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Staphylococcus saprophyticus Antibiotic resistance isolation from chronically urinary tract patients

Zainab Noori Hammed¹, Tareq Abdulrazzaq Alabdli², Safa Naji Alkaissy³, Kareem A. Hammadi⁴ ¹ AlHikma University College, Baghdad, Iraq. <u>zainab.nuri@hiuc.edu.iq</u> ² AlHikma University College, Baghdad, Iraq. <u>tariq.abd@hiuc.edu.iq</u> ³ AlHikma University College, Baghdad, Iraq. <u>Alkaissysafa@gmail.com</u> ⁴ AlHikma University College, Baghdad, Iraq. <u>kareem.hammady@hiuc.edu.iq</u>

Abstract :

The bacterium *Staphylococcus saprophyticus* is one of the common bacterial species in urinary tract patients. Seven isolates of this bacterium were diagnosed from the study population of fifty patients suffering from chronic urinary tract infections, men and women, with an average age of 20-50 years. The degree of sensitivity to vancomycin was 100% (zero resistance), tetracycline (85.7%), chloramphenicol (71.4%), cefaxitin (71.4%), while it was 100% resistant to oxacillin (zero sensitivity) and (57.1%) to erythromycin. The aim of the presenttraining is to find out the degree of sensitivity and resistance to *Staphylococcus saprophyticus* in chronically patientswith infectionsurinary tract. study concluded that the use of vancomycin in the administration of chronically infections with urinary tract for infected patients with *staphylococci saprophyticus* is the first against such an infection. On the contrary, we found that oxacillin is the most antibiotic resistant in these patients, which indicates that this bacterial type has overcome oxacillin.

Introduction :

S.saprophyticus is a coagulase-negative ,non-hemolytic Gram-positive, that is a communal source of unfussy infections in urinary tract (UTIs), predominantly inactively sexualof youngwomen. Often, it causes complications such as acute pyelonephritis, epididymitis ,urethritis and prostatitis. S.saprophyticus is share of the usual human microorganism(m.o) that lives in therectum, urethra, perineum, digestive tract and cervix,. It was likewise commonly present in the digestive tract of cattle and pigs by S. saprophyticus, therefore can be transmitted to individualsby the consumption of these products. (1,2). Patients with nosocomial UTIs, the young, pregnancy patients, and those with catheterization urinary bladder have an improvedoccurrence and colonization of S. saprophyticus. Males have a lesseroccurrence of S. saprophyticus infections. Overall possibility reasons for UTIs comprise the past of repeated UTIs, womanly sex, latest sexuallycontact, neurogenic bladder, pregnancy, benign prostatic hypertrophyand indwelling catheter (3,4).S. saprophyticusis stimulated by diversestyles of adhesives, likehemagglutinins with selfdestructive and adhesion possessions, and surface-attached lipases form fimbriae-like surface attachments that help bacteria maintainer strong adhesion to host surfaces. This greatcapacitycolonization of S. saprophyticus to the urinary tract is due in part to adhesions that allow the organism to inhabit the urinary epithelium with urease, resulting in severe S. saprophyticus infection. fold in antibiotic tolerance compared to non-biofilm-forming isolates (5). Inopportunely, UTIs are usually cured with broadspectrum antibiotics without a culture or sensitivity test. This unsuitable use of antibiotics has led to an increase in resistance to antibiotics, caused to the emergence of multidrug-resistant pathogenic bacteria. Changes in resistance of antibiotic have been reported in urological aetiologies. (6,7). Antibiotics are the substances used to kill or stop the growth of microbes and can be considered miraculous drugs in treatment of infectious diseases, but the increasing use of antibiotics in humans and animals has led to the development of antimicrobial resistance (10).A previous study showed biofilm establishment in Staphylococcus spp. It be contingent on the adhesive intracellular polysaccharide (PIA), whose is facilitated by the ica operonbiosynthesis. This operon encompasses the icaADBC genes and the icaR regulatory gene that is copied in the opposite route of the operon (ica). In the occasion of the icaR gene, some trainings have shown that its creationrepressor of transcriptional that shows an Adaptation part in regulating the expression of the operon (ica) depending on conservational environments. Various features such as growth anaerobically, the occurrence of antimicobial at sub-inhibitory meditations, and conservational stresses such as great osmolality can riseof operon(ica) expression. Adding to PIA,

