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Original Article

Prevalence of Methicillin-resistant *Staphylococcus aureus* (MRSA) Carrier in Hemodialysis Patients at Dr. Soetomo Academic General Hospital

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ABSTRACT

Chronic kidney disease (CKD) is now a global epidemic, and the prevalence is increasing worldwide. Hemodialysis is one of the ways to treat by kidney function replacement. Infection is the number two cause of death in patients with hemodialysis (HD). Methicillin-resistant Staphylococcus aureus (MRSA) is a common cause of bacteriemia in patients with dialysis. The epidemiological data of MRSA carriers in CKD in Indonesia are still scarce. This study was to determine the prevalence of MRSA carriers in patients at The Kidney and Hypertension Outpatient-clinic and Hemodialysis Installation at Dr. Soetomo Academic General Hospital, Surabaya Indonesia. The study design was descriptive-analytic with a cross-sectional study design. Sampling was collected consecutively. Data on the general characteristics of the research subjects will be analyzed using a Chi-Squared test. There were 150 CKD stage five patients included in this study, the number of patients has MRSA carrier were 6 (4%), among them, subjects underwent HD MRSA carrier were 2 subjects(2.7%), while for non-HD patients with MRSA were 4 subjects (5.3 %). There were no significant differences in MRSA carriers between HD and non HD groups (p=0.404). Comorbid factors that accompany MRSA carriers are diabetes mellitus, hypertension, kidney stones, gout, and systemic lupus erythematosus (SLE). ***Conclusions****: This study found, there were no significant differences in the incidence of MRSA carriers in stage five CKD non HD or HD groups. MRSA colonization exists in stage five CKD sufferers, so awareness of MRSA colonization.*

Keywords: *Chronic Kidney Disease, Hemodialysis, MRSA, Diabetes Mellitus, Hypertension, Indonesia.*

ABSTRAK

Penyakit ginjal kronis (CKD) saat in menjadi epidemi global, dan prevalensi meningkat di seluruh dunia. Hemodialisis adalah salah satu cara untuk terapi penggai ginjal. Infeksi merupakan penyebab kematian nomor dua pada pasien dengan hemodialisis (HD). Staphylococcus aureus yang resisten terhadap metisilin MRSA) adalah penyebab tersering bakteriemia pada pasien dengan dialisis. Saat ini data epidemiologis pembawa MRSA pada penderita CKD di Indonesia belum lengkap. Penelitian ini untuk mengetahui prevalensi pembawa MRSA pada pasien-pasien di Klinik Rawat Jalan Ginjal dan Hipertensi dan Instalasi Hemodialisis di Rumah Sakit Umum Dr. Soetomo, Surabaya Indonesia. Desain penelitian adalah deskriptif-analitik dengan desain penelitian cross-sectional. Pengambilan sampel dikumpulkan secara berurutan. Data karakteristik umum dari subjek penelitian akan dianalisis menggunakan uji Chi-Squared. Terdapat 150 pasien CKD stadium lima yang masuk didalam penelitian ini, jumlah pasien yang menjadi pembawa MRSA ada 6 subjek (4%), di antara mereka, subjek yang menjalani HD sebagai pembawa MRSA ada 2 subjek (2,7%), sedangkan untuk pasien non-HD dengan pembawa MRSA ada 4 subyek (5,3%). Tidak ada perbedaan yang signifikan antara pembawa MRSA antara kelompok HD dan non HD (p = 0,404). Faktor komorbid yang menyertai pembawa MRSA adalah diabetes mellitus, hipertensi, batu ginjal, asam urat, dan systemic lupus erythematosus (SLE). Penelitian ini mendapatkan, tidak ada perbedaan

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yang signifikan pada kejadian pembawa MRSA pada stadium lima CKD non HD atau kelompok HD. Kolonisasi MRSA ditemukan pada penderita CKD stadium lima, sehingga kesadaran pada kolonisasi MRSA.

