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PREVALENCE OF NASAL *STAPHYLOCOCCUS AUREUS* AND METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* IN HOSPITAL PERSONNEL AND ASSOCIATED RISK FACTORS

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Abstract: Hospital- and community-acquired *Staphylococcus aureus* infections pose a substantial burden in terms of morbidity, mortality and healthcare costs. The extent of nosocomial *S. aureus* transmission, in particular methicillin-resistant *S. aureus* (MRSA), the prevalence of *S. aureus* colonization in healthy personnel working in hospital was determined. Factors associated with *S. aureus* nasal carriage and antibiotic sensitivity pattern of the isolates were also analyzed. A total of 129 nasal swabs and epidemiological information concerning risk factors for nasal carriage were obtained from physicians, nurses, sanitary workers and administrative staff. Antibiotic susceptibility testing was performed using disk diffusion method. The prevalence of *S. aureus* and MRSA nasal carriage was significantly ($p < 0.05$) higher in physicians (51.8%, 18.5%), nurses (66.6%, 27.3%) and sanitary workers (59%, 13.6%) as compared to administrative staff (27.6%, 2.1%). There was no association between smoking and nasal *S. aureus* carriage ($p = 0.006$) and the isolates from physician. The nurses and sanitary workers were comparatively more resistant to various antibiotics than the isolates from administrative staff.

Keywords: nasal carriers, hospital personnel, prevalence, risk factors, *Staphylococcus aureus*, MRSA

The rate of *Staphylococcus aureus* infection has increased over the past 200 years. Nasal carriage of *S. aureus* has been identified as potential source of infection. *S. aureus* is one of the common naturally occurring cocci in human host, with an estimated 30–40% of the population proved as carriers (1). While often found on the nasal mucosa, it can also be isolated from other moist surfaces such as the axillae and perineum. The vast majority of carriers suffer no ill effects of colonization, but immunocompromised individuals, or patients recovering from surgery or serious diseases are more susceptible to infections (2, 3). *S. aureus* is equipped with a vast array of virulence factors, giving it the versatile ability to establish infections in virtually every organ in human body, causing everything from superficial skin lesions to serious systemic infections such as pneumonia and sepsis (4, 5).

A variety of workers reported 20 to 30% colonization of this bacterium in healthcare workers and they are responsible for transmition (6, 7). Infection outbreaks have been reported from critical units, including burn wards, nurseries, intensive care units as well as in clinical and surgical patients; they have been found to be due to inappropriate use of antibiotics, lack of hand washing, insufficient nursing care and presence of carriers among the staff. There are two types of *Staphylococcus aureus* found in nosocomial environments: permanent and transitory. The former can be found on healthcare-workers and in the hospital environment. The latter can be found in infected patients and in carriers, which are in transitory contact with the hospital (8).

The importance of *S. aureus* as a human pathogen, apart from its ability to cause a diverse range of life-threatening infections, is its extraordinary potential to develop antimicrobial resistance (9). Treatment of staphylococcal infections has become more challenging with the emergence of methicillin resistant *S. aureus* (MRSA), which are often also multi-drug resistant. Methicillin resistance was first reported in 1961, shortly after the introduction of methicillin. MRSA infections are additional to the burden of methicillin susceptible

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S. aureus and have serious sequelae. MRSA infections may be difficult to treat as there are reduced antimicrobial options; in addition, some of the agents can be difficult to administer, have side effects, and may not penetrate particular body compartments well, for example, in the treatment of bone infections or endocarditis. Also, the available agents may not be as effective against MRSA as standard agents are against methicillin susceptible *S. aureus*. The cost of treatment and prolonged stay in the hospital results in extra costs to health services.

The indiscriminate use of antibiotics in some parts of the world both in human and veterinary medicine has provoked selection of resistant strains, causing more serious infections. The healthcare workers inserted in this epidemic chain have great importance in the increasing resistance of contaminants.

