Methicillin-resistant *Staphylococcus aureus* carriage in a residential care institution for the elderly in Quezon City, Philippines

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Methicillin-resistant *Staphylococcus aureus* (MRSA) is a pathogen responsible for hospital- and community-acquired infections. While the prevalence of MRSA is well-documented in hospitals, its occurrence in other healthcare facilities is not well studied. The present study determined the prevalence, antimicrobial susceptibility patterns, SCC*mec* types, and risk factors associated with MRSA carriage in a residential care facility for the elderly in Quezon City. A total of 66 nasal swabs from asymptomatic residents were examined for the presence of MRSA. The isolates were identified and characterized through biochemical tests, amplification of the *nuc* and *mecA* genes, antimicrobial susceptibility tests, and staphylococcal cassette chromosome *mec* (SCC*mec*) typing. The prevalence of MRSA among the residents was 16.7%. All MRSA isolates carried the SCC*mec* type IV and majority were multidrug-resistant, showing cross-resistance to erythromycin (90.9%), clindamycin (90.9%), and rifampicin (81.8%). Intermediate susceptibility to trimethoprim-sulphamethoxazole was observed in 81.8% of the isolates. All the isolates were susceptible to ciprofloxacin, moxifloxacin, chloramphenicol, tetracycline, doxycycline, minocycline, gentamicin, linezolid, and vancomycin. Among the risk factors examined, only the history of pulmonary tuberculosis was significantly associated with MRSA carriage (p=0.033; OR=4.67; 95% CI=1.19-18.26). Results showed that asymptomatic residents of the care facility for the elderly may carry MRSA. Sanitary practices, infection control measures, and antibiotic therapy regimen within the facility should be evaluated with the objective of preventing the spread of MRSA.

KEYWORDS

Methicillin-resistant *S. aureus* (MRSA), multidrug resistance, *mecA* gene, SCC*mec*, elderly, nasal carriage, residential care facilities, Quezon City

INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the leading causes of healthcare-associated diseases, from skin and wound infections to invasive bloodstream infections (ARSP 2017; CDC 2013). More than 80,000 cases of invasive infections and 11,000 related deaths have been reported in the United States (CDC 2013). Infections are difficult to treat because MRSA is resistant to almost all β-lactam agents and often exhibits multidrug resistance to other classes of antimicrobial agents. Resistance to β-lactam agents is due to the acquisition of the *mecA* gene that is carried by a mobile genetic element known as staphylococcal cassette chromosome *mec* (SCC*mec*). Additional antimicrobial resistance determinants are often present within the SCC*mec* and are responsible for the multidrug resistance in MRSA (IWG-SCC 2009; Milheirico et al. 2007).

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Table 1: Primer sequences, targets and expected PCR products for *S. aureus* and MRSA identification and SCC*mec* typing

Primer	Sequence (5'-3')	Target	Amplicon length (bp)	Reference
Unibac-F	CGT GCC AGC CGC GGT AAT ACG	16S rDNA	611	Amit-Romach et al. 2004
Unibac-R	GGG TTG CGC TCG TTG CGG GAC TTA ACC CAA CAT			
SA-01 F	GCG ATT GAT GGT GAT ACG GTT	*nuc* gene	267	Brakstad et al. 1992
SA-02 R	AGC CAA GCC TTG ACG AAC TAA AGC			
mecA1 F	AAA ATC GAT GGT AAA GGT TGG C	*mecA* gene	533	Murakami et al. 1991
mecA2 R	AGT TCT GCA GTA CCG GAT TTG C			
CIF2 F2	TTC GAG TTG CTG ATG AAG AAG G	SCC*mec* I (locus A)	495	Oliveira and de Lencastre 2002
CIF2 R2	ATT TAC CAC AAG GAC TAC CAG C			
DCS F2	CAT CCT ATG ATA GCT TGG TC	SCC*mec* I, II, IV (*dcs* region, locus D)	342	Oliveira and de Lencastre 2002
DCS R1	CTA AAT CAT AGC CAT GAC CG			
RIF5 F10	TTC TTA AGT ACA CGC TGA ATC G	SCC*mec* III (locus F)	414	Oliveira and de Lencastre 2002
RIF5 R13	GTC ACA GTA ATT CCA TCA ATG C			
mecI P2	ATC AAG ACT TGC ATT CAG GC	SCC*mec* II, III (*mecI* gene, locus C)	209	Oliveira and de Lencastre 2002
mecI P3	GCG GTT TCA ATT CAC TTG TC			
ccrB2 F2	AGT TTC TCA GAA TTC GAA CG	SCC*mec* II, IV (*ccrB2* gene)	311	Milheirico et al. 2007
ccrB2 R2	CCG ATA TAG AAW GGG TTA GC			
SCCmec V J1 F	TTC TCC ATT CTT GTT CAT CC	SCC*mec* V (J1 region)	377	Milheirico et al. 2007
SCCmec V J1 R	AGA GAC TAC TGA CTT AAG TGG			

