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Methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* in allergic rhinitis patient and healthy individuals: Prevalence, antibiotic susceptibility and effect on disease severity

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Allergic rhinitis is a common condition affecting populations globally. It has been recently suggested to increase the risk of both methicillin resistant and susceptible *Staphylococcus aureus* (MRSA, MSSA) nasal carriage. The aim of this study was to assess the prevalence and antibiogram to MSSA and MRSA among allergic rhinitis patients and healthy individuals, and its effect on disease severity. Nasal swabs were collected from 74 allergic rhinitis patients and 74 healthy individuals. MSSA and MRSA were identified by culture and biochemical methods. Antibiogram was determined by the disc diffusion method. MRSA prevalence was 15% in allergic rhinitis group and 4% among healthy individuals (*P* = 0.024), however there was no significant difference between MSSA nasal carriage among allergic rhinitis (8.1%) and control group (13.5%) (*P* = 0.28). The MRSA carriage was also significantly different between mild (0%) and moderate/severe allergic rhinitis (20%) (*P* = 0.035). MSSA nasal carriage was not significantly different between both groups (*P* = 0.65). Four multidrug-resistant MRSA isolates from allergic rhinitis patients were detected compared to one isolate from healthy individuals. MRSA nasal carriage was higher among allergic rhinitis compared to controls. It was also higher among moderate/severe cases compared to mild cases. This suggests that allergic rhinitis increases the risk for MRSA nasal carriage. MRSA carriage also increases the severity of the disease. Therefore, decolonization of MRSA might be useful in managing severe cases.

Key words: Methicillin resistant *Staphylococcus aureus,* allergic rhinitis, antibiotic susceptibility.

INTRODUCTION

Methicillin resistant *Staphylococcus aureus* (MRSA) became an increasingly important pathogen since its isolation in 1960s (Jevons, 1961). It was initially recognized as a nosocomial pathogen. Nevertheless, since 1990s, there has been an increase in MRSA among population without exposure to health care environment which led to the

recognition of new MRSA strains often referred to as community-associated MRSA (CA- MRSA) (Centers for Disease Control and Prevention, 1999).

Isolates of MRSA are also resistant to penicillin and all other beta lactam antibiotics due to possession of *mec*A gene which codes for a penicillin binding protein (PBP2a) with low affinity to beta-lactams (David and Daum, 2010; Monecke et al., 2011; Pinho et al., 2001). Additionally, the emergence of MRSA isolates with resistance to several other antibiotics (multidrug resistance) represents another major challenge that restricts the available options for the treatment of MRSA infections (DeLeo et al., 2010).

Asymptomatic nasal colonization with MRSA was suggested as a risk factor for the development of subsequent infections such as skin infections and the more fatal necrotizing pneumonia (DeLeo et al., 2010). Risk factors such as children population, recent antibiotic usage and working within healthcare facilities were suggested to increase the risk of MRSA nasal carriage (Costelloe et al., 2011; Kuehnert et al., 2006; Albrich and Harbarth, 2008). However, risk factors for CA-MRSA colonization are not fully outlined and are still being studied (Chih-Jung et al., 2011). In addition, CA-MRSA was shown to infiltrate hospital settings (Otter and French, 2011). Therefore, continuous surveillance is necessary to assess the epidemiology, reservoirs and risk factors for MRSA colonization in the community to efficiently apply infection control and management policies in community and subsequently, in hospitals. Allergic rhinitis was previously reported to increase the risk of *S. aureus* carriage (Shiomori et al., 2000). However, few studies have recently documented increased risk of MRSA nasal carriage among allergic rhinitis patients (Cevik et al., 2014). The scarcity of studies that focused on detecting MRSA among allergic rhinitis patients mandates further exploration of this aspect.

The aim of this study was therefore, to assess the nasal carriage and antibiogram of MRSA and MSSA among allergic rhinitis and its effect on disease severity among patients from Al-Karak province, Jordan. The results of this study might help in guiding the infection control and management plans of probable CA-MRSA infections and its complications among allergic rhinitis patients.

