Antibiotic resistance and *mec*A gene characterization of *Staphylococcus epidermidis* isolated from some hospitals in Gaza strip

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Abstract

Antibiotic resistance of *S. epidermidis* isolated from biological specimens is a global problem to public health. In this study a total of 256 *S. epidermidis* isolates (128 clinical isolates and 128 nasal isolates) from Gaza strip, Palestine were investigated. All isolates were tested for its antimicrobial susceptibilities and carriage of the *mec*A gene. Out of the 256 isolates, 184 (71.9%) were resistant to multiple antibiotics with all displaying increased susceptibility toward rifampicin (100%), doxycycline (98.4%) and vancomycin (98%). Ninety-six isolates (37.5%) were multidrug resistant (MDR) while, 99 isolates (38.7%) were *mec*A positive. A significant difference was demonstrated between clinical and nasal isolates. Clinical isolates were significantly more resistant for 8/12 tested antibiotics including resistance to cefoxitin (30μg) (p=0.000) and significantly (p=0.000) represents the MDR isolates while nasal isolates were significantly (p=0.000) sensitive for all tested antibiotics. No significant difference between the two groups in carrying *mec*A. We find that clinical isolates gain an extra-feature that qualify it to cause a disease and methicillin resistance (MR) was not *mec*A dependent in all MR isolates.

Keywords: *Staphylococcus epidermidis*, Antibiotic resistance, Multidrug resistance, Methicillin resistance, *mec*A gene.

1. Introduction

S. epidermidis belongs to the coagulase-negative staphylococci (CoNS) is a permanent member of the normal human microbiota, commonly found on skin and mucous membranes [1, 2].

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Abundant colonization of human skin and mucus membranes by *S. epidermidis* gives it the opportunity to cause infections under special circumstances **[3]**. Hence it has appeared as an important opportunistic human pathogen, reflecting the increased infection among indwelling medical devices and an increasing number of immunocompromised patients **[3, 4]**.

Increased antibiotic-resistant among Staphylococci are a universal problem **[2]**. CoNS strains also constitute a therapeutic challenge due to their increasing frequency of the acquisition of the resistance to commonly used drugs **[5]**. This deteriorating situation is further aggravated by the phenomenon of multiresistance **[6]**.

Antibiotic resisting *S. epidermidis* strains is an opportunistic pathogen commonly isolated from patients and healthy individuals **[2]**.

Several investigations have found the antibiotic resistance rates for *S. epidermidis* to be higher than 90% of all samples tested **[7]** and its frequency of MR reaches up to 80% globally with a few exceptions as in Iceland and Denmark having a lower frequency of about 30% - 40% **[8]** where its strains receive resistance determinants through gene acquisition and genetic recombination **[2]**.

A wide variety of resistance genes contributes to the antimicrobial resistance among staphylococci. *mec*A gene encoding for a penicillin-binding protein (PBP), PBP-2a, contributes to its ability to resist methicillin, which is the most important **[9]**. Penicillin-binding protein catalyze the formation of peptide cross bridges in the bacterial cell wall. PBP1-4 are targeted by β-lactams. PBP2a, which is responsible for the MR phenotype and is a transpeptidase with a reduced affinity for transpeptidase-inhibiting β-lactams, allowing bacteria to continue cell wall synthesis and multiplication in the presence of β-lactams **[10]**.

This study aims to investigate the antibiotic resistance, MR and the occurrence of *mec*A gene among *S. epidermidis* isolated from clinical samples and compare it with commensal isolates from healthy individuals.

2. Material and methods

2.1. Sample collection

A total of 860 clinical isolates were collected from various biological sample cultures (284, 440, 106, 14 and 6 isolates from blood, pus, urine, sputum and cerebrospinal fluid, respectively). Samples were collected from five hospitals in Gaza strip, namely, Al Shifa Hospital, Alnassr Pediatric Hospital, European Gaza Hospital, Nasser Medical Complex and Al Aqsa Martyrs Hospital. Blood culture isolates related to blood stream infections were accepted following the Center of Disease Control **[11]**.

