DYNAMICS OF SENSITIVITY OF *STAPHYLOCOCCUS AUREUS* STRAINS TO ANTIBACTERIAL DRUGS

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https://doi.org/10.5281/zenodo.8395494

Abstract. *Objective: Based on the results of the reference laboratory of the Center for Antimicrobial Resistance (CAMR), to study the dynamics of resistance to antibacterial drugs in Staphylococcus aureus isolated from patients who were hospitalized for the period 2017-2021. Materials and methods: A study of 524 strains of Staphylococcus aureus was carried out using the bacteriological method of research, received by the CAMR reference laboratory from three medical institutions in Tashkent for the period from 2017 to 2021. Results: dynamics of resistance of Staphylococcus aureus strains isolated from patients did not have high resistance to all studied antimicrobial drugs. There was also a slight change in the resistance of strains based on the passage of time. Conclusions: Constant monitoring of the antibiotic sensitivity of microorganisms, carried out in hospitals, will make it possible to reasonably prescribe empirical therapy until an antibiogram of the strain is obtained.*

Keywords: *staphylococcus aureus, microbiological monitoring, antimicrobials, sensitivity, antibiotic resistance, sputum, blood, urine.*

Staphylococcus aureus is the etiological agent of more than 100 nosological forms of diseases. In Russia, according to the results of the Marathon study, the proportion of *Staphylococcus aureus* in the structure of bacterial pathogens of nosocominal infections is 11%. As an etiological factor *of Staphylococcus aureus* infections of soft tissues and skin - 43.7%, respiratory tract infections - 33.9% and bloodstream infections -12.6% [5].

In modern practice, antibacterial drugs are more often used to treat staphylococcal infections. Before the discovery of antibiotics, the mortality rate from invasive staph infections reached 90%. Antibiotics have significantly reduced mortality, but have not become a radical solution to the problem.

The inability to completely defeat an infection with antibiotics lies in a fundamental property of living matter - the same one that makes evolution possible - the ability to mutate. From an evolutionary point of view, any antibiotic is simply an unfavorable environmental factor. It does not act on a single bacterium, but on a large population in which the bacteria are not absolutely identical due to spontaneous mutations. As a rule, mutants are less viable than “normal” organisms [8].

In 2009, the Infectious Diseases Society of America identified six particularly dangerous antibiotic-resistant pathogenic bacteria, united in the ESKAPE group (these microorganisms, through the selection process, acquired the property of escaping the action of modern antibiotics), including *Staphylococcus aureus* (MRSA) [4].

The acquisition of drug resistance by microorganisms reduces the possibilities for treating the diseases that these microorganisms cause. The prevalence of this phenomenon is growing and threatens the health of both people and animals. The immediate consequences of infection with

resistant microorganisms can be serious, including longer illness, increased mortality, and longer hospitalization [2].

The main problem of antibiotic resistance *in Staphylococcus aureus* is resistant to beta-lactam antibiotics, which is often characterized by resistance to other classes of antibacterial drugs, in particular aminoglycosides, macrolides, linosalides, and fluoroquinolones [1]. The resistance of such strains to beta-lactams, as well as associated resistance to drugs of other groups, leads to the ineffectiveness of antimicrobial therapy [7].

Another reason for the ineffectiveness of treating infections with antibiotics is a strategy that many practitioners use. Often, bacteriological examination and verification of the infectious agent with subsequent testing of its sensitivity to antibiotics is not carried out. It turns out to be nonsense: treatment without diagnosis. Time is wasted, the patient suffers not only from the infection, but also from the side effects of the antibiotic [8].

Analysis of the sensitivity of microorganisms to antibacterial drugs, along with the study of changes in the occurrence of individual pathogens, is necessary in the selection of rational therapy and allows us to predict the success of the prescribed therapy [6].

