

## RISK FACTORS ASSOCIATION WITH MRSA NASAL COLONIZATION AMONG PREOPERATIVE PATIENTS IN AZADI TEACHING HOSPITAL-DUHOK, KURDISTAN REGION, IRAQ

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### ABSTRACT:

**Background:** Nasal colonization with Methicillin-resistant *Staphylococcus aureus* (MRSA) can predispose to subsequent infections in surgical and non-surgical patients, making the management challenging with increased rates of morbidity, mortality and cost burden.

**Objectives:** The present study was carried out to evaluate the risk factors of MRSA nasal colonization in preoperative patients in Azadi Teaching Hospital in Duhok Province - Kurdistan Region-Iraq.

**Methods:** Nasal swabs were obtained from 150 patients after completing a questionnaire. Conventional laboratory methods were carried out to identify *Staphylococcus aureus* (*S. aureus*) and antimicrobial susceptibility test was conducted for recognizing MRSA isolates.

**Results:** A total of 41 (27.3%) of 150 patients were MRSA carriers. The mean age of participants MRSA carriers was 35.27±20.40 years old. The highest prevalence rate of nasal colonization with MRSA was in males (27.94%) than females (26.82%). In logistic regression analysis, no significant differences was detected between MRSA carriage and the associated risk factors including age [OR: 0.99 (95% CI: 0.97- 1.01); *P* = 0.45], gender [OR: 1.05 (95% CI: 0.51- 2.17); *P* = 0.87] and medical comorbidities [OR: 1.11 (95% CI: 0.42- 2.92); *P* = 0.82].

**Conclusions:** Age, gender and medical comorbidities were not associated common risk factors for nasal colonization of MRSA in preoperative patients. This study should be considered preliminary and studies with larger sample sizes and with using advance molecular tools are needed in the future.

**KEYWORDS:** Risk factors, MRSA, Nasal Colonization, Preoperative patients, Duhok.

### 1. BACKGROUND

*Staphylococcus aureus* (*S. aureus*) is one of the most commonly isolated infectious *Staphylococcus* species and one of the main human bacterial pathogens (Wertheim *et al.*, 2005). It can predispose a wide range of minor to life-threatening diseases including osteomyelitis, pneumonia, endocarditis, toxic shock syndrome (TSS) and Skin and soft tissue infections (SSTIs) (Kong *et al.*, 2016). The main natural reservoirs are the asymptomatic human carriers and the main site of colonization is the frontal part of the nasal mucosal. Permanent nasal colonization can be found in up to 30% of the human population and is considered as the major predisposing aspect in the pathogenesis of disease (Sakr *et al.*, 2018).

Overuse and misuse of antibiotics have led to increased levels of antibiotics-resistance. Methicillin was invented for the treatment of penicillin-resistant *S. aureus*. However, MRSA strains started to emerged and at the beginning such strains were considered a challenge in hospitals and health care units. Then, MRSA turned into a public-health problem affecting healthy individuals and became the most frequent cause of skin and soft-tissue infections in communities (Zetola *et al.*, 2005, Zafar *et al.*, 2007). Until recently, MRSA infections were confined to patients with established risk factors within the system of healthcare service and considered hospital acquired

infection MRSA (Green *et al.*, 2012). Thereafter, community-acquired MRSA (CA-MRSA) appeared in healthy individuals within society settings without established risk factors (Wang *et al.*, 2009). The vast majority of MRSA strains carry *mecA* gene which is held by staphylococcal cassette chromosome *mec* (SCC*mec*) type (Ahmad *et al.*, 2009). Conversely, community-associated (MRSA-CA) and health care-associated MRSA (HA-MRSA) are diverse in several genetic and phenotypic characteristics, with CA-MRSA being more virulent as they usually contain Panton-Valentine Leukocidin (PVL) (Chen *et al.*, 2012). PVL is a cytotoxin that causes leukocyte destruction and tissue necrosis. It has been previously reported that PVL toxin is commonly associated with CA-MRSA (Gillet *et al.*, 2002)

MRSA colonization appears to play a key role in the acquisition of infection, therefore the identification of colonization risk factors is important for the prevention and control of bacterial infection (Sganga *et al.*, 2017). The most common reported associated risk factors for MRSA colonization are nursing home residence, hospitalization history within past 12 months, administration of antibiotic in the previous 3 months, previous MRSA infection, chronic skin disease, chronic hemodialysis, immunosuppression and presence of indwelling medical device (Torres *et al.*, 2012).

