrims, B and Y in university students, and B, C, and Y in military personnel. 'Other' serogroups were more prevalent in university students than Hajj pilgrims or military personnel. Risk factors for carriage varied by setting. Among Hajj pilgrims, a high endemicity in the country of origin increased the risk of carriage, while smoking, male sex, and frequently attending parties increased the carriage risk for university students. Similarly, smoking increased the carriage risk for professional soldiers. Data gaps remain for many regions.
Conclusions: Preventative vaccination policies for high-risk groups should be based on current disease data in individual countries, supplemented by carriage data. Meningococcal carriage studies and disease surveillance are critical for determining the local epidemiology, populations responsible for disease transmission, and the need for targeted vaccination.

Introduction

Invasive meningococcal disease (IMD) is a severe bacterial infection caused by *Neisseria meningitidis*, a Gram-negative bacterium often carried harmlessly in the pharynx of humans. IMD commonly presents as meningitis and septicaemia, but can more rarely cause diseases such as septic arthritis and pericarditis (Pace and Pollard, 2012). Despite advances in medical care, IMD case fatality is approximately 10–15%, and debilitating sequelae, such as amputation and neurological impairment, can result from infection in an estimated 10–15% of survivors (Pace and Pollard, 2012; Edmond et al., 2010). The incidence of IMD varies globally, with the highest burden in the African meningitis belt, young children and adolescents, and immunocompromised individuals (Harrison et al., 2009; McNamara et al., 2017a; Snydman et al., 2014; Jafri et al., 2013). Additionally, semi-closed populations are at high risk of infection, with numerous outbreaks reported among university students, Hajj/Umrah pilgrims, and military recruits (Brundage et al., 2002; Jean-François et al., 2002; National Foundation for Infectious Diseases (NFID), 2017). As such, preventative vaccination programmes have been introduced in these settings (National Foundation for Infectious Diseases (NFID), 2017; Yezli et al., 2016a; Michael et al., 2015).

Historically, carriage of the bacterium was estimated to occur in approximately 10% of the general population, with most people becoming a carrier multiple times in their lifetime (Cartwright et al., 1987). Transmission of the meningococcus occurs through droplet spread and thus through close contact with a carrier of *N. meningitidis* or an infected individual. Studies estimate that carriage peaks in early-to-late adolescence, depending on the region (Cooper et al., 2017; Christensen et al., 2010), indicating that persons of these ages are likely important transmitters of disease. Social behaviours, recent respiratory infections, and

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https://doi.org/10.1016/j.ijid.2018.05.022

environmental factors can also increase an individual's risk of carriage (MacLennan et al., 2006; Mueller et al., 2008).

Six of the 12 capsular groups of *N. meningitidis*—A, B, C, W, X, and Y—cause the majority of disease cases, and their distribution varies globally. There are vaccines currently available targeting five of the 12 meningococcal serogroups, i.e. A, B, C, W, and Y, although the 'B' vaccines include recombinant proteins or recombinant proteins plus outer membrane vesicles, not capsular polysaccharides like the other vaccines. While conjugate vaccines have induced herd immunity for some serogroups, in part through a reduction in carriage levels (Trotter and Maiden, 2009), it is as yet unclear whether the broad-protection MenB vaccines will have similar effects (Donnelly et al., 2010; Pajon et al., 2016). Knowledge of the locally circulating serogroups and disease incidence is key for appropriate vaccine recommendations.

Hitherto, reviews have focused on select regions/populations or have provided prevalence-only carriage data, and an updated carriage review is warranted (Soriano-Gabarro et al., 2011a; Trotter and Greenwood, 2007; Agier et al., 2017; Zhang et al., 2007; Yezli et al., 2016b). No review describing serogroup-specific carriage in the three high-risk settings of university students, military personnel, and Hajj/Umrah pilgrims at a global level could be identified. Understanding the serogroups carried by high-risk populations such as these is important in gaining a better understanding of disease transmission and potential populations for vaccination (Borrow et al., 2016; Vetter et al., 2016). Therefore, the aim of this review was to summarize the carriage studies with serogroup data conducted in these defined high-risk settings for the period 2007–2016.

