Detection and antibiotic resistance pattern of *Staphylococcus aureus* and (MRSA) isolated from healthcare workers Nares at three Gaza hospitals, Palestine

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Abstract

Background: *Staphylococcus aureus* is a significant cause of nosocomial morbidity and mortality and has been identified as an emerging problem in the community. Here we detect the carriage rate and antibiotic resistance pattern of *S. aureus* and MRSA isolated from 140 healthcare workers (HCWs) nares at Gaza hospitals.

Methods: A cross sectional study was conducted on a total of 140 HCWs. *S. aureus* were recovered and identified from nasal swabs by conventional and molecular laboratory techniques. Susceptibility to 13 commonly used antibiotics against *S. aureus* infections was determined by disk diffusion test according to the CLSI guidelines. Testing by PCR for the presence of *nuc*, *mecA*, *cap 5* and *cap 8* genes was performed on all isolates.

Results: The nasal carriage rate of *S. aureus* was 42.1% (59/140), of MRSA was 22.6% (32/140) and of MSSA was 19.3% (27/140), with the highest carriage rate of MRSA among HCWs from surgery wards. There was no significant difference between the gender or hospitals with regard to *S. aureus* and MRSA carriage rate. However, a statistically significant difference was found for ward type and work experience. All 59 strains of *S. aureus* were sensitive to vancomycin and doxycycline, while nearly all were resistant to penicillin and ampicillin. The antibiotic resistance among MRSA was much higher than that among MSSA with a statistically significant difference for most antibiotics tested. Nearly 61% of isolates were noted to be multidrug resistant with higher percentage in MRSA (24/32; 75%) in comparison to MSSA

(12/27; 44,44%). All isolates were successfully genotyped for capsular polymorphism type 5 (55.9%) and type 8 (44.1%).

Conclusion: This is the first study in Gaza Strip investigating the nasal carriage of *S. aureus* among HCWs. High rate of MRSA isolates were shown to be MDR. These results highlight the critical need for screening and tracking MRSA among HCWs and to monitor and manage the usage of antibiotics in the hospitals and community in Gaza, Palestine.

Keywords: *S. aureus*, MRSA, HCWs, Antibiotic resistance pattern, Gaza, Palestine

Introduction

Staphylococcus aureus is one of the most prevalent human pathogens isolated from hospitalized patients worldwide, and is of increasing importance in the community setting. It causes a wide range of localized and systemic diseases ranging from skin and soft-tissue infections to infective endocarditis, osteomyelitis, bacteremia and necrotizing pneumonia, as well as various toxin and superantigen-mediated diseases [1-4]. Methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the most significant health care associated (HA) and community-associated (CA) pathogen, causing a wide range of infections and are associated with higher morbidity, mortality, prolonged length of hospital stay and higher healthcare costs as compared to methicillin-susceptible staphylococci [1,5]. In recent decades, MRSA has emerged as the most frequently identified antibiotic-resistant pathogen in many parts of the world, including North Africa and the Middle East[6]. Fortunately, whereas HA-MRSA isolates are generally multi-drug resistant, CA-MRSA tends to be resistant

primarily to β -lactam antibiotics. However, recent studies indicate that many CA-MRSA lineages are becoming increasingly resistant to non β -lactam antibiotics [7], while a growing number of reports describe replacement of HA-MRSA by CA-MRSA in healthcare settings [7,8].

S. aureus permanently colonizes the anterior nares of about 20% to 30% of the general population. Health care workers (HCWs) are more likely to be colonized than persons in the general population, presumably because of increased exposure, So, HCWs constitute an important reservoir of *S. aureus* and MRSA [9,10]. Nasal colonization with *S. aureus* in HCWs has been associated with an increased risk of invasive *S. aureus* infection [9,11]. Increased rates of MRSA colonization among HCWs have at least 3 important implications. First, HCWs may become infected by their own MRSA carriage strains; second, they could serve as a route of cross-transmission to patients; and finally, they may introduce the pathogen into their communities [12]. Several studies in Arabic countries and worldwide have reported that the rate of the nasal carriage of *S. aureus* and MRSA among HCWs ranges from

10.1%-76% [10,12-26]. The screening of nasal carriage in HCWs is an important component in the control of MRSA in any health care facility [27].

