Original article

Screening of antibiotic-resistant staphylococci in the nasal cavity of patients and healthy individuals

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Abstract

The normal microbiota play critical roles in the general health of an individual and the functions of the microbiota colonized the nasal cavity in maintaining the health of the respiratory tract are well known. The nasal cavity is one of the potential bio-sources of the pathogenic opportunistic bacteria that have the ability to resist standard antibiotics. My aim was an evaluation of the prevalence of antibiotic-resistant staphylococci in the nasal cavity of healthy individuals and compared them with the strains isolated from patients. The work was designed as prospective, descriptive study in Medical University Hospital (MUH) and Botany and Microbiology Department, King Saud University (KSU), Riyadh, respectively. Strain isolation, purification, and preservation were performed according to standard protocols and the identification of pure bacterial cultures was carried out using a fully automatic system (VITEK 2 system). The isolates identified as Staphylococcus spp. were subjected to investigation. In patients, 34 out of 6668 isolates were Staphylococcus spp. obtained from the nasal cavity, while 32 out of 320 isolates from the nasal cavity of healthy individuals were Staphylococcus spp. The results confirmed that all the isolates were resistant to ampicillin and benzylpenicillin, but showed susceptibility to vancomycin, fusidic acid, gentamicin, linezolid, rifampicin, tetracycline, and trimethoprim/sulfamethoxazole. A significant association (P < 0.05) was observed between all the isolates resistant to ampicillin and clindamycin in patients and healthy individuals. The antibiotic-resistant staphylococci are prevalent in the nasal cavity among healthy individuals and patients, and a statistically significant association exists between sources of bacterial isolates and antibiotic resistance.

1. Introduction

Several microorganisms, including bacteria, archaea, fungi, and viruses, have been detected and isolated from healthy human tissues and biofluids. “Microbiota” is a scientific term that refers to any non-pathogenic microbes that have the ability to survive and colonize some human parts such as nose, mouth, and skin. The human nasal cavity is a section of the respiratory system and all the parts of the respiratory system receive the inhaled air through the nasal cavity (Bassis et al., 2014; Ramakrishnan et al., 2016; Bomar et al., 2018). Evidence indicates that the normal microorganisms of the nasal cavity maintain the health of the respiratory tract and functions of the defense system (Kumar and Chordia, 2017).

Rasmussen et al. reported that the nasal cavity of a healthy adult is colonized by several opportunistic bacteria such as Corynebacterium spp., Aureobacterium spp., Rhodococcus spp., and Staphylococcus spp. Numerous species of fungi have also been isolated from the healthy nasal cavity (Rasmussen et al., 2000). For instance, Sellart-Altisent et al. reported that Alternaria spp., Penicillium spp., Aspergillus spp., and Cladosporium may colonize the nasal cavity of healthy humans (Sellart-Altisent et al., 2007). There are several invasive and allergic fungi have been diagnosed in nasal cavity (Robson et al., 1989; deShazo, 1997).

Lina et al. confirmed that the microbiota have the ability to colonize the healthy human nasal cavity and live under constant competition conditions (Lina et al., 2003). Commensal microbes could prevent the colonization of the human nasal cavity by pathogenic bacteria. For instance, Staphylococcus epidermidis strains known to produce serine protease Esp2,3, have the ability to block biofilm formation by pathogenic S. aureus (Iwase et al., 2010).
**2. Material and methods**

**2.1. Design of the experiment**

In this study, the work was carried out in (MUH) and Botany and Microbiology Department, KSU, Riyadh from 1/1/2016 to 1/1/2017. Written informed consent and ethical approvals were obtained in conformity to the directions of the Ethics Committee (17/0449/IRB, Institutional Review Board of College of Medicine, KSU, Saudi Arabia). The data obtained from the Medical Microbiology Department in MUH were compared with those acquired from the healthy individuals in Botany and Microbiology Department to evaluate the association between the two sources of Staphylococcus strains. The study was a completely randomized design and the clinical samples and healthy individuals were randomly selected.

