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ORIGINAL ARTICLE

Antibiotic Susceptibility of *Staphylococcus epidermidis* among Undergraduate Students in Malaysia Public University Health Campus

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ABSTRAK

Staphylococcus epidermidis (S. epidermidis) menjadi salah satu keprihatinan utama dalam pengurusan hospital berikutan kebolehannya menyebabkan jangkitan perolehan hospital terutamanya daripada alatan perubatan yang tercemar. Pengurusan jangkitan S. epidermidis semakin mencabar dengan peningkatan kes kerintangan terhadap antibiotik sejak kebelakangan ini. Laporan terhad mengenai kerintangan terhadap antibiotik oleh S. epidermidis di kalangan kumpulan komuniti yang sihat meninggalkan satu persoalan mengenai tahap penyebaran bakteria rintang antibiotik di kalangan komuniti. Oleh itu, kajian ini bertujuan untuk mengenalpasti corak rentan antibiotik oleh S. epidermidis yang dipencilkan daripada pelajar-pelajar sihat di salah satu kampus kesihatan di universiti awam. Sebanyak 96 sampel sapuan telapak tangan telah diambil dan melalui beberapa ujikaji termasuk ujian pengenalpastian secara mikroskopik, biokimia dan juga ujian rentan antiobiotik untuk eryhtromycin, oxacillin, gentamicin, penicillin dan tetracycline menerusi ujian Kirby Bauer. Sejumlah 43 sampel menunjukkan kehadiran S. epidermidis (44.8%), di mana 72.1% daripada jumlah pencilan bakteria ini menunjukkan kerintangan terhadap sekurang-kurangnya satu jenis antibiotik. Tahap kerintangan tertinggi dan terendah masing-masing didapati pada penicillin dan gentamicin. Walaupun tiada perbezaan yang signifikan antara corak rentan antibiotik antara kumpulan jantina, tahap kerintangan antibiotik yang tinggi di kalangan komuniti sihat menunjukkan terdapat keperluan terhadap kajian lanjut kerana penyebaran strain bakteria rintang antibiotik boleh berlaku kepada populasi komuniti lain dengan lebih meluas dan tanpa disedari.

Kata kunci: *bakteria, kerintangan dadah, pelajar, Staphylococcus epidermidis, ujian antimikrob resapan cakera*

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ABSTRACT

Staphylococcus epidermidis (S. epidermidis) has become one of the major concerns in the hospital setting due to its ability to cause hospital-acquired infection particularly from medical device contamination. The management of *S. epidermidis* infections become more challenging with the increase of antimicrobial resistance cases over the past years. Limited reports on *S. epidermidis* antibiotic resistance among healthy people leave uncertainty about the magnitude of antimicrobial resistance spreads among the community. Therefore, this study aimed to identify the antibiotic susceptibility pattern of *S. epidermidis* isolated from healthy undergraduate students in one of Malaysia public universities-health campuses. Ninety-six hand palm swab samples were collected and undergo several tests, including microscopic, biochemical identification tests and antibiotic susceptibility test for erythromycin, oxacillin, gentamicin, penicillin and tetracycline following Kirby-Bauer test. A total of 43 samples showed the presence of *S. epidermidis* (44.8%), where 72.1% of the isolates showed resistance towards at least one type of antibiotic. The highest and lowest resistance was observed for penicillin and gentamycin, respectively. Although there is no significant difference of antibiotic susceptibility pattern was observed between genders, the presence of high antibiotic resistance in *S. epidermidis* among these healthy communities should warrant further investigation since the spreading of the resistant strain could occur in the wider community population without notice.

Keywords: bacterial, disk diffusion antimicrobial tests, drug resistance, *Staphylococcus epidermidis*, students