Epidemiological data about *S. aureus* and MRSA in HCWs in Palestine are generally scarce and insufficient [16,28] with current knowledge regarding the epidemiology of *S. aureus* in Gaza Strip based on two recent studies; a hospital-acquired and a community-based carriage respectively [29,30].

To that end, we aimed to determine the prevalence of asymptomatic nasal carriage of *S. aureus* and MRSA among HCWs who work in environments with varying degrees of exposure to patients and to determine its susceptibility profile to most common used antibiotics in our hospitals. To the best of our knowledge, this is the first study reporting the prevalence of *S. aureus* and MRSA in HCWs within the Gaza hospitals.

Methods

Study setting and sampling

This is a cross-sectional study of a convenience sample consisting of 140 HCWs that was conducted for six months between October 2010 and March 2011. The study was performed at three hospitals in Gaza Strip, two main hospitals (Al-Shifa, the largest public tertiary hospital in Gaza city and European-Gaza hospital in Rafah city), as well as from another public primary-care hospital (Odwan hospital in northern Gaza). HCWs including physicians, nurses, and medical technicians who are full-time workers from departments of surgery, internal medicine and intensive care units were involved in this study.

All HCWs included were healthy and had not used antibiotics in past two months prior to sample collection. Participation was on voluntary basis and written informed consent was taken from all participants prior to enrolment. A simple questionnaire was used to obtain demographic data including age, sex, place of work, employment status and length of healthcare service, where

data were recorded and analyzed anonymously. Ethical approval from the Helsinki committee at the ministry of health in Gaza Strip (Approval no. PHRC/HC/36/14) was obtained for performing the current study.

Sterile cotton swabs moistened with sterile saline were used for sample collection. The sample was obtained by rotating the swabs gently for five times on both nares so that the tip is entirely at the nasal osteum level [31], and it was directly streaked onto mannitol salt agar and blood agar plates (HiMedia Labs, Mumbai, India). Plates were incubated aerobically at 37°C for 24-48 hrs.

Isolation and Identification of *S. aureus* and MRSA

Conventional techniques: *S. aureus* isolates were identified phenotypically based on colonial morphology, Gram stain, and by using one or more of the following methods: catalase test, tube coagulase test, Pastorex™ Staph Plus latex agglutination (Bio-Rad, Hercules, California), and the Staph ID 32 API system (bioMérieux, France). Screening for MRSA was done by testing for oxacillin (1 µg) resistance using the Kirby-Bauer disc diffusion method as per instructions of Clinical and Laboratory Standards Institute (CLSI) (2009) [32]. Briefly, a 0.5 McFarland suspension of each *S. aureus* strain was streaked onto Mueller Hinton agar plate (HiMedia Labs, Mumbai, India) supplemented with 2% sodium chloride and incubated for 24h at 35 °C. The zone of inhibition was measured and isolates that have zones < 10 mm diameter were considered to be oxacillin resistant and presumptively diagnosed as MRSA.

Molecular techniques: *DNA isolation:* Isolates were overnight subcultured in brain heart infusion broth and pelleted by centrifugation at 5,000 rpm for 15 min, resuspended in 185 µl of TE buffer (20 mM Tris chloride, 2 mM EDTA [PH 8.0]) with 15 µl of recombinant lysostaphin (15 mg/ml; Sigma, St. Louis, Mo.) and incubated at 37°C for 30 min,

then boiled at 95°C for 15 minutes. After cooling to room temperature, the suspension was centrifuged at 10,000 rpm for 5 minutes, and the supernatant was used directly as template for PCR reactions[33].

Detection of *nuc* and *mecA* genes: Multiplex PCR was used for detection of the *nuc* (*S. aureus* species-specific) and *mecA* (methicillin-resistance) genes[34].

