

To Study the Correlation between Carrier Status of Nasal *Staphylococcus aureus* in Patients on Haemodialysis with Hepatitis C, Hepatitis B and Their Sociodemographic Features

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ABSTRACT

Aim: To study the correlation of nasal *Staphylococcus aureus* carrier status in patients on haemodialysis, infected by hepatitis C virus (HCV), hepatitis B virus (HBV), and their sociodemographic features.

Subjects and Methods: A survey, including patients' sociodemographic features, was applied to patients by physicians in face to face interviews. Medical records regarding their serologic data were recorded from haemodialysis centres. Nasal swab samples of 2 cm depth from both nostrils of patients were obtained for nasal culture. Samples were inoculated in 5% sheep blood agar and incubated in an incubator at a temperature of 37°C for 24 hours. The results were studied by the same microbiologist.

Results: A total of 185 patients were enrolled in the study. According to culture results, 14.1% of patients ($n = 26$) had methicillin sensitive *Staphylococcus aureus* (MSSA) and 1.1% ($n = 2$) had methicillin resistant *Staphylococcus aureus* (MRSA). Status of viral hepatitis was 3.8% ($n = 8$), 10.8% ($n = 20$) for HBV and HCV, respectively. Forty per cent ($n = 8$) of patients with HBV (+) had MSSA carrier status. Statistically significant positive correlation between MSSA and HCV carrier was detected ($r = 0.325$, $p = 0.001$) but not between HBV carrier and MSSA ($p = 0.255$).

Conclusion: In the present study, significant positivity was detected between MSSA carrier status and HCV in patients on haemodialysis and who have lived together with ≤ 2 family members at home. Particularly, statistically significant correlation between HCV (+) and MSSA carrier was observed.

Keywords: Haemodialysis, methicillin resistant *Staphylococcus aureus*, methicillin sensitive *Staphylococcus aureus*, hepatitis B virus, hepatitis C virus, *Staphylococcus aureus*

Estudiar la Correlación entre el Portador del *Estafilococo dorado* Nasal en Pacientes de Hemodiálisis con Hepatitis C, Hepatitis B y sus Características Sociodemográficas

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RESUMEN

Objetivo: Estudiar la correlación entre el portador del *Estafilococo dorado* (*Staphylococcus aureus*) nasal en pacientes de hemodiálisis infectados por el virus de la hepatitis C (VHC), el virus de la hepatitis B (VHB), y sus características sociodemográficas.

Sujetos y Métodos: Una encuesta que incluía características sociodemográficas de los pacientes fue aplicada a pacientes por médicos en entrevistas cara a cara. Historias clínicas contentivas de sus datos serológicos, fueron registradas a partir de los centros de hemodiálisis. Muestras de frotis nasales

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de 2 cm de profundidad de ambas fosas nasales, fueron obtenidas para un cultivo nasal. Se inocularon muestras en agar de sangre de oveja al 5%, e incubadas en una incubadora a una temperatura de 37°C por 24 horas. Los resultados fueron examinados por el mismo microbiólogo.

Resultados: Un total de 185 pacientes fueron enrolados en el estudio. Según los resultados del cultivo, 14.1% pacientes ($n = 26$) tenían estafilococo dorado sensible a la meticilina (MSSA) y 1.1% ($n = 2$) tenían estafilococo dorado resistente a la meticilina (MRSA). El estatus de las hepatitis virales fue 3.8% ($n = 8$), y 10.8% ($n = 20$) para HVB y HVC respectivamente. Cuarenta por ciento ($n = 8$) de los pacientes con HVB (+) eran portadores del MSSA. Estadísticamente, se detectó una correlación positiva significativa ($r = 0.325$, $p = 0.001$), entre MSSA y el portador de VHC, no así entre el portador del VHB y MSSA ($p = 0.255$).

Conclusión: En el estudio presente, se detectó una positividad significativa entre el estatus de; portador de MSSA y los pacientes de VHC en hemodiálisis, que vivían junto con [= dos o menos de dos] miembros de la familia en casa. En particular, se observó una correlación estadísticamente significativa entre HCV (+) y el portador MSSA.