Another 216 isolates were collected from healthy appeared volunteers have no relation to the healthcare field by swabbing the right nose nares using a sterile cotton swab **[12, 13, 14]**. Volunteers were chosen to be from different areas along Gaza strip.

2.2. Identification of *Staphylococcus epidermidis*

2.2.1. Conventional identification

Swabbed bacteria were cultured on an enriched and selective media called Brain Heart Infusion broth (Himedia Laboratories – M210I) supplemented with 5% blood and 7.5% Nacl.

The 1076 isolates were subcultured on blood agar (Himedia Laboratories) supplemented by 5% blood and incubated aerobically at 37°C for 18-24 hrs. and one isolated colony were selected and re-subcultured on 5% blood agar for subsequent procedures.

Gram stain were used to ensure the morphology, reaction and purity of the cultures. Catalase test and coagulase test were used to exclude non-staphylococcus and coagulase positive staphylococcus bacteria, respectively. DNase test and Mannitol fermentation test were used to exclude as possible isolates rather than *S. epidermidis*. All tests were done according to **[15, 16]**.

2.2.2. Molecular identification

DNA was extracted by using alkaline lysis method. Briefly, 2-3 colonies from freshly cultured bacterium on 5% blood agar were suspended in 30µl of lysis buffer (0.25% sodium dodecyl sulfate, 0.05 N NaOH) and heated at 95°C for 15 mins. using thermocycler then 170µl of nuclease free water were added to the lysate. Lysate were centrifuged at 16,000 g for 5mins. and supernatants were transferred to a new sterile 0.2ml eppindrofes and frozen at -20°C until further uses **[17]**.

S. epidermidis suspected isolates were confirmed by PCR using *S. epidermidis* species specific primers (*Sep*F: 5'-ATCAAAAAGTTGGCGAACCTTTTCA-3' & *Sep*R: 5'-CAAAAGAGCGTGGAGAAAAGTATCA-3') **[18]**.

PCR amplifications were carried out in a final volume of 15□l contains 5□l of staphylococcal DNA previously extracted and stored, a final concentration 0.4 □mol from each primer (*Sep*F & *Sep*R), 7□□l master mix (2x MyTac^{TM} Red Mix, Bioline, U.K.) and 2□□l nuclease free water (hy.labs). In each reaction *S. epidermidis* ATCC 12228 and *S. aureus* ATCC 5638 strains were used as a positive and negative controls, respectively, and a tube contains all except DNA were used as a blank.

PCR was performed under the following conditions: 1 min at 95°C, then 35 cycles of 15 sec at 95°C, 30 sec at 56°C, 10 sec at 72°C and a final hold of 5 min at 72°C with a (Biometra

T professional gradient Thermocycler). PCR products were resolved by electrophoresis in a 2% agarose gel (Agarose Molecular Grade, Bioline, U.K.) at 70V for 45min, prepared in 1×TBE buffer pH 8 and stained with 3□150% ethidium bromide/100ml gel (Sigma, U.K.). The sizes of the amplification products (124 bp) were estimated by comparison with a 50-bp molecular size ladder (iNTRON-SiZer^{TM}DNA Markers).

2.3. Antibiogram

Antibiotic sensitivity test was performed according to Kirby-Bauer method, Clinical Laboratory Standards Institute (2014) guidelines using Muller Hinton Agar. Cefoxitin (Fox; 30μg), vancomycin (VA; 30μg), erythromycin (E; 15μg), gentamicin (GN; 10μg), tetracycline (TE; 30μg), clindamycin (CD; 2μg), fusidic acid (FC; 10μg), doxycycline (DOX; 30μg), ciprofloxacin (CIP; 5μg), norfloxacin (NOR; 10μg), trimethoprim (TM; 2.5μg) and rifampicin (RD; 30μg) were used. Antibiotic disks were obtained from Liofilchem, Italy. A $1×10^8$ CFU/ml of bacterial suspension were spread on the plates; six disks were tested per each plate. Plates then were incubated at 37°C for 24hrs and zones of inhibitions were recorded in millimeters using metal ruler [16].

