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Staphylococcus aureus nasal carriage and bloodstream infection among conventional hemodialysis patients in Thailand: a prospective multicenter cohort study

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Abstract

Objective: Staphylococcus aureus nasal carriage screening among hemodialysis patients is not standard practice in Thailand, because of data lacking regarding prevalence and correlation with subsequent infection. We aimed to investigate the prevalence of *S. aureus* nasal carriage and its association with bloodstream infection among hemodialysis patients. In this prospective multicenter cohort study, participants were screened for *S. aureus* nasal carriage over 2 consecutive weeks. Incidence of *S. aureus* bloodstream infection over the next 12 months was observed.

Results: The prevalence of *S. aureus* nasal carriage was 11.67%. Incidence of *S. aureus* bacteremia among participants with and without *S. aureus* nasal carriage were 7.1% and 3.8%, respectively. The odds ratio for nasal carriage and subsequent bacteremia was 1.96 (95% CI 0.04–21.79; p = 0.553). Survival analysis showed that time to bacteremia among participants in the two groups did not significantly differ (p = 0.531). Prevalence of *S. aureus* nasal carriage among hemodialysis patients in Thailand was low. Patients presenting with *S. aureus* nasal carriage did not have increased risk of *S. aureus* bacteremia after 12-month follow-up. Nasal *S. aureus* screening and decolonization should not be encouraged in this setting.

Keywords: End-stage chronic kidney disease, Hemodialysis, S. aureus nasal carriage, S. aureus bloodstream infection

Introduction

Bloodstream infection is the most common type of infection among hemodialysis patients, with *Staphylococcus aureus* as the main causative pathogen [1]. *S. aureus* colonizes humans especially in the nasal area, and carriage is recognized as an important risk factor for subsequent bloodstream infection [2].

Hemodialysis patients appear to have a greater risk of *S. aureus* colonization. An observational study reported a high rate of *S. aureus* nasal carriage among hemodialysis patients (40%), compared to normal populations (27%) [3]. An artificial nasal colonization study found that the average duration of *S. aureus* colonization was 4 days in the non-carriage group, and 14 days in the intermittent *S. aureus* nasal carriage group. However, among patients with persistent *S. aureus* nasal carriage, duration of colonization has been observed for up to 157 days [4].

Screening of *S. aureus* nasal carriage among hemodialysis patients and decolonization using mupirocin ointments exhibited more than 80% reduction in *S. aureus* infection and bacteremia [5]. Therefore, screening for *S.*

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aureus nasal carriage among hemodialysis patients is a routine practice in several countries [6, 7].

In Thailand, community-acquired methicillin resistant *S. aureus* (CA-MRSA) has not been observed and there is a lack of data regarding the prevalence of nasal carriage and association with invasive diseases [8]. Given the difference in epidemiology, screening of *S. aureus* nasal carriage is not a standard practice in Thailand. We therefore aimed to investigate the prevalence of *S. aureus* nasal carriage and its association with *S. aureus* bloodstream infection among hemodialysis patients.

Main text

Material and methods

Study setting and design We conducted a prost

We conducted a prospective multicenter cohort study. Patients with end-stage renal disease (ESRD) who received hemodialysis at Phramongkutklao Hospital and Ananda Mahidol Hospital hemodialysis centers from July 2020 to September 2020 were enrolled. We estimated a sample size of 145 participants based on a previous study showing *S. aureus* nasal carriage among 40% of ESRD patients [3]. This provided 80% power to demonstrate the correlation between *S. aureus* nasal carriage and *S. aureus* bacteremia, with a two-sided alpha level of 0.05. The inclusion criteria included: age over 18 years, diagnosis of ESRD, receiving conventional hemodialysis, and regular follow up at two study hospitals. We excluded any patients who were undergoing hemodialysis for acute kidney injury.

Nose swab and bacterial isolates

All patients completed study questionnaires regarding their sociodemographic data and medical history. Bacterial swabs were obtained by study staff from the nasal mucosa at anterior nares once a week for 2 consecutive weeks. On each occasion, the cotton tip was inserted 1 cm into one nostril, rotated four times with slight pressure against the nasal septum, and transported with Amies transport medium. Each specimen was gently rolled and streaked on 5% sheep blood agar (BA) which were incubated at 37 °C for up to 24 h. Identification of S. aureus was carried out following standard microbiologic methods recommended by Clinical and Laboratory Standards Institute (CLSI) guidelines [9]. Positive swabs were defined as a colony forming unit (CFU) of $> 10^3$. S. aureus isolates were inoculated in Mueller Hinton Agar and methicillin susceptibility was identified by disc diffusion method using 30 μg cefoxitin disc. Isolates with zone diameters of \geq 25 mm were classified as methicillin-susceptible whereas zone diameters of ≤ 24 mm were classified as resistant, according to CLSI guidelines [9].