Palabras claves: Hemodiálisis, *Estafilococo dorado* resistente a la meticilina, *Estafilococo dorado* sensible a la meticilina, virus de la hepatitis B, virus de la hepatitis C

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INTRODUCTION

Nosocomial infections are important health problems. Among potential pathogenic bacteria in the nasal cavity, *Staphylococcus aureus*, *Neisseria meningitidis*, *Moraxella catarrhalis*, *Streptococcus pneumoniae* and *Haemophilus influenzae* are the major ones (1, 2). *Staphylococcus aureus* has stood in the forefront due to the high incidence of carrier infection and associated complications for community health (3, 4). Diabetic patients, intravenous (IV) drug-users, patients on haemodialysis and with cirrhosis of the liver, and hospitalized patients, particularly in intensive care units and on surgery wards, are at risk for staphylococcal infections (5–9). Nasal mucosa is the most common site that harbours *Staphylococcus aureus* in the body. Other regions are the perineum and axillary region, throat, other sites where skin integrity is disrupted and IV catheter insertion. Persons with persistent *Staphylococcus aureus* carrier status are about 10–20% of the normal population (10–13).

The most common reasons for mortality in patients on haemodialysis are infectious diseases. *Staphylococcus aureus* is the most common isolated pathogen leading to infectious diseases in these patients (14). Catheters have been primarily implicated in the development of infectious diseases in patients on haemodialysis. *Staphylococcus aureus* colonization of the nasal anterior mucosa of patients and health professionals is a reservoir for *Staphylococcus aureus* infection. Nosocomial infection usually results from contact between patients' catheter and patients, or health professionals (4). Kurutepe *et al* (15) conducted a study and reported that the ratio of *Staphylococcus aureus* was 33% in patients on haemodialysis. Carrier of nasal *Staphylococcus aureus* was between 10–40% in the normal population (16, 17). DeLeo *et al* reported that community acquired *Staphylococcus aureus* infection exceeded nosocomial infection due

to *Staphylococcus aureus* (18). Nowadays, increase in methicillin resistance to *Staphylococcus* species is an important health problem. Another problem is the increase in multiple antibiotic resistances against the bacteria with methicillin-resistant *Staphylococcus aureus* (MRSA) [+] all over the world (19). It is shown that not only antibiotic resistance against beta-lactam antibiotics, but also against macrolides, aminoglycosides, fluoroquinolones, lincosamides and chloramphenicols develop in some bacteria with MRSA [+] (20). Finally, patients on haemodialysis are at great risk for community and hospital acquired infection with *Staphylococcus aureus*.

Another problem in patients on haemodialysis is increased risk for hepatitis B virus (HBV) and hepatitis C virus (HCV). Patients on haemodialysis are more likely to be exposed to both HBV and HCV than the normal population (21, 22). In studies, it was shown that HBV and HCV carrier status in patients on haemodialysis is five times more than in the normal population (23).

In the present study, we aimed to investigate the relationship between nasal *Staphylococcus aureus* carrier status and status of HCV and HBV infection in patients on haemodialysis and their sociodemographic features from six different haemodialysis centres in Ankara.

SUBJECTS AND METHODS

The study was conducted by Gulhane Military Medical Academy, Department of Family Medicine, and performed in five discrete haemodialysis centres in Ankara, Turkey, between June 2009 and October 2009. Patients on haemodialysis were enrolled from those centres. The study survey, which included sociodemographic features, was applied by a physician in face to face interview after obtaining informed consent. Status of HBV, HCV and HIV carrier was recorded from the patients' medical records.

Nasal swab samples were collected from both nares of each patient at 2 cm depth *via* a sterilized swab. The specimens were immediately sent to the microbiology laboratory of our institute. Samples were incubated at 37°C for 24 hours in an incubator after inoculation on to 5% sheep blood agar. Cultures were evaluated by the same microbiology specialist. Samples displaying Gram (+) colony along with catalase (+) and catalase (-) were defined as *Staphylococcus aureus*. It was accepted as positive if the number of colonies multiplied was over ten on Agar. Antibiotic sensitivity of bacteria was evaluated by the disc diffusion method according to National Committee for Clinical Laboratories (NCCLS) criteria.

