

Factors associated with *Staphylococcus aureus* nasal carriage among healthy people in Northern China

X. Yan^{1,5}, Y. Song², X. Yu³, X. Tao^{1,5}, J. Yan³, F. Luo², H. Zhang^{1,5}, J. Zhang³, Q. Li², L. He^{1,5}, S. Li², F. Meng^{1,5}, J. Zhang^{1,5} and H. Grundmann⁴

1) State Key Laboratory for Infectious Disease Prevention and Control, National Institute for Communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, 2) Chaoyang Center for Disease Control and Prevention, Beijing, China, 3) Heilongjiang provincial Centre for Disease Control and Prevention, Harbin, China, 4) Department of Medical Microbiology, University Medical Center Groningen, Rijksuniversiteit Groningen, The Netherlands and 5) Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, Hangzhou, China

Abstract

There is still limited knowledge about the prevalence and risk factors of nasal carriage for *Staphylococcus aureus* among healthy carriers in China. We investigated 2448 healthy adults (≥ 18 years of age) from Beijing ($n = 1530$) and Harbin ($n = 918$) by nasal screening. Participants were checked for carriage of *S. aureus*, and health-related and demographic information between 2009 and 2011 was gathered. A total of 403 *S. aureus* (403/2448, 16.5%) were recovered, 8 of which were methicillin resistant (8/2448, 0.33%). Three factors were independently associated with *S. aureus* nasal carriage: Harbin as city of residence (odds ratio (OR) = 2.0, 95% confidence interval (CI) = 1.41 to 2.85), age ≤ 24 years (OR = 1.77, 95% CI = 1.30–2.44) and non-Han ethnicity (OR = 1.58, 95% CI = 1.05 to 2.38). On the basis of population genetic analysis using multiple locus variable number of tandem repeats analysis (MLVA) and *spa* typing, MLVA complex (MC) 398 and MC5a were the most prevalent clonal lineages in this collection. In multivariate models, residing in Harbin (OR = 1.77, 95% CI = 1.07–2.92) and having household members in the healthcare profession (OR = 3.69, 95% CI = 1.14–11.92) were factors associated with carriage of clonal lineage MC398. On the other hand, female sex (OR = 3.15, 95% CI = 1.35–7.33) and a history of chronic liver disease (OR = 16.93, 95% CI = 2.91–98.59) were associated with the clonal lineage MC5a. The three most common *spa* types were t571 (10.9%), t189 (9.9%) and t701 (7.2%). These findings provide insight into the determinants of nasal carriage and ecology for some of the most successful strains of *S. aureus* among healthy people in Northern China.

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Keywords: Epidemiology, healthy carriers, nasal carriage, *spa* typing, *Staphylococcus aureus*

Original Submission: 24 April 2014; **Revised Submission:** 20 July 2014; **Accepted:** 19 August 2014

Editor: G. Lina

Article published online: 29 October 2014

The first three authors contributed equally to this article, and all should be considered first author.

Corresponding author: H. Grundmann, Department of Medical Microbiology, University Medical Center Groningen, Rijksuniversiteit Groningen, Hanzeplein 1, 9713 GZ Groningen, The Netherlands

Corresponding author: J. Zhang, State Key Laboratory for Infectious Disease Prevention and Control, Chinese Center for Disease Control and Prevention, 155 Changbai Road, Changping District, Beijing 102206, China

E-mails: zhangjianzhong@icdc.cn (J. Zhang), h.grundmann@umcg.nl (H. Grundmann)

Introduction

Staphylococcus aureus is a leading cause of hospital-associated and community-onset bacterial infections in humans. The most important factors which contribute to the success of *S. aureus* as a pathogen are believed to be the ability to persist as a commensal, resistance to multiple antimicrobial agents and the diverse repertoire of virulence determinants [1,2].

Staphylococcus aureus can colonize multiple sites of the human body, but the anterior nares appear to be the main

ecological niche [3]. In healthy whites, it is estimated that 20% are persistent carriers and an additional 30% intermittent carriers, while approximately 50% are noncarriers. There are three lines of evidence that support the view that *S. aureus* nasal carriage is associated with a higher chance to develop staphylococcal infections. First, the rates of infection are higher in persistent carriers than others [4]. Second, high-resolution molecular typing using pulsed-field gel electrophoresis has shown that infecting strains of *S. aureus* were indistinguishable from carriage isolates previously isolated from the external nares of patients who later developed an invasive infection [5,6]. Finally, eradication of this microorganism is regarded as an effective means for reducing infections in surgical and dialysis patients [4,7].