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Staphylococcus spp. highlighted such as DNA and proteins (8,9). The species of Staphylococcus can arrangement biofilms reliant on polysaccharide intercellular adhesin (PIA), produced by operon(*ica*) (11). Biofilms can limit the system of host protectionaccess to *staphylococci* and reduce the effectiveness of antibiotics. In addition, conjugation can occur in staphylococcal cells at higher levels than planktonic cells in biofilms formation (12). Examination of 169 S. saprophyticusstraining showed that 70% of strains were able to a biofilm arrangement. Furthermore, formation of biofilm increased resistant to five antimicrobial (vancomycin, trimethoprim/sulfamethoxazole,oxacillin, norfloxacin and ciprofloxacin) approximately 32-fold(13). The capability of S. saprophyticus to effect infection may be related to urease as virulence factors (14,15), surface proteins([16) and protein D-serine deaminase (DsdA) (17). Were the first virulence factor is urease designated in S. saprophyticus. Trainings withinhibitor of urease have shown that reticence of urease action can deferral the growth of *S.saprophyticus* qualified analysis using a genome-wide method shows that S. saprophyticuslacks several other adhesion proteins and virulence factors when compared to other thrombus-negative Staphylococcus strains. Explains the differences at the clinical level (18). Additionalessential virulence factor for s. saprophyticus is the protein D-serine deaminase (DSDA), which is found in urine and actions as a bacteriostatic. A mutation in the DSDA gene shows attenuated virulence when examin to a rat model. The environs receives and transmits plasmids that can conveneresistance to antibiotic (19,20). Even though S. saprophyticus can transmitnumerous resistance genes, almost trainingscomprise this in a coagulase-negative organism set or work with a small number of models([21–22), and resistantelements in isolation are infrequently identified. Intelligences of genitourinary microbiotarelated with UTIs by this motime back to the 1980s (23)Consequently, there is no latestindication of such colonization by human microorganisms.Despite concerns about most infections by S. saprophyticus can easily extent in the surroundings. In addition, S. saprophyticus exhibits transient stability and may exhibit resistant to the cassettes of other types, as 93% of Brazilian isolates have resistance to ermC,msrBmsrA, linAand mphC erythromycin cassettes. (26).

Materials and methods

The current study includes 50 urine samples from patients suffering from chronic UTI taking into account the patient's consent, according to the specifications and instructions of scientific research ethics. The urine sample was collected according to international laboratory standards (25) in a sterile container was prepared for this purpose. To confirm *S. saprophyticus* infection, S. colonies were detected after culturing on blood agar and mannitol salt agar, testing for , trehalose, sucrose, xylose, novobiocin, nitrate reduction ,hemolysinand urease [26].

The Result:

Seven(14%) of *S. saprophyticus* were isolated from 50 urine samples, as the study population consisted of (38(76%) females and 12(24%) men) in the average age ranged between 20-50 years. The number of *S. saprophyticus* isolates was 5 (71%) females and 2(29%) men. The study found that the highest antibiotic resistance is for Oxacillin while the highest sensitivity. It is for vancomycin and according to Table (1).

| Antibiotics | Sensitivity % | Resistance % | | |
|--------------|---------------|--------------|--|--|
| vancomycin | 7(100%) | 0 | | |
| cefaxitin | 5(71.4%) | 2(28.5%) | | |
| tetracyclin | 6(85.7%) | 1(14.2%) | | |
| gentamycin | 4(57.1%) | 3(42.8%) | | |
| Erythromycin | 3(42.8%) | 4(57.1%) | | |

| Table(1):Antibiotic resist | ance and sensitivit | tv of S. sa | aprophyticus | with their | percentage. |
|----------------------------|---------------------|-------------|--------------|------------|-------------|
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| Chloramphenicol | 5(71.4%) | | 2(28.5%) | | |
|------------------------------------|-----------|-----------|-----------|-----------|--|
| Trimethoprim- sulphamethoxazole | 4(57.1%) | | 3(42.8%) | | |
| oxacillin | 0 | | 7(100%) | | |
| Std err =0.47 | Mean=4.85 | Sted=1.24 | Mean=2.14 | Sted=1.24 | |



figure(1): The number of S. saprophyticus according to their antibiotic resistance and sensitivity.