Staphylococcus aureus nasal carriage and S. aureus bacteremia

Participants were classified into three groups based on their S. aureus nasal carriage: no nasal carriage, intermittent nasal carriage, and persistent nasal carriage. Intermittent nasal carriage was defined as a positive nasal swab in only one of the two specimens, while persistent nasal carriage was defined as positive nasal swabs in both specimens [10, 11]. All participants were followed up until 12 months after the last nasal swab collection for their status of S. aureus bacteremia, defined as at least one isolation of S. aureus from a blood culture. Participants lost to follow up were excluded from the analysis but were interviewed by phone for the admission with signs or symptoms compatible with bacteremia. Participants and primary doctors were not informed of the carrier status and all participants presenting S. aureus nasal carriage did not receive any decolonization intervention.

Statistical analysis

Baseline characteristics were analyzed using descriptive statistics. Categorical data were presented as percentages while mean and standard deviation (SD) were used for continuous data. For categorical variables, Fisher's exact test or the Chi-square test was used, while Mann-Whitney test or Student's T-test was used to compare continuous variables. The relationship between S. aureus nasal carriage and S. aureus bloodstream infection was analyzed using odds ratios and was presented with a 95% confidence interval. We used Kaplan-Meier method to estimate the cumulative bacteremia and stratified logrank statistic to assess the risk of nasal carriage compared with non-nasal carriage. For all analyses, a two-sided p-value of 0.05 was considered significant. All statistical analyses were performed using Stata 12.0 Software (StataCorp, USA).

Result

From July 2020 to September 2020, 141 hemodialysis patients at the two hemodialysis centers were enrolled. Nine participants declined to participate in the study and 12 participants were excluded owing to changes in their hemodialysis center during this period. These 12 participants were all non-carriers. They did not report admission with signs or symptoms compatible with bacteremia upon phone interview. Hence, we included 120 participants (Additional file1: Fig S1).

Patient characteristics

Of 120 participants, the mean age was 54.9 ± 16.07 years. Half of the participants were female. The two most common routes of hemodialysis were arteriovenous fistula,

and tunneled hemodialysis catheter, respectively. The most common underlying diseases were hypertension, dyslipidemia, and diabetes. Female sex and dyslipidemia were significantly more common in the carrier group (OR 4.11; 95%CI 1.08–15.56, p=0.027, and OR 4.60; 95%CI 1.21–17.45, p=0.008 respectively). Baseline characteristics are described in Table 1.

The prevalence of *S. aureus* nasal carriage was 11.67% (14 /120), with ten cases classified as intermittent and four cases classified as persistent nasal carriage. The prevalence of *S. aureus* nasal carriage in hemodialysis patients of Phramongkutklao and Ananda Mahidol Hospital was 10.71% and 11.96%, respectively (p = 0.858). All *S. aureus* isolates were susceptible to methicillin (methicillin-susceptible *S. aureus*; MSSA).

Staphylococcus aureus bacteremia occurred in five participants after 12 month follow-up (incidence = 4.17%). Among participants with *S. aureus* nasal carriage, one participant in the intermittent nasal carriage group had *S. aureus* bacteremia (incidence = 7.1%; 1/14), while 4 participants in the non-nasal carriage group had *S. aureus* bacteremia (3.8%; 4/106). Participants with nasal carriage were not more likely to develop bacteremia than participants presenting non nasal carriage at 12 months (OR 1.96; p = 0.553).

Clinical characteristics of participants presenting bacteremia are described in Table 2. All *S. aureus* isolated

in blood culture were MSSA. Among participants presenting bacteremia, nasal carriage patients developed bacteremia in 41 days while non nasal carriage patients developed bacteremia at 89, 89, 111 and 153 days, respectively. Cumulative bacteremia did not significantly differ between the two groups (p = 0.531) (Fig. 1).