SCC*mec* elements are highly diverse in structure and genetic content and have been classified into several types. Currently, the typing of SCC*mec* elements has become an important tool in epidemiological studies to help track, control and prevent MRSA infections (Valle Jr. et al. 2016; Milheirico et al. 2007). MRSA infections are frequently acquired in hospitals but can also be spread to other healthcare facilities, such as nursing homes and residential care institutions (Zhang et al. 2015; Horner et al. 2013; Cabrera et al. 2010). These institutions, which often admit chronically ill and/or elderly residents, may serve as reservoirs for MRSA due to rampant use of antibiotics and close association with hospitals and the community (Tsao et al. 2015; Zhang et al. 2015). Colonized residents often acquire MRSA from previous hospital visits and transmit the pathogen into residential care facilities and the community (Zhang et al. 2015; Bradley 2002).

In the Philippines, an increase in MRSA prevalence from 53% to 61.5% was observed in hospitals from 2013 to 2016 (ARSP 2017). A similar kind of information for residential care institutions, however, is lacking. The objectives of this study were to determine the sample prevalence, antimicrobial susceptibility patterns, SCC*mec* types, and risk factors associated with MRSA carriage in a residential care institution for the elderly.

MATERIALS AND METHODS

Selection of participants and ethical considerations

Permit to conduct sample and data collection from residents of the Golden Reception and Action Center for the Elderly and other Special Cases (GRACES) in Quezon City was obtained from GRACES and the Office of the Regional Director of Department of Social Welfare and Development (DSWD)-National Capital Region. The study protocol was approved by the University of the Philippines Manila Research Ethics Board (UPMREB Code: 2015-281-01).

The study included consenting and asymptomatic elderly (≥60 years old) residents. Eligibility of the residents to participate in the study was determined with the assistance of an in-house

medical doctor and psychologist. The details of the study were explained to potential participants either individually or in groups. It was made clear that participation is voluntary, refusal to participate will not affect their access to care, treatment, and services, and participation can be discontinued at any time without penalty. Verbal and written consent were obtained. All information gathered were treated with full confidentiality while the identities of the participants were kept anonymous.

Sample and data collection

A cross-sectional study was performed and a single nasal swab was taken from each of the participants. Of the 213 residents housed in GRACES at the start of recruitment, 66 participants were enrolled in the study. Participants were not notified of the date and time of sample collection. Nasal swabs were collected from 32 females and 34 males from September to November 2015. Samples were obtained by swabbing both anterior nares, making sure that the swabs made contact with the nasal septum. Samples were placed in 3 mL mannitol salt broth (MSB) tubes, and were immediately transported to the Medical Microbiology Laboratory, Institute of Biology, University of the Philippines Diliman and incubated at 35±2°C for 24-48 hours.

Potential risk factors for nasal carriage were obtained from the medical records of the residents. Data that were extracted included demographics (e.g., age and sex), history of respiratory diseases/condition (e.g., asthma, pulmonary tuberculosis, and pneumonia), underlying conditions (e.g., diabetes), intake of antibiotics within six and three months prior to sampling, history of smoking, functional status (e.g., ambulant residents who can live independently or non-ambulant residents who require assistance for their medical and personal needs including those who are wheelchair-bound and bedridden), and length of stay at the facility. The frequency and duration of antibiotic use within the three and six month reckoning period were not included in the analysis.