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Among the postoperative complications; surgical site infections (SSI) are a major prevalent and they can arise as a consequence of several perioperative factors (Sakr *et al.*, 2018). It has been reported previously, that MRSA remains a common and serious causative bacterial pathogen for SSIs (Sganga *et al.*, 2017). MRSA colonization is associated with a fourfold increase in infection rate compared to methicillin-sensitive *S. aureus* (MSSA). Since nasal colonization of MRSA is associated with an increased infection risk of postoperative patients (Choi *et al.*, 2019), therefore, studies on the identification of colonization risk factors are critical to help in planning for preventive strategies and control of the MRSA-related infections.

This study aimed to investigate the most common associated risk factors with MRSA nasal colonization among preoperative patients in Azadi Teaching Hospital - Duhok Province, Kurdistan Region - Iraq.

## 2. METHODS

### 2.1. Study Design and Data Collection

A cross-sectional study was carried out at Azadi Teaching Hospital - Duhok province, Kurdistan Region, Iraq between April 2017 and April 2018 recruiting preoperative patients. A total of 150 patients who were scheduled for various elective surgeries were recruited in the present study. The participants were interviewed and information on risk factors associated with MRSA colonization was acquired by using a standardized questionnaire. Samples were obtained by inserting a moistened swab with sterile saline into both anterior nares to a depth for about 1 cm and then rotated gently for 3 seconds and directly transported for specimens processing. The collected data in the present study included age, gender, and medical comorbidities. The interview was completed by obtaining nasal swabs from enrolled subjects.

### 2.2. Identification of MRSA and Antimicrobial Susceptibility Testing

The collected swabs were inoculated into mannitol salt agar immediately after reaching the lab and then incubated at 35°C for 48 hs. *S. aureus* strains were identified based on mannitol fermentation, morphological characteristics, Gram stain, coagulase and catalase test. Antimicrobial susceptibility test to oxacillin (6 µg/ml) was performed on Mueller Hinton Agar (Oxoid Limited, UK) using disk diffusion by the Kirby Bauer methods according to the guidelines of the Clinical Laboratory Standards Institute (CLSI) to identify MRSA strains

### 2.3. Ethics consideration

The study protocol and informed agreement were accepted by the Research Ethics committee in the University of Duhok, College of Medicine - Kurdistan Region-Iraq. Informed agreement was acquired from all recruited subjects and for participants less than 18 years old; informed consent was acquired from legal guardians.

### 2.4. Statistics

Statistical analysis of findings was performed using Minitab software version 17.0 (Minitab, Inc., Pennsylvania 16801, USA). Continuous data were calculated as means ± standard deviations (SD) and frequencies were identified for categorical data using descriptive analysis. Logistic regression statistical analysis was applied to evaluate the association of risk factors with MRSA nasal colonization carriage. The strength of association was described according to the adjusted odds ratio (OR) and 95% confidence interval (95% CI). *P*-value of <0.05 was regarded as statistically significant differences.

## 3. RESULTS

A total of 150 participants were enrolled during the study period. Of these, 68 (45.3%) were males and 82 (54.7%) were females. The age of recruited subjects ranged from 2 to 84 years old, with an average mean of 36.99±17.23 years. In this study, 41/150 were MRSA carriers giving a prevalence rate of 27.3%. The average age of MRSA carriers was 35.27±20.40 years. The gender distribution of MRSA carriage for males and females was 19/68 (27.94%) and 22/82 (26.82%), respectively. Logistic regression statistical models were applied to recognize predictive risk factors of MRSA colonization. Of the studied risk factors, age [OR: 0.99 (95% CI: 0.97 - 1.01), *P* = 0.45], gender [OR: 1.05 (95% CI: 0.51 - 2.17), *P* = 0.87] and medical comorbidities [OR: 1.11 (95% CI: 0.42 - 2.92), *P* = 0.82] were not significantly associated with MRSA colonization.

