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Nasal Carriage of Methicillin-Resistant *Staphylococcus aureus* and Risk Factors Amongst Inpatients, Outpatients and Hospital Personnel

Hastanede Yatan Hastalar, Poliklinik Hastaları ve Hastane Personelinde Metisiline Dirençli *Staphylococcus aureus* Nazal Taşıyıcılık Oranları ve Risk Faktörleri

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ABSTRACT

Introduction: The aim of this study was to determine the ratio of nasal carriage of methicillin-resistant *Staphylococcus aureus* (MRSA) and the risk factors among 1500 subjects including 689 hospital staff, 609 inpatients, and 202 outpatients in Ankara Training and Research Hospital.

Materials and Methods: Nasal swabs were obtained from hospital staff, inpatients and outpatients, which were then inoculated-into mannitol-salt agar, oxacillin resistance screening agar base (ORSAB), and chromogenic MRSA agar media, respectively. Methicillin resistance was confirmed with cefoxitin disk by the disk-diffusion test. In statistical analyses, the Chi-square and the Kruskal Wall is tests were used, considering $p< 0.05$ value statistically significant.

Results: MRSA nasal carriage rate was determined 3.03%, 9.03% and 3.96% in hospital staff, inpatients and outpatients, respectively. The rate of nasal carriage of MRSA amongst doctors, nurses and auxiliary health personnel was 1.36%, 1.735% and 5.06% respectively.

Conclusion: Hospital staff,especially auxiliary health personnel, should be trained on hospital infections, routes of transmission, and protective measures. In addition, in clinics where MRSA infections and colonization is common, hospital staff and inpatients should be screened for MRSA nasal carriage at certain intervals and patients to be admitted to the intensive care and surgical units should undergo screening for MRSA nasal carriage before admission.

Key words: Inpatients, hospital staff, outpatients, MRSA, nasal carriage, risk factors

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ÖZET

Giriş: Bu çalışmanın amacı; Ankara Eğitim ve Araştırma Hastanesinde çalışan 689 hastane personeli, 609 yatan hasta ve 202 poliklinik hastasında metisiline dirençli *Staphylococcus aureus (MRSA)* nazal taşıyıcılığı oranını ve risk faktörlerini belirlemektir.

Materyal ve Metod: Hastane personeli, yatan hastalar ve poliklinik hastalarından alınan burun sürüntüleri sırasıyla; mannitol-salt agar, oksasilin direnç tarama agar (ORSAB) ve kromojenik MRSA agar besiyerlerine ekildi. Metisilin direnci sefoksitin disk difüzyon testiyle doğrulandı. İstatistiksel analizde ki-kare testi ve Kruskal Wallis testleri kullanıldı. p< 0.05 değeri istatistiksel olarak anlamlı kabul edildi.

Bulgular: MRSA nazal taşıyıcılığı oranı hastane personelinde %3.03, yatan hastalarda %9.03, poliklinik hastalarında ise %3.96 olarak belirlendi. MRSA nazal taşıyıcılık oranı doktorlar, hemşireler ve yardımcı sağlık personelinde sırasıyla; %1.36, %1.73 ve %5.06 olarak belirlendi.

Sonuç: Hastane personeli özellikle de yardımcı sağlık personeli hastane infeksiyonları, bulaş yolları ve korunma yolları hakkında eğitilmelidir. Bunun yanı sıra, MRSA infeksiyonlarının ve kolonizasyonunun yaygın olduğu kliniklerde çalışan hastane personeli ve yatan hastalar MRSA nazal taşıyıcılığı açısından belirli aralıklarla taranmalı ve yoğun bakım ünitesi ve cerrahi kliniklere yatacak hastalar hastaneye kabul edilmeden önce MRSA nazal taşıyıcılığı yönünden taranmalıdır.