2.4. *mec*A gene detection

PCR using (*mec*AF: 5´-TGGTATGTGGAAGTTAGATTGG-3´ & *mec*AR: 5´-AACGATTGTGACACGATAGC-3´) primers [19] was performed to detect the presence of *mec*A gene in a final volume of 25□l contains 5□l of staphylococcal DNA previously extracted, final concentration 0.4 □mol from each primer (forward & reverse), □□□□l master mix (2x MyTac^{TM} Red Mix, Bioline, U.K.) and □□□l nuclease free water (hy.labs). PCR performed under the following conditions: 5 min at 94°C, then 40 cycles of 45 sec at 94°C, 45 sec at 53°C, 45 sec at 72°C and a final hold of 5 min at 72°C with a (Biometra T professional gradient Thermocycler).

In each reaction *mec*A positive *S. aureus* ATCC33591, *mec*A negative *S. epidermidis* ATCC12228 and a tube contains all except DNA were used as a positive control, negative control and blank, respectively.

The PCR products were resolved by electrophoresis in a 2% agarose gel (Agarose Molecular Grade, Bioline, U.K.) at 70V for 45min, prepared in 1×TBE buffer pH 8 and stained with 3□l 50% ethidium bromide/100ml gel (Sigma, U.K.). A (547bp) band indicate the presence of the gene.

3. Statistical analysis

The results were tabulated and analyzed using version20 of the Statistical Package for the Social Sciences (SPSS). Frequencies, cross tabulation and appropriate statistical tests as Chi-square test and Z test were performed. A P-value of less than 0.05 was considered significant.

4. Results

4.1. *Staphylococcus epidermidis* identification

As described in the materials and methods, phenotypically and biochemically, 366 isolates out of the 1076 collected isolates were suspected to be *S. epidermidis* Table (1). All suspected isolates were confirmed by PCR and 256 isolates found to be *S. epidermidis* (128 clinical isolates and 128 nasal isolates) Figure (1). Clinical isolates were from various clinical samples (73, 45, 8 and 2 isolates from blood, pus, urine and cerebrospinal fluid, respectively), and nasal isolates were from different locations (32, 32, 33 and 31 isolates from Gaza City, Khan Younis down town, Khan Younis eastern areas and Rafah city).

Table (1): Phenotypic and biochemical characterization.

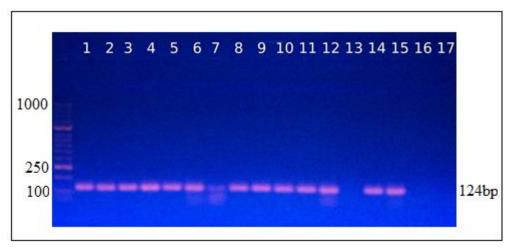|	Clinical isolates	Nasal isolates
Collected isolates	860	216
Gram positive cocci	860	216
Catalase positive	687	216
Coagulase negative		
DNase negative	196	186
Non mannitol fermenter		
Died or lost	16	0
Suspected *S. epidermidis*	180	186

Figure (1): PCR amplification with *S. epidermidis* specific primers. *S. epidermidis* ATCC12228 & *S. aureus* ATCC6538 were used as positive and negative controls, respectively. Lane1, 16, 17, positive control, negative control & blank, respectively. Lane 2-12 & 14 & 15, positive isolates (*S. epidermidis*). Lane 13 negative isolate (not-*S. epidermidis*).

4.2. Antibiogram

Antibiotic sensitivity test performed using Kirby-Bauer agar disk diffusion on Muller Hinton Agar method according to CLSI 2014 guidelines, Figure (2).
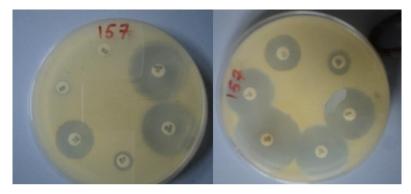

Figure (2): Kirby-Bauer agar disk diffusion test on Muller Hinton Agar.

