Prevalence of nasal carriage and diversity of *Staphylococcus aureus* among inpatients and hospital staff at Korle Bu Teaching Hospital, Ghana

Beverly Egyir a,b,c, Luca Guardabassi b, Soren Saxmose Nielsen d, Jesper Larsen a, Kennedy Kwasi Addo e, Mercy Jemima Newman e, Anders Rhod Larsen a

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**A B S T R A C T**

There is a paucity of data on *Staphylococcus aureus* epidemiology in Africa. Prevalence of nasal carriage and genetic diversity of *S. aureus* were determined among hospital staff (HS) and inpatients (IP) at the largest hospital in Ghana. In total, 632 nasal swabs were obtained from 452 IP and 180 HS in the Child Health Department (CHD) and Surgical Department (SD). *S. aureus* carriage prevalences were 13.9% in IP and 23.3% in HS. The chance of being a carrier was higher in HS (P = 0.005) and IP staying ≤7 days in hospital (P = 0.007). Resistance to penicillin (93%), tetracycline (28%) and fusidic acid (12%) was more common than for other agents (<5%). A higher chance of multidrug-resistant *S. aureus* carriage was observed among IP compared with HS (P = 0.01). High genetic diversity was shown by spa typing, with 55 spa types found among 105 isolates; the predominant spa types were t355 (10%) and t084 (10%). MRSA was detected in six IP with an overall carriage prevalence of ca. 1.3%, but not in HS. All three MRSA isolates from SD belonged to ST88–SCCmec IV, and two of them displayed the same spa type and antibiograms; three MRSA isolates from CHD belonged to distinct lineages (ST88–SCCmec IV, ST8–SCCmec V and ST72–SCCmec V). Altogether, these data indicate a high diversity of *S. aureus*, low levels of MRSA carriage, and a higher chance of nasal carriage of multidrug-resistant *S. aureus* among IP compared with HS in this hospital.

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**1. Introduction**

*Staphylococcus aureus* is an important pathogen associated with human infections in hospitals and communities worldwide [1]. Asymptomatic nasal carriage ranges between 15% and 40% of a population and is an established risk factor for *S. aureus* infection as well as for transmission between patients and healthcare workers [2,3].

Meticillin-resistant *S. aureus* (MRSA) infections are a major healthcare and socioeconomic problem in hospitals worldwide as they are more difficult and expensive to treat compared with infections caused by meticillin-susceptible *S. aureus* (MSSA) strains [4]. Efforts to diminish the spread of MRSA in hospitals are therefore pivotal and may include various infection control initiatives such as improved hand hygiene, rapid diagnostics, and eradication of MRSA in asymptomatic carriers especially prior to surgery [1,5].

Data on carriage, antibiotic susceptibility patterns and the molecular epidemiology of *S. aureus* in the African continent are limited. *S. aureus* carriage prevalences of 17–46% have been found among patients and hospital personnel in Somalia and Sudan [6,7]. A prevalence of 29% was reported by a recent study investigating *S. aureus* carriage in a remote indigenous population in Central Gabon [8]. Data available from different African countries indicate a prevalence of MRSA ranging from 4.8% to 20% in clinical isolates [9–11].

The objective of this large-scale surveillance study was to determine the prevalence of nasal carriage, antimicrobial susceptibility patterns and clonal diversity of *S. aureus* and MRSA among inpatients (IP) and hospital staff (HS) at the largest hospital in Ghana.

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* Corresponding author. at: Bacteriology Department, Noguchi Memorial Institute for Medical Research, Accra, Ghana. Tel.: +233 20 891 8099; fax: +233 30 250 2182.  
E-mail addresses: begyr@sund.ku.dk, begyr@noguchi.mimcom.org, bvg@ssi.dk (B. Egyir).

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2. Materials and methods

2.1. Study design, site and population

A cross-sectional study was conducted between September 2011 and May 2012 at Korle Bu Teaching Hospital, Ghana, which has over 2000 beds and an average admission of 250 patients daily. The hospital serves a population of over 3 million and acts as a major referral health facility for an estimated population of 24 million people across Ghana.

Nasal screening of IP and HS was conducted at the Child Health Department (CHD) (bed size, 168; staff, 180) and Surgical Department (SD) (bed size, 242; staff, 200), which are situated 200 m apart in different buildings. Clinical conditions of IP in the CHD ranged from febrile illnesses to cancer and various surgical conditions; in the SD, clinical conditions of IP were primarily surgery related. Participation was voluntary and nasal screening was done after receiving informed consent from participants. Descriptive information regarding participant’s age, sex, diagnosis, department and period of hospitalisation was collected. History of antibiotic use among IP was retrieved from IP records. Data regarding dosage and duration of antimicrobial therapy were not obtained for this study.