Anahtar kelimeler: Yatan hastalar, hastane personeli, poliklinik hastaları, MRSA, nazal taşıyıcılık, risk faktörleri

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INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* (MRSA) is an important nosocomial pathogen resistant to various antibiotics and disinfectants. It is very important to prevent the spread of MRSA infections. Morbidity and mortality rates of infections caused by MRSA strains and the cost of treatment are high[1-3]. It has been reported in many studies carried out in Turkey that the rate of MRSA infection varies between 37-71%[4]. MRSA usually spreads through direct contact with contaminated hands of health care workers; however, nasal carriage among hospital staff and inpatients may be accounted for some nosocomial MRSA infections[5]. Consequently, identification of patients and hospital staff colonized or infected with MRSA, subsequent isolation, and eradication of nasal carriage are necessary for the control of nosocomial MRSA infections[6-8].

The aim of this study was to determine the rate of nasal carriage of MRSA amongst hospital staff, inpatients, and outpatients.

MATERIALS and METHODS

Ethics Statement

Written informed consent was obtained from all patients, on whom the study was carried out in Ankara Training and Research Hospital. Information forms were prepared and the approval of the Ethics Committee was obtained from Ankara Training and Research Hospital.

Patients and Samples

In order to determine nasal carriage and risk factors (i.e. antibiotic use in the last six months, hospitalization or history of surgical operation in the previous year, and hospital stay) among hospital staff and patients hospitalized for surgery and/or in internal medicine clinics and intensive care units for more than one week, nasal swabs were taken from a total of one thousand five hundred subjects including 609 patients hospitalized for more than one week, 202 outpatients selected as the control group, and 689 hospital staff members.

Laboratory Study

Nasal swabs were inoculated into mannitol-salt agar (Oxoid, UK), oxacillin resistance screening agar (ORSAB, Oxoid, UK), and chromogenic MRSA agar

media (Chromagar MRSA, Dr. A. Rambach, Paris, France). Culture plates were kept in the incubator at 37°C and evaluated for growth at the 24th, 48th and 72nd hours. Catalase and coagulase test-positive colonies appearing yellow in the mannitol salt agar medium and staining as gram positive cocciin Gram staining were identified as *S. aureus* while colonies appearing yellow in mannitol agar, blue in ORSAB and/or pink or lilac in chromogenic MRSA agar medium were evaluated for methicillin resistance. Catalase and coagulase test-positive colonies which grew in mannitol agar and appeared yellow but did not grow in ORSAB and/or chromogenic MRSA agar medium and were stained gram-positive cocci in Gram staining were evaluated as methicillin-sensitive *S. aureus* (MSSA). Single colony passage was performed from the proper colonies. The confirmation of methicillin-resistance in *S. aureus* strains was made according to the Clinical and Laboratory Standards Institute (CLSI) criteria by the disk diffusion method using cefoxitin disk in Mueller-Hinton agar medium[9]. In addition, the sensitivity of isolated MRSA strains to various antibiotics was investigated with the Kirby-Bauer disk diffusion method with regard to CLSI recommendations[9]. In the quality control of media and antibiotic disks, ATCC 43300 (MRSA) and ATCC 25923 (MSSA) standard strains were used.Statistical analyses were carried out in the Depart-ment of Biostatistics in the Medical School of Ankara University.

Statistical Analysis

Chi-square and Kruskal Wall is tests were used in the statistical evaluation and A p value of < 0.05 was considered statistically significant.

RESULTS

Of the six hundred and eighty-nine staff members included into the study, 312 were male and 377 were female; the mean age was 33.08 years. Of the six hundred and nine hospitalized patients, 297 were male and 312 were female; the mean age was 52.37 years. Of the two hundred and two outpatients, 97 were male and 105 were female; the mean age was 39.56 years. Of the six hundred and eighty-nine hospital staff-screened for nasal carriage, 220 (32%) were physicians, 173 (25%) were nurses while 296 (43%) were auxiliary healthcare personnel. Both MRSA and MSSA carrier states were related to age. Median age for MRSA nasal carriage was 48.5 (range, 16-96) yearsand the median age for MSSA carriage was 42 (range, 16-86) years. The relationship between MRSA and MSSA carrier states and age was statistically significant ($p< 0.05$). Of the six hundred and eighty-nine hospital staff members included into the study, 21 were MRSA nasal carriers while 74 were MSSA nasal carriers. Of the twenty-one nasal carriers, 3 were physicians, 3 were nurses, and 15 were auxiliary healthcare staff. Of the seventy-four MSSA nasal carriers, 27 were physicians, 8 were nurses and 39 were auxiliary healthcare personnel. Among the six hundred and eighty-nine hospital staff screened in the study, 13.7% were *S. aureus* carriers (95/689) and 21 (3%) were MRSA carriers. When the correlation regarding occupations was investigated, MSSA nasal carriage was detected at a higher rate in nurses than in physicians; whereas, MRSA was detected at similar rates ($p= 0.02$). Among auxiliary healthcare staff, both MRSA and MSSA carriage were detected higher than those among physicians and nurses ($p< 0.01$). The distribution of the hospital staff who were nasal carriers of *S. aureus* is demonstrated in Table 1. According to the clinical presentation, the rate of nasal carriage was high in intensive care units (23.8%), surgical clinics (23.8%), operating theaters, anesthesia units (9.5%), sterilization units, and the laundry (9.5%). These units accounted for 66.6% of nasal carriers. The rate of