From the 256 tested isolates 231 (90.2%) shows resistance against at least one antibiotic and 25 (9.8%) were susceptible for all tested antibiotics and 49 were resistant for just single antibiotics, Figure (3).

All *S. epidermidis* isolates (100%) were susceptible for rifampicin. However, resistance was low, but with variable degrees, to doxycycline, vancomycin, tetracycline, clindamycin and gentamicin (1.6%, 2%, 12.5%, 14.5%, and 16.8% respectively, Table (2).

Different resistance patterns seen, where 29 (12.5%) shows resistance against 6 up to the 11 tested antibiotics and 111 (48.1%) were resistant to 3 or more antibiotics and 91 (39.4%) were resistant to two or less antibiotics. Also, 96 (41.5%) of the 231 resisting isolates exhibit resistance against at least one antibiotic from three different categories and were recorded as multidrug resistant (MDR), Figure (3).

A significant difference between the clinical and the nasal isolates shown in the response to 8/12 (66.7%) antibiotics (p<0.05). When compared with nasal isolates, clinical isolates express significantly higher resistance against Fox, E, GN, TE, FC, CIP, NOR & TM, Tables (2) and (3).

As shown in the Figure (3) aggressiveness increased significantly among clinical isolates, where out of the 96 MDR isolates 72 (75%) belongs to the clinical isolates (p=0.000) and out of the 25 isolates shows no resistance to any of the antibiotics, 22 (88%) belongs to the nasal isolates (p=0.000), where 33 (67.3%) out of the 49 isolates resisting a single antibiotics also belongs to the nasal isolates (p= 0.008), Figure (3)

Clinical isolates were significantly higher in resisting ≥6 antibiotics (p=0.000) and ≥3 antibiotics (p=0.004), while nasal isolates were significantly higher in resisting <3 antibiotics (p=0.000).

Table (2): Bacterial resistance against different antibiotic discs.

Antibiotic	256 isolates	CI (%)	NI (%)	*p* value
VA	5(2.0%)	4 (3.1)	1(0.80)	**0.370**
E	126(49.2%)	81(63.3)	45(35.1)	**0.000***
GN	43(16.8%)	34(26.6)	9(7.0)	**0.000***
TE	32(12.5%)	16(12.5)	16(12.5)	**0.007***
CD	37(14.5%)	23(18.0)	14(10.9)	**0.090**
FC	171(66.8%)	99 (77.3)	72 (56.2)	**0.000***
DOX	4(1.6%)	4(3.1)	0(0.00)	**0.055**
CIP	54(21.1%)	36(28.1)	18(14.1)	**0.003***
NOR	62(24.2%)	44(34.4)	18(14.1)	**0.001***
TM	92(35.9%)	67(52.4)	25(19.5)	**0.000***
RD	0(0.0%)	0(0.0%)	0(0.0%)	**1.000**

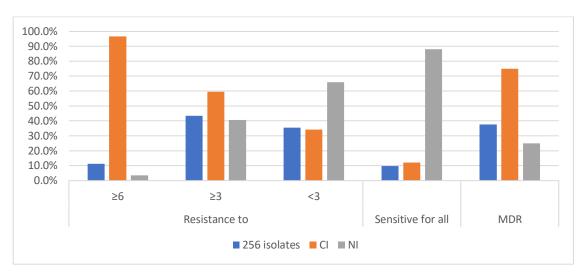**CI: Clinical isolates; NI: Nasal Isolates; *: Significance, *P*<0.05.**

Figure (3): Antibiotic resistance pattern and MDR among isolates. CI: clinical isolates; NI: nasal isolates.

4.3. Cefoxitin resistance and *mec*A gene distribution

Cefoxitin was resisted by 132 (51.6%) isolates, and significantly resisted by clinical isolates (p=0.000), Table (3).