**2.2. Isolation, purification, and preservation of strains**

The microbial strains were cultivated from the nasal cavity of healthy individuals (N = 50) on blood agar (base blood medium [Sigma-Aldrich, USA] contained defibrinated sheep blood (5%) [Wattin-Biolife, Saudi Arabia, Riyadh]) using wet sterile cotton swabs. The incubation of the plates were done at 37 °C for 24 h and purification was carried out by triple streaking method from the single colonies grown on the surface of blood agar using new blood agar medium. The purity of the bacterial cultures was determined using cultural and microscopic characteristics; all cultures with same characteristics were considered as a single or pure culture. The preservation of the pure bacterial cultures was carried out in sterile glycerol solution (30%) at −80 °C.

**2.3. Identification of microbial isolates**

The identification of all isolates were performed using a fully automated enclosed system (VITEK 2, Biomerieux, USA). The manufacturers’ guidelines were followed using AST-GN69, AST-XN06, or AST-GN69 cards. Strain identification was performed using a single colony of the bacterial isolates after cultivation on blood agar, followed by MacConkey Agar (Oxoid, UK). Only the isolates identified as Staphylococcus spp. were used in the subsequent tests.

**2.4. Antibacterial susceptibility testing**

VITEK 2 system was used to perform the antibacterial susceptibility tests. The antibacterial susceptibility tests using AST-GP71 card was carried out in fully automated system in Vitek 2 instrument according to the manufacturer’s guidelines. The susceptibility test was performed using pure cultures obtained from single colonies and cultivated on blood agar at 35 °C for 19 h.

**2.5. Statistical analysis**

Statistically significant association between the isolates from patients and healthy individuals was analyzed using Pearson’s chi-square test. The percentage of bacterial isolates resistance to antibiotics, relative risk, and odds ratio were calculated using statistical software of SPSS (IBM SPSS Statistics 25).

**3. Results**

The evaluation of the predominance of Staphylococcus species resistance standard antibacterial agents isolated from healthy individuals and patients was done, and the association between the clinical isolates and the isolated obtained from healthy individuals was investigated. Furthermore, the presence of potential antibiotic-resistant *Staphylococcus* in the isolates from healthy individuals was analyzed.

**3.1. Clinical bacterial isolates from nasal cavity**

The data obtained from 6668 clinical bacterial isolates were analyzed and summarized in Table 1. The results revealed the isolation of 0.7% of pathogenic bacteria from the nasal cavity of patients. *Escherichia coli*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Proteus mirabilis*, *Acinetobacter spp.*, *S. epidermidis*, *Enterococcus faecalis*, *E. faecium*, *Streptococcus group A*, *group B*, and *P. pneumonia* were absent in the nasal cavity samples from the patients, but *Klebsiella pneumonia*, *S. aureus* resistance to methicillin (MRSA), *P. aeruginosa*, and *S. aureus* were isolated. Among the clinical isolates, 12.4%, 1.5% and 0.0% of the isolates were MRSA, *S. aureus* and *S. epidermidis* respectively. The results showed that 65.9% of the isolates from the nasal cavities of patients were MRSA and 67.5% were *Staphylococcus* spp.

**3.2. Staphylococcus isolates from healthy nasal cavity**

Fig. 1 shows that approximately one-third of the bacterial isolates from the nasal cavity of healthy individuals were *S. aureus* and the other bacterial isolates were not *S. aureus* strains. Furthermore, 33.3% of the bacterial isolates were *S. epidermidis*, while *S. capitis* and *S. hominis* subsp. *hominis* represented 6.7% and 26.7% of the bacterial isolates, respectively.