Briefly, primers *mecA*-1 (5'-GGGATCATAGCG TCATTATTC-3') and *mecA*-2 (5'-AACGATTGTGAC ACGATAGCC-3') for the gene *mecA* and *nuc*-1 (5'-TCAGCAAATGCATCACAAACAG-3') and *nuc*-2 (5'-CGTAAATGCACTTGCTTCAGG-3') for the gene *nuc* were used in a multiplex PCR reaction on a T100™ Thermal Cycler (BioRad, USA) under the following conditions: an initial 5-min denaturation step at 95°C, followed by 30 cycles of 1 min of denaturation at 95°C, 1 min of annealing at 59°C, and 2 min of extension at 72°C; with a final extension step at 72°C for 10 min. PCR products were analyzed by electrophoresis on ethidiumbromide-stained 2% agarose gels. The sizes of the amplicons were 530bp and 280bp for *mecA* and *nuc* genes, respectively. *S. aureus* ATCC 33592 was used as positive control for *mecA* and *nuc* genes and *S. aureus* ATCC 29213 was used as positive control for only *nuc* gene, while *S. epidermidis* DSM 20044 was used as negative control [34, 35].

Detection of the capsular polysaccharide locus type 5 and 8: For identification of the capsular polysaccharide locus type that define the CP5 and CP8 serotypes, a monoplex PCR was performed with primers specific for the variable segment of the cap locus (*cap5*: 5'-GAAAGTGAACGATTAGTAGAA-3', 5'-GTACG AAGCGTTTTGATAGTT-3'; *cap8*: 5'-GTGGGATTT TTGTAGCTTTT- 3', 5'-CGCCTCGCTATATGAACTAT - 3') as described by Goerke et al., 2005 [36]. The sizes of the amplicons were 532bp and 437bp for *cap5* and *cap8* genes, respectively.

Antimicrobial susceptibility testing

S. aureus susceptibility to penicillin, ampicillin, oxacillin, erythromycin, clindamycin, gentamicin, cefoxitin, amikacin, doxycycline, ciprofloxacin, rifampin and trimethoprim/sulfamethoxazole were determined using the disk diffusion method in accordance with standards recommended by the CLSI [32]. All disks were purchased from HiMedia Laboratories Pvt. Limited, India, and *S. aureus* ATCC 33592 was used as a quality control strain. Multidrug resistance (MDR) phenotype was defined as resistance of *S. aureus* isolates to three or more distinct antimicrobial classes used in this study.

Statistical analysis

The results were tabulated, encoded and statistically analyzed using Statistical Package for Social Sciences (SPSS®) program version 17 (Chicago, IL, USA). Fisher's exact 2-tailed and Pearson's χ^2 tests were used for categorical variables to compare frequencies of *S. aureus* positivity and negativity and MRSA positivity and negativity. Likewise, percentages as of antibiotic resistance profiles of MRSA and MSSA were compared with Pearson's χ^2 or Fisher's exact test as appropriate. A *P* value of less than 0.05 was considered significant.

Results

In this study, 140 HCWs in three main hospitals in Gaza strip were screened for *S. aureus* and MRSA nasal colonization. The demographic characteristics of the participants are recorded in **Table 1**. Participants included 104 males and 36 females (ratio 1:2.9) and the majority (80%) were from surgery and medicine departments. Also, the majority of them (92.8%) have work experience ranged from 1-15 years.

Of the 140 HCWs tested in this study, 59 (42.1%) were positive for *S. aureus* by phenotypic

Table 1. Distribution of the study population by gender, hospital, ward and work experience.