Discussion :

The survival rate of S. saprophyticus is high in the urinary tract is believed to be owing in portion to the binding of cell wall adhesives, which, together with urease, allow the organism to efficiently attach and colonize the urinary epithelium, resulting in sustained growth and infection. The colonization of Bacterial in the bladder and ureteral epithelium by S.Saprophyticushappens through diversekinds of adhesives. These comprisehemagglutinins that self-destruct and have adhesive features, in addition to surface-bound lipases that surface fimbriae-like appendages that assistance bacteria conserverobust adhesion to these surfaces(27). The current results showed that the number of isolation in women is more than in men and this is compatible with (28,29,30,31). This organism is one of most common source of unfussy UTIs, particularly in women sexually active. UTIs are further communal in females than in males due to their structuralvariances: the expanse between the the urethra and anus with the narrowing of the urinary area(32). The present study showed that *staphylococci saprophyticus* was 100% sensitive to vancomycin, which is consistent with(40)Who found that vancomycin is the first choice for treatment of Gram-positive bacterial species. The formation of biofilm increases the resistance of some antibiotics such as oxycillin, trimithoprim/sulfamithoxazole,Biofilms can decreasecontact of the host protectioncoordination to Staphylococcus and weaken antibiotic achievement(33). The mechanism of resistance to Trimethoprine can be explained either by the presence of genes carried on the plasmid, as this plasmid provides the bacterial cell with a new metabolic enzyme that is insensitive to the antigen, which replaces the chromosomal enzyme, so the bacterial cell will continue in the pathway, and either by the presence of biochemical transposons, in the presence of this drug, which leads to the production of folic acid(37). The anti-Erythromycin, which belongs to the group of macrolides, which was resisted by the bacterial isolates under study in different proportions. The mechanism of resistance occurs either by changing the target

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site of the antibody binding to the ribosome, which leads to reducing the binding of the antibody, or by the production of enzymes that act on the esterification of the antibiotic, such as the Er esterase enzyme(38,39). Therefore, biofilms represent the main existencestratagems of these microorganisms, which describes why biofilms are important for public health. In addition, the closeness of cells within or between small colonies delivers an tremendousenvirons for the conversation of genetic elements. The conjugation mechanism, that is, the transmission of plasmids between bacteria, is more common among bacterial cells in biofilms than among planktonic cells(34). The World Financial Forum has described antibiotic resistant as ainternational threat that no single country or organization can eradicate or control(35). Antimicrobial resistant occurs when bacteria acclimate and propagate in the occurrence of these antibiotics. The improvement of this phenomenon is associated with the frequent use of antibiotics. For the reason that numerous antibiotics be appropriate to the similar drug class, resistant to a particular antimicrobial can chief to resistant in a linked class that spreads quickly and may not spread completely. In fact, resistance that occurs in an organism or at a genetic locus can also be predicted, for example, by the altercation of genetic elementsamongdiverse bacterial species and may influence antimicrobial therapy for different diseases and infections. bacteria have Drug-resistant can spread among animalsand humans viawater, food and the environment. Human and animal smuggling, migration and migration affect transmission. bacteria have Antibiotic-resistant can be present in animals from which nutrition is obtained and in foodstuffs intended for human consumption(36).

Conclusions

The current study concluded that the use of vancomycin in the management of chronically infections in urinary tract for infected patients with *staphylococci saprophyticus* is the first against such an infection. On the contrary, we found that oxacillinis the most antibiotic resistant in these patients, which indicates that this bacterial type has overcome oxacillin.