For sociodemographic features, gender, age, educational level, status of marriage, income, occupation, residency, catheter use, household members, start date of haemodialysis, status of health insurance, smoking and alcohol use were inquired. Additionally, medical history such as diabetes mellitus, hypertension, hyperlipidaemia, allergy, cardiac diseases, thyroid diseases, liver and renal diseases were inquired of patients and their families. Patients' weight and height measurements were recorded at morning time at the haemodialysis centre. Body mass index (BMI) was calculated by using the formula of kg/m², and their BMI classification was determined by the World Health Organization (WHO).

Statistical analysis

Statistical analysis was conducted using SPSS 15.0 (SPSS Inc, Chicago, IL, USA). In this study, descriptive analysis of data was conducted. When comparing values from two groups, independent sample *t*-test was used for parametric values and Chi-square (Fisher's exact test) test used in categorized data analysis. Odds ratio (OR) and confidence interval (CI 95%) were estimated for MSSA, HCV, HBV, and sociodemographic parameters (age, gender, marital status, income salary, disease duration, household members). Data were summarized as mean ± standard deviation. Significance was determined if *p*-value < 0.05.

Ethical consideration

The study protocol was approved by the Ethical Review Committee of Gulhane Military Medical Academy, Department of Family Medicine and all the participating haemodialysis centres in Ankara, Turkey. No financial incentives were provided to any study participant. Written informed consent and verbal assent was given by all participants or their surrogate prior to the interview.

RESULTS

One hundred and eighty-five patients (male = 119, 64.3%, female = 66, 35.7%) were enrolled in the study. The mean age in male, female and total patients were 58.9 ± 15.9, 58.2 ± 15.0 (*p* = 0.490) and 58.6 ± 15.6, respectively. Married patients comprised 80.5% (n = 149); 11.9% (n = 22) were single and the remaining 7.6% (n = 14) were widowed. Information about education level of subjects is stated in

Table 1. Seven patients (3.8%) were from rural residences and the remaining 96.2% (n = 178) were from urban residences; 30.1% of patients (n = 68) were current smokers. One hundred and seventeen patients (62.9%) were non-smokers. Only 2.7% (n = 5) were current alcohol drinkers. Among haemodialysis-related diseases, diabetes mellitus and hypertension were seen in 14.1% and 16.2% of patients, respectively. A family history of chronic renal failure was elicited in 23.4% of patients (n = 44). In maternal medical history, the percentage of chronic renal diseases was 23.4%, hypertension 27.4% and diabetes mellitus 18.6%. In father's medical history, the percentage of diabetes mellitus was 10.5% and hypertension 9.9%. Moreover, diabetes mellitus and hypertension were observed as 20.8% (n = 38) and 8.2% (n = 7), respectively, in other family members of patients.

In Table 1, status of methicillin sensitive *Staphylococcus aureus* (MSSA) positivity according to status of HBV and HCV seropositivity along with sociodemographic features in patients on haemodialysis was stated. Methicillin sensitive *Staphylococcus aureus* positivity was statistically significant in patients with HCV (+), haemodialysis duration over ten years, and those who live with ≤ 2 household members (*p* < 0.0001, *p* = 0.045 and *p* = 0.001, respectively). However, female patients and those with low educational level had MSSA (+), but this was not significant (*p* = 0.079 and *p* = 0.326, respectively). Methicillin sensitive *Staphylococcus aureus* (+) and MRSA (+) were observed in 14.1% (n = 26) and 1.1% (n = 2) of patients, respectively. Colony formation was not detected in the culture medium of 157 patients (84.8%) within 24 hours. No HIV infection was found in any patient. Seven (3.8%) and 20 (10.8%) patients had HBV and HCV carrier status, respectively. A significant difference between MSSA (+) in patients who were HCV (+) and HCV (-) was observed [*p* < 0.0001] (Figure). Hepatitis C virus positivity increased MSSA (+) 4.4 times [OR: 4.411, 95% CI for Exp (B) (1208, 16107) (*p* = 0.025)]. There was statistical significance between HCV (+) and MSSA (+) [*p* = 0.001], but not between HBV (+) and MSSA (+) [*p* = 0.255] (Table 2). Significant difference between *Staphylococcus aureus* and sociodemographic features such as educational level, status of smoking, health insurance, monthly salary, household member, residency, caring for bed-bound patients was not observed (*p* = 0.972, *p* = 0.536, *p* = 0.311, *p* = 0.699, *p* = 0.401, *p* = 0.157, *p* = 0.283 and *p* = 0.208, respectively). No significant difference was detected between status of patients' education and MSSA positivity (*p* = 0.291 and *p* = 0.246). A correlation between MSSA positivity and the number of household members was observed. When the number of household members was above two, marked decrease in MSSA positivity was detected (*p* = 0.022, 95% CI = 1.17, 5.77). However, this was not observed for status of MRSA positivity (*p* = 0.522). The difference between status of MSSA carrier and homecare provider was not observed (*p* = 0.068).

