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Prevalence of Methicillin Resistant *Staphylococcus aureus* and Assessment of Associated Factors among Patients Admitted at Jimma Medical Center, Southwest Ethiopia

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Abstract

Background: Methicillin Resistant *Staphylococcus aureus* (MRSA) is one of the most important hospital associated pathogens whose emergence has created clinical difficulties for nosocomial infections. The extent of nasal colonization during hospitalization, however, has not been investigated. Therefore, this study aimed to assess the prevalence and associated factors of methicillin resistant *Staphylococcus aureus* nasal colonization in inpatient wards at an Ethiopian teaching hospital offering tertiary care for the prevention and control of its transmission.

Methods: A hospital based prospective cross-sectional study was conducted among 388 admitted patients at Jimma medical center in Jimma town, southwest Ethiopia, from October 1 to December 30, 2020. Proportional stratification and systematic random sampling were employed to get a proportional number of participants and to recruit study participants from each ward. Socio-demographic data and data on associated factors were collected using a structured questionnaire. Two nasal swab samples were taken from each patient, the first within 48 hours of admission and the second at the time of discharge. The specimens were then inoculated on Mannitol salt agar and yellowish colonies were sub-cultured on nutrient agar. The isolate was further identified using gram reaction, catalase, and coagulase tests. The Cefoxitin disk was used for the detection of methicillin resistant *Staphylococcus aureus*. Multivariate logistic regression was employed for factors associated with Methicillin Resistant *Staphylococcus aureus* (MRSA) nasal colonization. A P-value <0.05 was defined as statistically significant for all results.

Results: The overall prevalence of MRSA nasal colonization was 29.9%. The prevalence of MRSA at the time of admission was 23.7%. From the total (116) MRSA isolated, 20.69% of patients were newly colonized. The isolates showed the highest resistance to penicillin (97.9%). History of hospitalization, chronic wound infection, and diabetes mellitus were significantly associated with MRSA nasal colonization.

Conclusion: The prevalence of MRSA was 29.9%. The isolated *S. aureus* showed the highest resistance to penicillin (97.9%) and the majority of the isolates were multidrug resistant. Having a history of hospitalization, chronic wound infection, and diabetes mellitus were significantly associated with MRSA nasal colonization. MRSA transmission in the hospital can be reduced by screening patients during their admission.

Keywords: Antibiotic resistance • Inpatients • Jimma • Jimma medical center • MRSA • Nasal colonization • Prevalence

Abbreviations: ART: Anti-Retroviral Treatment; AST: Antibiotics Susceptibility Test; ATCC: American Type Culture Collection; CAMRSA: Community Associated Methicillin Resistant *Staphylococcus aureus*; CLSI: Clinical and Laboratory Standards Institute;

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Co-NS: Coagulase Negative Staphylococcus; HAART: Highly Active Anti-Retroviral Treatment; HAMRSA: Healthcare Associated Methicillin Resistant *Staphylococcus aureus*; MDR: Multiple Drug Resistance; MRSA: Methicillin Resistant *Staphylococcus aureus*; MSA: Mannitol Salt Agar; MSSA: Methicillin-Sensitive *Staphylococcus aureus*; NA: Nutrient Agar; SOP: Standard Operating Procedure; SPSS: Statistical Package Software for Social Science; PBPs: Penicillin Binding Proteins

Introduction

Staphylococcus aureus (*S. aureus*) is a gram-positive bacterium that has a spherical shape and is characterized by its salt-tolerant nature. It can be cultivated in mannitol salt agar medium containing 7.5% sodium chloride, is negative for oxidase test and positive for catalase test [1,2]. This organism is a common cause of bacterial infections in both developed and developing countries [3,4]. The capability of this bacterium to cause disease is enhanced by its resistance to antibiotics used in its treatment and virulence factors, which can be exemplified by the arrival of Methicillin Resistant *Staphylococcus aureus* (MRSA) [5]. Nosocomial and community onset infections are caused by MRSA with an increasing endemic and epidemic spread [6,7]. This strain of *S. aureus* is a pathogenic strain responsible for many difficult to treat infections in humans [8,9], being one of the most important hospital-associated pathogens [10].

There are two types of MRSA, Health Care Associated (HAMRSA) and Community Associated (CAMRSA). Health care associated isolates are obtained from patients two or more days after hospitalization. Community associated MRSA is obtained from patients within two days of hospitalization and without the HAMRSA risk factors [10,11]. Methicillin resistant *Staphylococcus aureus* is resistant to many groups of antibiotics called the beta lactams. Self-medication and buying drugs without prescription are very common practice especially in developing countries which can contribute for the development of drug resistant antibiotics [12].

These MRSA associated infections impose a serious burden regarding medical and socio-economic costs, and cause significant morbidity and mortality [13]. It adapted to tolerate treatment with antibiotics, such us methicillin, dicloxacillin, nafcillin, and oxacillin, it may also be denoted as multidrug resistant *S. aureus*. The emergence of MRSA has created clinical difficulties for nosocomial infections worldwide [14]. It has become a major human pathogen and a public health problem globally, with 13% to 74% of global *S. aureus* infections being attributable to MRSA infections [15-17]. The prevalence of MRSA nares colonization in Ethiopia ranges from 8.3%to 77.3% and in the study area (inpatients of JUMC), the carriage rate of MRSA nares colonization among *S. aureus* was reported to be 51.8%. Infection with MRSA increase the duration of an antibiotic treatment with more than six days when compared to MSSA infection.