		No. (%)
Gender	Males	104 (74.3)
	Females	36 (25.7)
	Total	140 (100)
Hospital	European	58 (41.4)
	Al-Shefa	37 (26.4)
	Odwan	45 (32.1)
	Total	140 (100)
Ward	Surgery	60 (42.9)
	Medicine	52 (37.1)
	ICUs	28 (20.0)
	Total	140 (100)
Work experience	1-5 years	64 (45.7)
	6-15 years	66 (47.1)
	> 15 years	10 (7.1)
	Total	140 (100)

ICUs: Intensive Care Units.

characteristics and analysis of *nuc* gene (**Table 2, Figure 1**). Screening for MRSA by testing for oxacillin (phenotypically) and analysis of the *mecA* gene by PCR revealed that 32 (54.2%) of the *S. aureus* isolates were MRSA and 27 (45.8%) were MSSA. The overall colonization prevalence was 42.1% for *S. aureus* and 22.9% for MRSA (**Table 2, Figure 1**).

As stated in Table 2, the highest prevalence of *S. aureus* colonization occurred in medicine ward (23 of 59 [44.2%]), followed by surgery ward (25 of 59 [41.7%]). However, in regard to the work experience, the highest prevalence of *S. aureus* colonization was happened in HCWs who had work experience more than 15 years. There were no statistically significant differences in the rates of *S. aureus* carriage between males and females ($P = 0.395$), or among European, Al Shifa and Odwan hospitals ($P = 0.554$, 0.747 , and 0.775 respectively). However, a statistically significant

Table 2. Distribution of *S. aureus* that isolated from HCWs according to gender, hospital, ward and work experience.

		Positive No. (%)	Negative No. (%)	Total No. (%)	P- value
Gender	Males	46 (44.2)	58 (55.8)	104 (100)	0.395
	Females	13 (36.1)	23 (63.9)	36 (100)	
	Total	59 (42.1)	81 (57.9)	140 (100)	
Hospital	European	24 (41.4)	34 (58.6)	58 (100)	0.554
	Al-Shefa	15 (40.5)	22 (59.5)	37 (100)	0.747
	Odwan	20 (44.5)	25 (55.6)	45 (100)	0.775
	Total	59 (42.1)	81 (57.9)	140 (100)	
Ward	Surgery	25 (41.7)	35 (58.3)	60 (100)	0.001*
	Medicine	23 (44.2)	29 (55.8)	52 (100)	0.011*
	ICUs	11 (39.3)	17 (60.7)	28 (100)	0.925
	Total	59 (42.1)	81 (57.9)	140 (100)	
Work experience	1-5 years	18 (28.1)	46 (71.9)	64 (100)	0.644
	6-15 years	33 (50)	33 (50)	66 (100)	0.279
	< 15 years	8 (80)	2 (20)	10 (100)	0.002 [‡]
	Total	59 (42.1)	81 (57.9)	140 (100)	

* Statistical significant difference in prevalence of *S. aureus* among HCWs according to type of ward.[‡] Statistical significant difference in prevalence of *S. aureus* among HCWs according to work experience.

Figure 1. Agarose gel electrophoreses patterns showing PCR-amplified products in multiplex PCR for the detection of *nuc* and *mecA* genes. Lane: M, DNA molecular weight marker (100-bp/1 kb DNA ladder); 1-2, *S. aureus* ATCC 33592 (positive control for *nuc* and *mec* genes, MRSA); 3, *S. aureus* ATCC 29213 (positive control for *nuc* gene, MSSA); 4-5, 8-9, 11-12, 14-16, 18, MRSA (*mec* positive); 6-7, 10, 13, 17, MSSA (*mec* negative). Sizes are indicated in base pairs on the left and right of the figure.

differences were found between departments, where surgery and medicine departments had higher rate than ICUs departments ($P = 0.001$, 0.011), and between years of work experience of participants ($P = 0.002$).

As reported in **Table 3** and according to the type of ward and hospital, the highest prevalence of MRSA colonization occurred in surgery department (20 of 25 [80%]), followed by Al Shifa hospital (9 of 15 [60%]). The prevalence of MRSA colonization was significantly higher in surgery department (80%, $P = 0.003$), while there were no statistically significant differences in the rates of MRSA carriage according to hospital, gender or length of HCWs employment ($P = 0.827$, 0.974 , and 0.58 respectively). Although the HCWs with work experience longer than 15 years had the highest prevalence of *S. aureus* carriage (80%), they had the lowest prevalence of MRSA colonization (37.5%). Finally, HCWs who worked in the surgery department were more likely to harbor MRSA than those who worked in other areas.