However, using PCR targeting the *mec*A gene in *S. epidermidis* isolates, Figure (5), 99 (38.7%) isolates found to carry the gene with no significant difference between clinical and nasal isolates, Table (3).
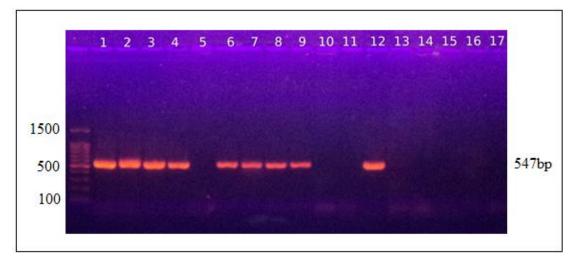

Figure (4): PCR amplification of *mec*A gene in *S. epidermidis* isolates. *S. aureus* ATCC33591 and *S. epidermidis* ATCC12228 were used as a positive and negative controls, respectively. 100bp DNA ladder was used. Product of 547bp indicates the presence of *mec*A gene. Lanes 1, 16 & 17; positive control, negative control & blank, respectively. Lanes 2-4, 6-9 & 12 *mec*A positive isolates. Lanes 5, 10, 11 & 13-15 *mec*A negative isolates.

Out of the 256 isolates, 17.6% and 34% of the isolates found to resist methicillin in the presence and absence of *mec*A gene respectively, while 21.1% and 27.3% were methicillin sensitive (MS) in the presence and absence of *mec*A gene respectively, Table (3). For methicillin resistance significance were recorded in the side of clinical isolates in both resistance patterns and vice versa for nasal isolates, Table (3).

Table (3): Cefoxitin resistance, *mec*A gene distribution and Relatedness between *mecA* gene and MR among isolates.

	256 isolates	**CI (%)**	**NI (%)**	***p* value**
Cefoxitin resistant	132(51.6%)	89(69.5)	43(33.6)	**0.000***
***mec*A +ve**	99(38.7)	48(37.5)	51(39.8)	**0.700**
***mec*A$^+$MR**	45(17.6)	28(62.2)	17(37.8)	**0.035***
***mec*A$^+$MS**	54(21.1)	20(37)	34(63)	**0.015***
***mec*A$^-$MS**	70(27.3)	19(27.1)	51(72.9)	**0.000***
***mec*A$^-$MR**	87(34)	61(70.1)	26(29.9)	**0.000***

5. Discussion

Antibiogram of the 256 isolates (128 clinical isolates and 128 nasal isolates) were tested for 12 antibiotics, including the cefoxitin as an indicator of the isolates' methicillin resistance and as a primary indication for the presence or absence of the *mec*A gene responsible for its resistance to methicillin [9].

Two hundred and thirty-one of the 256 (90.2%) isolates exhibit resistance against at least one antibiotic with different patterns, where from the 231 isolates exhibiting resistance, 12.5%, 48.1% and 39.4% shows resistance against ≥6, ≥3 and <3 antibiotics, respectively. Out of the 256 isolates, 96 (37.5%) shows resistance to at least one antibiotic from three or more antibiotic categories and considered as MDR isolates while 25 (9.8%) were sensitive for all antibiotics.

None of the isolates showed any resistance against rifampicin, followed by the doxycycline (1.6% resistance) and vancomycin (2% resistance) and moderate resistance was recorded against cefoxitin representing the ability of 51.6% of the isolates to be MR followed by the fusidic acid and a moderate resistance seen against the other 7 antibiotics.