Mortality and length of hospitalization are the short-term direct effects of resistance on the affected patient. The long-term effects may include having a resistant infection on future health, family time associated with increased hospitalization time and subsequent recovery, the loss of work, and even the emotional impact of having a resistant infection [18]. The MRSA frequently causes nosocomial infections and is resistant to most of the antibiotics. This is one of the greatest challenges for modern antimicrobial treatment [19].

The common sources of MRSA are human patients and carriers [20]. Asymptomatic carriers constitute important MRSA reservoirs. The occurrence of subsequent infections has been associated with the colonization of patients with MRSA. Acquisition and colonization of MRSA during a hospital stay not only complicates patient management but also has a significant impact on efforts to control and prevent Health Care Associated Infections (HCAIs).

Even though different studies were conducted on the nasal colonization of MRSA, the magnitude of this organism during hospitalization was not investigated. To the best of our knowledge, there is a gap in the prevalence of MRSA nasal colonization of admitted patients during their hospitalization. As a result, updated information is needed on the prevalence of MRSA nasal colonization (both at admission and during discharge) and its associated factors among admitted patients at JMC inpatient wards for prevention and control of its transmission. Therefore, the main objective of the study was to assess the prevalence of MRSA nasal colonization and its associated factors among admitted patients.

Materials and Methods

Study design and settings

A prospective cross-sectional study was conducted from October 1 to December 30, 2020 at Jimma Medical Centre (JMC). Jimma Medical Center, a tertiary teaching hospital, is located in Jimma town, 352 km southwest of Addis Ababa. It is the only teaching and referral hospital in the southwest of Ethiopia with a bed capacity of 660 and a catchment population of over 20 million. Here were 460 inpatient beds during sample collection. Separately, there are 120 beds in the medical ward, 60 beds in gynecology, 142 beds in the surgery ward, 52 beds in maternity, and 86 beds in the pediatric ward in the in-patient's ward. An average of 1372 patients per month was getting service in the mentioned department of the inpatient wards. Data from September to December 2019 indicated that 1908, 730, 1324, 990, and 536 patients were admitted to pediatrics wards, gynecology wards, medical wards, surgical wards, and maternity wards, respectively.

Population

All patients admitted to JMC inpatient wards less than 48 hours after hospitalization and who signed informed consent were included in the study. The patients who were critically ill and were not volunteers were excluded. Also, study participants with nasal anatomical deformities and nasal bleeding at the time of data collection were excluded because rolling of the swab may aggravate bleeding. Participants with clear nasal infections were also excluded from the study.

Sample size determination

The required sample size was calculated using a single population proportion formula ($n=(Z\ a/2)^2\ P\ (1-P)/d^2$). The assumptions used to calculate the sample size were: 59% (0.59) of *S. aureus* among in-patients of Jimma University hospital, using a 95% confidence interval (Z a/2=1.96) and a 5% (0.05) margin of error. Then, by adding a 5% non-response rate, the final sample size was 388.

Sampling technique

The total number of patients in the source population at the time of data collection was one thousand three hundred and seventy-two patients (1372). Proportional stratified sampling was used to get a proportional number of study participants from each ward. From each ward, study participants were enrolled using a systematic random sampling technique. The interval is equal to the total population divided by the sample size, which is three (K=3). The first sample was taken by the lottery method, and the rest of the samples were taken at intervals of three until the total sample size was achieved. The sampling frame was the list of the patients on the registration log book (Figure 1).

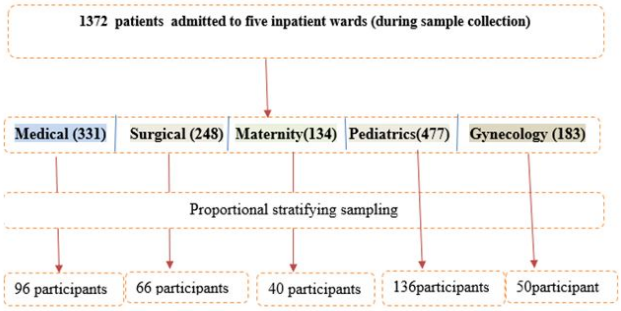

Figure 1. Schematic representation of sampling techniques used in the study.

Operational definitions

MRSA: *S. aureus* strain that had less than or equal to a 21 mm zone of inhibition to cefoxitin disk in a disk-diffusion test on Mueller-Hinton agar.

MDR: Bacteria that show resistance to antibiotic drugs belonging to at least three different classes of antibiotics.

History of diabetes mellitus: Patients who had diabetes and measured their blood sugar by themselves using a glycemic reader (glucose meter) or had follow-up at a health institution and were taking treatments.

History of HIV infection: Patients who were on ART follow-up

Nasal carriage: is the state of carrying bacteria in the nose without showing any signs of infection.

