Frequency of Nasal Carriage of *Staphylococcus Aureus* and Its Antimicrobial Resistance Pattern in Patients on Hemodialysis

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Introduction. *Staphylococcus aureus* is currently the most common cause of infection in hospitalized patients. Patients on hemodialysis are at increased risk due to their immunocompromised state. The present study was designed to determine the frequency of *S aureus* nasal carriage in patients on hemodialysis.

Materials and Methods. This study was undertaken in 2 dialysis centers to establish the frequency of *S aureus* nasal carriage at teaching hospitals of Mazandaran University of Medical Sciences, in the north of Iran. Standardized nose swabs were rotated into the anterior nares of the patients, and the samples were cultured on a blood-agar medium. Having grown the colony, gram stain, catalase, manitol, DNAase, and coagulase tests were all performed. Pattern of antibacterial sensitivity was determined by using the disc diffusion method. Also, agar dilution method was used to determine minimal inhibitory concentration of oxacillin and vancomycin.

Results. Of 84 patients on hemodialysis, 31 (36.9%) were nasal carriers of *S aureus*, of whom 23 (74.2%) were resistant to methicillin. Of the methicillin-resistant *S aureus* isolates, 3 (13.0%) were resistant to vancomycin and 7 (56.5%) had reduced susceptibility to vancomycin in agar dilution method. Resistance frequencies to clindamycin, ciprofloxacin, and trimethoprim-sulfamethoxsazole were 12.9%, 9.7%, and 19.3%, respectively. However, all microorganisms were sensitive to rifampicin.

Conclusions. Patients on hemodialysis are at an increased risk of *S aureus* infections; thus, screening of these susceptible patients should be considered as a health priority. Meanwhile, microbial sensitivity tests should be ordered for all cases in order to optimize treatment options.

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INTRODUCTION

Infection is a major cause of morbidity and the second most common cause of death in patients receiving hemodialysis.[1,2] Nasal carriage of *Staphylococcus aureus* plays a key role in the development of *S aureus* infections. The reservoir for *S aureus* skin infection is the anterior nares. It is a major risk factor for acquiring of infection in patients undergoing hemodialysis.[3] Patients on hemodialysis are more prone to staphylococcal infections because of their decreased immunity, increased skin colonization by *Staphylococci*, and

multiple needle punctures required for dialysis. The carrier state is significant not only in terms of predisposing to subsequent infections, but also as the potential of transmission among dialysis unit staff and their family members.[4]

The *S aureus* nasal carriers constitute 59.5% to 76% of the patients on dialysis in different dialysis centers.[5-7] A direct link between such a high nasal carriage of *S aureus* in patients on hemodialysis and subsequent infection by the same organism has been found in numerous studies.[7-9] consequently, elimination of staphylococcal nasal carriage results in a significantly lower infection rate.[1]

The rate of dialysis units that reported 1 patient or more receiving treatment for a methicillin-resistant *S aureus* (MRSA) infection increased from 40% in 1995 to 71% in 2000.[10] The increasing number of infections with MRSA strains makes therapy challenging.[11] Determination of in vitro resistance of *S aureus*, as a cause of hospital-originated infection, is crucial to apply appropriate antibiotics.[12,13] Despite rapid improvement in antimicrobial therapy, there are still great difficulties in the treatment of staphylococcal infections.

Certainly, determining the prevalence of nasal carriage, especially among patients on hemodialysis, and recognizing the appropriate pattern of antibacterial resistance, could pave the way for optimized antibiotic prescription and prevent resistance to newly developed antibiotics. In the present study, we evaluated the *S aureus* carriage state of our patients who were on hemodialysis during a 3-month period. The pattern of antibacterial resistance was determined according to the latest guidelines of the National Committee for Clinical Laboratory Standards (NCCLS).[14]

MATERIALS AND METHODS

Clinical samples were obtained from all patients on hemodialysis at Imam Khomeini Hospital and Fatemeh Zahra Hospital in Sari, Iran, from June of 2006 to December 2006. All patients undergoing regular hemodialysis that was not receiving antibiotics during the past 2 weeks and were not hospitalized for any reasons other than hemodialysis during the past 2 months were included in this study. Informed consent to participate the study was obtained from all eligible patients.