By returning to the field, rifampicin is rarely used in Gaza strip, and doxycycline is moderately or less prescribed and are effective, while vancomycin is one of those that are restricted for hospital use. Tetracycline, and gentamicin also are under restriction, tetracycline

because of its side effects and gentamicin is available only as injection and is restricted for hospital use. Clindamycin, ciprofloxacin, trimethoprim and norfloxacin shows a highly acceptable effectivity. Clindamycin and ciprofloxacin mainly used in Gaza strip because of their acceptable price and high effectivity, until now. Trimethoprim and norfloxacin are rarely used now a day. Also, it was found that there was an abuse of the cefoxitin, erythromycin and fucidic acid. First, Cefoxitin was used at a wide range because of its effectivity, erythromycin because of its low price and fucidic acid was the recommended ointment mostly for all skin infections, and now cefoxitin and erythromycin known to be ineffective against many cases. These data explain the variance in the results of the antibiogram among different antibiotics (Data collected by the researcher).

These results were drastically changed when the 256 isolates subdivided according to the source of isolation into clinical and nasal (commensal) isolates and a significant change become clear in the frequencies of antibiotic resistance, resistance patterns and MDR. These results come in consistency with what was mentioned previously in regard to the used antibiotics in Gaza strip and reflecting a selection pressure for hospital related clones.

To some extent, the results of this study in response to the general terms is compatible with other studies, also some differences are seen, between the present results and the literatures.

In Jordan, study the antibiogram of 24 CoNS nasal isolates for 13 different antibiotics were studied and 75% of the isolates are MR-CoNS and MDR phenotype exceeds 77% of the isolates with different resistance [20].

In China, the antibiogram of 223 and 106 *S. epidermidis* isolated from various clinical samples and from the urethral orifices of healthy volunteers against 11antibiotics was investigated. The resistance rates of clinical isolates were significantly higher than those among colonized isolates to all except linezolid where there was no significant difference (p=0.684) and vancomycin where all the 329 isolates were susceptible [21].

In a study where responses of 183 and 75 *S. epidermidis* isolated from prosthetic joint infections and nasal swabs, respectively were investigated a significant difference in all responses of the two groups against tested antibiotics except this against mupirocin was seen. MR and MDR among the clinical isolates were significantly higher than the nasal isolates [22].

In another investigation includes 64 *S. epidermidis* clinical isolates, isolates were grouped according to the resistant patterns, were 3 isolates (4.7%) were resistance to six antibiotics, 33 (51.6%) $\geq$ 3 antibiotics, 27 (42.2%) to < 3 antibiotic, and 1 (1.7%) was

susceptible to all the antibiotics. The present results agreed with two out of the four patterns of the present study [23].

In general, a divergence seen between these studies and became clearer with the present results. It was illustrated that the patterns of correlation between countries' resistance rates suggest predominantly independent profiles. And antibiotic resistance patterns largely correlated with volume of usage, affordability, endogenous factors such as strictness of practices for prescribing drugs [24].

Also, it was mentioned that the presence of large diversity in resistance patterns within and between sites and countries indicates the presence of more than one clone of the same organism. An antibiotic with no or reduced resistance is a relatively newly used antibiotic with a broad-spectrum activity against multidrug-resistant pathogens [25].

In 2019, it was stated that for different antibiotics, bacterial isolates have a different resistance pattern as well as variable resistance patterns from sample to sample are seen. And the majority of the bacterial isolates are resistant to the commonly used antibiotics in each country [26].

In addition to what was mentioned, Gaza strip nearly is a semi-isolated area, it is not surprising that its antibiotic resistance pattern shows its own domestic characters. Moreover, it is expected to be changed if it opens more to the world where it can import antibiotic resistance and the problem becomes worse.

MR was investigated phenotypically and genotypically by using cefoxitin discs and detecting the presence of *mec*A gene by PCR, respectively. Among the 256 tested isolates 132 (51.6%) were phenotypically cefoxitin resistant and MR was significantly higher among clinical isolates (p=0.000) where MR was recorded in 69.5% and 33.6% of the clinical and nasal isolates, respectively. That also related to the way of antibiotic using in Gaza strip and the difference in the clones inside the hospitals and in the community.