Table 1: Status of MSSA (\pm) in patients on haemodialysis according to their sociodemographic features and HBV (\pm) and HCV (\pm) status

		MSSA		p
		(+)	(-)	
Age	(years)	58.9 \pm 15.9	58.2 \pm 15.0	0.490
Duration of diseases	(years)	7.9 \pm 5.9	6.3 \pm 4.9	0.200
BMI	Kg/m ²	23.4 \pm 4.0	24.9 \pm 4.4	0.140
HBsAg	(+)	0	7	0.340
	(-)	26	152	
HCV	(+)	8	12	< 0.0001
	(-)	18	147	
Gender	Male	13	106	0.079
	Female	13	53	
Educational level	Illiterate	9	32	0.326
	Primary	13	94	
	Secondary	2	16	
	University	2	15	
Number of household members	\leq 2	13	44	0.045
	3–5	10	102	
	\geq 6	3	13	
Duration of haemodialysis	\leq 5	12	91	0.001
	6–10	6	42	
	> 10	8	26	
Total		26	159	185

MSSA = methicillin sensitive *Staphylococcus aureus*, HBV = hepatitis B virus, HCV = hepatitis C virus, BMI = body mass index, HBsAg = hepatitis B surface antigen

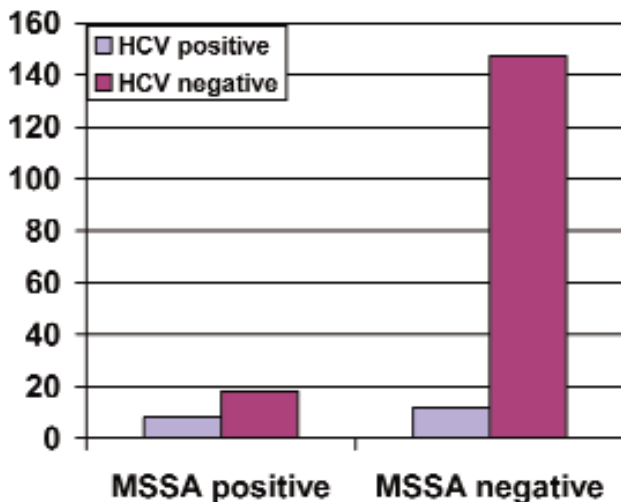


Figure: Methicillin sensitive *Staphylococcus aureus* (MSSA) carrier status according to hepatitis C virus (HCV) infection.

DISCUSSION

Infections due to *Staphylococcus aureus*, especially in patients on haemodialysis and hospitalized patients cause serious health problems. Since the 1960s, MRSA strains have been reported (24) and rates are increasing. The national nosocomial infection follow-up system, United States of America (USA), detected the ratio of nosocomial infection as 13% between 1979 and 1995 at hospitals in the USA. Moreover, its ratio gradually increased (25–27). While the ratio of MRSA was 2.3% in 1975 in the USA, it increased to 29% in 1991 (28). However, the frequency of MRSA was only 0.26% in the present study. In the same period, the rate of MRSA was reported as 0.8% in Nashville, USA. However, the study with similar age groups of persons was repeated by New York researchers at the same research centre in 2005, with the result of a total rate of MSSA of 46%, and carrier rate of MSSA was 9.2% in children. The nasal carrier rate of *Staphylococcus aureus* on healthy individuals in our country was reported as 14% by Kaleli *et al* (30), 16.8% by Kazaz *et*

Table 2: Distribution of HIV status and carrier status in *Staphylococcus aureus*, HBV, HCV in the present study

	(+)	%	(-)	%	Total
MSSA	26	14.1	159	85.9	185
MRSA	2	1.1	183	98.9	185
HBsAg	7	3.8	178	96.2	185
HCV	20	10.8	165	89.2	185
Anti-HIV	0	0	185	100	185

al (31) and 21.4% by Kantarcioglu *et al* (32). The rate of MRSA varied in several countries, ranging from 1.5% to 45% (33).