Isolation and identification of *Staphylococcus aureus*

Samples positive for mannitol fermentation in MSB tubes, as indicated by a color change of the medium from red to yellow-orange, were streak-inoculated on mannitol salt agar (MSA) plates. Cultures positive for mannitol fermentation in MSA, as indicated by yellow colonies with yellow zones, were purified and identified based on Gram stain, catalase, DNase and coagulase tests, following standard protocols (Harley and Prescott 2002; Sperber and Tatini 1975). Isolates that gave

Table 2: Antimicrobial susceptibility patterns of MRSA isolates among elderly residents of GRACES, 2015

Antimicrobial category	Antimicrobial agent	Code	MRSA n (%)		
			S	I	R
Cephamycins	Cefoxitin	FOX	-	-	11 (100)
Ansamycins	Rifampicin	RP	2 (18.2)	-	9 (81.8)
Folate pathway inhibitors	Trimethoprim-sulphamethoxazole	TS	1 (9.1)	9 (81.8)	1 (9.1)
Fluoroquinolones	Ciprofloxacin	CIP	11 (100)	-	-
	Moxifloxacin	MFX	11 (100)	-	-
Phenicols	Chloramphenicol	C	11 (100)	-	-
Tetracyclines	Tetracycline	T	11 (100)	-	-
	Minocycline	MN	11 (100)	-	-
	Doxycycline	DXT	11 (100)	-	-
Aminoglycosides	Gentamicin	GM	11 (100)	-	-
Oxazolidinones	Linezolid	LZD	11 (100)	-	-
Macrolides	Erythromycin	E	1 (9.1)	-	10 (90.9)
Lincosamides	Clindamycin	CD	1 (9.1)	-	10 (90.9)
Glycopeptides	Vancomycin	VAN	11 (100)	-	-
Multidrug resistance*		-	-	-	**10 (90.9)**

Interpretive criteria: S – Susceptible; I – Intermediate; R – Resistant
*Interim standard definition by Magiorakos et al. 2012

positive results to either coagulase or DNase test or both were confirmed by PCR amplification of the *nuc* gene, which encodes for an *S. aureus*-specific thermostable nuclease (Brakstad et al. 1992).

DNA extraction and purification

Genomic DNA was extracted using the microwave lysis method (Ahmed et al. 2014). Briefly, an 18- to 24-hour culture grown in brain heart infusion broth was pelletized by centrifugation at 10,000 x g for 5 minutes, washed with 1X TE buffer (10 mM Tris, pH 8.0, 1 mM EDTA), and lysed with TE buffer and 10% sodium dodecyl sulfate. Samples were heat-denatured by microwave treatment, extracted with phenol-chloroform-isoamyl alcohol (25:24:1), and DNA was precipitated with absolute ethanol. DNA yield and purity were determined by NanoDrop™ 2000 Spectrophotometer (Thermo Scientific, USA). DNA samples were stored at -20°C until use.

PCR amplification of the *nuc*, *mecA*, and 16S ribosomal DNA genes

Singleplex PCR amplifications of the *nuc* gene and 16S rDNA were performed to confirm the identity of the isolates and to rule out false-negative results, respectively. The primer sequences are listed in Table 1. Amplifications were carried out in a 25 µL final reaction mixture containing 45-50 ng DNA template, 3.5 µL nuclease-free water, 0.8 µM of each primer, and 1X GoTaq® Green Master Mix (Promega, USA) that consisted of 1.25 U GoTaq® DNA Polymerase, 1X Green GoTaq® Reaction Buffer (pH 8.5), 200 µM dATP, 200 µM dGTP, 200 µM dCTP, 200

