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Research Article

# Prevalence of *Staphylococcus Aureus* in External Ocular Infection and the Occurrence of Mrsa in Isolates

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## Abstract

**Background and aim:** *Staphylococcus Aureus* is an opportunist that causes ocular infection and systemic infections in the human body. This organism increases its resistance to many types of antibiotics every day and becomes more resistant, and this led to a growing concern in this era. Given this fact, the aims of this study were to determine the frequency of *S. aureus* in external ocular infections and to determine the prevalence of MRSA strains and the sensitivity of isolated *S. aureus* to antibiotics, in patients who attended selected ophthalmology clinics in major public hospitals and private clinics in the city of Sana'a - Yemen.

**Subjects and methods:** The study was conducted for a year, starting in September 2016 to October 2017, where a total of 197 patients with external eye infections were included in the study. Samples were collected and transferred to the National Center of Public Laboratories (NCPHL), in Sana'a. Possible bacterial pathogens have been isolated and identified using standard laboratory techniques. MRSA was determined by means of the disc diffusion method to 5 micrograms of methycillin disc and 1 micrograms of oxacillin disc; an antimicrobial sensitivity test was performed by means of disc diffusion method of selected antibiotics. The ocular infections include conjunctivitis, keratitis, blepharitis and blepharo-conjunctivitis.

**Results:** Of a total of 197 cultured swabs, only 146 swabs produced a positive culture (74.1%). Gram-positive bacteria formed 52.1% of the total isolates where *S. aureus* was the predominant pathogen (30.1%). The prevalence of MRSA was 34.1%. There was a higher rate of antibiotic resistance tested in MRSA isolates compared to a lower rate of resistance in MSSA.

**Conclusion:** It can be concluded, *S. aureus* was the most common bacterial isolate in external ocular infections, high rate of MRSA, the emergence of *S. aureus* isolates resistant to wide range of antibiotics have raised MRSA in ocular infections into a multi-drug-resistant, making it more and more dangerous in ocular infections. Regular surveillance of ocular associated infections and monitoring antibiotic sensitivity pattern and strict drug policy for antibiotics are recommend.

**Keywords: Antibiotic resistance; Ocular infection; MRSA; *S. aureus*; Sana'a; Yemen**

## Introduction

*S. aureus* is one of the most important isolated bacterial human pathogens. The isolated Methicillin-Resistant *S. aureus* (MRSA), which is usually resistant to other β-lactam-antimicrobial drugs, is called MRSA. MRSA, first identified in the 1960s, has traditionally been associated with health care facilities infections, but is now a dominant pathogen in community-related diseases [1]. MRSA is considered as a serious cause of morbidity and mortality worldwide with increasing prevalence, due to its multiple drug resistance, leaving limited treatment options. A series of MRSA catastrophic eye infections cases have been reported in patients after refractive surgery and cataracts surgeries [2-4]. According to the American Society of Cataract and Refractive Surgery report, MRSA bacteria replaced non-tuberculous mycobacteria as the most common pathogen causing infections after laser-assisted in situ keratomileusis [5].

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MRSA has been reported to account for 18.2% (6/33) culture-confirmed endophthalmitis in a referral vitreo-retinal practice [3]. The proportion of MRSA in ocular *S. aureus* infections of a single institution varied from 3% to 30%, with some reports showing an increase in the incidence of MRSA to 41% [6-8]. The surveillance network, which monitors patterns of sensitivity to antimicrobials for bacterial pathogens in the United States, reported an increase in the percentage of MRSA among *S. aureus* ocular infections in the USA, from 29.5% in 2000 to 71% in 2017, which showed that MRSA is an increased risk in the field of the eye [9-12].

In Yemen, the MRSA rate among *S. aureus* clinical isolates was range from 19.3% to 80% during 2015 to 2020 which is higher than the rate recorded in other regions of the world, [13-17] but the rate of eye infections due to MRSA is still unknown. Here, we performed this cross-sectional study to determine the rate of ocular MRSA infection and to determine the sensitivity of antibiotics to MRSA ocular infection by comparing those of ocular Methicillin Sensitive *S. aureus* (MSSA) infections.

## Patients, Materials and Methods

The study was conducted for a year, starting in September 2016 to October 2017, where a total of 197 patients with external eye infections were included in the study. Samples were collected and transferred to the National Center of Public Laboratories (NCPHL), in Sana'a. Possible bacterial pathogens have been isolated and identified using standard laboratory techniques.

### Data collection and processing

A questionnaire was filled out for each patient with the patient's personal and clinical data. This included age, gender, profession and relevant clinical information regarding bacterial and fungal ocular infections.