Purpose: based on the results of the reference laboratory of the Center for Antimicrobial Resistance (CAMR), to study the dynamics of resistance to antibacterial drugs in *Staphylococcus aureus* isolated from patients undergoing hospital treatment for the period 2017-2021.

Materials and methods: The studies were carried out within the framework of the Cooperation Agreement between CDC and the Republican Specialized Scientific and Practical Medical Center of Epidemiology, Microbiology, Infectious and Parasitic Diseases (RSSPMCEMIPD) under project No. U 01 GH 001653-01 “Increasing the potential of the Republic of Uzbekistan to counter the problem of resistance to antimicrobial drugs."

Isolates from patients isolated from biological materials (blood, urine, sputum, pharynx and purulent discharge) were supplied to the reference laboratory of the Central Medical Research Center from pilot institutions 1 - city clinical hospital (P3), Republican Scientific and Practical Medical Center of Pediatrics (P4), Republican Scientific Center for Emergency Medical Care (P5) for the period August 2017. until July 2021 Re-identification was carried out on the basis of the protocol (Surveillance of antimicrobial resistance among pathogens of community-acquired infections in Uzbekistan), approved by the ethics committee of the Ministry of Health of the Republic of Uzbekistan. No. 04/170 dated 04/28/16 and CDC Atlanta CGHHSR 2016-101. Himedia nutrient media (India) and discs with antimicrobial agents produced by Liofilchem (Italy) were used.

Sensitivity and interpretation of AST results to antimicrobial drugs was carried out using the disk diffusion method using the guidelines of the European Committee for Antimicrobial Susceptibility Testing (EUCAST 2017, 2018, 2019, 2020, 2021). The sensitivity of all strains to 8 antibacterial drugs was determined: cefoxitin (FOX), ciprofloxacin (CIP), levofloxacin (LVX), erythromycin (ERY), clindamycin (CLI), linezolid (LNZ), rifampicin (RIF). Reference strains *of Staphylococcus aureus* were used in this work ATCC 25923

The obtained sensitivity results were processed using the WHONET program.

Results and their discussion: From August 2017 to June 2021, 524 strains from blood, sputum, pharynx, cerebrospinal fluid, urine and purulent discharge of *Staphylococcus aureus* were received at the Center for Further Study, from three multidisciplinary hospitals. Of these, 86 strains were received in 2017; 2018 - 164 strains; 2019 - 136 strains; 2020 - 87 strains; 2021 - 51 *Staphylococcus aureus* strains.