The present study is aimed to estimate the rate of colonization of *S. aureus*, particularly MRSA, in hospital personnel, to determine its associated potential risk factors and antibiotic resistance status of the isolates.

MATERIALS AND METHODS

Study design

The study was conducted in the Children Hospital Complex (Multan, Pakistan), 300-bed tertiary care hospital. During one year study (2006–2007), 129 employees of the hospital were screened randomly for their nasal carriage. Specimens for culture were collected from various wards and an administrative site of the hospital. Several variables regarding age, gender, approximate weight, occupation, self-reported health sta-

Table 1. Demographic and clinical characteristics of the participants with *S. aureus* nasal carriage among health care personnel.

Factors	*Staphylococcus aureus*			
	Positive		Negative	
	n	%	n	%
Gender				
Male	29	43	38	57
Female	33	53	29	47
Age (Year)				
< 30	33	44	42	56
30–40	23	52	21	48
> 50	6	60	4	40
Working duration (year)				
< 1	16	38	26	62
1–2	24	49	25	51
> 2	22	58	16	42
Smoking exposure				
Yes	17	26	6	74
No	45	58	61	42
Antibiotics used in past 30 days				
Yes	8	38	5	62
No	54	53	62	47
Diabetes				
Yes	1	100	0	0
No	61	48	67	52
Asthma				
Yes	2	67	1	33
No	60	48	66	52

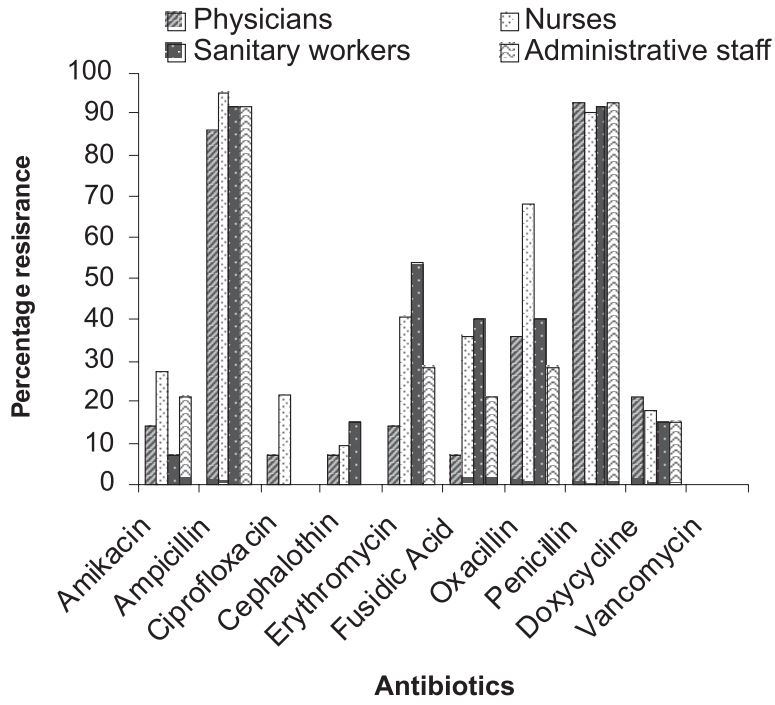

Figure 1. Antibiotic resistance pattern of nasal *S. aureus* among hospital personnel

tus, use of antibiotics in the past 30 days, self-report or physician diagnosis of diabetes, self-report or physician diagnosis of asthma, near past history of any other disease and current exposure to cigarette smoke were investigated as potential characteristics indicative of nasal carriage of *S. aureus*. A questionnaire concerning the demographic and medical profiles was completed by all the participants under the supervision of an expert interviewer.

Cultivation, identification and susceptibility testing

The samples were obtained by rubbing a sterile cotton swab (Becton Dickinson Culturette Systems, Sparks, MD.) in both nostrils consecutively and inoculated on 5% sheep blood agar and incubated for 24 h at 35°C. Morphologically, *S. aureus* was identified by Gram-staining, catalase, and coagulase test by standard methods (10). The *S. aureus* strains were then tested for sensitivity to antibiotics, following the technique of Kirby and Bauer, recommended by National Committee for Clinical Laboratory Standards, using antibiogram disks. The strains with oxacillin (1 mg) zone diameter = 13 mm were defined as MRSA (11, 12).