All *S. aureus* isolates tested were susceptible to vancomycin and doxycycline. The majority of *S. aureus* isolates were resistant to penicillin (96.6%) and ampicillin (93.2%). Rates of resistance to other antibiotics were 61% to erythromycin and cefoxitin, 59.3% to clindamycin, 30.5% to trimethoprim/sulfamethoxazole (SXT), 27.1 to ciprofloxacin, 20.3% to gentamicin, 15.3% to rifampin, and 10.2% to amikacin [**Figure 2**]. Resistance to multiple classes of antimicrobials was found among both MRSA and MSSA, including β -lactams, macrolides, aminoglycosides, fluoroquinolones, and tetracyclines. Overall, MRSA strains exhibited complete resistance to penicillin, oxacillin and cefoxitin (100%), and nearly complete resistance to ampicillin (96.9%). Meanwhile, high resistance was also observed to erythromycin (75%), clindamycin (75%), SXT (56.2%), ciprofloxacin (43.8%), and moderately to gentamicin (37.5%), rifampin (28.1%) and amikacin (15.6%). MSSA strains also exhibited nearly complete resistance to penicillin (92.6%) and ampicillin (88.9%). Resistance rate to erythromycin,

Table 3. Distribution of MRSA and MSSA that isolated from HCWs according to gender, hospital, ward and work experience.

Ward		MRSA No. (%)	MSSA No. (%)	Total No. (%)	P- value
Gender	Males	25 (54.3)	21 (45.7)	46 (100)	0.974
	Females	7 (53.8)	6 (46.2)	13 (100)	
	Total	32 (54.2)	27 (45.8)	59 (100)	
Hospital	European	12 (50)	12 (50)	24 (100)	0.827
	Al-Shefa	9 (60)	6 (40)	15 (100)	
	Odwan	11 (55)	9 (45)	20 (100)	
	Total	32 (54.2)	27 (45.8)	59 (100)	
Ward	Surgery	20 (80)	5 (20)	25 (100)	0.003*
	Medicine	8 (34.8)	15 (65.2)	23 (100)	
	ICUs	4 (36.4)	7 (63.6)	11 (100)	
	Total	32 (54.2)	27 (45.8)	59 (100)	
Work experience	1-5 years	11 (61.1)	7 (38.9)	18 (100)	0.580
	6-15 years	18 (54.5)	15 (45.5)	33 (100)	
	> 15 years	3 (37.5)	5 (62.5)	8 (100)	
	Total	32 (54.2)	27 (45.8)	59 (100)	

*Statistically significant difference in prevalence of MRSA and MSSA among HCWs according to type of ward

clindamycin, ciprofloxacin and amikacin was 44.4%, 40.7%, 7.4%, and 3.7% respectively. However, none of the MSSA strains (0%) were resistant to oxacillin, gentamicin, SXT, and rifampin along with aforementioned vancomycin and doxycycline. The resistance rates of MRSA isolates to erythromycin, clindamycin, gentamicin, ceftioxin, ciprofloxacin,

rifampin, and SXT were significantly higher than those among MSSA isolates (P value < 0.05) (**Figure 3**).

Multidrug resistance (MDR) among *S. aureus* isolates defined as resistance for β -lactam plus 2 or more antibiotics used in this study. Nearly 61%

Figure 2. Antibiotic resistant pattern of *S. aureus* isolated from health care workers to the common used antibiotics in Gaza hospitals. SXT: Trimethoprim/sulfamethoxazole.

Figure 3. Antibiotic resistant pattern of MRSA and MSSA isolates from health care workers to the common used antibiotics in Gaza hospitals.

*Statistically significant difference in resistance pattern between MRSA and MSSA (P -value < 0.05).