### Antimicrobial susceptibility test

Antibiotic resistance phenotypes (Methicillin/Oxacillin sensitivity test): All isolates of *S. aureus* were tested for the susceptibility to 5 µg Methicillin disc and 1 µg Oxacillin disc provided by Difco using the disk diffusion method as described by NCCLS. The resistance breakpoints were ≥ 14 mm to ≤ 10 mm for 5 µg Methicillin, and ≥ 12 mm to ≤ 10 mm for 1 µg Oxacillin. The ability of other antibiotic disc to inhibit MRSA or MSSA were estimated according to the guidelines provided by NCCLS using commercially available discs which include: Amikacin (AK, 30 µg), ceftriaxone (CRO, 30 µg), gentamicin (CN, 10 µg) ciprofloxacin (CIP, 5 µg), penicillin (P, 10U), tetracycline (TE, 30 µg), erythromycin (E, 15 µg), doxycycline (DO, 30 µg), chloramphenicol (C, 30 µg), trimethoprim-sulfamethoxazole (SXT, 1.25/23.75 µg ), and vancomycin (VA, 30 µg). The zone of inhibition produced by *S. aureus* against each antibiotic was measured and interpreted as resistant and susceptible according to standards of Clinical Laboratory and Standards Institute [18].

## Results

The positive culture rate was 74.1% (146 out of 197) and 25.9% of the specimens were negative (Table 1). Seventy-six (52.1%) were Gram positive bacteria, 70 (47.9%) were Gram negative bacteria. The most frequent microorganism isolated was *S. aureus* (44 isolates) (Table 2). The prevalence of MRSA was 34.1%. Table 3 shows the susceptibility patterns of *S. aureus* isolates towards the different commonly used antibiotics. As demonstrated above, we found that resistance to Methicillin was often accompanied by higher rates of co-resistance to other antimicrobial classes. MRSA was significantly more resistant than MSSA to Amikacin (23.3% *vs.* 4.5%), ceftriaxone (46.7% *vs.* 24.1%), gentamicin (20% *vs.* 3.4%), erythromycin (60% *vs.* 30%), ciprofloxacin (23.3% *vs.* 0.0%, and vancomycin (26.7% *vs.* 6.9%).

## Discussion

*S. aureus* are the predominant community-acquired pathogens and the main cause of hospital infection [19,20]. In part, the global spread of *S. aureus* is due to its ability to colonize the respiratory system and other epithelial and mucous surfaces effectively in healthy individuals, which act as trigger for spreading infection [21,22]. In addition, the capacity of *S. aureus* to arise resistance to multiple antibiotic classes increases the selection and expansion of epidemic antibiotic strains that can escalate in both society and hospitals, posing a serious public health threat [23]. Community-acquired Methicillin-resistant *S. aureus* (CA-MRSA), which cause mainly skin and soft tissue infections, have rapidly spread throughout the world following the first reported cases in the early sixties [1,8,9,24].

**Table 1:** Cultural results of the 197 patients with external bacterial ocular infections.

| Results | Frequency | |
|---|---|---|
| | No | % |
| Positive culture | 146 | 74 |
| Negative culture | 51 | 26 |
| Total | 197 | 100 |

**Table 2:** Distribution of bacterial isolates of external ocular infection.

| Bacterial isolates | Positive for bacterial growth N=146 | |
|---|---|---|
| | No | % |
| **Gram positive bacteria** | **76** | **52** |
| *S.aureus* | 44 | 30 |
| *Beta-haemolytic streptococcus* | 9 | 6.2 |
| *S. pneumonia* | 11 | 7.5 |
| CoNs | 12 | 8.2 |
| **Gram negative bacteria** | **70** | **48** |
| *H. influenzae* | 13 | 8.9 |
| *Pseudomonas aeruginosa* | 39 | 27 |
| *Moraxella lacunata* | 5 | 3.4 |
| *E. coli* | 11 | 7.5 |
| *Proteus spp* | 2 | 1.4 |
| Total n=197 | 146 | 74 |

Mixed infection cases were excluded.

MRSA has also become a principal cause of clinically relevant eye infections [1-8,25-27], which develops mainly in patients within the community and can lead to severe vision loss and poor outcomes for patients [28]. *S. aureus* infection, including MRSA strains, has not been well studied in Yemen. The current study represents the first study of *S. aureus* infection in ocular infections and the prevalence of MRSA among ocular *S. aureus* in Yemen. The present rate of 34.1% of MRSA in all isolates of *S. aureus* is lesser than the rate reported from Yemen in previous reports in which MRSA was isolated from 55% of health workers in Taiz, Yemen [13], and is also lower than that reported by al-Baidani and others [14] among health care workers in Al-Hodeidah, where MRSA was 86%. On the other hand, it was slightly higher than that reported by Al-Safani and others [15] (19.3%) among patients attending the military hospital in the city of Sana'a; and Alyahawi, and others among patients of some private hospitals in the city of Sana'a (17.6%) [16]. Our MRSA rate (34.1%) is lower than reported from Taiwan, where MRSA accounted for 53% to 83% of all *S. aureus* clinical isolates [29], and in the USA where MRSA accounted for 71% of isolated clinical eye infection [9]. Therefore, these data indicate that MRSA is low prevalence and with a stable percentage of MRSA infection in Yemen where other clinical studies also have indicated a low MRSA rate such as Alsafani et al. [15] (19%), and Al-Akwa'a et al. [17] (23%).