One of the most important sources of contamination for *Staphylococcus aureus* infections is hospital employees. The transmission occurs mostly through catheters by hand contamination from persons working in surgical services, intensive care, and haemodialysis units. Among hospital employees, nasal carrier rates were reported as 31% in doctors, 27% nurses and 39% in health-workers by Mert *et al* (34); 38% in health-workers by Kiriş *et al* (35), 33.3% in doctors, 25% in nurses and 30.1% in general by Sancak *et al* (36). This situation has great significance for the staff of haemodialysis centres. The rate of nasal carrier for *Staphylococcus aureus* in nurses working at haemodialysis units was found to be 26% in Turkey by Demirci *et al* (37). According to these data, the education of hospital staff on hand hygiene and nasal culture done at regular intervals is important in preventing complications that may occur in patients.

The nasal carrier for *Staphylococcus aureus* in haemodialysis patients was found to be 33% by Kurutepe *et al* (15) and 49.2% by Demirci *et al* (37). This frequency was found to be around 10–51% in studies in the USA and 30.1% in Italy by Zanelli *et al* (38). Kluytmans *et al* (39) reported that the nasal carrier for *Staphylococcus aureus* in haemodialysis patients was between 30.1% and 84.8%. In our study, the nasal carrier for *Staphylococcus aureus* was found to be 15.2% (14.1% MSSA, 1.1% MRSA). This rate is lower than previous studies. This lower rate might be because the study was done in special dialysis centres where the number of the patients was less than in state hospitals, and the number of staff per patient is high and the hygiene level is good in these centres.

Another important problem with haemodialysis patients is HBV and HCV carrier status. Shepard *et al* (23) found an 8% incidence of HCV in haemodialysis patients in the USA. During the same period in the USA, prevalence of HCV in the general population was 1.6%. This rate was nearly five times more than the general population (26). The study conducted by the Turkish Society of Nephrology included 5787 patients, and 3095 of these (52.6%) had antibodies against HCV (22). Recently, a study by Gultekin *et al* (5) found the rate of HBV to be 14.6% and HCV 9.8%. These rates are lower than in the old literature data, although in many European countries, the rates are below 5%.

In our study, the carriage of HBV was 10.8%, whereas in chronic haemodialysis patients with HCV carriage, it was found to be 3.8%. This rate is lower than our earlier studies. Haemodialysis patients are often investigated with nasal carriage of *Staphylococcus aureus*, this carriage is limited to the review of literature investigating the relationship between sociodemographic data. In our study, HCV-positive MSSA carriage increased 4.4-fold [OR: 4, 411 95% CI for Exp (B) (1208–16107) ($p = 0.025$)]. Cytokines are important in the host defense against viral infections, particularly against the

two major forms of human hepatitis virus, HBV and HCV (40). Tumour necrosis factor- α (TNF- α) is hyper-expressed in chronic renal failure (CRF) patients with hepatitis C and suggests a mechanism of inflammation in the liver (41). In the recent study from Turkey, it was considered that CRF, dialysis, and chronic liver parenchymal disease with HCV or HBV infection might reduce the effectiveness of the body's immune system, which could allow dormant bacteria to become reactivated (42). In our study, HCV carriers with a statistically significant positive correlation was present between MSSA carriage ($p = 0.001$). However, there was no significant difference between HBV-staphylococcal carriage [$p = 0.255$] (Table 2).

The present study indicated that significant MSSA (+) was observed in patients with HCV (+), duration of dialysis over 10 years and who lived with ≤ 2 household members. Significant correlation between MSSA (+) and HBV carrier was also detected in our study. *Staphylococcus aureus*, which is an important causal factor for morbidity and mortality in patients on haemodialysis, is transmitted through catheter contamination with patients' nasal mucosa and hands of health professionals. Therefore, the importance of hand washing should be emphasized. Nasal culture should be regularly taken from both the patients and health professionals within the interval period. Patients who are culture (+) should be treated with mupirocin.

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