MRSA: Methicillin resistant *S. aureus*; MSSA: Methicillin sensitive *S. aureus*; SXT: Trimethoprim/sulfamethoxazole.

Table 4. Antibigram resistance typing of the 32 MRSA isolates.

Resistance pattern*	Resistance type	No. of isolates (%)
Amp	I	5 (15.6)
Amp, Cip	II	2 (6.25)
Amp, R	III	1 (3.12)
Amp, Ery, Cli, Cip	IV	7 (21.88)
Amp, Ery, Cli, Cip, SXT	V	7 (21.88)
Amp, Ery, Cli, Gent, R, STX	VI	6 (18.75)
Amp, Ery, Cli, Gent, Ak, STX	VII	4 (12.5)

*Amp, Ampicillin; Cip, Ciprofloxacin; R, Rifampin; Ery, Erythromycin; Cli, Clindamycin; SXT, Trimethoprim/sulfamethoxazole; Gent, Gentamicin; Ak, Amikacin.

of isolates were noted to be MDR. Among MRSA isolates there were 24 out of 32 (75%) MDR, while in MSSA there were 12 out of 27 (44.44%) MDR. There was higher rate of MDR-MRSA in comparison to the MDR-MSSA. Seven different groups of antibiotypes were identified. Four of them were multiple resistant antibiotypes (resistant to 3 or more antimicrobial agents) and accounted for 75% of all *S. aureus* isolates (**Table 4**).

All *S. aureus* isolates were classified as containing either *cap5* (33 isolates [55.9%]) or *cap8* (26 isolates [44.1%]). There was higher rate of *cap5* among MRSA and MSSA than *cap8* (28.8% and 27.1% vs. 25.4% and 18.6% respectively) (**Table 5**).

Discussion

The main route of transmission of *S. aureus* and MRSA in the hospital setting is considered to be from patient to patient via the contaminated hands of HCWs. They have been implicated as the source of infection in a number of published outbreak reports around the world [37]. Data regarding *S. aureus* and MRSA in Palestine are very scant. Previous reports

Table 5. Capsule polymorphism (capsular types 5 and 8) of MRSA and MSSA HCWs isolates

Bacteria	cap5 (%)	cap8 (%)
MRSA	17 (28.8)	15 (25.4)
MSSA	16 (27.1)	11 (18.6)
<i>S. aureus</i>	33 (55.9)	26 (44.1)

have mostly focused on Northern Palestine [28] and the West Bank [16], with absence or relatively little details regarding epidemiology of *S. aureus* in HCWs. Recently, a community-based nasal carriage among healthy children and hospital-based studies addressed the epidemiology of *S. aureus* and MRSA in Gaza Strip for the first time[29,30]. In this study, we described the nasal colonization rate of *S. aureus* and MRSA among a convenience sample of HCWs in three Gaza hospitals. To the best of our knowledge, this is the first report describing the prevalence of *S. aureus* colonization and their resistance profiles among HCWs in the Gaza Strip.

The overall nasal carriage *S. aureus* prevalence in this study was 42.1%. Of these, 54.2% were MRSA (22.9% among the study population). Estimates of HCWs colonization rates from the worldwide literature vary widely depending on the country, hospital specialty and setting (endemic, non-endemic or outbreak) [37]. Our findings in the present study is comparable to the findings of other studies of *S. aureus* colonization rates among HCWs in developing countries as in Iran (31%)[20]Libya (39%) [22], Pakistan (48%) [23], India (50%) [24] or in developed countries as in Germany (33.8%) [21] and USA (30%, 43.8%) [12,19]. However, the nasal carriage rate in this study was higher than those found in other studies that conducted in Arabic countries and other developing countries as seen in a recent publications from Libya (12.4%) [38], India (17.5%) [39], West Bank of Palestine (20.8%) [16] and Kuwait (21%) [14]. Yet, other recent studies from Saudi Arabia (76%) [10], Taiwan (67.2%) [26]

and Senegal (56.1%) [25] showed nasal colonization among HCWs higher than our findings. A plausible explanation for the differences in the colonization rates of *S. aureus* and MRSA between different countries and even some time in the same country may be due in part to differences in sample size or frequency of sampling and using different conventional and/or molecular methods among others.