INTRODUCTION

Staphylococcus epidermidis (S. epidermidis) is one of the most common Staphylococci that colonises the human skin, particularly the nares (together with *Staphylococcus aureus*) and axilla, head, legs and arms (together with *Staphylococcus hominis*) (Kloos & Musselwhite 1975). As part of normal flora, *S. epidermidis* rarely reported to cause infections, even it has been proposed as an effective probiotic in preventing overgrowth of other pathogenic bacteria such as *Propionibacterium acnes* that leads to acne vulgaris (Wang et al. 2014). However, this skin commensal gained much attention due to its involvement in hospital-acquired infection or nosocomial infection. The infection, which usually involves indwelling catheters and any implanted devices such as central intravenous catheters become more complicated with the formation of biofilms that is difficult to be eradicated (Vuong & Otto 2002; Rogers et al. 2009). Even though life threatening *S. epidermidis* is rare, the treatment becomes harder once

it occurs and subsequently results in an increased burden on the public healthcare system (Otto 2009). Capability to resist antibiotics makes the management of this bacterium more challenging either at treatment or prevention phases. This coagulase-negative Staphylococci (CoNS) was reported to be resisted towards several antibiotics such as methicillin, aminoglycosides, macrolides, tetracycline, chloramphenicol and clindamycin (Otto 2012). One of the main contributors to antibiotic resistance is the overuse of antibiotics through prolonged and/or frequent usage of the prescribed drugs (Costelloe et al. 2010). This condition can lead to colonization of the resistant bacteria strain, especially in a high-risk patient such as infants and young children (Patel & Saiman 2010; Nesher & Rolston 2014).

The resistance patterns of this bacterium change over time, due to many factors, including the easy transmission of the bacteria from one person to another person (Massey et al. 2006). The resistance patterns also differed from one to another geographical place, and it was reported to be found among the healthy population as well (Domínguez et al. 2002; Cherifi et al. 2013). While most of the research focuses on patients and children, very little information regarding antimicrobial resistance of this bacteria is available among the healthy population. Most of the epidemiological related studies focus on the former groups since they are the most frequent individual exposed to the antimicrobial drugs. However, it is also important to study the pattern of antibiotic resistance among healthy people, in order to have a clearer picture of the spreading of antimicrobial resistance in the human population. There are probabilities that healthy people can be a carrier of antibiotic resistant bacteria, and without proper attention, it could be the silent spreader among communities. Thus, this study aimed to identify the antibiotic susceptibility pattern of *S. epidermidis* among those undergraduate students in health campus of one Malaysian public university. As health-background students, they are exposed to a hospital settings through few activities such as clinical attachment, laboratory practicum and educational visits, where they might have potential for nosocomial infection.

MATERIALS AND METHODS

Sample Collection and Bacterial Identification

The subjects were recruited upon obtaining the ethical approval by IIUM Research Ethics Committee (IREV 2017-042). The skin swab samples were taken from palm hands of the subjects who fulfilled the inclusion criteria as full time undergraduate and not under antibiotic treatment for the past one month prior to sample collection. The swabs that were transported in the Stuart's transport medium were cultured on Mannitol Salt (MS) agar and incubated for 24 hours at 37°C. Each colony with different morphology was inoculated on new MS agar and incubated at 37°C overnight prior to

bacterial identification tests.

The bacterial colonies on MS agar were identified through Gram staining and biochemical tests. Upon observing the bacterial colony as Gram-positive cocci under microscope, the bacterial isolates were further confirmed as *S. epidermidis* through observation of positive catalase test, negative coagulase test and susceptible towards novobiocin drug.

Antibiotic Susceptibility Test

Antimicrobial susceptibility tests for *S. epidermidis* isolates were done using Kirby-Bauer's disk diffusion method for 5 antibiotics; penicillin (10 µg), erythromycin (15 µg), oxacillin (1 µg), gentamicin (10 µg) and tetracycline (30 µg). Bacterial suspension equivalent to 0.5 McFarland opacity standard was prepared by transferring 24 hours grown bacteria on the MS agar into a test tube containing peptone water. Sterile cotton swab was dipped into the test tube and a full lawn of bacteria streak was made on a Mueller Hinton (MH) agar. Each antibiotic disk was placed on the MH agar and incubated for 24 hours at 37˚C. The inhibition zone was measured by taking the diameter (mm) of clear zone surrounding the disk. The antibiotic susceptibility pattern was categorized as susceptible, intermediate or resistant based on Clinical and Laboratory Standard Institute (CLSI) guidelines.

Statistical Analysis

The prevalence of *S. epidermidis* isolates and its antibiotic susceptibility pattern was recorded for total subjects and in specific gender of the subjects. The association between antibiotic susceptibility and gender were statistically analyzed through Pearson chi-square or Fisher's exact test by using Statistical Packages for Social Sciences (SPSS) version 12.01 (Chicago, Illinois, USA, SPSS Inc.), where the *p*-value less than 0.05 was considered as significant value.