The following data were collected: dialysis duration (time span since initiation of hemodialysis therapy), history of diabetes mellitus, and history of documented intravenous catheter infection with a positive blood or catheter tip culture for staphylococcal infection. Diabetes mellitus diagnosis was based on 2 consecutive fasting (minimum of 8 hour) blood glucose values of 126 mg/dL or higher, collected during ambulatory appointments.[15]

Nasal specimens were collected from 84 patients on long-term hemodialysis using 2 sterile dry cotton-wool swabs for each patient. The swab was circled through both nostrils consecutively while applying an even pressure. The swabs were immediately placed in a transport medium. The nasal swabs were inoculated onto sheep blood-agar plates and phenol-red mannitol salt agar plates. The plates were incubated at 37°C for 48 hours. The identification of *S aureus* was based on colony morphology, biochemical activities, and the coagulase test.

Antimicrobial susceptibility testing was performed in accordance with the guidelines of the NCCLS,[16] using the Kirby-Bauer disc diffusion method.[17] The susceptibilities of isolated *S aureus* strains were tested against oxacillin, 10 µg per disc; cephalotin, 30 µg per disc; trimethoprim-sulfamethoxazole, 1.25-23.75 µg per disc; rifampicin, 5 µg per disc; clindamycin, 2 µg per disc; gentamicin, 10 µg per disc; and ciprofloxacin, 5 µg per disc (supplied by Padtan Teb, Tehran, Iran).

The minimum inhibitory concentrations (MICs) of 2 antibiotics (meticillin and vancomycin) were determined by using the broth microdilution technique as described by the NCCLS.[14] All isolates with MICs greater than 4 µg/mL were considered resistant (MRSA). Vancomycin MICs were determined for each MRSA isolates. The plates were incubated for a full 24-hour period at 37°C before reading. Two individuals independently performed the reading. *Staphylococci*, especially methicillin-resistant isolates, for which the vancomycin MICs were 4 µg/mL or greater were considered to have reduced susceptibility, and a vancomycin MIC of 8 µg/mL or greater considered vancomycin-resistant *S aureus* (VRSA). As a control strain, *S aureus* ATCC 33591 (methicillin resistant) and *S aureus* ATCC 25923 (methicillin susceptible) were used for identification and susceptibility tests.

Data was analyzed by using the SPSS software (Statistical Package for the Social Sciences, version 13.0, SPSS Inc, Chicago, Ill, USA). The t test and

the chi-square test were used where appropriate. Continuous variables were presented as mean ± standard deviation. *P* values less than .05 were regarded as significant.

RESULTS

Of the 84 patients on hemodialysis, 45 (53.5%) were men and 39 (46.4%) were women. The average age of the patients was 52.4 ± 20.7 years. The mean period on hemodialysis was 33.6 ± 16.9 months (range, 12 to 168 months). Twenty-five patients (29.8%) were diabetic and 54 (64.3%) had hypertension.

Staphylococcus aureus nasal carrier state was determined in 31 of the 84 patients on hemodialysis (36.9%). A significant association was found between the hemodialysis duration and the isolation rate of *S aureus*; hemodialysis duration was 36.4 ± 14.3 months in patients with *S aureus* and 22.3 ± 16.5 months in the noncarriers ($P < .001$).

In the diabetic patients, *S aureus* isolation rate was 36.0% (9 of 25), and in nondiabetics, it was 37.3% ($P = .35$). History of central intravenous catheter infection was significantly more frequent among the patients with isolation of *S aureus* than those without it (9 [29.0%] versus 4 [7.5%], $P < .001$).

Methicillin resistance rate was 74.2% (23 of 31) among the *S aureus* strains. The MIC value was 0.5 µg/mL or lower in 8 isolates (defined as methicillin-sensitive *S aureus*, according to the NCCLS criteria) and it was greater than 4 µg/mL in 23 isolates (defined as MRSA, according to the NCCLS criteria). Vancomycin MIC ranges were as follows for the 23 isolates of MRSA: greater than 8 µg/mL for 3 isolates (13.0%; VRSA), between 2 µg/mL and 4 µg/mL for 7 (30.4%; reduced susceptibility to vancomycin), less than 2 µg/mL for 13 (56.5%; vancomycin susceptible). The resistance of *S aureus* to other antibiotics (by the disc diffusion test) was as follows: clindamycin, 12.9%; gentamicin, 26.0%; ciprofloxacin, 9.7%; trimethoprim-sulfamethoxazole, 19.3%; rifampicin, zero; and cephalotin, 87.0%.