**3.3. Antibiotic susceptibility testing of Staphylococcus spp.**

The results shown in Table 2 demonstrate that all *Staphylococcus* spp. isolated and identified from the patients were vancomycin, linezolid, and teicoplanin-susceptible strains whereas those isolated from the healthy individuals showed susceptibility to vancomycin, cefoxitin, gentamicin, linezolid, moxifloxacin, rifampicin, teicoplanin, and trimethoprim/sulfamethoxazole. More than 90% of the bacterial isolates from patients were resistant to ampicillin, oxacillin, amoxicillin/clavulanic acid, cefoxitin, cefaclor, and benzylpenicillin, while over 90% of the isolates from healthy individuals were resistant to only two antibiotics (ampicillin and benzylpenicillin). Statistical analysis indicated a significant association (P < 0.05) between ampicillin- and clindamycin-resistant strains isolated from patients and healthy individuals.
3.4. Antibiotic susceptibility testing of S. aureus

Fig. 2 shows that all S. aureus isolates obtained from the nasal cavity of patients and healthy individuals were resistant to ampicillin and benzylpenicillin but showed susceptibility to vancomycin, fusidic acid, gentamicin, linezolid, rifampicin, teicoplanin, tetracycline, and trimethoprim/sulfamethoxazole. No significant association (\(P < 0.05\)) was observed between S. aureus strains obtained from the nasal cavity of patients and healthy individuals based on susceptibility test for azithromycin, cefoxitin, cefaclor, clindamycin, erythromycin, and moxifloxacin.

3.5. Minimum variance criterion

The minimum variance criterion of bacterial isolates was evaluated with Ward’s method in SPSS. Fig. 3 shows that the bacterial isolates from the nasal cavity of healthy individuals could be...

### Table 1

Pathogenic bacterial isolates from the nasal cavity of patients.

| Clinical bacterial isolates | Total isolates from all clinical samples (N) | Clinical isolates from nasal cavity (N) | % |
|-----------------------------|---------------------------------------------|----------------------------------------|---|
| Staphylococcus spp.         |                                             |                                        |   |
| Methicillin-Resistant Staphylococcus aureus (MRSA) | 251.0 | 31.0 | 12.4 |
| Staphylococcus aureus       | 339.0 | 5.0  | 1.5  |
| Staphylococcus epidermidis  | 231.0 | 0.0  | 0.0  |
| Non-Staphylococcus spp.     |                                             |                                        |   |
| Klebsiella pneumoniae       | 704.0 | 9.0  | 1.3  |
| Pseudomonas aeruginosa      | 804.0 | 2.0  | 0.2  |
| Escherichia coli            | 1594.0| 0.0  | 0.0  |
| Proteus mirabilis           | 144.0 | 0.0  | 0.0  |
| Enterobacter cloacae        | 225.0 | 0.0  | 0.0  |
| Pseudomonas aeruginosa      | 1425.0| 0.0  | 0.0  |
| Acinetobacter spp.          | 276.0 | 0.0  | 0.0  |
| Enterococcus faecalis       | 249.0 | 0.0  | 0.0  |
| Enterococcus faecium        | 109.0 | 0.0  | 0.0  |
| Streptococcus group A       | 85.0  | 0.0  | 0.0  |
| Streptococcus group B       | 186.0 | 0.0  | 0.0  |
| Streptococcus pneumonia     | 46.0  | 0.0  | 0.0  |
| Total                       | 6668.0| 47.0 | 0.7  |

Table 1

Pathogenic bacterial isolates from the nasal cavity of patients.