RESULT

In this study, a total of 96 undergraduate students was recruited which consisted of 52 male and 44 female subjects. The present data showed that 43 out of 96 (44.8%) skin swabs were presented with *S. epidermidis* isolates. Female subjects (n=22; 50%) had a higher *S. epidermidis* isolates than male subjects (n=21; 40.4%) but no statistical significant differences was observed between gender (p=0.345).

In terms of antibiotic susceptibility findings, a total of 31 out of 43 (72.1%) *S. epidermidis* isolates had demonstrated resistance towards at least one type of antibiotic. Specifically, 20 of the isolates were found to be resistant to one antibiotic, regardless of the type of antibiotic. Other isolates were resistant to two antibiotics (5 isolates), three antibiotics (5 isolates) and four antibiotic (1 isolate). Non of the isolates were found to resist all five types of antibiotics. This makes 25.6% (11 out of 43) of the isolates are multidrug resistant strain. The bacteria showed highest resistance towards penicillin (n=27; 62.8%), followed by erythromycin and oxacillin (n=9; 20.9%, for each

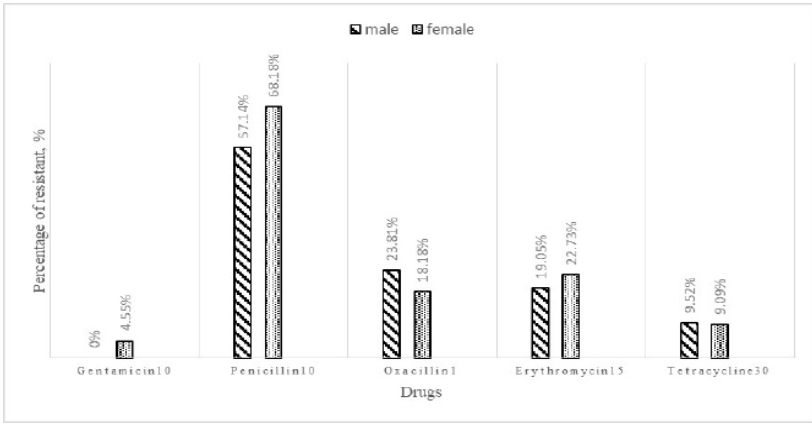

Figure 1: Percentage of *Staphylococcus epidermidis* resistance isolates towards each antibiotic drug for male and female subjects

antibiotic), tetracycline (n=4; 9.3%) and gentamycin (n=1; 2.3%). Comparison analysis of antibiotic susceptibility *S. epidermidis* showed no significant difference between gender variables in this study. Nevertheless, female subjects were more resistant to all types of antibiotics, except oxacillin and tetracycline, than males (Figure 1). Further analysis showed there was no significant association between the specific antibiotic susceptibility pattern and gender of the subjects (Table 1).

DISCUSSION

S. epidermidis is one of the most important coagulase-negative Staphylococci, which has increasingly reported as the main causes of hospital-acquired infection (Rogers et al. 2009). Infection caused by antibiotic-resistant *S. epidermidis* strain increases the risk of morbidity and mortality among the infected patients, resulting in the increment of the burden imposed upon public healthcare management and cost. This condition, however, can be improved by providing adequate and comprehensive information on the antimicrobial susceptibility pattern in the local population.

This study was conducted to provide additional information to the surveillance data available on the prevalence and antibiotic susceptibility pattern in *S. epidermidis* among the healthy population. Common misperception about the low risk of *S. epidermidis* infection among healthy people come down to limited antibiotic susceptibility profile reported in this population of interest. In our study, a high prevalence of *S. epidermidis* was found in the studied group (44.8%), which is superior to a study in Shanghai, China (Du et al. 2013). In addition, it is also observed that the female subjects (50%) had a slightly higher prevalence of *S. epidermidis* than male subjects (40.4%). Gender differences in the colonization of bacterial species were reported in several studies, for example, *Staphylococcus aureus* (*S. aureus*) nasal colonizer was highly found among female students in

Table 1: The association analysis of antibiotic susceptibility of *Staphylococcus epidermidis* and gender of the subjects