Colonization: The presence of methicillin-resistant *S. aureus* in nasal swab culture was defined.

Newly colonized patients: Patients whose nasal swabs were negative for MRSA during admission and positive during discharge time.

Nasal swab: Specimens collected from the anterior nares using sterile cotton swabs moistened with normal saline.

Hospitalized or admitted patients: They were patients who stayed in inpatient wards to receive their treatments and follow up under the supervision of health care providers.

Patient discharge time: It was the time when patients finished their time of treatments and decided (by their healthcare provider) to leave their admission ward.

Non carriers: Patients whose nasal swab did not show growth on mannitol salt agar.

Data collection procedures

Socio-demographic characteristics: A pretested structured questionnaire was used as a tool for the collection of socio-demographic data and factors associated with MRSA colonization. Relevant data regarding gender, age, educational status, occupation, history of hospitalization in the past six months, household member hospitalization, surgery within the past one year, chronic wounds, antibiotic usage within the past three months, diabetic disease, and HIV infection were collected by trained nurses.

Nasal swab sample collection and processing: Nasal specimens were collected from the anterior nares using sterile cotton swabs moistened with normal saline. Two nasal swab samples were collected from each participant. The first samples were taken within 48 hours of patient admission and the second samples were collected from the participant during their discharge time. Using a swab by rotating gently against the inner surface A pre-moistened swab with sterile normal saline was introduced into each nostril by rolling it 4 to 5 times (clockwise and anticlockwise) against the nostril wall. The collected nasal samples were placed in a tube containing Stuart's transport media (in-house made), labeled, stored in ice packs, and transported immediately to the microbiology laboratory for further processing. A total of 776 nasal samples were collected from 388 participants.

Phenotypic screening to identify ***Staphylococcus aureus*****:** After reaching the microbiology laboratory, nasal swabs were inoculated onto mannitol salt agar plates and incubated for 18-24 hours at 37°C. The characteristic golden yellow or cream colonies with a yellowish background rising from the overnight culture were noted as presumptive *S. aureus* colonies. The colonies were further characterized by standard bacteriological procedures such as the gram reaction, catalase test, and coagulase test. Colonies which were coagulase positive were considered to be *Staphylococcus aureus*. Whereas colonies with white colonies (not mannitol fermenters) and coagulase negative were taken as CoNS.

Antibiotic Susceptibility Testing (AST): The antimicrobial susceptibility testing was carried out by using Kirby-Bauer's disk diffusion method as per Clinical and Laboratory Standards Institute (CLSI) 2018 guidelines. The following antimicrobials (Sensi-Discs, Becton, Dickinson and Company, Sparks, MD) and disc potencies (ug) were used: Cefoxitin (FOX), Clindamycin (DA), Chloramphenicol (C) (30 µg), Ciprofloxacin (CIP), Erythromycin (E), gentamicin(CN), Penicillin (P), Sulphamethoxazole-trimethoprim (SXT), and Tetracycline(TTC). The results were recorded as interpreted values, "R"(Resistant),"I" (Intermediate) and "S" (Sensitive). The interpretation of the categories of

susceptible, intermediate, and resistant was based on the CLSI guidelines (CLSI, 2018).

Detection of Methicillin resistant *Staphylococcus aureus*: Cefoxitin is a potent inducer of the mecA regulatory system and can be used for the detection of heterogeneous populations of MRSA. When PCR detection for mecA gene detection is compared with the oxacillin (1 µg) and cefoxitin (30 µg) disc diffusion method and the oxacillin agar screening test (6 mg/ml oxacillin), cefoxitin disc diffusion has high sensitivity and specificity. In the absence of the availability of molecular biology techniques, the cefoxitin disc is the best detector of methicillin resistance in *S. aureus* related to the other phenotypic tests.

The methicillin sensitivity or resistance of each *S. aureus* was tested using surrogate antibiotics of 30 µg cefoxitin discs by the Kirby-Bauer disk diffusion method according to CLSI. In Mueller-Hinton agar plates, inoculum was adjusted to 0.5% McFarland standard and streaked uniformly with swab sticks. The plates were allowed to dry for 3-5 minutes before the disks were used. The plates were then incubated aerobically at 37°C for 24 hours. The zone of inhibition was interpreted according to CLSI guidelines. All isolates resistant to cefoxitin were considered MRSA. An inhibition zone of 21 mm or less around the cefoxitin disc was indicated by MRSA. *S. aureus* ATCC 25923 was used for quality control.

Data quality assurance and control: The questionnaire was written in English, translated into Amharic and Afaan Oromoo, and then translated back into English to ensure consistency. Prior to actual data collection, it was pre-tested for accuracy on 5% of patients at Mettu Karl hospital. Before collecting the data, all data collectors received the proper one-day training on the purpose of the study, confidentiality concerns, study participant rights, consenting, and interviewing techniques. Under the careful supervision of investigators, experienced and trained nurses gathered socio-demographic and clinical data. Every piece of collected data was checked for its completeness daily by the investigators.