Discussion

In this prospective multicenter cohort study among hemodialysis patients, the prevalence of S. aureus nasal carriage was 11.7%. This number was lower than reported in other studies. For example, a related systematic review and meta-analysis among 2,374 participants revealed the prevalence of *S. aureus* nasal carriage at 26% [5]. Another report also found a 40% prevalence of S. aureus nasal carriage among hemodialysis patients [3]. Several factors may have influenced this effect. Firstly, the prevalence of S. aureus nasal carriage in the general population in Thailand is low. Related studies in Thailand reported the prevalence of S. aureus nasal carriage at 20, 13.9, and 3.6% among patients with allergic rhinitis, patients undergoing elective cardiac surgery, and pre-admission screening, respectively [12-14]. These proportions are lower than the reported prevalence in the US and Germany at 22% and 40%, respectively [4, 15]. Although the prevalence of nasal carriage among hemodialysis patients is usually higher when compared with the general population [3],

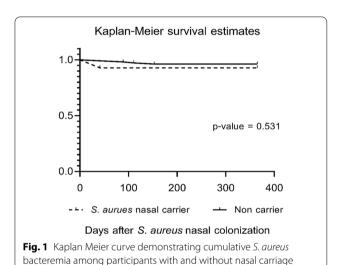
Table 1 Baseline characteristics of hemodialysis patients presenting *S. aureus* nasal carrier and non-carrier

Characteristic	Carrier (n = 14) n (%) Mean ± SD	Noncarrier (n = 106) n (%) Mean ± SD	Total (n $=$ 120) n (%) Mean \pm SD	p-value
Age	55.14±17.15	54.89 ± 16.10	54.9 ± 16.07	0.959
Female	11(78.57%)	50(47.17%)	61(50.83%)	0.027
BMI	22.01 ± 6.12	23 ± 4.32	21.4 ± 4.57	0.566
Route of hemodialysis				
Double lumen catheter	1(7.14%)	5(4.72%)	6(5%)	0.696
Tunneled hemodialysis catheter	5(35.71%)	35(33.02%)	38(31.67%)	0.841
AVF	6(42.86%)	57(53.77%)	63(52.5%)	0.442
AVG	2(14.29%)	9(8.49%)	11(9.17%)	0.480
Prior antibiotic	9(32.14%)	20(21.74%)	29 (24.17%)	0.260
Immunosuppressive use	1(7.14%)	8(7.54%)	9(7.5%)	0.957
Underlying disease				
Hypertension	12(85.71%)	98(92.45%)	110(91.67%)	0.391
Diabetic	4(28.57%)	29(27.36%)	33(27.5%)	0.924
Dyslipidemia	11(78.57%)	47(44.34%)	58(48.33%)	0.008
SLE	1(7.14%)	3(2.83%)	4(3.33%)	0.398
Skin disease	1(7.14%)	5(4.72%)	6(5%)	0.696
Malignancy	1(3.57%)	2(2.17%)	3(2.5%)	0.678
Renal cell cancer	1(7.14%)	0	1(0.83%)	1
Prostatic cancer	0	2(1.89%)	2(1.67%)	1

Table 2	Clinical	characteristics	of Caurous	hactoromia	narticinante
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No	Age/Sex	Vascular access	Nasal carriage status	Hemoculture (Bacteremia)	Clinical syndrome	Treatment/outcome
1	35/Female	DLC IJV	Intermittent	MSSA	CRBSI	IV Cloxacillin, removed catheter/ Cured
2	60/Male	Tunneled hemodialysis catheter	None	MSSA	CRBSI	IV Cloxacillin, removed catheter/ Cured
3	59/Male	Tunneled hemodialysis catheter	None	MSSA	CRBSI	IV Cloxacillin, removed catheter/ Cured
4	74/Female	Tunneled hemodialysis catheter	None	MSSA	CRBSI	IV Cefazolin, removed catheter / Cured
5	67/Male	AVG	None	MSSA	Infected AVG	IV Cefazolin, debridement/ Cured

AVF arteriovenous fistula, AVG arteriovenous graf, DLC double lumen catheter, IJV internal jugular vein, MSSA methicillin-susceptible Staphylococcus aureus, CRBSI catheter related blood stream infection



we found that the prevalence of carriage in our cohort was close to that of the general Thai population. This also correlated with the lower incidence of *S. aureus* infection in hospitals and the lower colonization rate among health care personnel in Thailand [13–17]. Secondly, in this present study, most participants had permanent vascular access. This was associated with a lower risk of *S. aureus* nasal carriage compared with temporary dialysis access [18]. Finally, the prevalence of *S. aureus* nasal carriage may depend on several factors particularly, ethnicity, previous antibiotic use, socioeconomic status, and geographic differences between countries, as well as personal hygiene [18, 19].

