

Methicillin-Resistant *Staphylococcus aureus* Nasal Carriage Among Patients and Healthcare Workers in a Hospital in Kelantan, Malaysia

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Abstract

Staphylococcus aureus nasal carriage is a common source of nosocomial infection and colonization. The aim of the present study was to assess the burden of methicillin-resistant *S. aureus* nasal carriage, its association with factors of interest including its genetic relationships. The prevalence of *S. aureus* nasal carriage was found to be 28.7%. This study showed that patients with a history of previous antibiotic intake, nasogastric tube, and longer hospitalization had a significantly high risk of being MRSA nasal carriers. The genetic relationship of all 34 nasal MRSA isolates revealed four major clusters of isolates, and there was a relationship between MRSA isolated from inpatients and healthcare workers.

Key words: MRSA, nasal carriage, nosocomial infection

Staphylococcus aureus is a common cause of hospital and community-acquired infections worldwide. *S. aureus* colonization is mainly found in the anterior nares (40%) (Kaplan, 2005). Several worldwide studies have reported that the rate of nasal carriage of *S. aureus* varies from 16.8% to 90% (Alghaithy *et al.*, 2000; Goyal *et al.*, 2002). In a study conducted in several hospitals in Malaysia in 1996, the prevalence rate was 40% (Rohani *et al.*, 2000). The principal mode of transmission from patient to patient is *via* the transiently colonized hands of healthcare workers (HCWs), who acquire the organism from patient contact or by handling contaminated materials (Solberg, 2000). Nasal carriage of *S. aureus* is a potential source of infection and colonization often precedes infection. In general, nasal carriage rates among hospital personal and patients (60–70%) are much higher compared to those among community carriers (30–50%) (Lowy, 1998). Identification and isolation of persons who are colonized or infected with methicillin-resistant *S. aureus* (MRSA) is recommended to minimize the spread of MRSA within hospitals. During 2005–2007, we identified an ongoing increase of both MRSA and *S. aureus* infection rates in Hospital Universiti Sains Malaysia (HUSM) despite high compliance with intensified control measures that

were implemented during admission (Al-Talib *et al.*, 2010). Thus, this study was carried out to determine the prevalence of *S. aureus* nasal carriage, and MRSA burden at HUSM, Kelantan state, Malaysia. This study was carried out at HUSM which is a 747-bed, tertiary care, teaching hospital. It is the referral center for Kelantan state and the nearby states, and is located at Kubang Kerian, which is about 7 km from Kota Bharu. The Research and Ethics Committee, School of Medical Sciences, Universiti Sains Malaysia, approved the study protocol. This was a cross-sectional study that was carried out from 1 March to 31 August 2008 among patients, relatives and staff nurses in all of the wards in HUSM. A total of 550 subjects were included in this study. Informed consent was obtained from all participants before specimen collection. Epidemiological information was obtained by interviewing the participants at the time that the nasal swabs were collected. Demographic (sex, race, and occupation) and clinical conditions data (history of antibiotic usage in the past 2 weeks, duration of hospitalization, and history of fever in the past 2 weeks) were included in this study. The specimens were taken from the subjects by using a sterile moistened swab inserted into the nostril, to a depth of approximately 1 cm, and rotated five times.

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For each subject, both nostrils were sampled using the same swab. Trypticase soy broth was used as the transport medium. The specimens were quickly sent to the laboratory and inoculated onto mannitol salt agar (MSA) plates. All colonies surrounded by yellow zones on MSA after 48 h of incubation at 37°C were selected. Colonies with pink or red zones were excluded. Identification of *S. aureus* was made based on the colony characteristics on MSA, Gram staining and a positive tube coagulase test. Molecular typing was conducted using pulsed-field gel electrophoresis (PFGE) as described by McDougal *et al.* (McDougal *et al.*, 2003). Restriction digestion was performed with *Sma*I, and restriction fragments were separated in a CHEF-DRII system (Bio-Rad, Hercules, CA, USA). Analysis of DNA fragments was conducted using both visual inspection and Bio-Rad software. Strain relatedness was interpreted according to published guidelines (Tenover *et al.*, 1995). A total of 550 *Staphylococcus* species were isolated from the anterior nares of patients, relatives and HCWs. The total prevalence of *S. aureus* nasal carriage was 28.7%, which was higher than that in other studies (Choi *et al.*, 2006; Santhosh, 2008). Norazah *et al.*, in a study conducted in Malaysia in 2002, reported a higher prevalence of *S. aureus* nasal carriage which varied from 45% to 76% (Norazah *et al.*, 2001). By analyzing all subjects with *S. aureus* nasal colonization, 34 were found to be colonized with MRSA and 124 were methicillin-sensitive *S. aureus* (MSSA) nasal carriers. *S. aureus* and particularly MRSA pose a major hazard in hospitals and contribute to the wider problem of hospital-acquired infection (Aldeyab *et al.*, 2008). A marked increase in the prevalence of MRSA infections has been reported in Malaysia since the mid-1985 (Choi *et al.*, 2006). A wide range of MRSA nasal carriage rates have been observed (Choi *et al.*, 2006; Askarian *et al.*, 2009; Johnson *et al.*, 2009), which could be attributed to different study populations, interpretation guidelines and culture techniques. Out of these 550 *Staphylococcus* species isolates, 312 were isolated from inpatients, 156 were from patients accompanied relatives, and 82 were from HCWs. Among the 550 nasal swabs, 392 (71.3%) were found to be coagulase-negative staphylococci and 158 (28.7%) were *S. aureus*. Among the 158 *S. aureus* isolates, 34 (21.5%) were found to be MRSA.