Table 3: Risk factors for MRSA carriage among elderly residents of GRACES, 2015

Variable		No. (%) of residents who were:		Odds Ratio (95% Confidence Interval)	*P*
		MRSA carriers (n=11)	non-MRSA carriers (n=55)		
Age	(Mean ± SD)[a]	71 ± 7.5	72 ± 8.4	[c]	0.879
Sex	Male	6 (54.5)	28 (50.9)	0.86 (0.24–3.17)	0.826
	Female	5 (45.5)	27 (49.1)		
Asthma	Yes	2 (18.2)	5 (9.1)	2.22 (0.37–13.27)	0.330
	No	9 (81.8)	50 (90.9)		
Pulmonary tuberculosis	Yes	7 (63.6)	15 (27.3)	4.67 (1.19–18.26)	**0.033**[b]
	No	4 (36.4)	40 (72.7)		
Pneumonia	Yes	6 (54.5)	28 (50.9)	1.16 (0.32–4.24)	0.826
	No	5 (45.5)	27 (49.1)		
Diabetes	Yes	1 (9.1)	6 (10.9)	0.82 (0.09–7.55)	1.000
	No	10 (90.9)	49 (89.1)		
Antibiotic use (6 months)	Yes	10 (90.9)	40 (72.7)	3.75 (0.44–31.86)	0.271
	No	1 (9.1)	15 (27.3)		
Antibiotic use (3 months)	Yes	8 (72.7)	39 (70.9)	1.09 (0.26–4.66)	1.000
	No	3 (27.3)	16 (29.1)		
Smoking history	Yes	2 (18.2)	5 (9.1)	2.22 (0.37–13.27)	0.330
	No	9 (81.8)	50 (90.9)		
Functional status	Ambulatory	8 (72.7)	40 (72.7)	1.00 (0.23–4.28)	1.000
	Non-ambulatory	3 (27.3)	15 (27.3)		
Length of stay at the facility	<1	2 (18.2)	22 (40.0)	[c]	0.202
	≥1	4 (36.4)	21 (38.2)		
	≥2	5 (45.5)	12 (21.8)		

[a] SD: Standard deviation
[b] Statistically significant: $p<0.05$
[c] Risk estimate statistics could not be computed

µM dTTP, and 1.5 mM $MgCl_2$. Singleplex PCR amplification of the *nuc* gene was performed under the following conditions: 94°C for 2 minutes; 37 cycles of 94°C for 1 minute, 42°C for 30 seconds, and 72°C for 1 minute; and a final extension at 72°C for 7 minutes. The thermocycling conditions for 16S rDNA amplification were adopted from Amit-Romach et al. (2004).

Multiplex PCR amplification of the *nuc* and *mecA* genes (Table 1) was conducted to identify MRSA. PCR was performed in a 20 µL reaction mixture with 240 ng DNA template, 2.6 µL nuclease-free water, 0.8 µM of each primer, and 1X GoTaq® Green Master Mix (Promega, USA). Thermocycling conditions were as follows: 94°C for 4 minutes; 30 cycles of 94°C for 30 seconds, 53°C for 30 seconds, and 72°C for 1 minute; and a final extension at 72°C for 4 minutes. All PCR amplifications were conducted in a MyCycler™ Thermal Cycler (Bio-Rad, USA).

Amplicons were resolved by electrophoresis on 1.5% (w/v) agarose gel stained with 0.5 µg/mL ethidium bromide and then visualized using UV transilluminator. All PCR assays included the following control organisms: *S. aureus* ATCC 6538, MRSA BIOTECH 10378, and *S. epidermidis* BIOTECH 10098.

Antimicrobial susceptibility testing

The antimicrobial susceptibility patterns of the isolates were determined using the agar dilution method for vancomycin, and disk diffusion method for gentamicin (10 µg), rifampicin (5 µg), ciprofloxacin (5 µg), moxifloxacin (5 µg), clindamycin (2 µg), linezolid (30 µg), chloramphenicol (30 µg), erythromycin (15 µg), tetracycline (30 µg), doxycycline (30 µg), minocycline (30 µg), trimethoprim-sulphamethoxazole (1.25/23.75 µg), and cefoxitin (30 µg), in accordance with the Clinical and Laboratory Standard Institute (CLSI) guidelines (2014). Cefoxitin test was used to detect methicillin resistance. Isolates that were resistant to at least one antimicrobial agent in three or more categories were considered as multidrug-resistant (Magiorakos et al. 2012).