Antibiotic	Gender	Susceptibility			p-value
		Susceptible	Intermediate	Resistance	
Gentamicin	Male	21	-	0	0.323
	Female	21	-	1	
Penicillin	Male	9	-	12	0.454
	Female	7	-	15	
Oxacillin	Male	16	-	5	0.650
	Female	18	-	4	
Erythromycin	Male	17	0	4	0.331
	Female	15	2	5	
Tetracycline	Male	19	-	2	0.961
	Female	20	-	2	

Yemen as compared to male students (Al-Haj et al. 2018). Similarly, a study by Callewaert et al. (2013) also found a high preponderance of Staphylococci and Corynebacterium colonization on female and male subjects, respectively. The association between bacterial species and gender of the host was not clearly understood to date. However, Giacomoni et al. (2009) suggested that the above differences could be due to different anatomy and physiology of male and female skin, such as the hair growth, skin thickness, hormone and production of sweat and sebum.

Surveillance study on antibiotic susceptibility in *S. epidermidis* among healthy populations rarely reported as compared to the other Staphylococcus species, for example *S. aureus* (Tigabu et al. 2018; Kateete et al. 2019). Yet, the importance of studying this opportunistic pathogen should not be neglected, considering the potential of the bacterium to cause severe complications to the infected patients. Known as one of major biofilm producers, *S. epidermidis* is difficult to be eradicated due to its resistance towards many treatments including the antibiotic drugs. In certain antibiotic, such as mupirocin, a higher resistance level was detected among *S. epidermidis* (3.3%) than more established Staphylococci, *S. aureus* (0.9%) (Kresken et al. 2004). In the present study, 25.6% isolates were multidrug resistant, which was higher than multidrug resistant *S. epidermidis* (1.7%) isolated in healthy student in Riyadh, regardless of the type of antibiotic (Eladli et al. 2018).

Among all types of antibiotics tested in this study, *S. epidermidis* isolates showed the highest resistance towards penicillin (62.8%). This figure was lower than the findings by Domínguez et al. (2002) who had detected 87% penicillin resistant *S. epidermidis* isolated from healthy children in Spain. In contrast, lower percentage of penicillin resistant isolates were reported among healthy subjects in Mymensingh Medical College, Bangaladesh, which was

only 10% of 30 subjects (Haque et al. 2009). Penicillin resistance was recorded as early as in 1940, soon after its discovery (Abraham & Chain 1940). One of the possible reasons for the severe resistance cases of penicillin is the overuse and misuse of the drugs, either used for treatment or in food-producing animals (Prestinaci et al. 2015). As the first antibiotic introduced to treat infection, penicillin was rampantly used all over the world. Clear evidence had shown the relationship between antibiotic consumption and resistance development in the bacteria (Olesen et al. 2018). In Malaysia, penicillin has been recorded as the most common antibiotic prescribed for infection's treatment (National Healthcare Statistics Initiative 2006). Frequent exposure to the antibiotic may increase the spread rate of antibiotic resistance strain in the community, since *S. epidermidis* easily transmitted between individuals (Massey et al. 2006). The usage of penicillin was considered obsolete in few European countries such as France, Spain and Romania (Mossialos et al. 2010).

Oxacillin, another type of beta-lactam antibiotic shows a lower resistance (20.9%) against *S. epidermidis* in the subjects of the present study compared to the previous study by Eladli et al. (2018) who found 40% oxacillin resistance in their healthy subjects. Oxacillin is the second generation of penicillin was developed due to the emergence of penicillinase-producing strains which showed resistance towards penicillin (Lobanovska & Pilla 2017). This semisynthetic, beta-lactamase-resistant penicillin was introduced due to their ability to resist penicillinase produced by the bacteria (Lobanovska & Pilla 2017). Oxacillin acts by inhibiting the bacterial cell wall synthesis via penicillin-binding proteins (PBPs). The resistance towards this antibiotic was developed through the acquisition of *mec*A gene that encodes modified penicillin-binding protein (designated as PBP-2a) which has no inhibitory effect by β-lactam antibiotics (Finan et al. 2002).