The reliability of the study findings was guaranteed by implementing QC measures throughout the whole process of the laboratory activities. Culture media, biochemical reagents, staining reagents, and antibiotic discs were checked for their normal shelf life before use. All culture plates were stored at the recommended refrigeration temperature (2°C-8°C) after being prepared. Antibiotic discs were also stored at the same temperature range before use. The standard reference strain *S. aureus* ATCC 25923 was used as a positive control on the biochemical tests and agar plates, including Mueller Hinton with antibiotic discs. Proper sample collection and handling was done by experienced and trained nurses who were working at each ward. In general, all laboratory procedures were conducted based on recommended standard laboratory procedures by strictly following the pre-analytical, analytical, and post-analytical stages of quality assurance that are incorporated into standard operating procedures.

Data management and analysis: The data was coded and entered into Epidata version 3.1 before being cleaned and analysed with SPSS for Windows version 21.0. Both descriptive and inferential statistics were employed for the analysis of the data. Frequencies were used to determine the prevalence of MRSA among patients admitted to inpatient wards. Bivariate and multivariable logistic regression was also employed to assess the significantly associated factors with nasal colonization of MRSA. Variables with a P-value of less than 0.25 were taken as candidates for multivariable logistic regression. P-values of less than 0.05 on multivariate logistic analysis were considered statistically significant.

Results

Sociodemographic characteristics of the participants

A total of 409 participants were recruited to participate in this study of which 388 provided full information. A total of 776 nasal samples (during admission and during discharge time) were obtained from 388 participants across five wards of the in patients within three month (October 01, 2020 to December 30, 2020) study period. Response rate was 94.9% (388/409). Briefly 192 samples from medical ward, 272 paediatric ward, 80 Maternity, 132 surgical wards and 100 Gynecology ward. A summary of study participants is presented in Tables 1 and 2.

Categories		No.	Percent (%)
Gender	Male	163	42
	Female	225	58
	Under five	30	7.7
	5-9	48	12.4
	10-14	58	14.9
	15-19	10	2.6
Age group	20-24	25	6.4
	25-29	34	8.8
	30-34	40	10.3
	35-39	29	7.5
	40-44	35	9

	>45	79	20.4
Educational status	No formal education	112	28.9
	Pre-school age	29	7.5
	KG	9	2.3
	Elementary	193	49.7
	High school	35	9
	Diploma and above	10	2.6
Occupation	Merchant	15	4.1
	Farmer	60	16.71
	Student	135	37.6
	House wife	140	39
	Employed	6	1.67

Table 1. Sociodemographic characteristics of study participants admitted to inpatient wards of JMC, Jimma, southwestern Ethiopia, October 01 to December 30, 2020.

Categories		No.	Percent (%)
Ward	Medical	96	24.7
	Surgical	66	17
	Maternity	40	10.3
	Pediatric	136	35.1
	Gynecology	50	12.9
Antibiotics	Yes	104	26.8
	No	284	73.2
Hospitalization	Yes	95	24.5
	No	293	75.5
Surgery	Yes	21	5.4
	No	367	94.6
Chronic wound	Yes	130	33.5
	No	258	66.5
History of HIV	Yes	5	1.29
	No	383	98.71
Diabetics	Yes	49	12.63
	No	339	87.37
House member hospitalization	Yes	33	8.5
	No	355	91.5

Table 2. Other clinical and admission data of study participants admitted to inpatient wards of JMC, Jimma, southwestern Ethiopia, and October to December 2020.

From the 388 inpatients from whom nasal swabs were collected and cultured on MSA, 368 (94.85%) showed growth. Out of which 210 (57.06%) were S. aureus and 158 (42.94%) were found to be coagulase negative during their admission.

During the time of discharge, out of 388 samples recollected from the patients 375(96.65%) samples showed growth on MSA. Two hundred thirty six (62.93%) isolate were *S. aureus* and 139 (37.07%) were coagulase negative staphylococci.

The rest thirteen (3.35%) swabs did not showed growth.

In this study; 163 (42%) were males and 225 (58%) were females. The ages of study subjects ranged from 1 year to 80 years. The median and range duration of hospitalization for MRSA carriers was 11 and 30 days while it was 8 and 20 days for MSSA carriers and 7 and 11 for whose swabs were not grown on MSA. Around 95% of the patients were referred from other health facilities.

Antimicrobial susceptibility test

The Kirby-Bauer sensitivity test for the 210 isolates of *S. aureus* at admission and 236 isolate during discharge time against ten commonly used antibiotics showed resistance rate of 96.2% for penicillin, 51.% for chloramphenicol, 48.5% for trimethoprim-sulphamethoxazole, 43.8% for cefoxitin, 43.3% for tetracycline 38.1%for erythromycin, 33.3% for Ciprofloxacin, 14.8% for gentamicin and 11% for clindamycin. During discharge time the sensitivity test for these isolate showed resistance rate of 97.9 for penicillin, 56% for chloramphenicol, 54.2% for trimethoprim-sulphamethoxazole, 49.2%for cefoxitin, and 47.9% for tetracycline 44.1% for erythromycin, 38.6% for Ciprofloxacin, 14.4% for clindamycin and 15.7% for gentamicin (Table 3).