SCC*mec* typing

Multiplex PCR assays were conducted using primers (Table 1) that targeted the loci of SCC*mec* types I-V (Milheirico et al. 2007; Oliveira and de Lencastre 2002). Primers for locus A, locus F, and *dcs* region (locus D) were combined in Primer set A while primers for *mecI* gene (locus C), SCC*mec* type V J1 region, and *ccrB2* gene were combined in Primer set B. Primers for the *mecA* gene were incorporated in both primer sets as an internal control. Each reaction was performed in a 20 µL final volume containing approximately 240 ng DNA template, 2.6 µL nuclease-free water, 0.8 µM of each primer, and 1X GoTaq® Green Master Mix (Promega, USA). Thermocycling conditions in a MyCycler™ Thermal Cycler (Bio-Rad, USA) were as follows: 94°C for 4 minutes; 30 cycles of 94°C for 30 seconds,

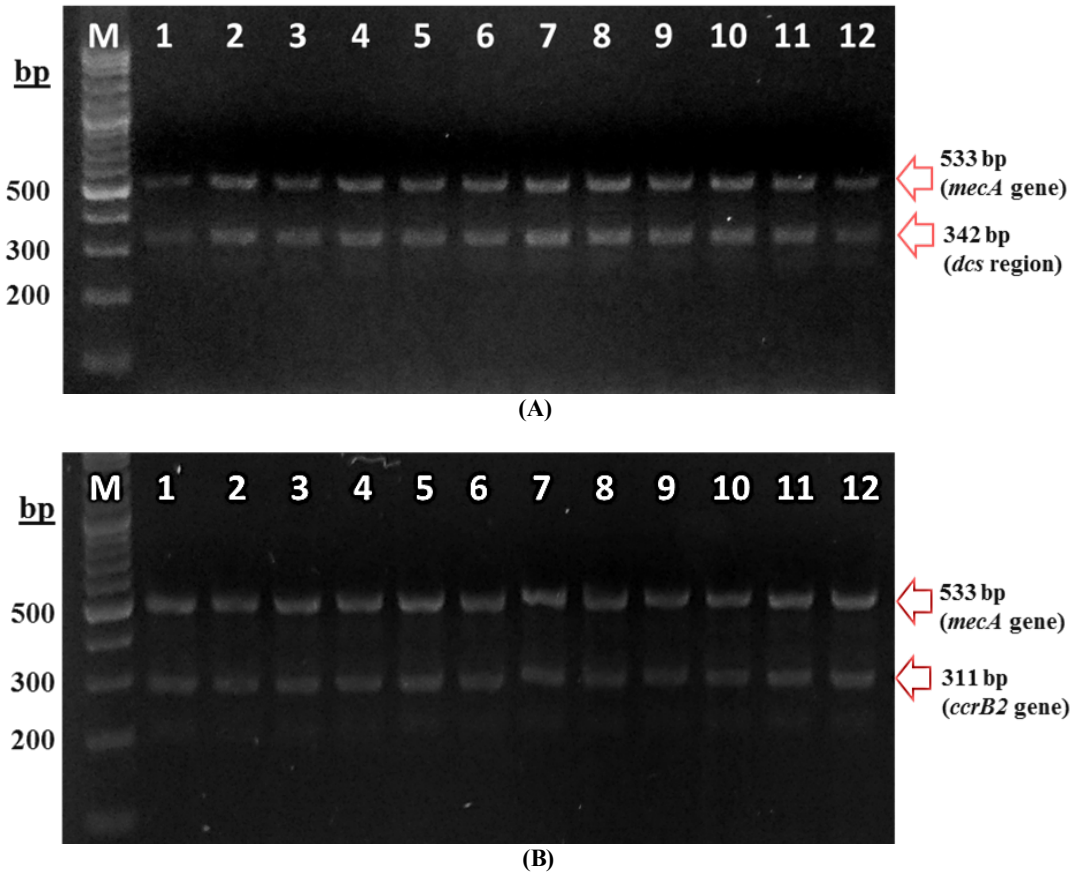

Figure 1: AGE results for SCC*mec* typing using primer set A (A) and primer set B (B) of MRSA reference strain and isolates. Lanes 1-11: MRSA isolates (Isolates 1, 6, 10, 17, 44, 46, 47, 58, 61, 65, 66, respectively) and Lane 12: positive control, MRSA (BIOTECH 10378) showing the approximate amplification products for the *mecA* gene (533 bp) internal control. Amplification products of 342 bp for *dcs* region (A) and 311 bp for *ccrB2* gene (B) were present in all the MRSA isolates and control strain. All MRSA isolates and control showed no amplification product in SCC*mec* V J1 region (377 bp) and in *mecI* gene (209 bp) (A). No amplification products were observed either in CIF2 (495 bp) and RIF5 (414 bp) (B). M: DNA molecular size marker (VC 100 bp Plus DNA Ladder; Vivantis Technologies, USA).

48°C for 30 seconds, and 72°C for 1 minute; and a final extension at 72°C for 4 minutes. Amplicons were resolved by electrophoresis on 1.7% (w/v) agarose gel stained with 0.5 µg/mL ethidium bromide and then visualized under UV transilluminator.

Statistical analysis
The software IBM® SPSS® Ver. 20.0 (SPSS Inc., Chicago) was used for statistical analysis of data. Prevalence was calculated based on the positive results of nasal cultures. For the risk factor analysis, the demographics and clinical characteristics of MRSA carriers were compared to non-carriers. Significant associations between continuous variables were compared using Student's *t*-test for independent samples (Lim et al. 2014). Categorical variables were analyzed by Fisher's exact test. A *p*-value of ≤0.05 was considered statistically significant. Odds ratio (OR) and 95% confidence intervals (CI) were determined for each variable.