References

- 1. Argemi X, Hansmann Y, Prola K, Prévost G. Coagulase-Negative Staphylococci Pathogenomics. Int J Mol Sci. 2019 Mar 11;20(5)
- Pinault L, Chabrière E, Raoult D, Fenollar F. Direct Identification of Pathogens in Urine by Use of a Specific Matrix-Assisted Laser Desorption Ionization-Time of Flight Spectrum Database. J ClinMicrobiol. 2019 Apr;57(4).
- 3. Flores-Mireles AL, Walker JN, Caparon M, Hultgren SJ. Urinary tract infections: epidemiology, mechanisms of infection and treatment options. Nat Rev Microbiol. 2015 May;13(5):269-84.
- 4. Becker K, Heilmann C, Peters G. Coagulase-negative staphylococci. ClinMicrobiol Rev. 2014 Oct;27(4):870-926.
- Martins, K. B., Ferreira, A. M., Pereira, V. C., Pinheiro, L., Oliveira, A. D., & Cunha, M. D. L. R. D. S. D. (2019). In vitro effects of antimicrobial agents on planktonic and biofilm forms of Staphylococcus saprophyticus isolated from patients with urinary tract infections. *Frontiers in Microbiology*, 10, 40.
- 6. Ahmed S.S., Shariq A., Alsalloom A.A., Babikir I.H., Alhomoud B.N. Uropathogens and their antimicrobial resistance patterns: relationship with urinary tract infections. *Int J Health Sci.* 2019;13:48.
- 7. 24. Paul R. State of the globe: rising antimicrobial resistance of pathogens in urinary tract infection. *J Glob Infect Dis.* 2018;10:117.
- 8. Li, H., Wang, J., Wen, Y., Vuong, C., Otto, M., and Gao, Q. (2005). Conversion of *Staphylococcus epidermidis* strains from commensal to invasive by expression of the ica locus encoding production of biofilm exopolysaccharide. *Infect. Immun.* 73, 3188–3191. doi: 10.1128/IAI.73.5.3188-3191.2005.
- Mendoza-Olazarán, S., Morfín-Otero, R., Villarreal-Treviño, L., Rodríguez-Noriega, E., Llaca-Díaz, J., Camacho-Ortiz, A., et al. (2015). Antibiotic susceptibility of biofilm cells and molecular characterisation of *Staphylococcus hominis* isolates from blood. *PLoS One* 10:e0144684. doi: 10.1371/journal.pone.0144684.
- 10. WHO. *Global strategy for containment of antimicrobial resistance*. 2001.