Name of drug/disc content break point		At admission				During discharge			
		No.	R (%)	I (%)	S (%)	No.	R (%)	I (%)	S (%)
Penicillin (10 µg)	>28	210	96.2	--	3.8	236	97.9	--	2.1
Cefoxitin (30 µg)	>22	210	43.8	---	56.2	236	49.15	---	50.8
Erythromycin (15 µg)	14-22	210	30	8.1	61.9	236	36	8.1	55.9
Clindamycin (2 µg)	15-20	210	4.8	6.2	89	236	6.8	8.9	84.3
SXT (25 µg)	11-15	210	47.1	1.4	51.4	236	54.2	0	45.8
Tetracycline (30 µg)	15-18	210	31.9	11.4	56.7	236	29.7	18.2	52.1
Ciprofloxacin (5 µg)	16-20	210	25.7	7.6	66.7	236	30.5	8.1	61.4
Chloramphenicol (30 µg)	13-17	210	46.2	4.8	49	236	49.6	6.4	44.1
Gentamycin (10 µg)	13-14	210	13.8	1	85.2	236	13.1	1.3	85.7

Key: R=Rsistant, I=Intermediate, S=Susceptible, SXT-Trimethoprim Sulphamethoxazol, N-Number, % percent

Table 3. Overall antibiotic susceptibility profiles of *Staphylococcus aureus* isolates among patients admitted to inpatient wards of JMC, Jimma, southwestern Ethiopia, from October 1 to December 30, 2020.

The MRSA isolates were 0% sensitive to penicillin, 81.9% sensitive to gentamycin, 74.1% to clindamycin, 26.7% to ciprofloxacin, 18.1% to trimethoprim-sulphamethoxazole, 17.24% to chloramphenicol, 27.6% to erythromycin and 27.6% to tetracycline. In this case intermediates isolates were also taken (counted) as resistant. This study also revealed that 66.67% (154/231) of *S. aureusisolates* were multidrug resistant (Tables 4-6).

Ward	Drugs (N/%)								
	P	FOX	C	SXT	E	CIP	TTC	CN	DA
Medical	60 (26)	30 (25.9)	35 (26.5)	33 (25.8)	29 (27.9)	20 (22)	27 (23.9)	16 (47.1)	15 (39.5)
Surgical	40 (17.3)	29 (25)	24 (18.18)	22 (17.2)	24 (23.1)	14 (15.4)	14 (12.4)	13 (38.3)	8 (21.1)
Maternity	20 (8.65)	1 (.9)	7 (5.3)	10 (7.8)	6 (5.8)	1 (1.1)	8 (7.08)	0 (0)	4 (10.53)
Pediatrics	70 (30.3)	38 (32.8)	44 (33.3)	46 (36)	30 (28.8)	40 (43.95)	41 (36.3)	1 (2.94)	4 (10.53)
Gynecology	39 (16.9)	18 (15.5)	22 (16.6)	17 (13.3)	15 (14.4)	16 (17.6)	23 (20.4)	4 (11.8)	7 (18.4)

Note: N: Number; %: Percent; P: Penicillin; FOX-Cefoxitin; SXT: TrimethoprimSulphamethoxazol; C: Chloramphenicol; E: Erythromycin; DA: Clindamycin, CIP: Ciprofloxacilline; CN: Gentamycin; TTC: Tetracycline

Table 4. Antibiotic resistance profiles of *S. aureus* isolates from respective wards among patients admitted to inpatient wards JMC, Jimma, southwestern Ethiopia, from October 1 to December 30, 2020.

Drugs	Number	Percent	Remark
P	42	18.18	

P, C	26	11.26	
P, E	9	3.9	
P, E, DA	5	2.2	
P, SXT, TTC	20	8.7	
P, C, SXT, CN	4	1.7	MDR
P, C, FOX, CIP	1	0.43	
P, C, SXT, FOX	31	13.4	
P, SXT, TTC, CN, DA	3	1.3	
P, FOX, TTC, E, CIP, CN	20	8.7	
P, C, SXT, TTC, E, CIP, CN	6	2.6	
P, C, SXT, FOX, TTC, E, CIP	34	14.7	
P, C, SXT, FOX, TTC, E, CIP, DA	29	12.55	
P, SXT, C, FOX, TTC, E, CIP, CN, DA	1	0.43	

Note: P: Penicillin; FOX: Cefoxitin; SXT: Trimethoprim Sulphamethoxazol; C: Chloramphenicol; E: Erythromycin; DA: Clindamycin; CIP: Ciprofloxacilline; CN: Gentamycin; TTC:Tetracycline

Table 5. Overall resistance pattern of *S. aureus* isolates across commonly used drugs at JMC, Jimma, southwestern Ethiopia, from October 1 to December 30, 2020.