The present study describes female sex and dyslipidemia being associated with *S. aureus* carriage. Association between sex and *S. aureus* nasal carriage status remains controversial [20, 21]. Women with low levels of circulating testosterone may have increased probability of persistent *S. aureus* carriage [22]. The nasal

colonization of *S. aureus* among patients undergoing hemodialysis depends on underlying host conditions especially skin disease and diabetic mellitus. Nevertheless, dyslipidemia has not been established as a risk factor in related studies [23]. However, the association that we found in this present study may not represent the true relationship, because other confounding variables were not explored or controlled for. Well-designed studies are warranted to resolve this situation.

This study did not find any association between S. aureus nasal carriage and bacteremia. This may be explained by the unexpectedly low prevalence of S. aureus nasal carriage, compared with the prevalence at 40-65% reported in several studies which described associations between nasal carriage and bacteremia [3, 10, 24]. However, the rate of invasive infection within 6 to 20 months of nasal carriage was 19% [25], much higher than the 4.17% found in this study. Therefore, another possible explanation is the difference in the virulence of S. aureus between the studies. Although this study was conducted in tertiary hospital hemodialysis centers, we did not find MRSA. This conforms with reported data in Thailand which indicated an extremely low rate of MRSA nasal colonization either among patients or healthcare personnel [13, 14, 17]. The molecular basis and biofilm-forming capacity of S. aureus in each strain play a major role in the ability to colonize and develop invasive diseases [2, 26-28]. Molecular characterization as well as biofilm production of the isolated S. aureus nasal carriage strain should be further investigated.

To our knowledge, this study constitutes the first report of the prevalence of *S. aureus* nasal carriers and the relationship between nasal carriage and *S. aureus* bloodstream infection among hemodialysis patients in Thailand.

Conclusion

Prevalence of *S. aureus* nasal carriage among hemodialysis patients at two Thai tertiary hospitals was 11.67%. Patients who had *S. aureus* nasal carriage did not have increased risk of *S. aureus* bacteremia after 12 month follow-up. In healthcare centers with low *S. aureus* nasal carriage prevalence, nasal *S. aureus* screening and decolonization should not be encouraged.

Limitations

First, some participants were lost to follow up, which might have influenced the study result. However, this subset of patients were all non-carriers and did not report admission with signs or symptoms compatible with bacteremia. Therefore, the true incidence of bacteremia of the non-carrier group, but not in carrier group, might be underreported. Second, the molecular characteristics of the S. aureus isolates were not identified. Therefore, we could not confirm the linkage between colonization and bacteremia. Nevertheless, only one patient was found in this group. Finally, the adherence to basic infection prevention strategies among hemodialysis centers was not monitored. Therefore, we could not ensure that the lower rate of S. aureus nasal colonization and infection was due to good adherence to basic infection control. However, no difference was found in colonization between the two study sites.

Abbreviations

AVF: Arteriovenous fistula; AVG: Arteriovenous graft; DLC: Double lumen catheter; CKD: Chronic kidney disease; RRT: Renal replacement therapy; *S. aureus: Staphylococcus aureus*; ESRD: End stage renal disease; CA: Cancer; RCC: Renal cell carcinoma; HT: Hypertension; DLP: Dyslipidemia; SLE: Systemic lupus erythematous; MRSA: Methicillin-resistant *Staphylococcus aureus*; MSSA: Methicillin-susceptible *Staphylococcus aureus*; CRBSI: Catheter related blood stream infection.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13104-022-06185-y.

Additional file 1: Figure S1. Participant enrollment.

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Author contributions

Conceptualization, TT, WN, NV, NR and VV; methodology, TT, WN and VV; software, TT, WN and VV; validation, TT, WN and VV; formal analysis, TT, WN and VV; investigation, TT, WN, NV, NR and VV; resources, TT, WN, NV, NR and VV; data curation, TT, WN, NV, NR and VV; writing—original draft preparation, TT, WN and VV; writing—review and editing, TT, WN, NV, NR and VV visualization, TT, WN and VV; supervision, WN, and VV; project administration, WN; funding

acquisition, WN, and TT All authors have read and agreed to the published version of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Declarations

Ethics approval and consent to participate

The study was reviewed and approved by the Institutional Review Board, Royal Thai Army Medical Department in compliance with the Declaration of Helsinki, the Belmont Report, CIOMS Guidelines and the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use—Good Clinical Practice (ICH-GCP), approval number R071 h/63. Informed consent was obtained in written from all participants in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare they have no potential conflict of interest relevant to this article.

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