MATERIALS AND METHODS

Study design and data collection

This case - control study was carried out from March until April, 2014, at Al-Karak province in Jordan. The study was approved by the scientific and the ethics committees at the faculty of medicine, University of Mutah, Jordan, number 20147. All participants gave a written informed consent after procedure being fully explained.

Study population

A total of 115 samples were collected from allergic rhinitis patients. Another 115 samples were also collected from non-allergic rhinitis patients who served as a control. A questionnaire was filled in with information on age, sex, education level, profession and the severity score of allergic rhinitis (Bousquet et al., 2008). The questionnaire had also information on illnesses, having a family member who is a healthcare worker and antibiotic consumption over the last 3 months which were considered as exclusion criteria in this study. A total of 41 samples out of the 115 samples were excluded based on those criteria. This brought the study samples to 74 samples from each study group.

Nasal swabs culture, bacterial identification and antimicrobial susceptibility testing of the isolates

This was carried out as previously described elsewhere (Alzoubi et al., 2013). Briefly, the anterior nares of each participant were sampled by rotating a cotton swab three times in the vestibule of both anterior nares. The nasal swabs were then inoculated directly on Mannitol Salt Agar (MSA, BBL Microbiology System, Becton Dickinson Company, MD, U.S.A) and incubated at 35 ± 1°C and examined for growth within 48 h. Each single distinctive morphotype of a mannitol-positive colony was then selected from the MSA plate, subcultured on nutrient agar (BBL Microbiology Systems, Becton Dickinson, Company, MD, U.S.A.) and incubated at 37°C in a humidified incubator overnight for 18 h. Colonies from Nutrient agar were identified as *S. aureus* by Gram's staining, catalase and tube coagulase tests. Identification of the MRSA isolates was performed using 30 µg/ml cefoxitin disc in Mueller-Hinton agar supplemented with NaCl (4% w/v; 0.68 mol/L) according to Clinical and Laboratory Standard Institute (CLSI) guidelines (Clinical and Laboratory Standards Institute, 2012). Antimicrobial susceptibility to fusidic acid, erythromycin, mupirocin, gentamicin, linezolid, teicoplanin, ciprofloxacin, trimethoprim-sulfamethoxazole, tetracyclin, rifampicin, and cefoxitin was performed by disk diffusion that was performed according to the European Committee on Antimicrobial Susceptibility Testing for fusidic acid, and according to the Clinical Laboratory Standards Institute (CLSI) guidelines for the remaining antibiotics (The European Committee on Antimicrobial Susceptibility Testing, 2010; Clinical and Laboratory Standards Institute, 2012). *S. aureus* ATCC 25923 was used as control strain. Discs were purchased from Oxoid, Hampshire, England.

Statistical analysis

The statistical analysis was performed with STATA10 (Stata Corp. 2007. *Stata Statistical Software: Release 10*. College Station, TX: StataCorp LP, USA) to evaluate the significance of results. A *P* value of less than 0.05 was considered as significant using chi-square test.

RESULTS

The prevalence of MRSA nasal carriage in allergic rhinitis patients was about 15% (11/74) and in healthy individuals was 4% (3/74). Table 1 shows the distribution of isolates and statistical analysis. There was a significant difference

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Table 1. Numbers and percentages of MRSA and MSSA nasal carriage and *P* values among healthy individuals (controls) and allergic rhinitis patients.

Population	Controls (no.=74)	Allergic rhinitis (no.=74)	Allergic rhinitis (no.=74)	
			Mild (no.=19)	Moderate/Severe (no.=55)
No. MRSA +ve	3 (4%)	11(15%)	0 (0%)	11 (20%)
P value	0.024	0.024	0.035	0.035
No. MSSA +ve	10 (13.5%)	6 (8%)	2 (10.5%)	4 (7%)
P value	0.28	0.28	0.65	0.65

MRSA, Methicillin resistant *staphylococcus aureus*; MSSA, methicillin sensitive *staphylococcus aureus*, +ve, positive. Significant P value < 0.05.