Surgical wards and ICUs showed higher percentages of MRSA nasal carriage (35.3% and 29%, respectively). This could be due to the traumatic and postoperative immunological suppression of the patients. The higher percentage with MRSA isolates from the surgical wards and ICUs in our study could be due to environmental factors that were probably related to the higher rate of MRSA infection in these locations. The higher proportion of MRSA nasal carriers among Malay race was due to the large proportion of that ethnic group in the

Table I
Socio-demographic characteristics of 158 MRSA/MSSA nasal carriers

Variables	MRSA (n = 34)	MSSA (n = 124)	P value
	No. of subjects (%)	No. of subjects (%)	
Sex			0.036**
Male	24 (70.6)	52 (41.9)	
Female	10 (29.4)	72 (58.1)	
Race			0.292*
Malay	30 (88.2)	118 (95.2)	
Chinese	4 (11.8)	6 (4.8)	
Age group (yr)			
<18	6 (17.6)	6 (4.8)	
18–30	8 (23.5)	30 (24.2)	
31–45	2 (5.9)	52 (41.9)	
45–60	14 (41.2)	26 (21.0)	
>61	4 (11.8)	10 (8.1)	
Level of education			
Tertiary	4 (11.8)	12 (9.7)	
Secondary	16 (47)	56 (45.2)	
Primary	2 (5.9)	10 (8.1)	
Not educated	12 (35.3)	46 (37)	

* Fisher's exact test; ** Pearson χ^2 test

present study (Table I). There are many risk factors for MRSA nasal colonization including age, sex, duration of hospitalization and previous antibiotic treatment (Corea *et al.*, 2003). In our multivariate analysis, the only significant independent risk factors for nasal carriage of MRSA versus MSSA were patients with a history of previous antibiotic intake, longer duration of hospitalization, and nasogastric intubation ($P = 0.005$, 0.006 , 0.013 , respectively). Previous studies on factors associated with outbreaks of infection and MRSA nasal colonization have reported similar findings (Corea *et al.*, 2003; Marshall *et al.*, 2003). Routine screening of all patients for MRSA on admission is impractical due to financial and other constraints. Screening high-risk groups for MRSA carriage and instituting control measures might limit introduction of new strains into the hospital. In our study, patients with a history of antibiotic treatment had a 9.7-fold greater chance of being nasal carriers of MRSA than MSSA. Previous antibiotic administration has been shown to be significantly associated with acquisition of MRSA as compared to MSSA. Oztoprak *et al.* have reported that 86% of patients with previous antibiotic treatment developed MRSA infection compared to 63% who developed MSSA infection (Oztoprak *et al.*, 2006). Schaefer *et al.* have shown that 41% of MRSA nasal carriers had received two or more antibiotics compared to 21% in the control group (Schaefer *et al.*, 2009). The excessive use and abuse of antibiotics are the main contributing factors to bacte-

Table II
Multiple logistic regression for the associated factors of MRSA nasal colonization.

Variables	B	Wald	Adjusted OR*	(95%CI)		P value
				Lower	Upper	
Previous antibiotic intake	2.275	0.035	9.72	2.017	45.97	0.005
Duration of hospitalization	0.74	7.433	1.077	1.02	1.136	0.006
Nasogastric tube	1.96	6.2	7.15	1.155	32.121	0.013

rial resistance; therefore, antibiotics must be prescribed only when indicated, and the drug chosen is the most narrow spectrum agent, and should be given with appropriate dose and duration. Nasogastric intubation represents one of the main risk factors for nosocomial acquisition of MRSA (Erbay *et al.*, 2003), and our study showed that it was significantly ($P = 0.013$) associated with MRSA nasal carriage, which could have been due to interference of the nasogastric tube with the normal lining epithelium of the upper respiratory tract, or the tube acting as a vehicle that facilitated transmission of MRSA to the respiratory tract (Table II). Another important confounder was the duration of hospital stay. The excess length of hospital stay was significantly ($P = 0.006$) longer among MRSA carriers than MSSA carriers. Therefore, an increase of 1 day duration of hospitalization increases by 1.077 times the acquisition risk of MRSA nasal colonization. Our findings were comparable to those of two previous studies. In Belgium, Blot *et al.* have reported that the mean length of stay for MRSA patients was 29 days as compared to 10 days for those with MSSA (Blot *et al.*, 2002). Another study has found that length of stay > 16 days was significantly associated with MRSA nosocomial infection (Wang *et al.*, 2008). These studies have indicated that patients who require longer hospitalization usually have more severe underlying illness or are critically ill.