Another antibiotic, erythromycin, a macrolide group of antibiotics also showed low resistance cases in the present study (20.9%). This value was low to compare with the findings by Eladli et al. (2018), who had recorded 60% erythromycin-resistant isolates in their study group and Juda et al. (2016) who had found 38.1% erythromycin resistant *S. epidermidis* in hospitalized patients with non small cell lung cancer. Since firstly reported in 1950s, various resistance mechanisms have been proposed for macrolide-resistant staphylococci. Two resistance mechanisms that have been identified in the macrolide were prevention of protein synthesis interruption by erythromycin-resistant methylase and elimination of the drug from the bacteria through the bacterial efflux system (Mazzei et al. 1993; Pechere 2001; Roberts 2004; Juda et al. 2016).

The least resistant antibiotic recorded in this study was tetracycline (9.3%) and gentamicin (2.3%). These findings suggest that these antibiotics are still effective to treat the *S. epidermidis* infection and the prevalence of antibiotic-resistant strain in the healthy

community is low. The present finding, however, is contrary to the study by Eladli et al. (2018), where 60% of their healthy subjects were colonized by *S. epidermidis* tetracycline resistant strain. The mechanism of tetracycline to kill or inhibit the bacteria is through ribosomal binding disruption which can prevent the cell cycle. However, the capability of the bacterium to acquire tetracycline resistance (*tet*) and oxytetracycilene (*otr*) genes which have been identified to disrupt the binding site of the antibiotic and enhance the drug efflux from the cells, had led to antibiotic resistance occurrences (Connell et al. 2003; Butaye et al. 2003; Thaker et al. 2010).

Gentamicin, a broad spectrum aminoglycosides group of antibiotic being the most susceptible drug in this study. The finding was superior to Eladli et al. (2018) who found 100% susceptible gentamicin in their healthy subjects. The mechanism of action of gentamicin is through bacteria ribosomal RNA (rRNA) binding that leads to mistranslated non-functional protein, eventually lead to cell death (Hermann 2007). Resistance to gentamicin or aminoglycosides may occur through few mechanisms, including modification of the antibiotic mediated by aminoglycoside-modifying enzymes, drug efflux, decreasing cell permeability and modification of the aminoglycoside binding site (Ramirez & Tolmasky 2010; Doi et al. 2016).

The frequency of multidrug-resistant *S. epidermidis* in the current study (25.6%) was higher than other study reported elsewhere (Eladli et al. 2018). However, this percentage was lower compared with multidrug resistance percentage from clinical samples or hospital settings (Cherifi et al. 2013; Eladli et al. 2018). Increasing trends of multidrug-resistant *S. epidermidis* in hospital settings reaching serious level, where limited option of antibiotic leads to increasing of mortality, morbidity and hospital management cost. Vancomycin remains as the drug of choice even the resistance towards this drug have been reported (Raad et al. 1998; Haque et al. 2010; de Benito et al. 2018). Thus, more surveillance and epidemiological data on the antibiotic resistance profiles are needed to identify the spreading occurrence of resistant bacteria not only in the hospital settings, but in the healthy community as well.

In the present study, a few different patterns of antibiotic susceptibility have been observed among male and female subjects, with no significant differences between groups. Although the difference was not statistically significant, it is worth to note that *S. epidermidis* isolated from female subjects showed slightly higher resistance towards gentamicin, penicillin, and erythromycin as compared to male students. On the other hand, *S. epidermidis* isolated from the male subjects were fully susceptible to gentamicin, followed by tetracycline, oxacillin, erythromycin and penicillin. In a previous study, methicillin resistant *S. epidermidis (*MRSE) isolated from nasal exudate were significantly higher in male (33.7%) as compared to female (8.6%) podiatrist (de Benito et al. 2018). The

differences in other staphylococci have been observed in other studies, including a study by Pomorska-Wesolowska et al. (2017), who had found higher methicillin-resistant *Staphylococcus aureus* (MRSA) among male subjects compared to female subjects in long-term care facilities in southern Poland (Pomorska-Wesolowska et al. 2017). Similarly, Humphreys et al. (2015) suggest that male host has a higher risk of MRSA carriage and bloodstream infection (BSI); as supported by another study, where female subjects showed a poorer prognosis from MRSA BSI (Lamagni et al. 2011). There is yet a clear explanation for the association of the antibiotic susceptibility pattern and gender of the host, although the risk for MRSE has been postulated to be higher in a male host (de Benito et al. 2018).