DISCUSSION

Staphylococcus aureus carriage in the nose has been shown to be more common in patients receiving long-term hemodialysis than in the general population.[9] In this study, the nasal carriage rate of *S aureus* was found to be 36.9% in 84 patients on hemodialysis. Whereas, in studies from other countries, the rate of *S aureus* nasal carriers ranged from 59.5% to 76% in different dialysis centers.[18]

Piraino and coworkers investigated the relationship between *S aureus* infections and nasal carriage in 138 patients on peritoneal dialysis. They established that approximately 50% of the patients were carriers.[17] Aminzadeh and colleagues reported the nasal carrier state in 45.8% of their patients on hemodialysis in Tehran.[19] Ghazvini and Hekmat reported a rate of 40.5% in their patients on long-term hemodialysis in Mashhad.[20] Although our results were lower than their reported rates, the MRSA rate in our study was significantly higher than theirs.[19]

In our study, no significant correlation was found regarding the nasal carriage of *S aureus* and diabetic mellitus in patients on hemodialysis. However, history of central intravenous catheter infection was more frequent and the dialysis vintage was longer in patients with the isolation of *S aureus*. We speculate that while the length of admission to hemodialysis is an important risk factor for *S aureus* carriage, diabetes mellitus is not. Furthermore, in our study, age and gender were not important risk factors for *S aureus* carriage. Similarly, Aminzadeh and colleagues[19] did not find any difference between genders. In contrast, Saxena and coworkers found a significant correlation between age and nasal carrier state.[21] Carrying *S aureus* in nares was shown in several studies performed in different countries among patients on hemodialysis, and the risk of their becoming infected with their own strains was quite high.[22] Furthermore, *S aureus* infections can cause considerable morbidity and mortality in these patients.

While MRSA rate was 36.9% in our patients, based on in vitro sensitivity test results, resistance rates of *S aureus* strains isolated from patients on hemodialysis to methicillin and vancomycin were at 74.2%, 9.6%, respectively. There were no strains resistant to rifampicin among our cases; therefore, the most effective antibiotic in our isolates could be rifampicin. Although Aminzadeh and colleagues[19] found MRSA in 100% of their patients, they reported all their *S aureus* were sensitive to vancomycin. Most of these differences could be due to the method of microbial sensitivity test. We used the MIC to find the MRSA and vancomycin resistant rate, whereas they used only disc antibiogram method

that is less accurate compared to the MIC method.

Duran and coworkers[9] reported MRSA in 36% of their patients on hemodialysis, and all of their MRSA isolates were sensitive to vancomycin. The rate of MRSA in their study was significantly lower than our isolates; however, the differences between the vancomycin resistant rates are considerable. These differences simply reveal that resistant rate to the most important antibiotics is inappropriately high in *S aureus* isolates in our patients on hemodialysis. Unfortunately, the rate of antibiotic usage, especially vancomycin, is very high in our hospitals and it could be the reason for such a high resistant rate of our *S aureus* isolates. In addition, the choices of suitable antibiotics with positive effects on MRSA are limited in our country. As a result, we do not have any choice against VRSA at present. Furthermore, it was shown that *S aureus* strains isolated from our patients on hemodialysis have developed high resistance to many of the known antibiotics. The colonization of the resistant strains rather than the frequency of *S aureus* colonization are a threat to the patients on hemodialysis.[11]

With respect to the increasing rate of MRSA and VRSA and transmission of infection from carriers to others,[23] especially immunocompromised individuals, MRSA and particularly VRSA carriers should be isolated and the medical staff should be obliged to wash their hands routinely prior to taking care of their patients.[7] Meanwhile, we strongly suggest effective antibiotics for experimental therapy of *S aureus* and prescription of vancomycin, only if the microorganism was revealed to be oxacillin and methicillin resistant.

CONCLUSIONS

In summary, patients subjected to hemodialysis are more susceptible to *S aureus* infection. Screening of these patients is a cost-effective strategy. As it was shown that *S aureus* strains isolated from our patients on hemodialysis have developed high resistance to many of known antibiotics, therapy with antibiotics must be according to the microbial sensitivity tests. Because of the significantly high prevalence of these resistant pathogens in this high risk population, epidemiological studies to clarifying the prevalence and transmission patterns of antimicrobial resistant pathogens other than MRSA and vancomycin resistant pathogens are needed.

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CONFLICT OF INTEREST

None declared.

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