Statistical analysis

Statistical Package for Social Sciences (SPSS) for windows (Version-12; SPSS, Chicago, IL, USA) software was used for the statistical analysis of the data. Univariate analysis of the potential factors for *S. aureus* carriage were carried out using χ^2 test and Fisher exact test (when cells had expected counts less than 5). Tests were two-tailed and $p < 0.05$ was considered to be significant (13, 14).

RESULTS AND DISCUSSION

Among the 129 samples, 27 were collected from physicians, 33 from nurses, 22 from sanitary workers and 47 from administrative staff. Clinical and demographic characteristics of personnel and Univariate Analysis of potential risk factors for *S. aureus* nasal carriage (Table 1) showed no difference between carriers and non-carriers with regard to fever or antibiotic usage in the past 30 days, diabetes mellitus, asthma and working duration, while smoking exposure was significantly associated ($p = 0.006$) with *S. aureus* carriage.

The prevalence of nasal *S. aureus* and MRSA was 48 and 13.95%, respectively. The highest car-

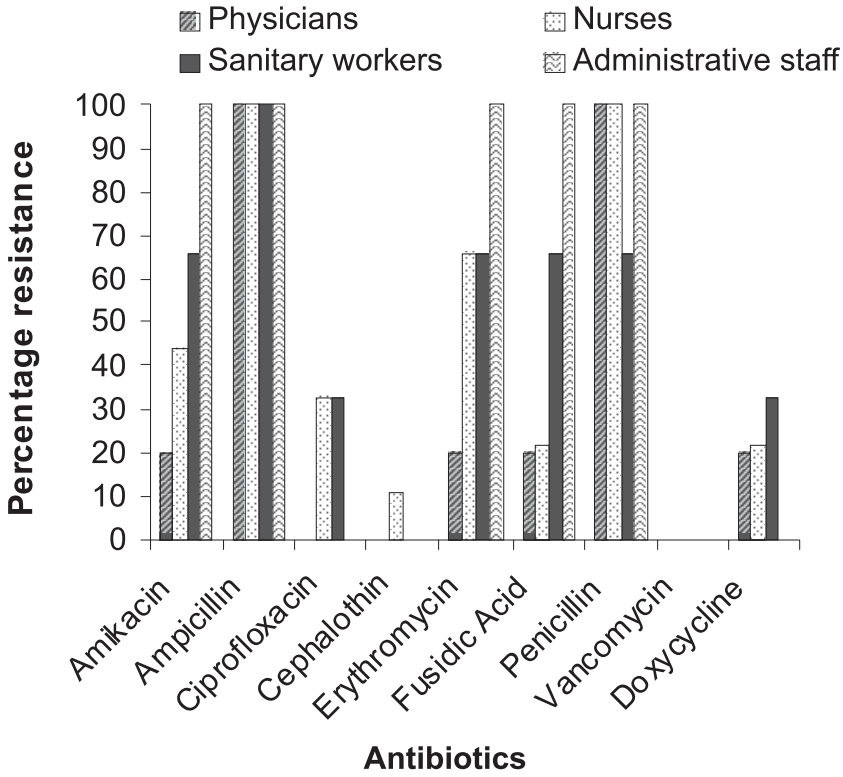

Figure 2. Antibiotic resistance pattern of nasal MRSA among hospital personnel

riage rates were seen in nurses (66.6% *S. aureus,* 27.3% MRSA), followed by sanitary workers (59% *S. aureus*, 13.6% MRSA), physicians (51.8% *S. aureus,* 18.5% MRSA), and administrative staff (27.6% *S. aureus,* 2.1% MRSA). The antibiotic susceptibility pattern varied among hospital personnel (Figs. 1 and 2).