Variables		N	MRSA		COR (95% CI)	AOR (95% CI)	P-Value
			Yes (%)	No (%)			
Gender	Female	141	59 (41.85)	82 (58.15)	.480 (.282-.815)	1.407 (.646-3.065)	0.389
	Male	95	57 (60)	38 (40)	Ref		.
History of diabetic	Yes	40	28 (70)	12 (30)	2.864 (1.377-5.957)	2.641 (1.029-6.776)	0.041
	No	196	88 (44.9)	108 (55.1)	Ref		
Hospitalization	Yes	72	64 (88.9)	8 (11.1)	17.231 (7.702-38.548)	16.67 (6.230-44.570)	<.001
	No	164	52 (31.7)	112 (68.3)	Ref		
History of surgery	Yes	10	7 (70)	3 (30)	0.39 (0.101-1.583)	1.360 (083-22.270)	0.829
	No	226	109(48.23)	117 (51.77)	Ref		
Chronic wound	Yes	63	55 (87.3)	8 (12.7)	12.63 (5.646-28.221)	9.79 (3.756-25.533)	<0.001
	No	173	61 (35.26)	112 (64.74)	Ref		

Note: N: Number; COR: Crude Odd Ratio; AOR: Adjusted Odd Ratio; CI: Confidence Interval

Table 6. Multivariate logistic regression analysis of associated factors for MRSA nasal colonization among patients admitted to inpatient wards of JMC, Jimma, Southwest Ethiopia, from October 1 to December 30, 2020.

Prevalence of MRSA

At the time of admission, 210/388 (54.12%) of the total study participants (388) were carriers of *S. aureus*, and 92/388 (23.7%) were colonized with MRSA. From the total study participants,236/388(60.8%) were carriers of S. aureus and 116/388 (29.9%) were colonized with MRSA during discharge time. Among these, 210/236 (88.99%) and 92/116 (79.3%) were dual-time (at admission and during discharge) nostril carriers of *S. aureus* and MRSA colonized respectively. The rest of the 24 (20.6%) participants were newly nasally colonized by MRSA during discharge time. From the overall MRSA colonization at admission and during discharge, the hospital acquiring MRSA accounted for 20.69% (24/116).

From the isolates grown on MSA, the carriage rates of participants for *S. aureus* and MRSA were 62.9% (236/375) and 49.15% (116/236), respectively. This meant that the overall prevalence of nasal colonization among participants was 236/388 (60.8%) for *S. aureus* and 116/388 (29.9%) for MRSA. The carriage rates of *S. aureus* and MRSA from grown isolates were 57.06% (210/368) and 43.8% (92/210) at admission time, respectively. Both the carriage rate of *S. aureus* and MRSA increased during discharge time, which was 6.93% (236/375) and 49.15% (116/236) respectively.

Twenty-six participants who were negative for *S. aureus* became nasal carriers during discharge time. Out of these, 11 (42.3%) were non-carriers and 15 (57.7%) were CoNS positive at admission time. All 24 participants who became MRSA carriers during discharge time were previously (at admission) carriers for *S. aureus*. Out of these new MRSA colonized participants, 8 (33.33%) medical ward, 8 (33.33%) surgical ward, 3 (12.5%) paediatrics ward, and 5 (20.83%) were detected in gynecology. The distribution of *S. aureus* and MRSA across the wards with respect to admission time and discharge time was shown in Figures 2 and 3.

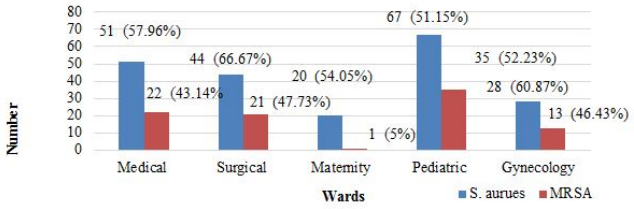

Figure 2. Distribution of *S. aureus* and MRSA at admission among participants in relationship with inpatient wards in JMC, Jimma, southwestern Ethiopia, from October 1 to December 30, 2020.

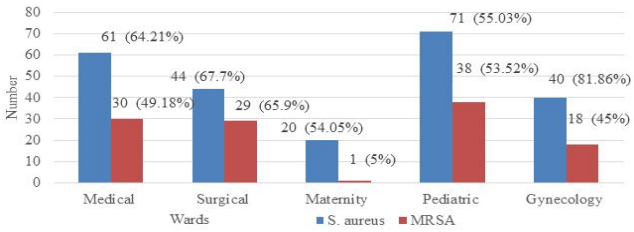

Figure 3. Distribution of *S. aureus* and MRSA at discharge among participants in relationship with inpatient wards in JMC, Jimma, southwestern Ethiopia, from October 1 to December 30, 2020.

The median and range of hospital stays for those participants who became (newly) nasal colonized by MRSA during discharge time were 18 days and 23 days, while it was 9 days and 24 days for those MRSA carriers at both times (admission time and during discharge).

Factors associated with MRSA nasal colonization

Gender, history of diabetic disease, history of hospitalization in the previous six months, history of surgery, and history of chronic wound were candidate variables for multivariate logistic analysis with a p-value of <0.25 in bivariate logistic regression. After controlling for confounders by means of multivariate logistic analysis, three variables showed statistical significance (P-value <0.05) with nasal colonization of MRSA. These variables were: History of hospitalization in the past six months; chronic wound infection; and history of diabetic disease.