Table 1. The distribution of nasal carrier hospital staff of *Staphylococcus aureus*

	MRSA nasal carriers n (%)	MSSA nasal carriers n (%)	Total n (%)
Doctor (n= 220)	3 (1.36%)	27 (12.2%)	30 (13.63%)
Nurse (n= 173)	3 (1.73%)	8 (4.6%)	11 (6.35%)
Auxiliary staff (n= 296)	15 (5.06%)	39 (13.1%)	54 (18.24%)
Total (n= 689)	21 (3.04%)	74 (10.7%)	95 (13.7%)

MRSA: Methicillin-resistant *Staphylococcus aureus,* MSSA: Methicillin-sensitive *Staphylococcus aureus.*

Table 2. The comparison of MRSA nasal carriage rates among hospital personnel, inpatients, and outpatients

	Hospital staff (n= 689)		Inpatients (n= 609)		Outpatients (n= 202)	
	Number	%	Number	%	Number	%
MRSA	21	3.04	55	9.03	8	3.96
MSSA	74	10.7	91	14.9	32	15.84
Total	95	13.7	146	23.9	40	19.8

Table 3. Rates of antibiotic resistance to various antibiotics in MRSA strains isolated from nasal cultures of hospital staff and inpatients

	Hospital staff (n= 21)		Inpatients (n= 50)	
Antibiotics	**Number**	**%**	**Number**	**%**
Cefoxitin	21	100	50	100
Tetracycline	12	57	25	50
Trimethoprim-sulfamethoxazole	4	19	17	34
Rifampicin	11	52	26	52
Ciprofloxacin	11	52	41	82
Erythromycin	15	71	47	94
Clindamycin	8	38	24	48
Fusidic acid	3	14	18	36
Mupirocin	1	4.8	15	30

MRSA: Methicillin-resistant *Staphylococcus aureus*

MRSA nasal carriage was established as 57% in surgical clinics and 34% in internal medicine clinics. MRSA nasal carriage was higher in surgical clinics ($p< 0.05$); whereas, MSSA nasal carriage was higher in internal medicine clinics (56%) than in surgical clinics (34%) ($p< 0.05$). When MRSA and MSSA nasal carriers were compared in terms of antibiotic use, it was demonstrated that the use of antibiotics was significantly-higher among MRSA nasal carriers (67%) than among MSSA carriers (34%) ($p< 0.001$). There was no difference in antibiotic use between surgical and internal medicine clinics ($p> 0.05$). Twenty-one hospital staff, who were MRSA nasal carriers, were evaluated for risk factors. The history of antibiotic use in the last six months was determined in twelve out of the 21 MRSA-carrier personnel. It was reported that one of them used beta-lactam antibiotics while the others used antibiotics whose names they could not remember. Among the hospital personnel, there was no history of operation and/or hospitalization within a year. Among MRSA-carrier personnel, only one had a concurrent disease (Behcet's disease). Among the MRSA-carrier personnel, there was no history of contact with patient, or hospital personnel in the family. MRSA nasal carrier inpatients and outpatients were also evaluated for risk factors as the hospital personnel by using a form. Among inpatients, established risk factors for nasal carrier status were antibiotic use (73%), hospitalization and/or a history of surgical operation in the previous year (25.4%), and concurrent disease (43.6%). There was no history of personnel working in the hospital or in institutions. Of MRSA nasal carrier inpatients, 63.6% (35/55) were admitted in surgical clinics and intensive care units while 36.4% (20/55) were admitted in internal medicine clinics. The number of MRSA carriers in surgical clinics were significantly higher ($p< 0.05$).The rate of MRSA and MSSA nasal carriage were determined 3.04%, 9.03% and 3.96% among hospital personnel, inpatients and outpatients, respectively. These results are demonstrated in Table 2. The rate of MRSA nasal carriage was higher in inpatients than in hospital staff and outpatients ($p< 0.05$). Results are shown in Table 3.