Researchers in different parts of the world have shown an increase in the occurrence of ocular MRSA, for example in the United States of America rates increase from 12% to 33% over 5 years (2000 to 2004) [7], as another researcher reported a similar increase in the rate of infections MRSA in kind from 4.1% in 1998 to 1999 to 16.7% in 2005 to 2006 to 71% in 2019 [8,9]. These results expect that MRSA could be more common than MSSA within the last feature, based on the rate of increase [30].

Although the rates of resistance to Methicillin in our population were lower than that seen among hospitalized patients elsewhere [15,7-9], approximately one third of our *S. aureus* isolates (34.1%) were resistant to this important antibiotic. Additionally, as described above, we found that resistance to Methicillin was often accompanied by higher rates of co-resistance to other antimicrobial classes; where MRSA was significantly more resistant than MSSA to Amikacin (23.3% *vs.* 4.5%), ceftriaxone (46.7% *vs.* 24.1%), gentamicin (20% *vs.* 3.4%), erythromycin (60% *vs.* 30%), ciprofloxacin (23.3% *vs.*0.0%) and vancomycin (26.7% *vs.*6.9%) although most other studies reported increased MRSA resistance strains to others antibiotics [7-9].

In the current study the resistant rate of MRSA to vancomycin was 26.7% higher than that of MSSA 6.9%, and this shows that vancomycin in MRSA is less effective. Previous studies support this finding [7,8,25]. Although vancomycin maintains extremely high efficacy against MRSA, *S. aureus* with reduced susceptibility to vancomycin was identified [30]. Because prior vancomycin use is a risk factor for MRSA with decreased vancomycin susceptibility, [31]

**Table 3:** The antibiotic sensitivity for 44 isolated MRSA and MSSA for tested antibiotics.

| Antibiotics | MRSA n=15 (34.1%) | | MSSA | | Total | |
|---|---|---|---|---|---|---|
| | Sensitive | Resistant | Sensitive | Resistant | sensitive | Resistant |
| Amikacin (30 µg) | 13(86.7) | 2(23.3) | 29(100) | 0(0.0) | 42(95.5) | 2(4.5) |
| Ceftriaxone (30 µg) | 8(53.3) | 7(46.7) | 22(75.9) | 7(24.1) | 30(68.2) | 14(31.8) |
| Chloroamphenicol (30 µg) | 7(46.7) | 8(53.3) | 16(55.2) | 13(44.8) | 23(52.3) | 21(47.7) |
| Ciprofloxacin(30 µg) | 13(86.7) | 2(23.3) | 29(100) | 0(0.0) | 42(95.5) | 2(4.5) |
| Doxycycline (30 µg) | 9(60) | 6(40) | 25(86.2) | 4(13.8) | 34(77.3) | 10(22.7) |
| Erthromycin (15 µg) | 6(40) | 9(60) | 20(70) | 9(30) | 26(59) | 18(41) |
| Gentamycin (10 µg) | 12(80) | 3(20) | 28(96.6) | 1(3.4) | 40(90.9) | 4(9.1) |
| Penicillin (30 µg) | 0(0.0) | 15(100) | 1(3.4) | 28(96.6) | 1(2.3) | 43(97.7) |
| Tetracycline (30 µg) | 10(66.7) | 5(33.3) | 20(70) | 9(30) | 30(68.2) | 14(31.8) |
| Trimethoprim-sulphamethoxazole (1.25/23.75 µg) | 8(53.3) | 7(46.7) | 24(82.8) | 5(17.2) | 32(72.7) | 12(27.3) |
| Vancomycin (30 µg) | 11(73.3) | 4(26.7) | 27(93.1) | 2(6.9) | 38(86.4) | 6(23.6) |

and no realistic evidence shows that routine vancomycin prophylaxis is effective in elective cataract surgery [32,33], it is recommended that ophthalmologists should follow guidelines of the Centers for Disease Control and Prevention [34] and the American Academy of Ophthalmology [35] against the routine use of vancomycin for prophylaxis to stop the spread of resistance.

The current study and other previous studies show that there is a risk of antimicrobial resistance, so there is a need to increase public calls for global collective action to tackle the threat, including proposing an international treaty on antimicrobial resistance. More details and attention are still needed in order to identify and measure resistance trends at the national and international levels; the idea of a global tracking system was suggested but implementation has yet to happen. A system of this type will offer insight into areas with high resistance as well as information needed to evaluate programs and other changes that have been made to fight or reverse antibiotic resistance. Yemen should also participate in several national and international monitoring programs for drug-resistant threats, including Methicillin-Resistant *S. aureus* (MRSA), Vancomycin-Resistant *S. aureus* (VRSA), Extended Spectrum Beta-Lactamase (ESBL), Vancomycin- Resistant *Enterococcus* (VRE), Multidrug-Resistant *Acinetobacter Baumannii* (MRAB) [36-38].

## Conclusion

Prevalence of S. Aureus in external ocular patients is quite high and showed resistance to commonly used antibiotics as well as carried moderate rate of MRSA. Despite these results, the sample size of this study is not sufficient and study period was too short to uncover actual picture of MRSA involved in ocular infection in Sana'a city, Yemen. Large scale studies could be done both in hospitalized patients and in community to identify prevalence of MRSA, genome analysis, identification of toxin gene and other antibiotic resistant gene.

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## Author's Contribution

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