Patients with a history of diabetic disease had 2.64 (95% Confidence Interval (CI): 1.029-6.776; p=0.041) times the risk of being MRSA nasal carriers as compared to patients who had no history of diabetic disease. Additionally, patients with a history of hospitalization in the past six months had 16.67 (95% Confidence Interval (CI): 6.230–44.570; p=<0.001) times the risk of being MRSA carriers compared to patients who had no history of hospitalization in the past six months. Patients diagnosed with chronic wound infection had 9.79 (95% Confidence Interval (CI): 3.756-25.533; p=<0.001) times the risk of being MRSA carriers compared to patients with no chronic wound infection.

Discussion

Methicillin resistant *Staphylococcus aureus* is a major human pathogen and a leading cause of nosocomial infections. This study focused on *S. aureus* and MRSA isolates from the anterior nares of participants from five inpatient wards in Jimma university medical center. In this study, we documented carriage rates of 62.93% and 49.15% for *S. aureus* and MRSA. These expressed rates are consistent with the burden of MRSA being lower and *S. aureus* being higher than 50% in several African studies (36-38). These reported rates may be related to non-adherence to drug prescriptions, self-medication, and poor hygiene practices in African countries, as well as suboptimal sanitation and water supply facilities.

Our findings on the carriage rate of *S. aureus* (62.3%) and MRSA (49.15%) were comparable to the 59% (*S. aureus*) and 51.8% (MRSA) carriage rates of a previous study (21) on patients admitted to Jimma university hospital inpatient wards. Specifically, the overall carriage rate of *S. aureus* and MRSA from the medical ward, surgical ward, maternity ward, pediatric ward, and gynecology ward were 64.21%and 49.18%, 67.7%and 65.9%, 54.05% and 5%, 55.03% and 53.52%, 81.86% and 45%, respectively. When compared to the previous study, this finding indicated that there was higher carriage of both *S. aureus* and MRSA across the inpatient wards, which could be attributed to differences in study design and study period.

The carriage rate of *S. aureus* (62.94%) and MRSA (49.15%) were higher during discharge when compared to time of admission which was 57.07% and 43.8%. As well as the prevalence of *S. aureus* (60.8%) and MRSA (29.9%) were higher during discharge time in relation to admission time which was 54.1% and 23.7% respectively. This difference may be contributed by exposure of the patients to the exogenous strain of the organism which were acquired during hospital stay.

The overall prevalence of MRSA among patients admitted to inpatient wards was 29.9%. The nasal colonization of MRSA detected in this study is higher than the rate reported in Kenya (7%) Ghana (0.9%), Atlanta, Georgia (7.3%), and Texas (3.4%). This might be due to differences in environmental factors, strains of the bacterium, the standard of medical care, awareness of antibiotic usage, and policy for antibiotic usage across the countries.

The MRSA colonization rate of patients at admission was 43.8%, and 8.1% of patients had MRSA on discharge from the screened participants who were negative for MRSA during admission.

This finding was comparable to the findings obtained from studies conducted in Tanzania (10.3%) and in Australia (11.7%). Isolates from the second swab taken during the patients' discharge showed increased resistance to commonly used antibiotics than those identified at admission. This may be contributed by the exposure of the patient to resistant exogenous clones of circulating microbes in the hospital.

This study also showed that 56.8% (n=134) and 51.1% (n=90) of the participants who were *S. aureus* carriers and MRSA colonized, respectively, had taken antibiotics before testing (3 months). In addition to the increased probability of *S. aureus* becoming resistant to antibiotics after prior antibiotic exposure, factors such as surgical procedures that disturb the mucocutaneous barriers, in addition to abuse or misuse of antimicrobial agents, may collectively contribute to a decrease in a patient's resistance to invading bacteria, with an increased risk of antibiotic resistant staphylococcal infection. This agrees with the study conducted by Ansari et al.

In justification with some studies, we could not statistically associate gender and previous antibiotic usage as risk factors for MRSA colonization. The role of antibiotic use as a risk factor is improved by a prolonged period from admission to isolation of MRSA, as it adds the time for exogenous acquisition of drug or antibiotic resistant strains. The significance of antibiotic usage as a risk factor may have been underestimated in this study because we were unable to document the antibiotic history of respondents during their hospitalization.

In terms of age, the highest prevalence rates of MRSA and *S. aureus* occurred among the age group of above 45 years 27.8% (n=32) and 22.9% (n=54) respectively. This may be related to a decline in immune function, malnutrition, and physiological and anatomical changes. This agrees with the study done by Maroof et al.

This study also revealed a lower prevalence rate of MRSA and *S. aureus* colonization among participants who had a history of HIV infection: 1.7% (n=4). This finding was consistent with the findings of. HIV infected patients are at greater risk (poor immunity, exposure to antibiotics from recent hospitalizations, and earlier MRSA infection or colonization) of MRSA colonization relative to the general population. However, it was exciting that nasal colonization with MRSA was more often seen in respondents without HIV/AIDS in the present study.

In fact, decreased MRSA colonization has been reported among HIV/AIDS patients on Highly Active Antiretroviral Therapy (HAART) elsewhere. This unintentional outcome of antiretroviral drugs could help to explain our findings. Less MRSA colonization may be due to non-selection of drug-resistant microorganisms as a result of reduced antibiotic usage in HAART patients. Moreover, a reduced incidence of HIV disease development in patients undertaking treatment might have led to a decreased frequency of MRSA and *S. aureus* colonization.