Combating *S. epidermidis* infections become harder due to increasing resistance to antibiotics. The complexity of treating these resistant bacteria rely on a few factors, including the capability of the bacteria to develop biofilm and acquire resistance genes (Otto 2009). The recent genomics study discovered that three multidrug-resistant, hospital-adapted lineages of *S. epidermidis* which resistant to rifampicin and last-line glycopeptide antibiotics (vancomycin and teicoplanin) have emerged in the past ten years and spread worldwide (Lee et al. 2018). In addition to surveillance research, study on possible host factors that may contribute to antibiotic susceptibility pattern is still lacking and need to be conducted in the future. Studying the host factors will give more information towards preventing the antimicrobial resistance spreading in communities.

The outcome from the present study may benefit future study with the same focus on *S. epidermidis*. However, these findings would be more significant with a larger number of sample size, where increasing numbers of sample size may decrease the margin of error, thus increases the efficiency of the study.

CONCLUSION

This study concludes that the distribution of *S. epidermidis* colonization on human palms was not affected by gender of the host. Higher percentage of antibiotic resistance has been observed, with highest and lowest resistance towards penicillin and gentamicin, respectively. A higher multiple antibiotic resistance in health community should be regarded as serious issues, and warrants further investigation since the spreading of the resistant strain could occur in the wider population without notice. The present findings provide new insights into *S. epidermidis* resistance spreading and serve as the basis for future investigation on searching treatment and prevention plan against its infections.

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REFERENCES

Abraham, E.P., Chain, E. 1940. An enzyme from bacteria able to destroy penicillin. *Nature* **146**: 837.

Al-Haj, N.A., Hauter, J.M., Al-Bulili, N.H., Al-Hotami, R.A., Al-Horaibi, M.T. 2018. Nasal carriage of *Staphylococcus aureus* among students of public schools in Sana'a, Yemen. *Res J Microbiol* **13**(1): 65-9.

Butaye, P., Cloeckaert, A., Schwarz, S. 2003. Mobile genes coding for efflux-mediated antimicrobial resistance in Gram-positive and Gram-negative bacteria. *Int J Antimicrob Agents* **22**: 205-10.

Callewaert, C., Kerckhof, F. M., Granitsiotis, M. S., Gele, M.V., Wiele, T.V.D., Boon, N. 2013. Characterization of Staphylococcus and Corynebacterium clusters in the human axillary region. *PLoS ONE* **8**(8): e70538.

Cherifi, S., Byl, B., Deplano, A., Nonhoff, C., Denis, O., Hallin, M. 2013. Comparative epidemiology of *Staphylococcus epidermidis* isolates from patients with catheter-related bacteremia and from healthy volunteers. *J Clin Microbiol* **51**(5): 1541-7.

Connell, S.R., Tracz, D.M., Nierhaus, K.H., Taylor, D.E. 2003. Ribosomal protection proteins and their mechanism of tetracycline resistance. *Antimicrob Agents Chemother* **47**: 3675-81.

Costelloe, C., Metcalfe, C., Lovering, A., Mant, D., Hay, A.D. 2010. Effects of antibiotics prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. *BMJ* **340**: c2096.

de Benito, S., Alou, L., Becerro-de-Bengoa-Vallejo, R., Losa-Iglesias, M.E., Gómez-Lus, M.L., Collado, L., Sevillano, D. 2018. Prevalence of Staphylococcus spp. nasal colonization among doctors of podiatric medicine and associated risk factors in Spain. *Antimicrob Resist Infect Control* **7**: 24.

Doi, Y., Wachino, J., Arakawa, Y. 2016. Aminoglycoside resistance the emergence of acquired 16S ribosomal RNA methyltransferase. *Infect Dis Clin* North Am **30**(2): 523-37.

Domínguez, E., Zarazaga, M., Torres, C. 2002. Antibiotic resistance in Staphylococcus isolates obtained from fecal samples of healthy children. *J Clin Microbiol* **40**(7): 2638-41.

Du, X., Zhu, Y., Song, Y., Tianming, L., Luo, T., Sun, G., Chongguang, Y., Cao, C., Lu, M., Li, M. 2013. Molecular analysis of *Staphylococcus epidermidis* strains isolated from community and hospital environments in China. *PLoS ONE* **8**(5): e62742.