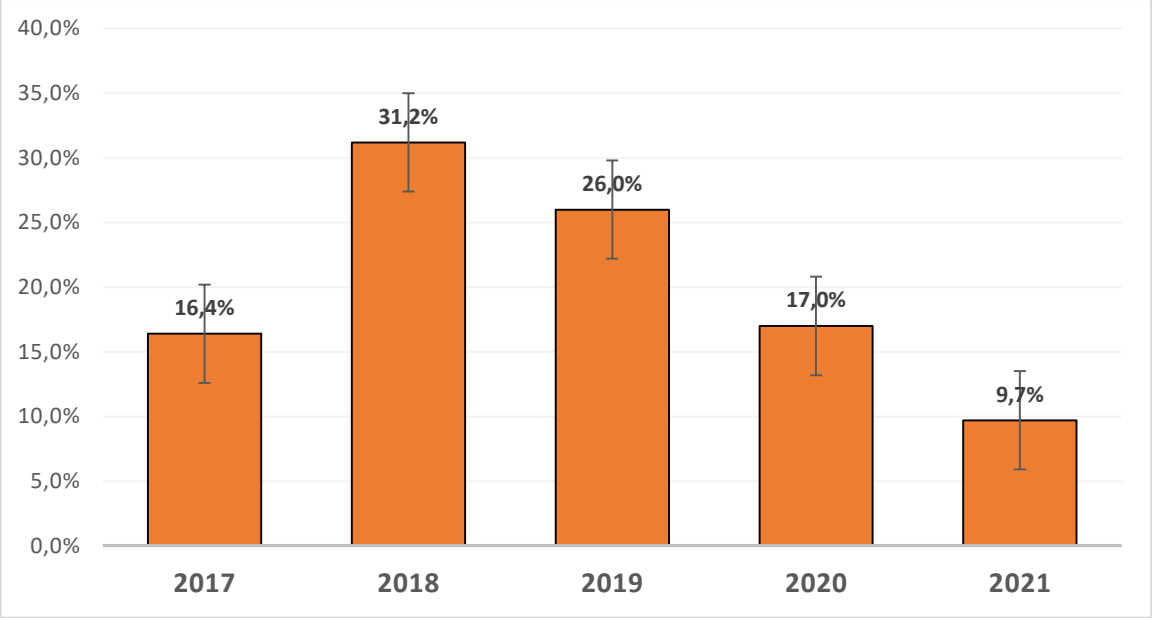

Fig. 1 Revenue dynamics Staphylococcus aureus to the reference laboratory (n =524)

Analysis of the sensitivity profiles of *Staphylococcus aureus* strains to antimicrobial drugs isolated from patients in hospitals, showed a high level of sensitivity to linezolid 99.0% and rifampicin 98.6%. The isolates had resistance rates to cefatoxitin, which amounted to 21.9%, to the fluoroquinolone class, ranging from 6.7%-8.0%, to erythromycin, 22.0%, while to clindamycin, 19.2% (Figure 1).

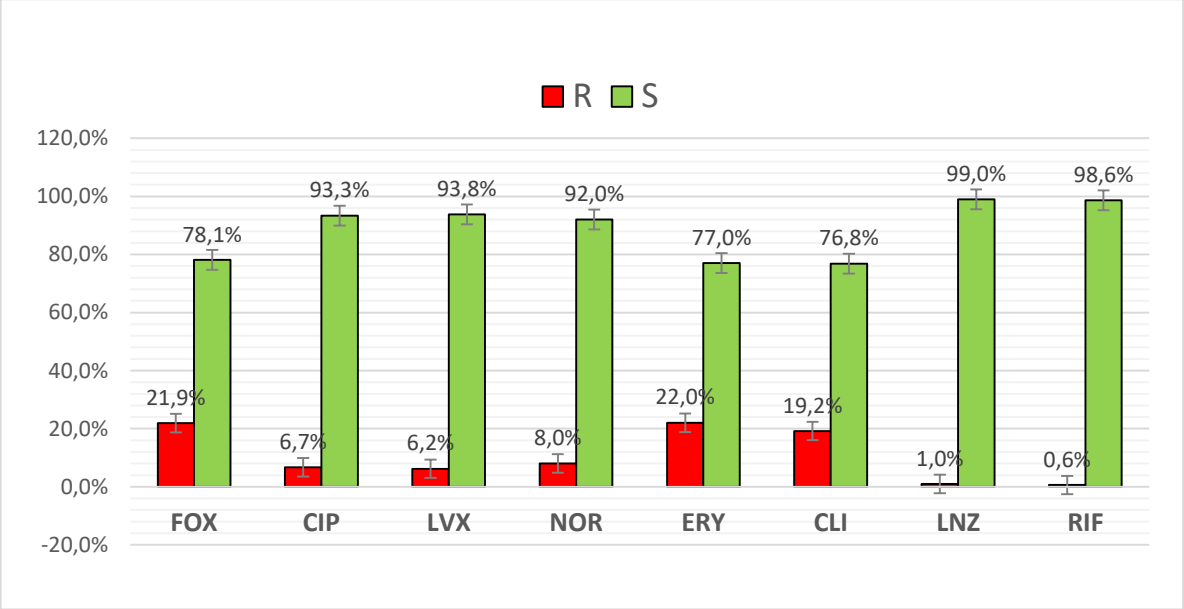

Fig.2 Susceptibility profile of Staphylococcus aureus strains to antimicrobials

Laboratory identification of the MRSA phenotype is based on the use of the marker antibiotic cefoxitin, which is more sensitive than oxacillin.