### Table 2

Antibiotic susceptibility testing of Staphylococcus spp. isolated from the nasal cavity of patients and healthy individuals.

| Antibiotics                              | Patients | Healthy individuals | \(\chi(1)^{*}\) | p   |
|------------------------------------------|----------|---------------------|-----------------|-----|
|                                          | S        | R       | N     | %    | N     | %    | N     | %    | 1     | 1     |
| Vancomycin\(^{**}\)                      | 34       | 100     | 0     | 0    | 32    | 100   | 0     | 0    | 25.1  | 0.00  |
| Amoxicillin/Clavulanic acid              | 3        | 8.8     | 31    | 91.2 | 22    | 68.8  | 10    | 31.2 | 3.92  | 0.048 |
| Ampicillin\(^{*}\)                       | 1        | 2.9     | 33    | 97.1 | 2     | 6.3   | 30    | 93.8 | 0.416 | 0.519 |
| Azithromycin                             | 20       | 58.8    | 14    | 41.2 | 26    | 81.3  | 6     | 18.8 | 3.92  | 0.048 |
| Cefoxitin                                | 2        | 5.9     | 32    | 94.1 | 32    | 100   | 0     | 0    | 58.46 | 0.00  |
| Cefaclor                                 | 3        | 8.8     | 31    | 91.2 | 24    | 75    | 8     | 25   | 29.86 | 0.00  |
| Ciprofloxacin                            | 20       | 58.8    | 14    | 41.2 | 30    | 93.8  | 0     | 0    | 17.95 | 0.00  |
| Clindamycin                              | 21       | 61.8    | 12    | 35.3 | 22    | 68.8  | 10    | 31.3 | 1.146 | 0.564 |
| Erythromycin                             | 19       | 55.9    | 14    | 41.2 | 26    | 81.3  | 6     | 18.8 | 1.146 | 0.564 |
| Fusidic acid                             | 18       | 52.9    | 2     | 4.1  | 18    | 56.3  | 14    | 43.8 | 22.96 | 0.00  |
| Gentamicin                               | 27       | 79.4    | 6     | 20.6 | 32    | 100   | 0     | 0    | 7.37  | 0.025 |
| Imipenem                                 | 4        | 11.8    | 30    | 88.2 | 24    | 75    | 8     | 25   | 26.98 | 0.00  |
| Levofloxacin                             | 21       | 61.8    | 13    | 38.2 | 30    | 93.8  | 0     | 0    | 16.54 | 0.00  |
| linezolid\(^{*}\)                        | 34       | 100     | 0     | 0    | 32    | 100   | 0     | 0    | 18.27 | 0.00  |
| Moxifloxacin                             | 19       | 55.9    | 15    | 44.1 | 32    | 100   | 0     | 0    | 18.27 | 0.00  |
| Oxacillin                                | 2        | 5.9     | 32    | 94.1 | 24    | 75    | 8     | 25   | 32.98 | 0.00  |
| Benzylpenicillin                         | 0        | 0       | 34    | 100  | 2     | 6.3   | 30    | 93.8 | 2.191 | 0.139 |
| Rifampicin                               | 33       | 97.1    | 0     | 3.9  | 32    | 100   | 0     | 0    | 0.95  | 0.328 |
| Teicoplanin                              | 34       | 100     | 0     | 0    | 32    | 100   | 0     | 0    | 5.09  | 0.024 |
| Tetracycline                             | 26       | 76.5    | 6     | 23.5 | 30    | 93.8  | 2     | 6.3  | 4.22  | 0.121 |
| Trimethoprim/sulfamethoxazole            | 29       | 85.3    | 5     | 14.7 | 32    | 100   | 0     | 0    | 5.09  | 0.024 |

R = resistance, S = susceptible, \((100 - \text{％}) \times 3\%\) = intermediate %.

\(^{*}\) Statistically significant association between source of bacterial isolates and antibiotic resistance \((P < 0.05)\).

\(^{**}\) No statistics were computed because the results were identical among all the isolates.
Fig. 2. Prevalence of Staphylococcus aureus strains resistant to antibiotics in the nasal cavity of patients and healthy individuals. *No statistically significant association between the isolates from patients and healthy individuals, as analyzed with Pearson’s chi-square test (P < 0.05). **No statistics were computed because the resistance to antibiotics was constant.