Table 2. Antibiotic resistance pattern of MRSA and MSSA isolates from allergic rhinitis patients (AR) and healthy individuals (control group).

Pathogen / number	Antibiotic susceptibility (number, %)										
	E	Mup	G	LZD	Teic	Cip	SXT	Tet	Rd	F	Cef
AR-MRSA/11	(7) 63.7	(0) 0	(3) 27.3	(0) 0	(0) 0	(0) 0	(1) 9	(2) 18.2	(0) 0	(5) 45.5	11 100
AR-MSSA/6	(3) 50	(0) 0	(0) 0	(0)0	(0) 0	(0) 0	(0) 0	(1) 17	(0) 0	(2) 33	(0) 0
Control-MRSA/3	(1) 33.3	(0) 0	(0) 0	(0) 0	(0) 0	(1) 33.3	(1) 33.3	(1) 33.3	(0) 0	(2) 66.6	11 100
Control-MSSA/10	(4) 40	(0) 0	(0) 0	(0) 0	(0) 0	(0) 0	(0) 0	(0) 0	(0) 0	(10) 100	(0) 0

E, Erythromycin; Mup, Mupirocin; G, Gentamicin; LZD, Linezolid; Teic, Teicoplanin ; Cip, Ciprofloxacin; SXT, Trimethoprim-sulfamethoxazole; Tet, Tetracycline; Rd, Rifampicin; F, Fusidic acid; Cef, Cefoxitin. MRSA, Methicillin resistant *staphylococcus aureus;* MSSA, Methicillin sensitive *staphylococcus aureus.*

between nasal carriages of MRSA in both groups (p = 0.024). On the other hand, MSSA nasal carriage was about 80% in allergic rhinitis patients and was 13.5% in healthy individuals (Table 1). There was no significant difference between both groups (p = 0.28).

MRSA nasal carriage was significantly different between Mild and moderate/severe allergic rhinitis cases (p = 0.035) as can be seen in Table 1. MSSA nasal carriage was not significantly different among both groups (p = 0.65)

Antibiotic susceptibility of MRSA and MSSA isolates from allergic rhinitis and healthy individuals

The antibiogram of all isolates is shown in Table 2. The highest level of resistance in the 11 MRSA isolates from allergic rhinitis patients was found against erythromycin (63.7%), fusidic acid (45.5%) gentamicin (27.3%) and tetracycline (18.2%) followed by trimethoprim-sulfamethoxazole (9%). MRSA isolates were susceptible to the remaining antibiotic profile. Four MRSA isolates were multidrug resistant. These isolates were resistant to three or more of erythromycin, gentamicin, tetracycline and fusidic acid.

A total of 50, 17 and 33% of MSSA isolates were resistant to erythromycin, tetracycline and fusidic acid respectively. MSSA isolates were sensitive to all remaining antibiotics used in this study.

Within the healthy individuals group, one third of MRSA isolates were resistant to erythromycin, ciprofloxacin, trimethoprim-sulfamethoxazole and tetracycline, while two thirds were resistant to fusidic acid. One MRSA isolate showed multi-resistance pattern to cefoxitin and to four other antibiotics including erythromycin, ciprofloxacin, tetracycline and fusidic acid. On the other hand, 40% of MSSA isolates showed resistance to erythromycin but were sensitive to the remaining antibiotic profile used in this study.

DISCUSSION

Colonization with MRSA is a risk for developing subsequent infections (DeLeo et al., 2010). Risk factors for MRSA nasal carriage in community are still not fully determined and studies are continuing to define these factors (Chih-Jung et al., 2011).