All isolates were investigated for the presence of the *mec*A gene, regardless of its response against the cefoxitin disc. The gene were investigated in 99/256 (38.7%) of the isolates, where not all who harbor the gene were resistant to cefoxitin, and vice versa. There was no significant difference in the *mec*A gene frequencies between clinical (37.5%) and nasal (39.8%) isolates (p=0.7).

Four patterns were observed in methicillin resistance and presence/absence of the *mec*A gene, namely, *mec*A$^+$ MR, *mec*A$^+$ MS, *mec*A$^-$ MS and *mec*A$^-$ MR. Among the 256 isolates, the patterns were investigated in 17.6%, 21.1%, 27.3%, 34% of the isolates, respectively. The four

patterns were observed among both, clinical and nasal isolates and significant difference was seen in three of the patterns. *mec*A⁻ MR was significantly higher among clinical isolates (p=0.000), while *mec*A⁺ MS (p=0.028) and *mec*A⁻ MS (p=0.000) were significantly higher in nasal isolates, reflecting the clinical isolates' ability to resist methicillin by mechanisms rather than the *mec*A gene as hyper production of β-lactamase or the presence of *mec*B gene that enable the isolates to resist methicillin, while nasal isolates are MR despite of the presence of *mec*A and in general are more susceptible for methicillin. These results show more aggressivity of clinical isolates and reflect the deference between clones recovered from the hospitals and those from the community, beside an evidence of pressure selection in the healthcare centers that increase the frequency of *mec*A⁻ MR.

In response to the prevalence of the *mec*A gene among the isolates, the present results were agreed with some published results, while other studies display lower results.

When investigating the prevalence of *mec*A gene by PCR among clinical isolates of *S. epidermidis*, *mec*A gene was found to be harbored by 45.6% of the tested isolates **[27]**.

In a study conducted in India where 728 *Staphylococcus* isolates isolated from various sources were investigated for *mec*A gene, and 66 (9%) isolates were positive and *S. epidermidis* (28/66 isolates, 42.4%) was the most predominant species **[28]**.

Also, *mec*A gene among *S. aureus* isolated from nasal swabs collected from high school students was investigated and out of the 60 tested isolates 32 (54.4%) were *mec*A positive strains **[29]**.

A similar study was conducted in Gaza strip, Palestine, on 62 *S. aureus* isolates recovered from nasal swabs from healthcare workers in Al Shifa Hospital where 64.5% of the isolates found to harbor the *mec*A gene **[17]**.

Several studies investigate the occurrence of *mec*A gene among *Staphylococcus* species and the relatedness between its presence and the methicillin resistance and the phenomena of *mec*A positive strains which is MS and the opposite one was mentioned by several investigators.

Several researchers highlight the presence of some differences between the results of the phenotypic and genotypic *mec*A investigating methods.

In 2018, a study carried in Tunisia, where MR was investigated phenotypically by cefoxitin disc and genotypically by investigating the presence of *mec*A gene among 68 CoNS isolates from milk collected from cows with clinical mastitis. Out of the 68 isolates 20 (29.4%) were MR strains phenotypically, and only 14 (70%) out of the 20 harbors the *mecA* gene

(*mec*A$^+$ MR) and the reminder 6 (30%) cefoxitin resisting isolates were non *mec*A or *mec*C genes harbors (*mec*A$^-$ MR) **[30]**.

Also, MR among *S. aureus* isolated from nasal swabs collected from high school students was investigated using oxacillin and cefoxitin and *via* detecting the presence of *mec*A gene. Out of the 60 tested isolates 32 (54.4%) were *mec*A positive strains while just 7 (11.7%) and 11 (18.3%) were oxacillin and cefoxitin resistance, respectively (*mec*A$^+$ MR), what indicates the presence of cefoxitin sensitive strains regardless of the presence of the *mec*A gene (*mec*A$^+$ MS) **[31]**.

A similar study was conducted in Gaza strip, Palestine, on 62 *S. aureus* isolates recovered from nasal swabs from healthcare workers in Al Shifa Hospital where 82.3% and 64.5% were oxacillin resistant and *mec*A positive, respectively, reflecting the presence of the different phenomena regarding to the methicillin resistance/sensitive pattern **[19]**.