Methods

Search strategy and data sources

A systematic review of the literature was conducted to identify serogroup-specific meningococcal carriage studies conducted between January 1, 2007 and December 31, 2016 in university students, military personnel, or Hajj/Umrah pilgrims (PROSPERO number CRD42017074671). Two authors (MEP and RM) searched six databases (MEDLINE, Embase, Global Health Database, WHO Global Health Library, Web of Science, Current Contents Connects) in July 2017. Search terms were developed for MEDLINE (Supplementary material, Table S1) and adapted for the remaining databases. Two Chinese literature databases (CNKI and Wanfang) were searched in June 2017 by a native speaker (YL), who translated the Chinese search terms from the English version. Google Scholar forward citations, relevant conference abstract lists, and references of identified studies and reviews were also searched. Forward searches on Google Scholar and conference abstracts were searched again in January 2018 as an update. No exclusion was made based upon language, and Google Translate was used to assist in the screening of foreign language articles. If questions remained, native speakers were contacted for assistance in translation.

Inclusion and exclusion criteria

Studies were considered for inclusion if they reported serogroup-specific pharyngeal carriage in asymptomatic individuals in a high-risk setting (Hajj/Umrah pilgrimage, university, or military), provided a clear geographic location for the participants, and were sampled only from the setting in question.

Studies were not eligible for inclusion if they were not in humans, only provided disease data, were carriage studies among cases or close-contacts of cases, only reported secondary data, were case studies, commentaries, or reviews, did not specify the geographic location or included global samples together, had unclear reporting of serogroups or participants sampled, only tested for one serogroup, could not be obtained and the author could not be contacted, or serogrouped or reported less than 75% of positive carriage specimens.

Data collection and management

Studies identified were imported into EndNote, where duplicates were removed. Two authors (MEP and RM) independently screened the titles and abstracts of all studies and the relevant full-text articles from the English databases. Data from studies selected for inclusion were independently extracted into Microsoft Access by two authors (MEP and RM). One author screened the Chinese articles (YL) with input from another (MEP). Any disagreements in eligibility or extractions were discussed and a consensus reached before moving forward.

Quality assessment

Studies identified for inclusion were assessed for quality using a modified Joanna Briggs Institute Checklist for Prevalence Studies. The quality of studies was ranked as high (0–3 no/unclear), medium (4–6 no/unclear), or low (7–9 no/unclear).

Data analysis

A narrative synthesis was performed for identified studies. Results were reported by high-risk setting and World Health Organization (WHO) region. Meta-analyses of serogroup carriage prevalence were deemed inappropriate due to heterogeneity between study populations and settings and/or insufficient data by WHO region.

Results

A total of 7014 records were identified and 331 were screened in full. Of these, 23 met the inclusion criteria (Figure 1). Three studies were among Hajj pilgrims, 14 among university students, five among military personnel, and one among university students and military personnel. Ten studies sampled participants in the high-risk settings of interest and reported serogroup-specific carriage but did not meet other eligibility criteria (Supplementary material, Table S2). Most studies received medium-level quality scores, primarily due to underreporting of study or population characteristics (Supplementary material, Table S3). Since no methodological 'gold standard' exists for carriage studies, no studies were excluded from the review based on quality scores.

Hajj pilgrims

Three studies among Hajj pilgrims met the inclusion criteria (Azeem et al., 2017; Ceyhan et al., 2013; Memish et al., 2017), and no eligible studies were conducted among Umrah pilgrims. Each of the included studies investigated serogroup-specific carriage among pilgrims both before and after the Hajj. However, the location of the 'before' and 'after' time point was inconsistent between studies and was a combination of swabbing pilgrims in their home countries and/or while in Mina. In total, 2774 pilgrims were sampled, representing 14 nationalities. One study included was a cohort study among Turkish pilgrims in 2010 (Ceyhan et al., 2013), while the other two studies were repeat cross-sectional studies with a nested cohort, one among Australian pilgrims in 2014 and the other among pilgrims from 12 countries in 2014 (Azeem et al., 2017; Memish et al., 2017).

Please cite this article in press as: M.E. Peterson, et al., Meningococcal carriage in high-risk settings: A systematic review, Int J Infect Dis (2018), https://doi.org/10.1016/j.ijid.2018.05.022