RESULTS

Prevalence of *S. aureus* and MRSA nasal carriage among the elderly at GRACES
Staphylococcus aureus was isolated from 13 females and 12 males, corresponding to a prevalence of 37.9% (25/66). Based on the cefoxitin challenge and amplification of the *mecA* gene, 44% (11/25) of the isolates were MRSA corresponding to a sample prevalence of 16.7% MRSA carriage among the residents.

Antimicrobial susceptibility patterns
Nineteen *S. aureus* isolates (76%) were resistant to at least one antimicrobial agent while 11 isolates were resistant to cefoxitin (Table 2). Majority (10/11; 90.9%) of the MRSA isolates were multidrug-resistant, and showed cross-resistance to erythromycin (90.9%), clindamycin (90.9%), and rifampicin (81.8%). One MRSA isolate was susceptible to all the non-β-lactam antibiotics tested. High rates of intermediate susceptibility to trimethoprim-sulphamethoxazole (81.8%) were also observed. None of the isolates was resistant to ciprofloxacin, moxifloxacin, chloramphenicol, tetracycline, doxycycline, minocycline, gentamicin, linezolid, and vancomycin.

SCC*mec* typing
SCC*mec* typing assigned all MRSA isolates to SCC*mec* type IV. The isolates displayed two bands of >300 bp for the *ccrB2* gene and *dcs* region (Figures 1A and 1B). Both of these amplification products are present in SCC*mec* types II and IV. The absence of a band for the *mecI* gene, which is present in SCC*mec* type II only, confirmed that the isolates carried the SCC*mec* type IV element.

Risk factors for MRSA nasal carriage
A history of pulmonary tuberculosis was significantly associated with MRSA carriage (*p*=0.033; OR=4.67; 95% CI=1.19-18.26) (Table 3). The prevalence of MRSA in residents with a history of tuberculosis (7/22; 31.8%) was higher than that of the residents without tuberculosis (4/44; 9%). The same risk factor was significantly associated with *S. aureus* and multidrug-resistant MRSA carriage (data not shown). No significant association was observed between MRSA carriage and the other categories examined.