Kata kunci: *Penyakit Ginjal Kronis, Hemodialisis, MRSA, Diabetes Mellitus, Hipertensi, Indonesia.*

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INTRODUCTION

Chronic kidney disease is a serious public health problem because there has been an increase in the number of patients, morbidity, and mortality.[1] MRSA can be spreading from hospital to community, in addition to hospital-hospital transfers.[2] In CKD patients with a history of hemodialysis with the use of vascular access, they should always be aware of the possibility of bacterial infections, it causes of death number 2 in patients with hemodialysis.[3,4,5] Vascular access is needed to obtain a large, enough blood flow. This access can be in the form of a fistula (artery-vein), graft, or intravenous catheter, which functions to drain blood during HD. Vascular access is one of the main risk factors for bacteremia (15.16%) and infections associated with frequent hospitalization and death (about 17.18%) in patients with hemodialysis.[6] The percentage of fatalities in CKD stage 5 patients due to infection is quite large. Patients who undergo hemodialysis are very susceptible to infection, especially Methicillin-resistant Staphylococcus aureus (MRSA). There was a meta-analysis study that estimates the prevalence of MRSA colonization in dialysis patients, the time and long-term risk of MRSA infection. From the data of 5596 dialysis patients, the prevalence of MRSA colonization was 6.2% (95% confidence interval, 4.2% to 8.5%). Prevalence increased over time but remained stable after 2000. Over a long period (6-20 months), the likelihood of developing MRSA is around 19% in patients who have hemodialysis compared with patients with hemodialysis without MRSA colonization of about 2%.[7] The infection will also worsen kidney function or will add a burden to the already poor kidney function, which will contribute to the increase in morbidity, mortality, and costs, therefore infection problems in stage five CKD patients are critical.[8]

Chronic kidney disease (CKD) is often associated with several immunological abnormalities, both congenital immune system disorders, and adaptive immune systems and, therefore, can increase susceptibility to infection.[9] Infection enhanced with the use of a central catheter compared to AV fistula. Infections originating from the use of vascular access are often associated with microorganisms *Staphylococcus aureus* and *Staphylococcus epidermidis*.[10] MRSA is a major nosocomial pathogen that affects inpatients. Endemic MRSA strains originate from the hospital. Most of the HD units have had patients with MRSA colonization of bacteria.[5] Bacteriemia or infection through the blood caused by S. aureus is a significant cause of high morbidity and mortality.[5,11]

Based on the above considerations, the researcher wants to examine the prevalence of MRSA carriers in CKD stage five patients in the Outpatient Clinic and Hemodialysis Installation, as an essential data on the incidence of MRSA carriers.

METHODS

The study was a descriptive-analytic study with a cross-sectional design. The research subjects were obtained by consecutive sampling. The study was conducted in the Outpatient Clinic and Hemodialysis Installation of Dr. Soetomo general hospital, Surabaya Indonesia in July - August 2018. There were two research groups, namely Stage five non-HD CKD and the Stage five CKD who had undergone HD treatment.

The study sample was selected through the inclusion and exclusion criteria of the population of Stage five CKD patients in the Hemodialysis Unit and Kidney and Hypertension Outpatient clinic. The requirements of participants: over 18 years old, willing to take part in this study, and signed informed consent.

Participants who were not included in the study, if one or more of the following criteria found: Subjects with decreased consciousness or sepsis.

Specimens were collected by using sterile dry cotton swabs, and instructions were given on how to take swab samples from anterior nares and throat. One swab was used for both nostrils. All swabs were transported to the Laboratory and directly inoculated into 5 ml of Phenyl mannitol salt broth (Difco), incubated overnight at 37^{o}C and then subcultured onto MRSA-Chromagar, and further identification using Vitex 2, as standard microbiological procedure in the Microbiology Laboratory at Dr. Soetomo General Hospital.[12,13,14]