In the current study, higher MRSA nasal carriage rate occurred in allergic rhinitis patients with about 15% carriage rate compared to 4% in healthy individuals group. This is similar to the finding of a recently published paper by Cevik et al. (2014) in Turkey, which revealed higher MRSA carriage rate among allergic rhinitis patients (3.7%) compared to controls (1.5%). The difference in MRSA prevalence among both studies might be explained by the fact that Jordan was shown to have a high prevalence of MRSA in general compared to other Mediterranean and European countries, which was attributed to inefficient

infection prevention and control measures (Borg et al., 2007). This caused increased rates of MRSA isolates in hospitals which could subsequently be infiltrated into community. This was also supported by other two studies from Jordan that found a prevalence of 7.4 (Al-Bakri et al., 2013) and 13.2% (Shehabi et al., 2013) of the community MRSA in Jordan. Other factors such as difference in host factors and difference in the population of the two studies might contribute to the difference in the MRSA prevalence in the current study and that found by Cevik et al. (2014).

The MSSA carriage was not significantly different between both groups of the current study though it was higher in controls (13.5%) compared to allergic rhinitis patients (8.1%).

Among allergic rhinitis patients, 20% of moderate-/severe cases carried MRSA compared to 0% in mild cases. MSSA was found in 7.3% of moderate/severe cases compared to 10.5% in mild cases but was not significantly different. Therefore, MRSA but not MSSA nasal carriage was found to be statistically higher among allergic rhinitis patients than controls, and also higher among moderate/severe allergic rhinitis than mild allergic rhinitis. This finding support the assumption that allergic rhinitis may be a risk factor for MRSA nasal colonization. Taking into consideration how common is allergic rhinitis which was estimated to affect 40-50% of people globally (Bousquet et al., 2008), treatment options should be selected carefully. The possibility of MRSA as the causative agent should be raised when dealing with infections among this category of patients such as sinusitis, otitis media and other body infections. On the other hand, the current study findings suggest that MRSA nasal carriage may be an important factor in exacerbating the severity of symptoms and probably the persistence of chronic sinusitis as has been previously suggested for *S.aureus* (Refaat et al., 2008). Allergic rhinitis results from allergens re-exposure in the nasal membranes such as dust, mite and pollens (Bousquet et al., 2008). Similarly, the MRSA nasal carriage may act as an allergen probably by some of its enterotoxins and this was previously suggested for *S. aureus* (Tang et al., 2011; Rossi and Monasterolo, 2004).

In guinea pigs, it was suggested that persistent allergic rhinitis is mediated by staphylococcus enterotoxin B via stimulating the TH2 response which leads to increased antigen specific IgE production (Tang et al., 2011). Therefore, screening and decolonization of MRSA nasal carriage in allergic rhinitis patient might not only decrease the morbidity and mortality of MRSA associated infections, but it might be recommended as a part of the treatment regime for moderate and severe cases of persistent allergic rhinitis cases, this was also suggested previously for *S. aureus* colonization in general (Refaat et al., 2008). However, further studies might be needed to assess the therapeutic role of MRSA decolonization among moderate/severe allergic rhinitis patients.

The antibiotic sensitivity of MRSA among allergic rhinitis in this study revealed high resistance to erythromycin and fusidic acid followed by gentamicin, tetracycline, and trimethoprim-sulfamethoxazole. There was no resistance for the remaining antibiotics that were used in this study, importantly to teicoplanin and linezolid which is nearly similar to what was found by some studies in Jordan (Al-Bakri et al., 2013). Therefore, it is recommended to avoid using the antibiotics for which MRSA was found to be resistant in the current study for the empirical treatment of MRSA infections such as pneumonia and bacteremia among allergic rhinitis patients.

The current study shows that there was a significant nasal carriage of MRSA among allergic rhinitis. The carriage was higher among moderate/severe cases compared to mild cases. This suggests that allergic rhinitis is a risk factor for MRSA nasal carriage. Additionally, MRSA carriage was shown to be associated with increased disease severity therefore, decolonization of MRSA might therefore be useful in managing moderate/severe and resistant cases of allergic rhinitis in line with other management protocols.

Conflict of Interests

The author(s) have not declared any conflict of interest.

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