To determine the incidence of MRSA in hospitals in Tashkent, we analyzed data on the resistance of *Staphylococcus aureus* strains We analyzed the dynamics of resistance of *Staphylococcus aureus* strains to the drug cefoxitin allocated in the period 2018-2021. (Fig. 3),

which showed that the greatest resistance was observed in 2020, amounting to 31.8%, while in 2021 it showed insignificant resistance of strains (9.8%).

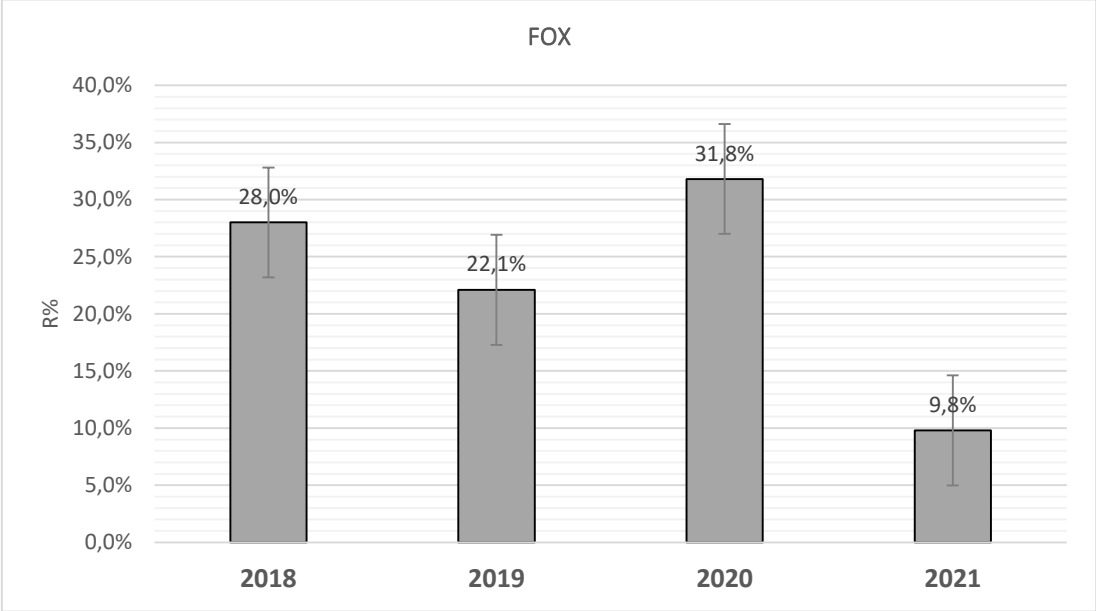

Fig 3. Dynamics of strain resistance to cefoxitin

A study of the dynamics of resistance of the marker antibiotic cefoxitin shows variation. This suggests that it is necessary to monitor the level of sensitivity, which is an important element in developing a strategy for rational antibacterial therapy.

Infections caused by MRSA are of great medical and social importance, as they are accompanied by higher mortality and require greater material costs for treatment [5].

Due to the fact that statistics on the consumption of antibiotics in Uzbekistan showed the widespread use of antimicrobial drugs of the fluoroquinolone series. Next, we analyzed the dynamics of resistance to fluoroquinolone antibacterial drugs. As can be seen from Fig. 5, the highest resistance rates were shown in 2020 (10.8%) and 2021 (10.3%),