Table 1. General characteristics

Characteristics Subject	N (%)
Age (Years)	
- Average ± SD	52.1±11.8
- age range	19-78
Co-morbid Factors	
- Diabetes mellitus	69 (46%)
- hypertension	129 (86%)
- Kidney stones	29 (19%)
- Gout	30 (20%)
- Hepatitis B	2(1.3%)
- SLE	1(0,66%)
- Cervical cancer	6(4%)
- HIV	1(0.66%)
- Others (Hepatitis C, ovarian cyst, UTI)	0 (0%)
Types of Vascular Access	
- AV fistula	74(49%)
- CVC	1(0.66%)
HD Frequency	
- Never been HD	75(50%)
- HD 1x / week	1(0,66%)
- HD 2x / week	74(49%)
Long HD	
<4 years	51(34%)
4-6 years	14(9.3%)
> 6 years	10(6.660%)

RESULTS

There were 75 subjects in the HD group, and 75 subjects in the non HD group, prevalence MRSA carriers were found in 6/150(4%) of total samples. Data on the general characteristics of research subjects in Table 1. In the non HD group, there were 45 male subjects (60%), and 30 female subjects (40%). In the HD group, there were 36 male subjects (48%), and 39 female subjects (52%).

In this study, the number of subjects with MRSA (+) carriers in patients who received hemodialysis was two (2.7%), and the number of MRSA carriers (+) in patients who have not undergone hemodialysis as many as four patients (5.3%). See Table 2.

Carrier prevalence of MRSA with comorbid DM, there were 69 (46%) patients suffering from DM, and 4 of them became MRSA carriers.

In this study in the non HD group who suffered HT as many as 65 (86.7%) with MRSA carrier incidence rates of 4 patients. Whereas in the HD group, who suffered HT as much as 64 (85.3%) with MRSA carrier incidence rate of 1 patient.

In the non-HD group who suffered kidney stones as many as 20 (26.7%), one patient with an MRSA carrier.

In the HD group suffering from kidney stones as many as 9 (12%), none of them with MRSA

In this study in the non-HD group who suffered from hepatitis B was 2 (2.7%). In the HD group subject suffering from hepatitis B were 9 (12%), but from both groups, there were no carriers of MRSA

In this study, the hepatitis C comorbid factor was not found, because the HD group with the hepatitis C comorbid factor was not willing to participate in this study.

In this study, there were no MRSA carriers with comorbid factors in urinary tract infections in either group HD and non HD subjects.

This study found only one patient with SLE in the HD group, and also as a carrier of MRSA.

Table 2. Prevalence of MRSA carriers

Characteristics Subject	MRSA Carriers (N)
Co-morbid factors	
- Diabetes mellitus	4(5.8%)
- hypertension	5(3.9%)
- Kidney stones	1(3.4%)
- Gout	2(6.67%)
- Hepatitis B	0(0%)
- SLE	1(100%)
- Cervical cancer	0(0%)
- HIV	0(0%)
- Others (Hepatitis C, ovarian cyst, UTI)	0 (0%)
Types of vascular access	
- AV fistula	2(2.7%)
- CVC	0(0%)
HD frequency	
- Never been HD	4(5.3%)
- HD 1x / week	0(0%)
- HD 2x / week	2(2.7%)
Long HD	
<4 years	2(3.9%)
4-6 years	0(%)
> 6 years	0(%)

For other comorbid factors such as cervical cancer, ovarian cancer, ovarian cyst, and HIV, there were no MRSA carriers.

The HD group that used double-lumen vascular access was one (1.33%) with an MRSA carrier occurrence rate of zero, while in the HD group who used AV Shunt vascular access as many as 73 (97.3%) with an MRSA carrier of two patients.

The HD group who had done two times/week was 74 (97.3%) patients, with two MRSA carriers. There was no MRSA carriers found in HD group who had done one time/week.

In the HD group with a length of time of HD less than 4 years as many as 51(68%) patients, with MRSA carriers of two (3.9%) patients, while the period of time undergoing HD 4-6 years was 14 (18.6%) patients, with MRSA carrier event of zero, while the length of time to experience HD more than 6 years was 10 (13.3%) patients, with MRSA carrier was zero.

DISCUSSION

Patients undergoing dialysis are vulnerable to get MRSA infections, especially they have carries or colonization of MRSA in their nose or throat.