DISCUSSION

The 37.9% prevalence of *S. aureus* among the elderly residents of GRACES was higher than the >20% carriage rate reported recently among the residents in nursing homes in France (Rondeau et al. 2016) and China (Zhang et al. 2015). In terms of MRSA carriage, the 16.7% prevalence in GRACES was comparable to the 16-20% carriage rates in care facilities in Australia (Lim et al. 2014), UK (Horner et al. 2013), and Taiwan (Tsao et al. 2015), but relatively higher than the 10% carriage rate in China (Zhang et al. 2015). Differences in the reported carriage rates can be attributed to variations in sample size, study sites, antimicrobial therapy, and sanitary and infection control practices (Zhang et al. 2015; Cabrera et al. 2010).

The high prevalence of *S. aureus* and MRSA nasal carriage may be due to overcrowding and poor personal hygiene among the residents. During the period of sample collection, GRACES accommodated more than 200 residents which exceeded the facility's capacity of 150 residents only. There were about 10 rooms which were occupied on a shared basis depending on the functional status of the residents. Each room was shared by either five to 20 ambulant residents or approximately 30 to 40 non-ambulant residents who require assistance for their medical and personal needs including those who are wheelchair-bound and bedridden. The residents were confined to crowded and poorly-ventilated rooms where the bacterium multiplied easily. It is likely that the bacterium was transmitted from one resident to another considering that switching of beds and sharing of personal items, such as clothes, towels, and bed linens, were common among the residents. Because some residents switched places and roamed around the facility, it was difficult to determine whether the carriers were in close proximity to each other and/or residing in the same room. Moreover, the screening and cohort isolation of residents with non-healing wounds, symptomatic infections, and communicable diseases (except pulmonary tuberculosis) remain a challenge for GRACES, due to the high number of admissions, scarcity of resources, and limited isolation facilities. Understaffing may have also contributed to poor compliance to infection control measures because of the high workload and increased demands for basic care and special needs of the residents. In GRACES, one houseparent can serve 10-20 residents depending on the residents' functional status. Since GRACES also houses elderly with special needs, such as those with debilitating conditions, Alzheimer's disease, dementia, tuberculosis, and other chronic illnesses, the overcrowding and understaffing may compromise the sanitation and disinfection protocols, with the staff prioritizing the completion of resident care duties over the strict compliance to aseptic work practices and proper hygiene, such as regular hand washing.

Residents found to be *S. aureus* and MRSA carriers may either be persistently- or intermittently-colonized while those classified as non-carriers could be intermittent carriers. Persistent carriers have higher bacterial loads and greater risk of developing subsequent infections than intermittent carriers (Wertheim et al. 2005; Bradley 2002). A longitudinal study may be conducted to distinguish these patterns of nasal carriage and to determine the risks of acquiring subsequent infections among residents.

Infections caused by MRSA are serious burden to public health as the emergence of multidrug-resistant strains complicates treatment (CDC 2013). Multidrug-resistant strains are not confined to hospitals as these can be transmitted to other healthcare facilities and the community (Zhang et al. 2015; Horner et al. 2013; Cabrera et al. 2010). More than 35% of long-term care residents are carriers of at least one type of multidrug-resistant bacteria (Lim et al. 2014), and one of the most prevalent is MRSA, which is the common cause of skin and soft tissue infections among the residents (Zhang et al. 2015; Bradley 2002).