Fig. 3. Dendrogram using Ward linkage (rescaled distance cluster) of Staphylococcus isolates from nasal cavity of patients and healthy subjects. Numbers on Y axis indicate the number of bacterial isolates and numbers on X axis indicate the distance or dissimilarity between clusters.


3.6. Risk estimate

Risk estimate of the predominance of antibiotic-resistant strains of *Staphylococcus* isolated from the nasal cavity of healthy individuals and patients is shown in Table 3. The results reported risk factor in patients over healthy individuals for all strains except *S. aureus* standard antibiotics.

### Table 3

| Strains                  | Value | 95% Confidence interval | Odds ratio for case (patient/healthy) |
|--------------------------|-------|-------------------------|--------------------------------------|
|                          | lower | upper                   | lower | upper |
| Azithromycin-resistant strain | 2.039 | 0.882                   | 4.715 |       |
| Clindamycin - resistant strain | 1.129 | 0.568                   | 2.244 |       |
| Cefaclor - resistant strain | 3.444 | 1.864                   | 6.366 |       |
| Erythromycin-resistant strain | 2.074 | 0.905                   | 4.754 |       |
| Fusidic acid - resistant strain | 0.134 | 0.033                   | 0.546 |       |
| Imipenem - resistant strain | 3.333 | 1.797                   | 6.182 |       |
| Oxacillin-resistant strain | 3.556 | 1.930                   | 6.551 |       |
| Tetracycline-resistant strain | 2.833 | 0.613                   | 13.086 |     |

* Antibiotics resisted by all bacterial isolates (from patients and healthy individuals/from patients or healthy individuals) were excluded.

4. Discussion

Investigation of antibiotic-resistant bacteria among healthy subjects and patients is an important scientific purpose associated with community health. This information may help predict the prevalence of dangerous pathogenic bacteria, including opportunistic pathogens, among healthy subjects. Furthermore, it may reveal some bio-sources of pathogenic bacteria resistant to the standard antibiotics. *S. aureus* is renowned for its ability to gain resistance to antibacterial agents, and the risks multiply once the bacterial strains acquire resistance to multiple antibiotics (Chambers and DeLeo, 2009). In this study, 12.4% of MRSA were identified from the non-healthy nasal cavity; however, this number is not an indicator that the lower respiratory tract infected with MRSA, as per the findings reported by Sarikonda et al. (2010). Although the nasal cavity of healthy humans is known to be colonized by *S. epidermidis* (Chen et al., 2016), we failed to isolate this bacterium from the nasal cavity of patients but isolated it from healthy individuals (33.3% of the isolates were *S. epidermidis*). More than 60% of the bacterial isolates from the nasal cavity of patients that underwent refractive surgery were *S. epidermidis* (Kitazawa et al., 2016).