In our study, there was no differences in the frequency of *S. aureus* between males and females HCWs or according to the type of hospital. Nevertheless, gender was found as a significant factor for *S. aureus* nasal colonization among HCWs in two studies in USA and Kenya where both studies indicated that males had higher rate of colonization [40]. On the other hand, there was significant higher rates of *S. aureus* colonization in surgery and medicine wards (Table 2) in comparison to ICUs departments. These results show those of Shibabaw et al., [18] who found that the highest rate of *S. aureus* carriers (35.7%) and MRSA carriers (57.1%) were among HCWs in pediatrics and surgery wards, respectively. A reason for this could be due to the higher exposure of HCWs in these departments to high numbers of patients and the crowd of these departments.

Our study revealed a high rate of MRSA nasal carriage among HCWs in this cohort (45.2% out of *S. aureus*; 22.9% of all HCWs). To our knowledge, this is the highest rate of MRSA colonization reported in HCWs in Palestine. Kaibni et al., from West Bank, Palestine identified 13.9% MRSA in 72 HCWs working in internal medicine department at Ramallah Governmental hospital [16]. All other reports of MRSA prevalence in Palestine have involved nasal carriage among healthy personnel who have not contact with hospital environment or hospital-based studies [16,28-30,41], although notably, 45% of the *S. aureus* isolates from the Gaza carriage study were methicillin-resistant [30]. Other studies from Arabic countries and worldwide

showed lower prevalence of MRSA among HCWs as in Jordan (10.1%) [13], in USA (12%, 15.2%) [12,19], in Iran (17.2%) [20] and in Libya (36.8%) [22]. Interestingly, a higher prevalence (73%) of MRSA than our findings was detected among HCWs in a recent study conducted in Saudi Arabia [10]. Therefore, the MRSA frequencies described in this report may be considered among the highest described in the region thus far. An important findings of our study is the highest occurrence of MRSA among HCWs in surgery departments (80%, $P= 0.003$). This finding could be due to increased physical contact of surgeons and nurses with patients and over-crowding in surgery departments at our hospitals. Nasal carriage of *S. aureus* and MRSA in HCWs can reflect carriage of their 'own' isolate versus a transiently acquired isolate from patients. Accordingly, the MRSA prevalence rate detected here among HCWs could reflect a high MRSA rate in hospitalized patients, as was recently investigated in Gaza [29] but also a high MRSA carriage rate in the community as was shown in a recent community-based nasal carriage study in Gaza [30]. Both studies showed a predominant lineage of *S. aureus*, with *spa* type t223, ST22-MRSA-IVa. Likewise, molecular typing of *S. aureus* isolated from HCWs in Portugal revealed that 88.6% of these isolates belong to the same clone (ST22-MRSA-IV) [42]. We think that same clone is present among our HCWs isolates, however, this needs to be approved by molecular epidemiology typing methods such as PFGE, *spa*, *SCCmec* and MLST.

In our present study, the antibiogram pattern of all *S. aureus* isolates showed resistance to most of the antibiotics tested, mainly penicillin, ampicillin, erythromycin and clindamycin. Almost all MRSA and MSSA were resistant to penicillin and ampicillin. This pattern of resistance was shown in previous studies from Gaza Strip and West Bank [16,28,29] and also mirrored others elsewhere [5,13,18,20,22-24]. High resistance to tested antibiotics could be mainly due to the excessive use, misuse, and great prescription

of these medication in Gaza for both hospital and community acquired infections and also in agriculture and animal feeding. Moreover, the lack of an antibiotic policy and the availability of antibiotics sold without a medical doctor prescription in Palestine worsen the case. In view of the high resistance rates of *S. aureus* to these aforementioned antibiotics, treatment of *S. aureus* infections at our hospitals with these antibiotics may not be effective. On the other hand, all *S. aureus* isolates including both MRSA and MSSA, were susceptible to vancomycin and doxycycline, and mostly to amikacin and rifampin (89.8%, 84.7% respectively). This could be due to the limited prescription and use of these antibiotics in Gaza Strip. So, the full sensitivity to vancomycin and doxycycline can work perfectly against *S. aureus* infections in our community and hospitals as indicated in recent studies in Gaza [29,30].