In the present study, multidrug resistance was common in the MRSA isolates (Table 2). Majority of the isolates showed cross-resistance to erythromycin (90.9%), clindamycin (90.9%), and rifampicin (81.8%), which could be due to the extensive use of these antibiotics in GRACES. Amoxicillin and clarithromycin, which are closely related to cefoxitin and erythromycin,

respectively, are commonly used as empirical treatment for upper respiratory tract infections. Clindamycin is often used for wound infections while rifampicin is used for at least six months in combination with other drugs for treating pulmonary tuberculosis. These antibiotics are, therefore, not suitable for treating staphylococcal infections in GRACES. Incidentally, only the history of pulmonary tuberculosis was observed as a significant risk factor for MRSA carriage (Table 3). Considering the high rates of rifampicin resistance among the isolates and the high prevalence of MRSA carriage in residents with a history of pulmonary tuberculosis, it is likely that prolonged exposure to rifampicin as a treatment for tuberculosis led to the proliferation of rifampicin-resistant MRSA. This assumption is consistent with a previous report in Japan where MRSA strains isolated from tuberculosis wards were significantly resistant to rifampicin (Sekiguchi et al. 2006). Modifying the multidrug therapy regimen for tuberculosis patients by eliminating rifampicin may help prevent the increase of rifampicin resistance. It is important that further studies and consultations be conducted as the current diagnosis and treatment strategy being implemented in GRACES is based on the National Tuberculosis Control Program. Furthermore, the high rates of intermediate susceptibility to trimethoprim-sulphamethoxazole among the isolates may have resulted as this antibiotic is commonly used for the treatment of urinary tract infections. Caution should be observed as intermediate isolates may develop resistance during prolonged and frequent exposure to this drug.

Several antimicrobial agents, such as ciprofloxacin, moxifloxacin, chloramphenicol, tetracycline, doxycycline, minocycline, gentamicin, linezolid, and vancomycin have remained effective against MRSA (Table 2). Nonetheless, it is important that these antibiotics be used rationally. Isolates initially reported as susceptible may become intermediate or resistant during treatment, resulting in clinical failure. Some *S. aureus* isolates tend to develop resistance to quinolones (e.g., ciprofloxacin, moxifloxacin) immediately after the start of treatment while others may exhibit reduced susceptibility to vancomycin during prolonged treatment. It is advisable to repeat the tests on subsequent isolates from the same body site upon the start of treatment with these antibiotics (CLSI 2014). A regular update on the susceptibility/resistance data in GRACES is essential for the appropriate treatment of MRSA infections.

All MRSA isolates carried the SCC*mec* type IV element. SCC*mec* IV-carrying MRSA, which is traditionally associated with the community (Zhang et al. 2015; Cabrera et al. 2010), has also been reported to be prevalent in care homes in China (Zhang et al. 2015), Taiwan (Tsao et al. 2015), and UK (Horner et al. 2013). It is likely that community-acquired MRSA may have spread to the residential care facility through the residents and their guests. However, it is difficult to validate this as residents and visitors are not screened for MRSA carriage prior to admission at GRACES. In the Philippines, SCC*mec* type IV is commonly carried by MRSA isolated from both hospitals and the community (Valle Jr. et al. 2016; Song et al. 2011; Cabrera et al. 2010), indicating that it may be the predominant SCC*mec* type circulating in the country.

The results provide baseline data for future epidemiological studies on the prevalence and risk factors associated with MRSA carriage. Due to the high resistance rates to cefoxitin, erythromycin, clindamycin, and rifampicin, these drugs are not recommended for empirical treatment of staphylococcal infections. There is a need to review and update policies on infection control and treatment plans in GRACES as these drugs are commonly used in the treatment of various infections. The treatment options for staphylococcal infections should be based on available resistance data. Improvements in basic personal hygiene and sanitary practices among the residents and healthcare workers can help reduce the prevalence and transmission of MRSA. It is recommended that longitudinal studies be conducted to determine the patterns of MRSA carriage and transmission among residents and healthcare workers. Routine surveillance should also be considered in order to determine the association of resistance and transmission patterns between healthcare facilities and communities to prevent outbreaks of infections.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

CONTRIBUTIONS OF INDIVIDUAL AUTHORS

MGBA and GMP conceptualized the study design. MGBA conducted the data and sample collection, laboratory experiments and data analyses, and prepared the manuscript. GMP supervised the study, provided materials and reagents for the experiments, and contributed to writing and editing of the manuscript. ECC contributed to the improvement of the study. The authors have read and approved the final version of the manuscript.

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