There was no significant difference between hospital personnel and inpatients in terms of antibiotic resistance, except for erythromycin and ciprofloxacin. Resistance to erythromycin and ciprofloxacin was higher in strains isolated from inpatients than those isolated from healthcare personnel ($p< 0.05$).

DISCUSSION

It is reported that nasal carriage of MRSA increase the risk for the development of MRSA infections. The most common risk factors for the acquisition of MRSA include administration of multiple antibiotics[8,10]. In a study carried out in Italy, community-acquired nasal carriage was found to be very rare while referral to hospital or outpatient clinics and the history of hospitalization in the last six months had been detected as risk factors for MRSA carriage and spread through institutions[11]. In another study carried out in Turkey, Baykam et al.reported that the history of hospitalization within the previous twelve month sand insulin use were the risk factors for community-acquired nasal carriage of MRSA[12].

In a study by Lucet et al., all patients in fourteen intensive care units were screened for nasal cultures[10]. Patients were inquired for previous hospitalization, surgical operation, antibiotic use, chronic diseases, and immunosuppression. A total of two thousand three hundred and forty-eight patients were screened and MRSA carriage was in 6.9% (162 cases). In multivariate analysis, the risk factors for MRSA carriage were age over 60 years, long period of hospitalization of patients referred from other hospitals, previous history of hospitalization, surgical operation, and open skin lesions. Porter et al. investigated the prevalence of MRSA and MSSA nasal carriage during hospitalization in the surgical intensive care[13]. They reported MSSA nasal carriage in 22.3% of the patients (126/565) admitted to the ICU and 3% (n= 16) MRSA nasal carriage. Mortality rate was higher in MRSA carriers than that of in MSSA carriers and non-carriers. Friedmann et al. reported that fifteen out of 167 patients were nasal carriers of MRSA upon admission to the hospital[14]. Eveillard et al. have demonstrated MRSA nasal carriage in sixty (6.2%) out of 965 healthcare workers[15]. MRSA prevalence was higher in those working in clinical services than in those working in non-clinical service departments (9.25% and 2.15%, respectively).

Baykam et al. screened nine hundred patients for MRSA upon hospital admission, and 11 MRSA strains (1.2%) were detected[12]. All MRSA strains were positive for the mecA and Panton-Valentine leucocidin gene. Eight of the 11 MRSA-positive patients (72%) had a history of hospitalization within the previous 12 months.

In the present study, the rate of MRSA nasal carriage was 3.04%, 9.03% and 3.96% in hospital staff, inpatients and outpatients, respectively. It was significantly higher in inpatients ($p< 0.001$). Among the hospital personnel, carriage rate was 1.36% among physicians, 1.73% among nurses and 5.06% among auxiliary healthcare personnel. The rate in auxiliary healthcare personnel was significantly higher than the rates among physicians and nurses ($p< 0.05$). Carriage rate was higher in surgical clinics for both healthcare personnel and inpatients ($p< 0.05$). Of the MRSA-carrier inpatients, 63.6% had admitted in surgical clinics and 36.4% in internal medicine clinics. *S. aureus* nasal carriage and MRSA nasal carriage rates in inpatients and outpatients in various studies are shown in Table 4. Risk factors for MRSA infection and colonization include recent admission to the hospital, surgical intervention, intravenous drug use, underlying disease, close contact with hospital personnel, antibiotic use in the last six months, institutionalization and the presence of hospital personnel among family members[5,8,11,16]. In our study, hospital personnel, inpatients and outpatients were evaluated for risk factors for MRSA nasal carriage. In inpatients and outpatients, the rate of antibiotic use was higher than that of the hospital personnel ($p< 0.05$). Among inpatients, the rate of admission to hospital and surgical operation was higher than those of hospital personnel and outpatients ($p< 0.05$). Moreover, the rate of underlying diseases was also higher among inpatients (diabetes, chronic renal failure, hypertension etc.) ($p< 0.05$). The limitation to this study was that the presence of the mecA gene was not detected by polymerase chain reaction method regarded as the gold standard for the detection of methicillin resistance. Askarian et al. have reported the prevalence of nasal carriage of MSSA to be 25.7% and MRSA to be 5.3% in 600 healthcare workers in Iran[17]. In this study, it was reported that the