By binary logistic regression analysis, five factors (gender, history of diabetic disease, history of hospitalization in the past six months, history of surgery, and history of chronic wounds) were selected as candidates for multivariate logistic analysis. After controlling confounders by means of multivariate logistic analysis, only three variables showed statistical significance with colonization of MRSA (history of hospitalization in the past six months, chronic wound infection, and history of diabetic disease). History of hospitalization probably indicates that there was another underlying condition (patients' risk factor) which was not studied in this work and exposure to the organism colonization pressure in a hospital setting. Nelwan et al. study in Indonesia agrees with current findings. It is known that MRSA can cause different infections, which may include wound infection. This organism might be transmitted from the wounded area to the nostrils by the hands of the patient through cross contact. It is in agreement with the work of Marshall et al. Lung dysfunction and immune disorders commonly related to diabetes might lead to a worsening response to antibiotic treatment and hence increased carriage of MRSA among these patients compared with non-diabetic patients. This agrees with a study from Nigeria.

According to our findings, nearly all of the isolates (97.9%) were penicillin resistant, and all of the methicillin resistant isolates were completely penicillin resistant. The majority of the isolates were resistant to Sulfamethoxazole-trimethoprim (54.2%), Chloramphenicol (56%), and cefoxitin (49.15%). The susceptibility profile identified 154 multi-drug resistant strains of *S. aureus* (66.67%, 154/231). Most (125/154) of these were clustered in a group with 18.4% to 100% similarity. This could reflect the fact that the bacteria were raised in an environment where most of these antibiotics were in use. Multiple drug resistance may be an alarm that shows a very large percentage of bacterial isolates has been exposed to many antibiotics.

In general, the highest percentage of resistance observed was to penicillin (97.8%, n=231), followed by chloramphenicol (56%, n=132), SXT (54.2%, n=128), cefoxitin (49.15%, n=116), and tetracycline (47.9%, n=113). About 38.6% (n=91) of the *S. aureus* isolates were resistant to ciprofloxacilline, 44.06% (n=104, 95%) to erythromycin, 16.1% (n=38) to toclindamycin, and 14.4% (n=34) to gentamicin.

The isolated bacteria during discharge time were more resistant to different antibiotics. Many reasons have been intended to explain why hospital isolates of bacteria are resistant to multiple antibiotics. This is due to the inherent resistance of some isolates to the drug, which can be attributed to the acquisition of plasmids, inability of the drug to transit through the organism's cell wall or membrane and reach its site of action, drug efflux and target site modification or permeability, or lack of the target site for that drug.

In the current study, gentamycin was the most effective against *S. aureus*. One reason for its effectiveness could be related to the fact that gentamycin is rarely used as it is administered by injection. This form of administration is far less agreeable to self-medication than orally ordered antibiotics.

Several reports have documented that resistance to cefoxitin induced by disk diffusion can be helpful for MRSA strain detection in routine testing, for cefoxitin is considered as a potential inducer of the system that controls the *mecA* gene. Consequently, isolates which were shown to be resistant to cefoxitin were also regarded as methicillin resistant.

Strength and limitation of the study

This study revealed MRSA colonization both at admission and discharge time. But the identified strain at admission time and during discharge time could not be differentiated for those who were positive during both times. Even though different associated factors for MRSA

nasal colonization were identified, we could not identify risk factors for newly colonized patients [20].

Conclusion

We summarized that the overall prevalence of MRSA nasal colonization of patients admitted to inpatient wards was 29.9%. The isolated *S. aureus* showed high resistance to Penicillin (97.9%), Chloramphenicol (56%), and Sulphamethoxazole-trimethoprim (54.2%) and the majority of the isolates were multidrug resistant. A history of hospitalization, a history of diabetes, and a history of chronic wounds were all significantly associated with nasal MRSA colonization.

Recommendation

The findings of the present study revealed that the nares of patients admitted to inpatient wards were not free from colonization of MRSA. It is known that MRSA nasal colonization is a predisposing factor for the development of MRSA infection and transmission. In light of our study, we recommend that the hospital screen patients during their admission to inpatient wards as it helps to know the colonization status of the patients in control of its transmission in the hospital since those who had MRSA at admission time were positive for MRSA until discharge time. Researchers should do further study on the associated risk factors for acquiring MRSA colonization in hospitals.

Ethical Consideration

Ethical clearance was obtained from the institutional review board of health sciences faculty, Jimma University. A letter of cooperation was written from Jimma university's research coordination office to Jimma university medical center. The purpose, benefit, and method of the study were clearly explained to the participants in language they could understand. All of the participants were informed that their responses would be kept confidential. The written informed consent was taken from the participants and those who had a willingness to participate in the study were included. Participation in the study was voluntary and refusal was permitted. To ensure confidentiality of data, study participants were identified using codes, and unauthorized persons were not able to access the collected data. Furthermore, the specimen collected during the study period was only used for the stated objectives. The study participants' results were reported to the physician for proper management as necessary. This study was conducted in accordance with the principles of the declaration of Helsinki II.

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