Herein, we confirmed that all the *S. aureus* strains obtained from the patients and healthy individuals were susceptible to vancomycin, linezolid, and teicoplanin. Cell wall biosynthesis of *S. aureus* is inhibited by vancomycin, a glycopeptide antimicrobial agent applied for the treatment of MRSA diseases (McGuinness et al., 2017). Vancomycin-resistant *S. aureus* strains were frequently identified in several studies performed in different countries (Hiramatsu et al., 1997; Centers for Disease Control and Prevention (CDC), 2002); however, we failed to report similar observation. Vancomycin remains a viable option for the treatment of bacterial infections resulted from *S. aureus*. The results reported with linezolid and teicoplanin were the same as those observed with vancomycin, wherein the isolation of *Staphylococcus* strains resistant to linezolid and teicoplanin has been previously reported (Tsiodras et al., 2001; Cepeda et al., 2003; Stefani et al., 2010); however, we could not observe these results in the present study. The most important risk indicator found in the present work was the isolation of the strains that have resistance to ampicillin and benzylpenicillin; more than 90% of the bacterial strains were ampicillin- and benzylpenicillin-resistant *Staphylococcus* species in both patients and healthy individuals. Ampicillin may be used to treat microbial diseases caused by *S. aureus* except for the strains resistant to penicillin or methicillin. The results obtained herein suggest that ampicillin may be excluded for the treatment of all infections caused by *Staphylococcus*. We found that the nasal cavity of healthy individuals is not a bio-source for cefoxitin-resistant *Staphylococcus* isolates, which were obtained from more than 90% of patients. However, the nasal cavity of healthy individuals served as a potential bio-source for the strains resistant to oxacillin. Methicillin resistance in species of *Staphylococcus* is screened using cefoxitin and oxacillin disc diffusion test (Jain et al., 2008; Broekema et al., 2009). In healthy individuals, the oxacillin test results showed that approximately one-third of the isolates were methicillin-resistant staphylococci, although cefoxitin test results confirmed that all the strains were non-methicillin-resistant staphylococci. Velasco et al. reported that cefoxitin test is the best analysis method to screen methicillin resistance in staphylococci (Velasco et al., 2005). Risk estimate of oxacillin-resistant staphylococci indicated that the risk prevalence of these strains is more than the other groups; this classification may help us detect the groups of antibiotics that may be used to treat the bacterial diseases caused by staphylococci. Thus, the antibiotic-resistant staphylococci are prevalent in the nasal cavity among healthy individuals and patients, and a statistically significant
association exists between sources of bacterial isolates and antibiotic resistance. The risk factor of prevalence of approximately all the isolates resistant to antibiotics is higher in patients than in healthy individuals.

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References

Bassis, C.M., Tang, A.L., Young, V.B., Pynnönen, M.A., 2014. The nasal cavity microbiota of healthy adults. Microbiome 2, 27.

Bomar, L., Brugger, S.D., Lennon, K.P., 2018. Bacterial microbiota of the nasal passages across the span of human life. Curr. Opin. Microbiol. 41, 8–14.

Broekema, N.M., Van, T.T., Monson, T.A., Marshall, S.A., Warshauer, D.M., 2009. Comparison of cefotaxin and oxacillin disk diffusion methods for detection of mecA-mediated resistance in Staphylococcus aureus in a large-scale study. J. Clin. Microbiol. 47, 217–219.

Centers for Disease Control and Prevention (CDC). 2002. Staphylococcus aureus resistant to vancomycin—United States. MMWR Morb. Mortal. Wkly. Rep. 51, 565–567.

Cepeda, J., Hayman, S., Whitehouse, T., Kibbler, C.C., Livermore, D., Singer, M., Wilson, A.P., 2003. Teicoplanin resistance in methicillin-resistant Staphylococcus aureus in an intensive care unit. J. Antimicrob. Chemother. 52, 533–534.

Chambers, H.F., DeLeo, F.R., 2009. Waves of resistance: Staphylococcus aureus in the antibiotic era. Nat. Rev. Microbiol. 7, 629–641.

Chen, H.W., Liu, P.F., Liu, Y.T., Kuo, S., Zhang, X.Q., Schooley, R.T., Gallo, R.L., Huang, C.M., 2016. Nasal commensal Staphylococcus epidermidis counteracts influenza virus. Sci. Rep. 6, 27870.

Cole, A.M., Tahk, S., Oren, A., Yoshioika, D., Kim, Y.H., Park, A., Ganz, T., 2001. Determinants of Staphylococcus aureus nasal carriage. Clin. Diagn. Lab. Immunol. 8, 1064–1069.

deShazo, R.D., O’Brien, M., Chapin, K., Soto-Aguilar, M., Gardner, L., Swain, R., 1997. A new classification and diagnostic criteria for invasive fungal sinusitis. Arch. Otolarngol. Head Neck Surg. 123, 1181–1188.