In a phenotypically investigation for MR *S. aureus* which completely absence of the five major SCCmec types, *mec*A gene as well as any production of PBP2a, what was explained as a probability of hyper production of β-lactamase **[31]**.

In another study, *mec*A and *mec*C genes was not detected in the 179 *S. aureus* isolates isolated from clinical samples in Turkey and were detected as MR by phenotypic method using cefoxitin. Cikman give the reason back to, the PCR method used in this study which may be not accurate enough to detect the presence of the *mec*A and *mec*C genes or the presence of a different *mec* gene, specifically mentioned as *mec*B **[32]**.

In Iran, investigation of the methicillin resistance among 146 *S. epidermidis* isolates isolated from clinical samples, and record both phenomena, MR *mec*A negative and MS *mec*A positive strains, encoding the two phenomena by false negative and false positive, respectively. False negative results were explained by the heterogeneousness of *mec*A gene while false positive results were due to the overproduction of penicillinase and/or great variation of PBPs **[33]**.

6. Conclusion

Infection related *S. epidermidis* is highly resistance when compared to commensal ones, and are significantly methicillin resistance also. Methicillin resistance mediated by mechanisms rather than *mec*A gene. Infection causing clones harbors mechanisms make it more aggressive than commensal clones, and make it more able to cause disease. More characterization and differences between disease causing and commensal *S. epidermidis* investigations are recommended.

7. Acknowledgments

8. References

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مقاومة المضادات الحيوية وجين مقاومة المثيسيلين في المكورات العنقودية البشروية المعزولة من بعض المستشفيات في قطاع غزة

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الملخص

تعتبر مقاومة المضادات الحيوية في المكورات العنقودية البشروية المعزولة من العينات السريرية تشكل مشكلة عالمية للصحة العامة. في هذه الدراسة تم فحص 256 عزلة من المكورات العنقودية البشروية (128 عزلة من عينات سريرية و128 عزلة من مسحات أنفية) من قطاع غزة بفلسطين. تم اختبار جميع العزلات لمعرفة حساسيتها لاثني عشر مضاد حيوي وتم الكشف عن مدى انتشار جين الـ$mecA$. مائة وأربعة وثمانون (71.9٪) عزلة من الـ256 عزلة وجدت لتكون مقاومة للعديد من المضادات الحيوية مع إظهار حساسية كاملة تجاه الريفامبيسين (100٪) وحساسية عالية تجاه الدوكسيسيكلين (98.4٪) والفانكومايسين (98٪)، كما أن 96 (37.5٪) من العزلات كانت متعددة المقاومة للمضادات الحيوية (MDR). هذا ووجد جين الـ$mecA$ في 99 (38.7٪) عزلة.

ظهرت فروق ذات دلالة إحصائية معنوية بين العزلات السريرية والأنفية حيث كانت العزلات السريرية أكثر مقاومة لـ 8/12 من المضادات الحيوية المختبرة بما في ذلك مقاومة سيفوكسيتين (30 ميكروغرام) (0.000 = P) وكما كانت العزلات السريرية الأكثر تمثيلاً للعزلات متعددة المقاومات وبفارق ذات دلالة إحصائية (P=0.000)، بينما كانت العزلات الحساسة لجميع المضادات المختبرة وبفارق ذات دلالة إحصائية تنتمي للعزلات الأنفية (P=0.000). هذا ولم يكن هناك فارق ذات دلالة إحصائية بين المجموعتين في مدى انتشار جين الـ$mecA$. وقد وجد أن العزلات السريرية تكتسب صفة إضافية تزيد من قدرتها الإمراضية ومقاومتها المثيسيلين بطرق إضافية غير جين الـ$mecA$ حيث أن مقاومة المثيسيلين لم تكن تعتمد على جين الـ $mecA$ في جميع العزلات المقاومة المثيسيلين.