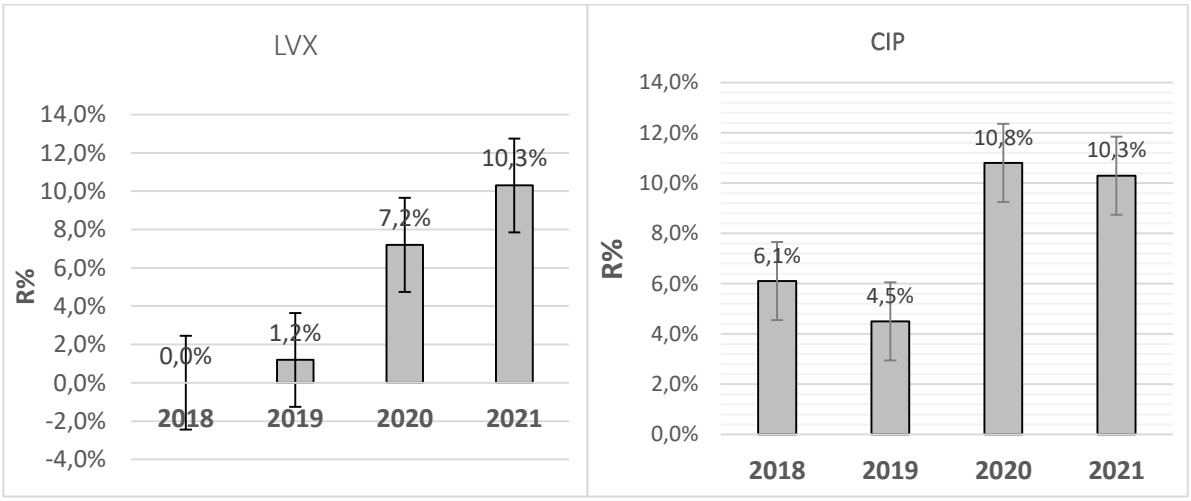

Fig 4. Dynamics of resistance strains to antibacterial drugs of the fluoroquinol series

Linezolid is the first drug from the oxazolidinone group with high activity against gram-positive flora.

According to studies, linezolid has greater clinical and microbiological efficacy compared to vancomycin in the treatment of various diseases caused by MRSA [3].

In this regard, an analysis of the dynamics of linezolid resistance was carried out; as the results showed, over time, a low proportion of isolates resistant to this antibiotic remains, so in 2020 it was 3.5%, while in 2021 it was 0.0%.