Eladli, M.G., Alharbi, N.S., Khaled, J.M., Kadaikunnan, S., Alobaidi, A.S., Alyahya, S.A. 2018. Antibiotic-resistant *Staphylococcus epidermidis* isolated from patients and healthy students comparing with antibiotic-resistant bacteria isolated from pasteurized milk. *Saudi J Biol Sci* **26**(6): 1285-90.

Finan, J.E., Rosato, A.E., Dickinson, T.M., Ko, D., Archer, G.L. 2002. Conversion of oxacillin-resistant staphylococci from heterotypic to homotypic resistance expression. *Antimicrob Agents Chemother* **46**(1): 24-30.

Giacomoni, P.U., Mammone, T., Teri, M. 2009. Gender-linked differences in human skin. *J Dermatol Sci* **55:** 144-9.

Haque, N., Bari, M.S., Bilkis, L., Hossain, M.A., Haque, S., Haque, N., Islam, M.A., Mahmud, N.U., Kalam, A., Hasan, M.S., Haque, M.A. 2010. Prevalence and antimicrobial resistance of methicillin resistant *Staphylococcus epidermidis* isolated at Mymensingh Medical College Hospital. *Mymensingh Med J* **19**(2): 163-9.

Haque, N., Hossain, M.A., Bilkis, L., Musa, A.K., Mahamud, C., Bari, M.S., Haque, N., Muhammad, N., Parvin, U.S., Islam, M.T., Khan, S.I., Islam, M.A., Haque, S. 2009. Antibiotic susceptibility pattern of *Staphylococcus epidermidis. Mymensingh Med J* **18**(2): 142-7.

Hermann, T. 2007. Aminoglycoside antibiotics: old drugs and new therapeutic approaches. *Cell Mol Life Sci* **64**(14): 1841-52.

Humphreys, H., Fitzpatick, F., Harvey, B.J. 2015. Gender differences in rates of carriage and bloodstream infection caused by methicillin-resistant *Staphylococcus aureus* : are they real, do they matter and why? *Clin Infect Dis* **61**(11): 1708-14.

Juda, M., Chudzik-Rzad, B., Malm, A. 2016. The prevalence of genotypes that determine resistance to macrolides, lincosamides, and streptogramins B compared with spiramycin susceptibility among erythromycin-resistant *Staphylococcus epidermidis*. *Memorias do Instituto Oswaldo Cruz* **111**(3): 155-60.

Kateete, D.P., Asiimwe, B.B., Mayanja, R., Mujuni, B., Bwanga, F., Najjuka, C.F., Kallander, K., Rutebemberwa, E. 2019. Nasopharyngeal carriage, spa types and antibiotic susceptibility profiles of *Staphylococcus aureus* from healthy children less than 5 years in Eastern Uganda. *BMC Infect Dis* **19**: 1023.

Kloos, W.E., Musselwhite, M.S. 1975. Distribution and persistence of Staphylococcus and Micrococcus species and other aerobic bacteria on human skin. *Appl Microbiol* **30**(3): 381-5.

Kresken, M., Hafner, D., Schmitz, F.J., Wichelhaus,

T.A. 2004. Prevalence of mupirocin resistance in clinical isolates of *Staphylococcus aureus* and *Staphylococcus epidermidis*: result of the antimicrobial resistance surveillance study of the Paul-Ehrlich-Society for chemotherapy, 2001. *Int J Antimicrob Agents* **23**(6): 577-81.

Lamagni, T.L., Potz, N., Powell, D., Pebody, R., Wilson, J., Duckworth, G. 2011. Mortality in patients with meticillin-resistant *Staphylococcus aureus* bacteraemia, England 2004–2005. *J Hosp Infect* **77**(1): 16-20.

Lee, J.Y.H., Monk, I.R., Gonçalves da Silva, A., Seemann, T., Chua, K.Y.L., Kearns, A., Howden, B.P. 2018. Global spread of three multidrug-resistant lineages of *Staphylococcus epidermidis*. *Nat Microbiol* **3**(10): 1175-85.

Lobanovska, M., Pilla, G. 2017. Penicillin's Discovery and Antibiotic Resistance: Lessons for the Future? *Yale J Biol Med* **90**(1): 135-45.