This study found 150 patients, consist of 81 (54%) male and 69 women (46%), total MRSA carriers there were 6 (4%), in women as many as 3 (4.3%) patients, and 3 (3.7%) patients in male, where statistically was no significant difference ($p = 0.84$). This result of MRSA carriers were lower than the result from a previous study in the same hospital in surgical and medical wards in the year 2016, there were 52 (8.1%) of 643 patients on admission were colonized with MRSA, this result was higher than our study, This is possible because most of the patients were referred from other hospitals.[15]

In this study, the prevalence of MRSA carriers who had not received HD treatment 4(5.3%) patients, compared to those who had received HD treatment 2(2.7%) patients, but the statistical difference was not significant ($p = 0.45$). In the research of Wang et al. found a little higher prevalence of MRSA carriers in patients with HD, the prevalence of S. aureus colonization in hemodialysis patients around 22.4% consisting of 16.5% MSSA and 5.9% MRSA.[16]

This study had a mean age of 54 research subjects with the youngest age range of 19 years and the oldest 78 years in the non-HD group, with MRSA carrier incidence rates of four patients (50, 52, 61, and 76 years). As for the HD group, the average age of the study subjects was 49 years, with the youngest age range being 29 years and the oldest being 75 years with MRSA carrier incidence rates of two patients (ages 44 and 74 years). This research similar to the following study conducted by Celik et al., 2011 which reported that patients with hemodialysis found higher MRSA carriers incidence rates in the age group between 55-64 years (30.55%) and MRSA carrier incidence rates that were the youngest with a range between 25-34 years.[17]

Non-HD group research subjects having comorbid diabetes mellitus as many as 45 people (60%) with an MRSA carrier occurrence rate of four patients. Whereas for the HD group, who had DM comorbid factors as many as 24 patients (32%) with an MRSA carrier incidence rate of zero. Other studies also reported similar data based on data from Kang et al., 2012 found that out of a total of 296 research subjects. HD group with DM comorbid factors were 125 people.[18] MRSA colonization was 11 patients (57.9%), while MRSA colonization was not found 114 (41.2%). Research conducted by Lai et al., 2011 found that of 306 research subjects with DM comorbid factors in HD patients with MRSA carriers as many as 11 people (37.93%), while subjects without MRSA carriers were 147 people (53.07%).[19] Another study Yeoh et al., 2014, found that DM increases the high risk for MRSA colonization infection (odds ratio 4.2).[20] Research conducted by Saxena et al., 2009 found that the prevalence of type 2 DM increases three times higher risk factors for MRSA nasal carriers compared to non-DMs (72.4% vs. 24.6%) in patients with hemodialysis (RR. 2.97, $p < 0.0001$). In nasal carriers, about 72.4% in dialysis patients with type 2 diabetes, 29% higher than in non-DM HD patients.[21]

This study found hypertension in the non-HD group was sixty-five patients (86.7%) with an MRSA carrier occurrence rate of four patients. Whereas for the HD group, who had hypertension comorbid factors as many as sixty-four patients (85.3%) with an MRSA carrier occurrence rate of one patients. A study conducted by Kang et al., 2012, found that MRSA carriers in HD patients with hypertension as comorbid as many as 84.2%.[18]

This study found that hepatitis B comorbid factors in the non-HD group were two patients (2.7%) with an incidence of MRSA carrier of zero (0%). Whereas for the HD group who had hepatitis B comorbid factors as many as nine patients (12%) with an MRSA carrier occurrence rate of zero (0%). This result concordance with research conducted by Kang et al., 2012 found that of the subjects as many as 296 patients who had hepatitis B comorbid factors as many as 32 patients (10.8%) with MRSA carrier events as much as zero (0%).[18]

CONCLUSION

In this study, the prevalence of MRSA in subjects with stage five CKD were 6/150 (4%) there were no significant differences in the incidence of MRSA carriers in stage five CKD non HD or HD groups. This study shows that MRSA colonization exists in stage five CKD sufferers who have or who have not received HD therapy.

CONFLICT OF INTEREST

There is no conflict of interest of this paper.

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