The trimethoprim-sulfamethoxazole showed moderate activity against *S. aureus* isolates in general (69.5%), but surprisingly, with 100% and 43.8% activity against MSSA and MRSA respectively (**Fig. 2, 3**). This picture contradict several studies reporting low rates of resistance to SXT against *S. aureus* isolated from HCWs with percentage of 1.9%, 4.7% and 21.4% [43], but in accordance with a hospital-based study in Gaza [29] and other study in China that revealed 93% resistance to SXT of HCWs nasal *S. aureus* isolates [43]. The MRSA isolates recovered in this study were resistant to quit high number of tested antimicrobial agents, and were found to be multidrug resistant (75%) (**Fig. 3, Table 4**). They were significantly have higher resistance to erythromycin, clindamycin, gentamycin, amikacin, ciprofloxacin, rifampin and SXT than MSSA (**Fig. 3**). This finding contradict the results of a recent study from Jordan that showed MRSA isolates were susceptible to a broad range of tested

antibiotics, and none were MDR [13]. Meanwhile, Kaibni et al., showed also less resistant to non- β -lactam antimicrobial agents but with 14.7% being MDR [16]. This percentage of MDR *S. aureus* nasal isolates is lower than our findings (75%), yet, a study from Serbia showed 83.9% MDR *S. aureus* nasal carriage isolates from HCWs [5].

On regard to the capsular polymorphism, Table 5 showed that all *S. aureus* isolates in this study encoded *cap5* or *cap8* gene. Many previous studies reported the majority of human *S. aureus* strains (70–80%) possess either *cap5* and/or *cap8* [44]. Nevertheless, a study from USA revealed that all pediatric isolates contained either *cap5* or *cap8* genes [45], while a recent study from Australia shows absence of *cap8* and *cap5* (non-typable strains) in 19.4% of their isolates [44]. Capsular polysaccharide plays an important role in the pathogenicity and immunogenicity of *S. aureus*, notably as anti-phagocytic factor but also as a vaccine target. However, loss of capsule expression, may lead to *S. aureus* persistence in a chronically infected host as shown in chronic osteomyelitis patients [46].

Our study has several limitations. First, we may have over or under estimated the prevalence of *S. aureus* and MRSA nasal carriage in HCWs because this was a simple point prevalence study, using a convenience sample of subjects. Also, only nasal swabs were collected and assessed, and other body sites such as throat, axilla and rectum that could be colonized were not collected. Second, we did not use an enrichment step and just directly inoculated the swabs on culture media. So, this may underestimate the prevalence of *S. aureus* and MRSA among the study subjects. Likewise, molecular typing was not performed in this study, such that the clonality of the MRSA and MSSA strains cannot be assessed. Lastly, we were not able to determine whether the *S. aureus* and MRSA colonization state is transient,

short-term, or persistent because we only screened the participants once and only one swab was collected.

Nevertheless, several themes of potential concern are raised by our findings. Most noteworthy is the high prevalence of MRSA, particularly among surgery departments. Also, the high resistance profile of MRSA against most common used antibiotics in our hospitals, and the high percentage of MDR-MRSA strains. Further studies should address the molecular characterization and virulence factors of *S. aureus* isolated from HCWs in Gaza.

In conclusion, this study demonstrates high rate of MDR isolates of MRSA. These results highlight the critical need for screening and tracking MRSA among HCWs as well as patients and to monitor and manage the usage of antibiotics in the hospitals and community.

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Conflict of interest

The author declares that there is no conflict of interests to declare.

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