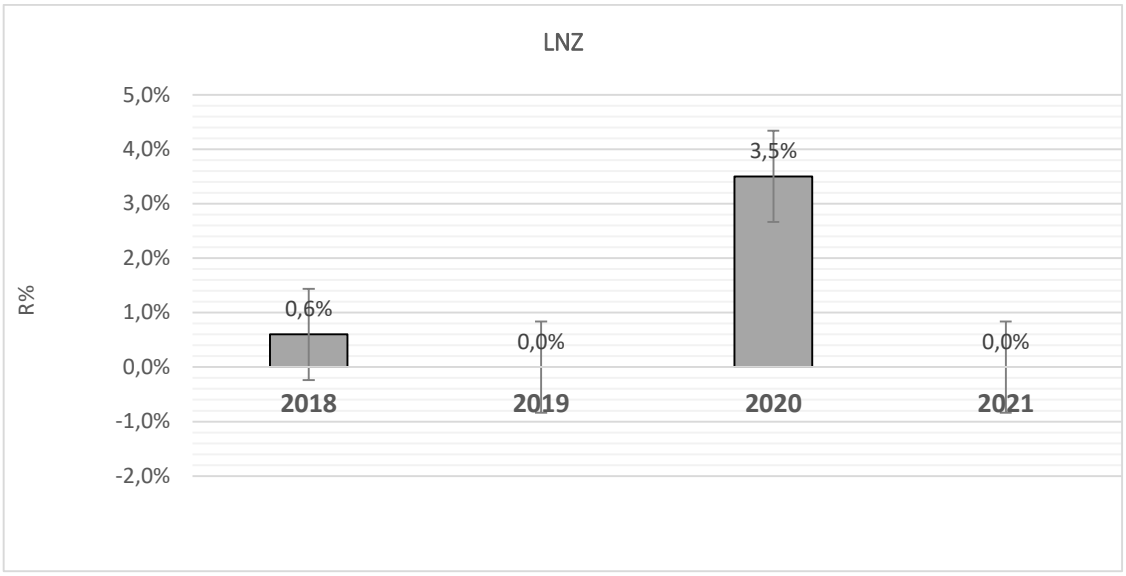

Figure 5. Dynamics of resistance of strains to linezolid

The data we obtained on the dynamics of resistance to macrolides correlates as follows: among strains of *Staphylococcus aureus* isolated from three hospitals in the city of Tashkent in the period from 2018-2021, the proportion of strains resistant to macrolides varied depending on the year of admission, so for erythromycin it was from 22.0% to 24.7% to clindamycin from 15.2% to 23.1%.

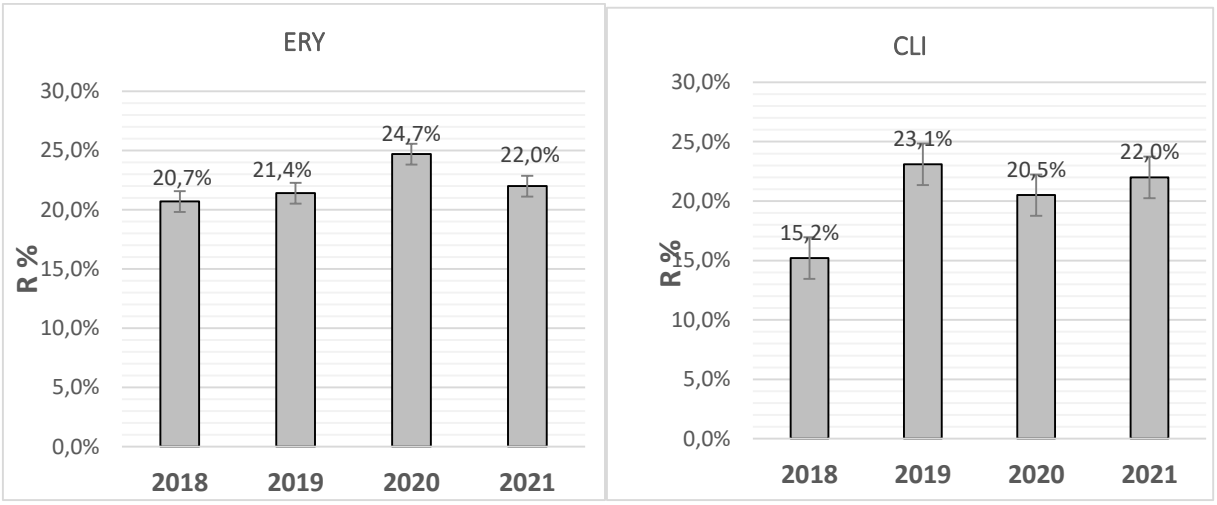

Figure 6. Dynamics of resistance of strains to macrolides

The development of resistance of staphylococci to clindamycin occurs rather slowly and gradually. Clindamycin, like lincomycin, exhibits dissociated cross-resistance to erythromycin.

The present study showed that the dynamics of resistance of *Staphylococcus aureus* strains isolated from patients were not highly resistant to all antimicrobial drugs. There was also a slight change in the resistance of the strains based on the passage of time.

Conclusion: The study thus conducted reflects the current state of the level of antibiotic sensitivity of *Staphylococcus aureus* circulating in the territory of Tashkent. Despite the seriousness of infections caused by *Staphylococcus aureus,* the level of resistance is not that critical.

Constant monitoring of the antibiotic sensitivity of microorganisms carried out in hospitals will make it possible to reasonably prescribe empirical therapy before obtaining an antibiogram of the strain.

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