Therefore, we consider that longer hospitalization is a risk factor for transmission of MRSA among patients. Many hospitals have recently implemented active surveillance to identify MRSA nasal carriers among patients, accompanying relatives, and HCWs, however, ongoing MRSA transmission can persist in endemic environments despite active surveillance (Ben-David *et al.*, 2008). There are several possible explanations for ongoing nosocomial MRSA transmission, including poor compliance with obtaining surveillance cultures, unscrubbed patients who are not included among high-risk patients, poor hand hygiene compliance, transmission of MRSA during the 72 h before colonized patients are identified and isolated, and insufficient measures to clean the contaminated environment. The genetic relationship of all 34 MRSA isolates was determined by PFGE (Fig. 1). A dendrogram of similarity percentage was calculated using dice coefficients from the PFGE data, based on an 80% cutoff value, which revealed four major clusters of isolates that were designated as pulsed-field type A-D. In the present study, four of the HCWs from surgical and ICUs wards were found to be MRSA nasal carriers. PFGE fingerprinting showed that the dominant PFGE pattern C was the dominant strain in 28 subjects (82.35%), and found in HCWs and patients. However, patterns A and B were found in another four patients, and pattern D in two patients'

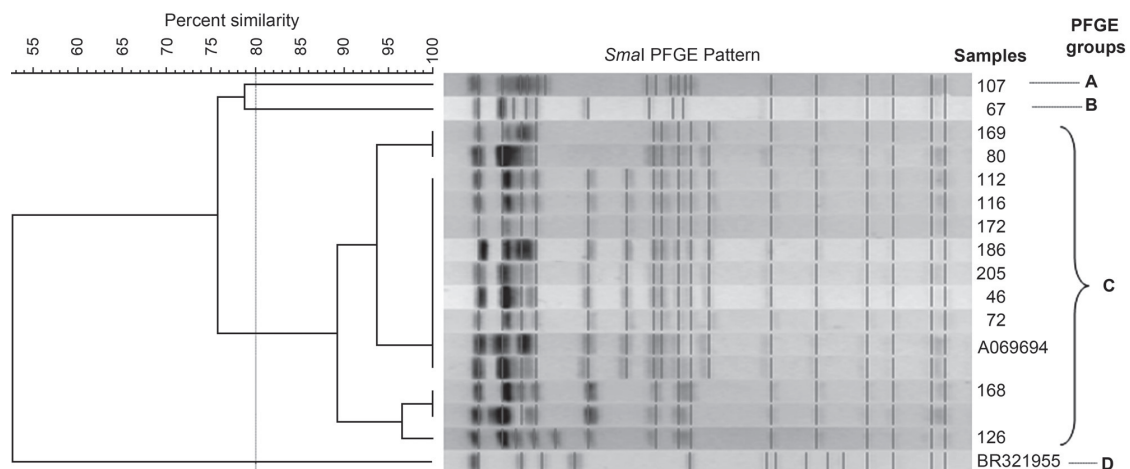


Fig. 1. Dendrogram of nasal MRSA samples (107, 67, 169, 80, 112, 116, 172, 186, 205, 46, 72, A069694, Staff 2 intan, 168, staffICU, 126, BR321955) and PFGE groups A, B, C, and D

relatives. There was a relationship between MRSA isolated from inpatients and HCWs. Unfortunately, our evidence is still insufficient to prove spread of MRSA between inpatients and HCWs, hence, more epidemiological information about MRSA isolates from HCWs and health residences would be useful. More surveys should be focused on HCWs' behavior because direct-contact droplets and air-borne transmission seem to be the major routes of transmission in nosocomial infection (<http://www.cdc.gov/mmwr/PDF/rr/rr5116.pdf>). Therefore, hand washing, and use of gloves, masks, eye protection, and face shields should be advocated as standard precautions for HCWs (Popovic *et al.*, 2000). In conclusion, this study revealed that the prevalence of nasal carriage of *S. aureus* strains among the HUSM population was higher than that found in other studies in our country. Logistic regression showed that previous antibiotic intake, longer hospitalization and nasogastric intubation were independently associated with MRSA carriage. PFGE fingerprinting of the MRSA isolated from patients was related to that of HCWs.

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