Massey, R.C., Horsburgh, M.J., Lina, G., Hook, M., Recker, M. 2006. The evolution and maintenance of virulence in *Staphylococcus aureus*: a role for host-to-host transmission? *Nat Rev Microbiol* **4**(12): 953-8.

Mazzei, T., Mini, E., Novelli, A., Periti, P. 1993. Chemistry and mode of action of macrolides. *J Antimicrob Chemother* **13**: 1-9.

Mossialos, E., Morel, C.M., Edwards, S., Berenson, J., Gemmill-Toyama, M., Brogan, D. 2010. *Policies and incentives for promoting innovation in antibiotic research*. Copenhagen. World Health Organization.

National Healthcare Statistics Initiative. 2006. Malaysian Statistics on Medicine 2006. Malaysia.

Nesher, L., Rolston, K.V. 2014) The current spectrum of infection in cancer patients with chemotherapy related neutropenia. *Infect* **42**(1): 5-13.

Olesen, S.W., Barnett, M.L., MacFadden, D.R., Brownstein, J.S., Hernandez-Diaz, S., Lipsitch, M., Grad, Y.H. 2018. The distribution of antibiotic use and its association with antibiotic resistance. *eLife* **7:** e39435.

Otto, M. 2009. *Staphylococcus epidermidis*—the "accidental" pathogen. *Nat Rev Microbiol* **7**(8): 555-567.

Otto, M. 2012. Molecular basis of *Staphylococcus epidermidis* infections. *Semin Immunopathol* **34**(2): 201–214.

Patel, S.J., Saiman, L. 2010. Antibiotic resistance in neonatal intensive care unit pathogens: mechanisms, clinical impact, and prevention including antibiotic stewardship. *Clin Perinatol* **37**(3): 547-63.

Pechere, J.C. 2001. Macrolide resistance mechanism in Gram-positive cocci. International *J Antimicrob Agents* **18**(1): S25-28.

Pomorska-Wesolowska, M., Rózanska, A., Natkaniec, J., Gryglewska, B., Szczypta, A., Dzikowska, M., Wójkowska-Mach, J. 2017. Longevity and gender as the risk factors of methicillin-resistant *Staphylococcus aureus* infections in southern Poland. *BMC Geriatr* **17**(1): 51.

Prestinaci, F., Pezzoti, P., Pantosti, A. 2015. Antimicrobial resistance: a global multifaceted phenomenon. *Pathogen and Global Health* **109**(7): 309-18.

Raad, I., Alrahwan, A., Rolston, K. 1998. *Staphylococcus epidermidis*: Emerging resistance and need for alternative agents. *Clini Infect Dis* **16**: 1182-7.

Ramirez, M.S., Tolmasky, M.E. 2010. Aminoglycoside modifying enzymes. *Drug Resist Updat* **13**(6): 151-71.

Roberts, M.C. 2004. Update on macrolide-lincosamide-streptogramin, ketolide, and oxazolidinone resistance genes. *FEMS Microbiol Lett* **282**: 147-59.

Rogers, K.L., Fey, P.D., Rupp, M.E. 2009. Coagulase-negative staphylococcal infections. *Infect Dis Clin* North Am **23**(1): 73-98.

Thaker, M., Spanogiannopoulos, P., Wright, G.D. 2010. The tetracycline resistome. *Cell Mol Life Sci* **67**(3): 419-31.

Tigabu, A., Tiruneh, M., Mekonnen, F. 2018. Nasal carriage rate, antimicrobial susceptibility pattern, and association factors of *Staphylococcus aureus* with special emphasis on MRSA among urban and rural elementary school children in Gondar, Northwest Ethiopia: A comparative cross-sectional study. *Adv Prev Med* **2018**: 9364757.

Vuong, C., Otto, M. 2002. *Staphylococcus epidermidis* infections. *Microbes Infect* **4**(4): 481-9.

Wang, Y., Kuo, S., Shu, M., Yu, J., Huang, S., Dai, A., Two, A., Gallo, R.L., Huang, C.M. 2014. *Staphylococcus epidermidis* in the human skin microbiome mediates fermentation to inhibit the growth of *Propionibacterium acnes*: Implications of probiotics in acnes vulgaris. *Appl Microbiol Biotechnol* **98**(1): 411-24.

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