2.2. Sample collection and isolation of S. aureus

Samples were taken by rotating a sterile cotton swab five times in both anterior nares. Nasal swabs were pre-enriched in 5 mL of Mueller–Hinton broth (Oxoid Ltd., Basingstoke, UK) supplemented with 6.5% NaCl, incubated at 37 °C for 24 h and plated on 5% sheep blood agar (Oxoid Ltd.). S. aureus isolates were identified phenotypically by colony morphology, haemolysis, catalase test and Gram staining and were confirmed by tube coagulase, SlideX Staph Plus (bioMérieux, Marcy-l’Étoile, France) and PCR amplification of the spa gene [12].

2.3. Antimicrobial susceptibility testing

Antimicrobial susceptibility testing was performed by the disk diffusion method according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) 2012 guidelines (http://www.eucast.org) using 30 µg of cefoxitin, 30 µg of tetracycline, 1 µg of penicillin, 2 µg of clindamycin, 15 µg of erythromycin, 10 µg of gentamicin, 10 µg of linezolid, 5 µg of rifampicin, 10 µg of ofloxacin, 1.25/2.5/7.5 µg of trimethoprim/sulphamethoxazole (SXT), 10 µg of fusidic acid and 200 µg of muipricin (Neo-Sensitabs; Rosco Diagnostica, Taastrup, Denmark). MRSA isolates were screened for glycopeptide resistance by spot test on brain–heart infusion agar (Becton Dickinson, Denmark) containing teicoplanin (5 mg/L). Isolates demonstrating ≥10 CFUs were subjected to Etest using vancomycin and teicoplanin strips (bioMérieux) as described by Fitzgibbon et al. [13]. Multidrug resistance was arbitrarily defined as resistance of MSSA to three or more distinct antimicrobial classes; MRSA found in this study were included in the multidrug-resistant (MDR) category irrespective of their susceptibility profiles.

2.4. Molecular characterisation

Crude bacterial lysates obtained by boiling for 10 min were used as the DNA template for multiplex PCR detection of spa, mecA and the lukF-PV gene encoding Panton–Valentine leukocidin (PVL), with subsequent sequencing of spa amplicons [14]. spa types were assigned, clustered and displayed as a minimum spanning tree with the spa typing plugin for BioNumerics v.6.5 using default settings (Applied Maths, Sint-Martens-Latem, Belgium). Multi locus sequence typing (MLST) was done on all MRSA isolates as described previously [15], and STs were assigned through the MLST database (http://www.mlst.net). Staphylococcal cassette chromosome mec (SCCmec) typing was performed using multiplex PCR assays [16].

2.5. Statistical analysis

Demographic characteristics of IP and HS were described and compared using the χ² test. The prevalences of S. aureus and MRSA were calculated overall and were stratified by demographic characteristics. Since S. aureus carriage is influenced by the duration of hospitalisation (DOH), data were categorised at two levels: ≤7 days and more >7 days, referred to as short and long DOH. The age of study participants was also categorised at two levels: ≤14 years (children) and >14 (adults). The patient’s underlying diagnosis was categorised as surgical for IP with surgical conditions and non-surgical for IP without surgical conditions. Logistic regression was used to determine the association of the two outcomes, S. aureus and MDR carriage (separately), with department, sex, age group, DOH group, patient underlying diagnosis, and IP or HS status. Data were analysed using the glm-function in R v.2.15.2 [17].

3. Results

3.1. Nasal carriage

Demographic characteristics of the study population are shown in Table 1. Distributions of S. aureus carriers and non-carriers stratified by population characteristics are shown in Table 2. A total of 632 participants were recruited, including 452 IP (71.5%) and 180 HS (28.5%). S. aureus was isolated from 105/632 (16.6%) of the study population. The S. aureus carrier prevalence in the two

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Demographic characteristics of inpatients (IP) and hospital staff (HS) in the Child Health Department (CHD) and Surgical Department (SD) at Korle Bu Teaching Hospital, Ghana, 2011–2012.</th>
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<tbody>
<tr>
<td>Characteristic</td>
<td>Level</td>
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<td>Sex [n (%)]</td>
<td>Female</td>
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<td></td>
<td>Male</td>
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<td>Department [n (%)]</td>
<td>SD</td>
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<td>CHD</td>
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<td>Age group [n (%)]</td>
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<td>&gt;14 years</td>
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<tr>
<td>Patient underlying diagnosis [n (%)]</td>
<td>Surgical</td>
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<td>Non-surgical</td>
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<td>Duration of hospitalisation [n (%)]</td>
<td>≤7 days</td>
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<td>&gt;7 days</td>
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</table>

¹ Difference in characteristic between IP and HS as assessed by χ² statistic.