Hiramatsu, K., Arita, N., Hanaki, H., Kawasaki, S., Hosoda, Y., Hori, S., Fukuchi, Y., Kobayashi, I., 1997. Dissemination in Japanese hospitals of strains of Staphylococcus aureus heterogeneously resistant to vancomycin. Lancet 350, 1670–1673.

Iwase, T., Uehara, Y., Shinji, H., Tajima, A., Sea, H., Takada, K., Agata, T., Mizuno, Y., 2010. Staphylococcus epidermidis Esp inhibits Staphylococcus aureus biofilm formation and nasal colonization. Nature 465, 346–349.

Jain, A., Agarwal, A., Verma, R.K., 2008. Cefotaxin disc diffusion test for detection of meticillin-resistant staphylococci. J. Med. Microbiol. 57, 957–961.

Kifazawa, K., Sotozono, C., Sakamoto, M., Sasaki, M., Hieda, O., Yamasaki, T., Kinosita, S., 2016. Nasal and conjunctival screening prior to refractive surgery: an observational and cross-sectional study. BMJ Open 6, e010733.

Kluymans, J., Belkum, A.V., Verbrugh, H., 1997. Nasal carriage of Staphylococcus aureus: epidemiology, underlying mechanisms, and associated risks. Clin. Microbiol. Rev. 10, 505–520.

Kumar, A., Chordia, N., 2017. Role of microbes in human health. Appl. Microb. Open Access 3.

Lina, G., Boutièe, F., Tristan, A., Michèle, B., Etienne, J., Vandenesch, F., 2003. Bacterial competition for human nasal cavity colonization: role of Staphylococcal agr alleles. Appl. Environ. Microbiol. 69, 18–23.

McGuinness, W.A., Malachowa, N., DeLeo, F.R., 2017. Vancomycin resistance in Staphylococcus aureus. Yale J. Biol. Med. 23, 269–281.

Ramakrishnan, V.R., Hauser, I.J., Frank, D.N., 2016. The sinonasal bacterial microbiome in health and disease. Curr. Opin. Otolaryngol. Head Neck Surg. 24, 20–25.

Rasmussen, T.T., Kirkeby, L.P., Poulsen, K., Reinholdt, J., Kilian, M., 2000. Resident aerobic microbiota of the adult human nasal cavity. APMS 108, 663–675.

Robson, J.M., Hogan, P.C., Benn, R.A., Gatesby, P.A., 1989. Allergic fungal sinusitis presenting as a paranasal sinus tumour. Aust. N. Z. J. Med. 19, 351–353.

Sarkonka, K.V., Micek, S.T., Doherty, J.A., Reichley, R.M., Warren, D., Kollef, M.H., 2010. Methicillin-resistant Staphylococcus aureus nasal colonization is a poor predictor of intensive care unit-acquired meticillin-resistant Staphylococcus aureus infections requiring antibiotic treatment. Crit. Care Med. 38, 1991–1995.

Sellart-Altisent, M., Torres-Rodríguez, J.M., Gómez de Ana, S., Alvarado-Ramírez, E., 2007. Nasal fungal microbiota in allergic and healthy subjects. Rev. Iberoam. Micol. 24, 125–130.

Stefani, S., Bongiorno, D., Mongelli, G., Campanile, F., 2010. Linezolid resistance in staphylococci. Pharmaceuticals 3, 1988–2006.

Tsiodras, S., Gold, H.S., Sakoulas, G., Eliopoulos, G.M., Wennersten, C., Venkataraman, L., Moellerling Jr, R.C., Ferraro, M.J., 2001. Linezolid resistance in a clinical isolate of Staphylococcus aureus. Lancet 358, 207–208.

Velasco, D., del Mar Tomas, M., Cartelle, M., Beceiro, A., Perez, A., Molina, F., Moure, R., Villanueva, R., Ros, G., 2005. Evaluation of different methods for detecting meticillin (oxacillin) resistance in Staphylococcus aureus. J. Antimicrob. Chemother. 55, 379–382.