In the present study, it was observed that the highest carriage rate was in nurses (66% *S. aureus* and 27.3 % MRSA), followed by physicians (51.8% *S. aureus*, 18.5% MRSA) and sanitary workers (59% *S. aureus*, 13.6% MRSA), while carriage rate among administrative staff was comparatively low. In 2003, Dimitrov and his co-workers found 21% and 14.4% *S. aureus* carriage in physicians and nurses, respectively (15). In accordance with previous studies, we found that smoking was associated with *S. aureus* colonization. Smoking is known to alter the respiratory mucosal surface, facilitating the binding of potential pathogens, *Streptococcus pneumoniae* and *Haemophilus influenzae*, and to lesser extent *S. aureus*. This led to an increased risk of colonization and development of pneumonia (16, 17). Other variables studied were not risk factors for colonization of *S. aureus*. This was contrary to some findings carried out previously, *S. aureus* carriage rates vary among different gender, age and ethnic groups (18–20). In addition, some other studies showed certain chronic illnesses such as diabetes, rhinitis, and asthma and skin diseases resulted in higher carriage rate of *S. aureus* (5, 21–23). In this study, there was only one individual with diabetes, therefore, association of diabetes was not possible to evaluate.

It is well known that the excessive use of antibiotics promotes the emergence of bacterial resistance. The presence of residues of antibiotics used in agriculture and in livestock, as well as the bacterial selection due to such use could be responsible for development of resistant strains in environments (24, 25). Patients and healthcare workers were indirectly exposed to the antimicrobials that act on endogenous microbiota, selecting resistant bacteria that are dispersed through individual contact (26). The healthcare workers inserted in this epidemic chain have great importance in the increasing resistance of contaminants, serving as a source of transmission and information for empirical prescription of antibiotics.

In our study, it was found that isolates from physicians (93%, 86%), nurses (90%, 86%) and san-

itary workers (92%, 92%) showed higher resistance against penicillin and ampicillin as compared to isolates from administrative staff (76%, 69%). The penicillins were found to be very effective against Gram-positive and Gram-negative cocci. Ampicillin, a derivative of penicillin, has been in use for more than forty years in treating the patients. Cephalothin proved to be relatively more effective antimicrobial than other ß-lactam antibiotics. The overall resistance against cephalothin was 8% in *S. aureus* isolates. Cephalothin proved to be relatively more effective antimicrobial than other ß-lactam antibiotics. The resistant *S. aureus* strains were isolated from physicians (7%), nurses (9%) and sanitary workers (15%) only. Similar reports were observed by Cespedes and co-workers (27), they found that only the strains isolated from the group of individuals with exposure to patients (physician, nurses) showed 11.4% resistance against cephalothin.

The overall resistance of *S. aureus* strains against ciprofloxacin was 10%. The resistance was only observed in those strains of *S. aureus* which were isolated from physicians (7%) and nurses (23%). The development of *S. aureus* resistance to ciprofloxacin might be due to previous antimicrobial chemotherapy of patient before hospitalization and use of combinations of antibiotics during treatment. Moreover, wide use of ciprofloxacin has resulted in a steady increase in incidence of fluoroquinolone resistant staphylococci (10, 28).When quinolones are used to treat infections caused by other bacterial pathogens, subjects colonized with *S. aureus* (e.g., on their skin or mucosal surfaces) are likely to be exposed to sub therapeutic antibiotic doses and are therefore at risk of becoming colonized with resistant strains. These resident, resistant strains then become the reservoir for future infections. Hoiby and coworkers (32) demonstrated that ciprofloxacin therapy rapidly increased the proportion of coagulase-negative staphylococcal strains colonizing the nares and skin that were resistant to both ciprofloxacin and methicillin. Since *S. aureus* is also a part of our commensal flora, a similar selection process is likely to occur (29, 30).