² Percentage of IP and HS with a particular characteristic among all patients with that characteristic.

³ Percentage of IP with that characteristic among all IP.
groups was 63/452 (13.9%) in IP and 42/180 (23.3%) in HS. HS had a higher chance of being S. aureus carriers than IP [odds ratio (OR) = 1.9, 95% confidence interval (CI) 1.2–2.9; P = 0.005]. IP staying ≤7 days in hospital were found to have a higher chance of being S. aureus carriers than those staying in the hospital for longer periods (OR = 2.5, 95% CI 1.3–4.8; P = 0.007).

### 3.2. Antimicrobial susceptibility

The highest prevalence of antimicrobial resistance was observed for penicillin (93%), tetracycline (28%) and fusidic acid (12%). The percentages of resistance were <5% for erythromycin, clindamycin, SXT, norfloxacin, gentamicin, rifampicin and mupirocin (Table 3). Resistance to linezolid and glycopeptides was not detected. Isolates obtained from IP tended to be more resistant than isolates from HS; tetracycline resistance was found to be 33% and 19% among IP and HS, respectively; resistance to fusidic acid was 17% in IP and 5% in HS (Table 3).

Of the 105 S. aureus isolates, 99 (94.3%) were MSSA and the remaining 6 isolates (5.7%) were resistant to cefoxitin and confirmed to be MRSA by meca PCR. All MRSA were isolated from IP, leading to a carriage prevalence of 1.3% (6/452) in this group and an MRSA prevalence of ca. 10% (6/63) among S. aureus isolates from IP.

Of the 105 S. aureus isolates, 14 (13.3%) were MDR. IP had a higher chance of MDR carriage compared with HS (OR = 2.4, 95% CI 1.5–4.6; P = 0.01). MDR carriage was not associated with sex, patient underlying diagnosis, department or DOH. The genotypes and resistance profiles of MDR S. aureus isolates are shown in Table 4 along with information on the IP they were isolated from.

### 3.3. Genetic diversity

A total of 55 spa types were found among the 105 isolates. The most frequent spa types were t084 (10%), t355 (10%), t127 (5.7%), t002 (3.8%), t537 (3.8%), t008 (2.9%), t304 (2.9%), t630 (2.9%), t861 (2.9%), t1510 (2.9%), t1082 (2.9%), t314 (1.9%), t636 (1.9%), t701 (1.9%), t1476 (1.9%), t2649 (1.9%), t2700 (1.9%) and t10822 (1.9%); the remaining 37 spa types were singletons. A minimum spanning tree displaying the relationships between the different spa types is illustrated in Fig. 1.

Among the six MRSA isolates, three from the SD and one from the CHD were ST88–SCCmec IV. Three of these four MRSA isolates displayed the same susceptibility profile, and two of them had the same spa type (Table 4). The two remaining isolates from the CHD
belonged to ST8–SCmec V and ST72–SCmec V. All MRSA isolates were negative for PVL, whereas a high percentage (23%) of PVL-positive isolates was observed among MSSA.

3.4. Antimicrobial usage

History of antimicrobial usage retrieved from 198 (43.8%) records of IP showed that 20%, 16% and 13% of IP had received cefuroxime, ciprofloxacin and ceftriaxone, respectively.

4. Discussion

This is the first baseline study that provides insight into the prevalence of nasal carriage, antimicrobial susceptibility and clonal structure of S. aureus and MRSA among IP and HS in Ghana. The study reveals a statistically significant lower S. aureus carrier prevalence among IP (13.9%) compared with HS (23.3%). The difference in S. aureus carrier prevalence among IP and HS could be due to the observation that >44% of the IP received antibiotic therapy at the time of sampling. In line with this hypothesis, S. aureus carriage was less frequent among IP with a long DOH (8%) compared with IP with shorter stays (17%).