Over the past decade, reports about community-onset methicillin-resistant *S. aureus* (MRSA) infections have raised concern about the public health implications of *S. aureus* transmission among healthy individuals. Therefore, unravelling the risk factors for carriage of *S. aureus* is crucial for understanding the transmission potential of both MRSA and methicillin-sensitive *S. aureus* (MSSA). To date, there have been only few reports on the prevalence and the risk factors of *S. aureus* nasal carriage in China. Previous studies revealed 15.4% to 23.1% *S. aureus* nasal carriage in Chinese medical students from different regions, of which 3.0% to 9.4% were MRSA [8,9]. Another study revealed a similar nasal carriage rate (20%) in 1044 military volunteers from Beijing with no MRSA strains identified [10]. Both studies focused on populations that typically lived under crowded conditions and thus had higher opportunities for transmission. It still remains unclear whether carriage rates and risk factors among the Chinese general population are in the same range. We therefore performed a population-based survey to determine the prevalence and risk factors of *S. aureus* nasal carriage in two cities in Northern China.

Materials and methods

Population and study design

A cross-sectional study was conducted in two northern cities, Beijing and Harbin. Individuals presenting for mandatory occupational health screenings from food and public service industries as well as public health workers were chosen as healthy volunteers for the present survey. Between 2009 and 2011, 1530 and 918 nasal swabs were sampled in Beijing and Harbin, respectively. A self-administered questionnaire was completed by each volunteer to collect pertinent demographic and medical information, as well as factors that are potentially related to *S. aureus* nasal carriage and transmission as identified in the literature.

Bacterial strains

Nasal swabs from both nares were enriched in tryptic soy broth (Oxoid, Basingstoke, England, UK) with 7% NaCl at 37°C for 24 hours, plated onto mannitol salt agar (Oxoid) and cultured at 37°C for 24 hours. Presumptive *S. aureus* colonies were confirmed by colony morphology, Gram staining, catalase production, coagulase production using the Slidex Staph Plus kit (Murex Biotech, Kent, France) and polymerase chain reaction (PCR) for the *nuc* and *mecA* genes [11].

Molecular typing and Panton-Valentine leukocidin (*pvl*) gene detection

Multiple locus variable number of tandem repeats analysis (MLVA) was carried out for all 403 isolates, and representative strains of each MLVA complex (MC) were analysed by multi-locus sequence typing (MLST) in a previous unpublished study. All the isolates were also characterized using *spa* typing [12]. The *pvl* gene was detected by PCR, as previously described [13].

Simpson's index of diversity and 95% confidence intervals were used to calculate the genetic diversity of strains by Ridom EpiCompare software, version 1.0 (Ridom GmbH, Münster, Germany).

Potential risk factors

Several variables were investigated as potential risk factors of *S. aureus* nasal carriage. These included general demographic variables such as age, sex, ethnicity and immune system impairment. Immune system impairment was defined as diagnosis of primary and secondary immunodeficiency disorders, and systemic immune suppressive therapy was also included. Additional risk factors, such as skin and soft tissue infections, hospitalization, use of antibiotics and frequent contact with animals or animal products in the past 6 months, were also recorded. At the same time, we were also interested in transmission between family members at the household level. Therefore, risk factors of other household members were also investigated (Online Appendix S1).

Statistical analysis

The questionnaires were manually imported into EpiData (v3.02) software (EpiData Association, Odense, Denmark). Statistical comparisons were performed with SPSS (PASW Statistics 18.0.3) software (IBM, Armonk, NY). The only continuous variable, age, was transformed into a categorical variable using the quartiles of the frequency distribution (≤ 24 , $>24-30$, $>30-40$, >40 years). Furthermore, the different occupations were grouped into four categories that involved the following: (1) physical contact with healthy people (such as hairdressing and kindergarten teacher); (2) physical contact with animals or animal products (such as animal handlers, meat

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