Resistance against amikacin, an aminoglycoside, results through mutations, decrease uptake of the antibiotic and modification of aminoglycoside by aminoglycoside-modifying enzymes. In the present study, administrative staff had the highest carriage rate of amikacin-resistant *S. aureus* (28%), whereas physicians and nurses had 27% and 14% of the isolates resistant to amikacin, respectively. Resistance against fusidic acid and erythromycin was higher in sanitary workers (40%, 54%), nurses (36%, 41%) and administrative staff (21%, 28%) as compared to physicians (7%, 15%).

Methicillin, the first of the semi-synthetic penicillinase-resistant penicillins, was introduced in 1961 to target strains of penicillinase-producing *S. aureus* (10, 33). In the present study, 29% of the *S. aureus* strains were resistant against methicillin. The highest resistance was found in strains isolated from nurses (41%) followed by physicians (36%), sanitary workers (31%) and administrative staff (14%). The incidence of resistance is decreasing with decreasing exposure to patients. Busato and his coworkers (34) found 19% resistant strains in 1996 and 12% resistant strains in 1999. We found that MRSA strains were also resistant to other antibiotics. In recent years, MRSA has become a particularly significant problem in Pakistani hospitals. The reason for this increase in Pakistan could be justified by the injudicious use of antibiotic in hospitals and community and because of the easy availability of antibiotics without prescription (35, 36).

Consistently with previous studies we found that all of the isolates of *S. aureus* and MRSA were sensitive to vancomycin (14, 27, 34). There was only one MRSA strain isolated from administrative staff which was also resistant to ampicillin, penicillin, amikacin, erythromycin, and fusidic acid. Strains isolated from sanitary workers showed 100% resistant to ampicillin, 66% resistance to amikacin, erythromycin, fusidic acid and penicillin each and 33% resistance against ciprofloxacin and doxycycline. On the other hand, MRSA strains isolated from nurses were also resistant to ampicillin and penicillin (100%), erythromycin (66%), amikacin (44%), ciprofloxacin (33%), fusidic acid (22%) and cephalothin (11%), while MRSA strains isolated from physician were only resistant to ampicillin (100%), penicillin (100%), amikacin (20%), erythromycin (20%) and doxycycline (20%). We observed that MRSA strains isolated from physicians and nurses were comparatively less resistant to other commonly used antibiotics than the isolates from sanitary workers and administrative staff.

The greater resistance offered by isolates against commonly used antibiotics could be attributed to many factors like misuse and overuse of antibiotics. Antibiotic use provides selective pressure favoring resistant bacterial strains. Inappropriate use increases the risk for selection and dissemination of antibiotic-resistant bacteria. Therefore, the drugs, which are more commonly used, which are generally inexpensive (37–39), lead to development of bacterial resistance in developing countries. Besides this selective pressure, new

strains can be introduced into a nosocomial area through patients or by healthcare workers (5, 40–43). Moreover, the use of antibiotics in poultry feed also exert a selective pressure that allows the drug resistant strains in intimate human biosphere from an inexhaustible pool of nature (44, 45). The excessive use of antibiotics is practically responsible for increase rate of resistance throughout the world in hospital settings. Another factor responsible for development of antibiotic resistance in bacteria could be due to non-access of health workers to health information (46). Well-trained health personnel are scarce and cannot serve the entire population; especially in rural areas (47). Unskilled personnel are less aware of the deleterious effects of inappropriate antibiotic use (48). Unqualified drug sellers offer alternative drugs when the prescribed drugs are out of stock or refill prescription without consulting the prescriber. Moreover, the addition of prosthetic materials leads to an increase in degree of resistance (49–51).

CONCLUSIONS

In conclusion, our study confirms the high prevalence of *S. aureus* and MRSA nasal colonization hospital personnel especially in physicians and nurses. However, MRSA carriage rate is low. Few demographic or clinical characteristics are related to carriage. As hospital personnel are at high risk of transmitting *S. aureus*, they should remain vigilant to follow appropriate measures (e.g., use of facemasks) for minimizing transmission. The appropriate use of antibiotics could retard or prevent the emergence and spread of resistant bacteria.

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