Previous studies have reported an association of age and sex with S. aureus carriage [18], but this study only found an association between nasal carriage of S. aureus with being a HS, which is in agreement with a recent study in Gabon [8]. The overall MRSA carrier prevalence of 0.9% (6/632) observed in this study is comparable with those reported by previous carriage studies in African hospitals: 0.0% (0/496) in Sudan [6]; 0.7% (1/145) in Somalia [7]; and 1.4% (4/295) in Gabon [8].

MRSA was recovered from six IP with various surgical conditions. The finding of four IP carrying MRSA ST88–IV was not surprising as this clone has been frequently reported in communities and hospitals in major African cities [8–10]. Two IP who stayed in the same ward 4 months apart carried isolates with the same spa type (t2649) and antibiogram (Table 4). However, there was no direct evidence of transmission of this MRSA lineage between the IP and from HS to IP. Possible environmental sources were not investigated in the study. It is of interest to note that two of the MRSA were isolated from IP receiving cefuroxime, ceftriaxone and cloxacinil. Routine nasal screening of IP, especially surgical patients, which is currently not performed in the health facility, could be considered to prevent treatment failure to further ameliorate morbidity, mortality and cost of stay at the hospital. In addition, active surveillance has been shown to minimise MRSA transmission to other patients and hospital staff [19].

The relatively high prevalence of resistance to fusidic acid, especially among IP (17%), is surprising, although of limited clinical relevance since fusidic acid is not frequently used in Ghana. This resistance pattern is in contrast to studies in South Africa where full susceptibility to fusidic acid was observed [20,21]. The genetic background of fusidic acid resistance was not investigated in this study and the reason for the high prevalence of resistance observed in the absence of any apparent selective pressure remains unknown. The occurrence of mobile fus genes has been reported in the USA where fusidic acid is not available in the market [22]. Further studies are needed to throw light on possible co-selecting factors favouring the spread of fusidic acid resistance in the absence of selective pressure.

The high prevalence of resistance to penicillin and tetracycline is comparable with previous reports from other African studies [6,7,11] and may reflect the frequent usage of these antibiotics in the community in Ghana, where they can be purchased over the counter without prescription. However, this finding has limited clinical relevance since penicillin and tetracycline are not routinely used for treatment of staphylococcal infections. According to the Standard Treatment Guidelines in Ghana, flucloxacillin should be the drug of choice for the treatment of staphylococcal infections. The observed high rate of susceptibility to vancomycin, teicoplanin and linezolid indicates that these agents remain excellent reserve drugs for the treatment of severe S. aureus infections in Ghana. Even though the resistance trends for norfloxacin, clindamycin, erythromycin, SXT, gentamicin and rifampicin were low (<5%), prudent usage of these antimicrobial agents should be encouraged to prevent selection of resistance of S. aureus to these drugs.

A high genetic diversity was observed among the S. aureus isolates, with t084 and t355 being the most prevalent spa types. S. aureus with spa type t084 has been reported frequently in healthy human nasal isolates elsewhere [4]. Noteworthy, PVL-positive MSSA belonging to t355 associated with ST152 was abundant in
this study and has been recognised in communities and hospitals in West Africa [23,24] and as a community-acquired MRSA in Central Europe [25].

ST88 was the most common MRSA lineage and appears to be one of the predominant MRSA clones in Africa as it was previously reported as a major MRSA clone in Nigeria, Mali, Gabon and other African countries [8–10,24]. In contrast, this MRSA lineage is uncommon in Europe [9,26,27]. Among the other MRSA isolated from Korle Bu Teaching Hospital in Ghana, ST8 has also been found in Cameroon and Madagascar; it has also been reported to be one of the major epidemic clones in Nigeria [9,10]. ST72 has been reported in Nigeria and Gabon as a MSSA clone [10,28], but only as major MRSA clone from communities in Australia and South Korea [29,30].

In conclusion, this study provides the first baseline epidemiological information on the prevalence of nasal carriage and genetic diversity of S. aureus and MRSA among IP and HS at a major referral hospital in Ghana. The results indicate a low frequency of MRSA carriage, high genetic diversity among S. aureus isolates, and a higher risk of nasal carriage of MDR S. aureus among IP compared with HS. The finding of MRSA among surgical patients suggests that screening of IP before surgery, which is not a routine practice in the hospital, may be an important infection control measure to be implemented in the future.

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Ethical approval

Ethical approval was obtained from the University of Ghana Medical School Ethical and Protocol Review Board (Accra, Ghana) [reference no. MS-EI/M.9 – P.3.212010-11].

Competing interests

None declared.

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