## 4. DISCUSSION

*S. aureus* infections are of great importance because of invasiveness, toxin-mediated virulence, and resistance to antimicrobial agents (Qiu *et al.*, 2010). MRSA is one of the main multi-drug-resistant organisms (MDROs) and there has been an increase in its incidence over the past decade, making a public health issue worldwide (Peters *et al.*, 2019). Furthermore, MRSA is a growing concern in both hospital and community setting since it has increased the disease burden due to prolonged hospital stays, increased medical costs and high mortality (Kadariya *et al.*, 2019). Numerous researches verified that *S. aureus* nasal colonization including MRSA is an important independent infection risk factor (Datta *et al.*, 2014, Wertheim *et al.*, 2005). A large percentage of MRSA infections comes from endogenous origin and are induced by the same strain that generally colonizes the nasal mucosa (von Eiff *et al.*, 2001).

Globally, there is a statistically significant difference in the nasal carriage rate of MRSA as it varies geographically. The prevalence rate of MRSA colonization in healthcare workers in Germany, Turkey, China, Argentina, Egypt and Iran was 1.6% (Peters *et al.*, 2017), 2.9% (Oguzkaya-Artan *et al.*, 2015), 4.1% (Kong *et al.*, 2018), 6.3% (Boncompain *et al.*, 2017), 17.8% (Hashim *et al.*, 2018) and 22.5% (Pourramezan *et al.*, 2019), respectively. These variations are likely due to differences in the usage of antimicrobial and infection control measures (Diekema *et al.*, 2001). In Iraq, several studies have reported nasal carriage rate of MRSA colonization in society and hospital varying from 4.2% to 10% (Assafi *et al.*, 2015, Hussein *et al.*, 2015, Hussein *et al.*, 2019) and 50.4% to 61% (Hussein, 2016, Hussein *et al.*, 2017, Hussein *et al.*, 2019), respectively. These reports indicated high rates of MRSA colonization. Therefore, an exploration of the colonization risk factors is very crucial. In the current study, we evaluated the association of MRSA colonization with each of age, gender and medical comorbidities. We found that there was no statistically significant association between age and MRSA carriage and our findings were in agreement with several other studies, worldwide (Berrocal *et al.*, 2012, Altunbas *et al.*, 2013). Our results contradict a previous study conducted in Iraq as well as the majority of reports elsewhere where they found a rise in the nasal colonization rate of MRSA with advancing age (Kuehnert *et al.*, 2006, Hussein *et al.*, 2017). Elder are expected to be a higher risk infection category towards MRSA because they are likely to have frequent hospital visits due to chronic illnesses and age-related issues (Sfeir *et al.*, 2014). However, other studies showed that younger people have an increased risk for MRSA colonization (Munckhof *et al.*, 2009, Halablab *et al.*, 2010). Therefore, the association between age and MRSA nasal colonization remains controversial; further studies using advance molecular tools are required to discover this.

In the present study, gender was not a significant risk factor association for MRSA carrier, resulting that both sexes had a roughly similar infection rate of MRSA carriage (27.94% for male and 26.82% for female). These results are consistent with the data of the previous study conducted in Duhok province, Iraq (Hussein *et al.*, 2017). Similar findings were also detected in a study carried out in Georgia (Hidron *et al.*, 2005). However, several of the previous studies reported that male gender is a major associated risk factor for the nasal colonization for MRSA (Munckhof *et al.*, 2009, Halablab *et al.*, 2010). The male predominance in MRSA carriage could be due to gender differences in behavior and hand-hygiene practice with males being less compliant (Sharir *et al.*, 2001). Furthermore, several researches have demonstrated that female hormones particularly estrogens have immune-modulating roles, and that may attribute to lower colonization and infection rates in females (Fish, 2008, Humphreys *et al.*, 2015).

In a previous study conducted in Taiwan among community individuals, presence of chronic medical diseases was not associated with MRSA colonization (Wang *et al.*, 2009). In agreement with prior studies in Turkey (Altınbas *et al.*, 2013), Lebanon (Sfeir *et al.*, 2014) and Korea (Choi *et al.*, 2019), our results found no significant differences between colonization MRSA carriage and medical comorbidities. This contrasts with other studies where they reported medical comorbidities as a significant risk factor for MRSA colonization (Haddadin *et al.*, 2002, Halablab *et al.*, 2010). A further research with a larger population sample from different provinces in Iraq is required to explore such relationships.

To conclude, age, gender and medical comorbidities were not recorded as a major risk factors for nasal colonization with MRSA in preoperative patients. The present study should be considered preliminary and studies with larger sample sizes are needed in the future. Furthermore, more risk factors such as family socioeconomic status, history of previous antibiotic usage, previous MRSA infection and surgeries should be evaluated.

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