Table 4. Rates of *Staphylococcus aureus* nasal carriage and MRSA nasal carriage in inpatients and outpatients

	Hospital staff		Inpatients		Outpatients	
Authors	***S. aureus***	**MRSA**	***S. aureus***	**MRSA**	***S. aureus***	**MRSA**
Cesur and Cokca[5]	18	6			11	2.6
Reboli, et al.[6]	8	2.1				
Lucet, et al.[10]				6.9		
Baykam, et al.[12]					13.4	1.2
Porter, et al.[13]				3		
Eveillard, et al.[15]		6.2				
Askarian, et al.[17]	25.7	5.3				
Çaylan, et al.[18]	15.1	4				
Kaleli, et al.[19]	29.2	16				
Erdenizmenli, et al.[20]	9.8	0.98			9.4	0
Akoua, et al.[21]	45.4	17.8				
Na'was, et al.[22]	19.8	2.5				
Hidron, et al.[23]			23.6	7.3		
Troillet, et al.[24]				2.6		
Kenner, et al.[25]					40	2

MRSA: Methicillin-resistant *Staphylococcus aureus*.

highest MRSA carriage rates were in the surgical wards and the emergency department. It was also reported that the occupation of nursing was an independent risk factor for nasal MRSA carriage. In Turkey, the rate of nasal MRSA carriage has been reported between 4-16% in various studies[18,19]. Cesur and Cokca have reported the rate of MRSA nasal carriage to be 6% among hospital personnel and 2.6% among outpatients[5]. In this study, MRSA nasal carriage rate was 6.12% among physicians, 6.57% among nurses, and 5.17% among auxiliary health personnel. Erdenizmenli et al. have investigated the rate of MSSA and MRSA nasal carriage in five hundred outpatients and 102 healthcare workers[20]. They reported the rate of MSSA nasal carriage to be 9.4% among outpatients; whereas, no MRSA carriage could be detected. In healthcare workers, they have reported the rate of MSSA nasal carriage to be 8.8% and the rate of MRSA nasal carriage to be 0.98% (only in one person). In the present study, the MRSA nasal carriage rate was significantly higher among auxiliary healthcare staff than those among physicians and nurses. This difference may be due to the fact that auxiliary healthcare staff is not adequately informed about hospital infections.

There was no significant difference between hospital personnel and inpatients in terms of antibiotic resistance, except for erythromycin and ciprofloxacin. Resistance to erythromycin and ciprofloxacin was higher in strains isolated from inpatients than those isolated from healthcare personnel. In a study by Cesur and Cokca, no statistically significant difference was reported between the rates of resistance in MRSA strains isolated from hospital personnel and outpatients[5].

As a result, in order to prevent MRSA nasal carriage and development of infection, infection control measures should be developed and strictly implemented. Antibiotic use is an important risk factor for MRSA colonization. Training hospital personnel, especially auxiliary healthcare personnel, is very important. Low education level among auxiliary healthcare personnel and the lack of information about hospital infections may account for the high rate of nasal carriage in this group. We recommend that the hospital personnel should be trained on hospital infections, their routes of contamination, and preventive measures for the prevention and control of hospital infections. On the other hand, hospital personnel and inpatients admitted in clinics where hospital infections and colonization are common should be screened at certain intervals for

MRSA carriage, and patients should be screened for MRSA nasal carriage before admission to intensive care and surgical units.

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