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- 11. Li, H., Xu, L., Wang, J., Wen, Y., Vuong, C., Otto, M., &Gao, Q. (2005). Conversion of Staphylococcus epidermidis strains from commensal to invasive by expression of the ica locus encoding production of biofilm exopolysaccharide. *Infection and immunity*, *73*(5), 3188-3191.
- Águila-Arcos, S., Álvarez-Rodríguez, I., Garaiyurrebaso, O., Garbisu, C., Grohmann, E., &Alkorta, I. (2017). Biofilm-forming clinical Staphylococcus isolates harbor horizontal transfer and antibiotic resistance genes. *Frontiers in microbiology*, 8, 2018.
- Martins, K. B., Ferreira, A. M., Pereira, V. C., Pinheiro, L., Oliveira, A. D., & Cunha, M. D. L. R. D. S. D. (2019). In vitro effects of antimicrobial agents on planktonic and biofilm forms of Staphylococcus saprophyticus isolated from patients with urinary tract infections. *Frontiers in Microbiology*, 10, 40.
- 14. Gatermann, S. O. R. E. N., John, J. O. R. G., & Marre, R. E. I. N. H. A. R. D. (1989). Staphylococcus saprophyticus urease: characterization and contribution to uropathogenicity in unobstructed urinary tract infection of rats. *Infection and immunity*, *57*(1), 110-116.
- 15. Loes, A. N., Ruyle, L., Arvizu, M., Gresko, K. E., Wilson, A. L., &Deutch, C. E. (2014). Inhibition of urease activity in the urinary tract pathogen Staphylococcus saprophyticus. *Letters in applied microbiology*, *58*(1), 31-41.
- 16. Gatermann, S., Meyer, H. G. W., Marre, R., &Wanner, G. (1993). Identification and characterization of surface proteins from Staphylococcus saprophyticus. *ZentralblattfürBakteriologie*, 278(2-3), 258-274.
- 17. Korte-Berwanger, M., Sakinc, T., Kline, K., Nielsen, H. V., Hultgren, S., &Gatermann, S. G. (2013). Significance of the D-serine-deaminase and D-serine metabolism of Staphylococcus saprophyticus for virulence. *Infection and immunity*, *81*(12), 4525-4533.
- 18. Argemi, X., Hansmann, Y., Prola, K., & Prévost, G. (2019). Coagulase-negative staphylococci pathogenomics. *International journal of molecular sciences*, 20(5), 1215.
- 19. Lee, J. H., Heo, S., Jeong, M., &Jeong, D. W. (2019). Transfer of a mobile Staphylococcus saprophyticus plasmid isolated from fermented seafood that confers tetracycline resistance. *PLoS One*, *14*(2), e0213289.
- 20. Sousa, V. S. D., da-Silva, A. P. D. S., Sorenson, L., Paschoal, R. P., Rabello, R. F., Campana, E. H., ... & Moreira, B. M. (2017). Staphylococcus saprophyticus recovered from humans, food, and recreational waters in Rio de Janeiro, Brazil. *International Journal of Microbiology*, 2017.
- 21. Sousa, M., Silva, N., Igrejas, G., Silva, F., Sargo, R., Alegria, N., ... &Poeta, P. (2014). Antimicrobial resistance determinants in Staphylococcus spp. recovered from birds of prey in Portugal. *Veterinary Microbiology*, *171*(3-4), 436-440.
- 22. Dubin, D. T., Fitzgibbon, J. E., Nahvi, M. D., & John, J. F. (1999). Topoisomerase sequences of coagulase-negative staphylococcal isolates resistant to ciprofloxacin or trovafloxacin. *Antimicrobial Agents and Chemotherapy*, *43*(7), 1631-1637.
- 23. Jordan, P. A., Iravani, A., Richard, G. A., & Baer, H. (1980). Urinary tract infection caused by Staphylococcus saprophyticus. *Journal of Infectious Diseases*, *142*(4), 510-515.
- 24. Korte-Berwanger, M., Sakinc, T., Kline, K., Nielsen, H. V., Hultgren, S., &Gatermann, S. G. (2013). Significance of the D-serine-deaminase and D-serine metabolism of Staphylococcus saprophyticus for virulence. *Infection and immunity*, *81*(12), 4525-4533.
- 25. Code Implementation Support Program(2021). Guidelines for Sample Collection. Version1.
- 26. Mahon, C. R., Mt, M. S., & Lehman, D. C. (2022). *Textbook of diagnostic microbiology-e-book*. Elsevier Health Sciences.
- 27. Ehlers S. and Merrill S. A.(2022). *Staphylococcus Saprophyticus*. Kingman Regional Medical Center.
- 28. Gupta, K., Hooton, T. M., Wobbe, C. L., &Stamm, W. E. (1999). The prevalence of antimicrobial resistance among uropathogens causing acute uncomplicated cystitis in young women. *International journal of antimicrobial agents*, *11*(3-4), 305-308.
- 29. Bennett J. E. MD, (2020) in Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, Staphylococcus epidermidis and Other Coagulase-Negative Staphylococci.

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ISSN NO: 2230-5807

- 30. Argemi, X., Hansmann, Y., Prola, K., &Prévost, G. (2019). Coagulase-negative staphylococci pathogenomics. *International journal of molecular sciences*, *20*(5), 1215.
- 31. Hashemzadeh M, Dezfuli AAZ, Nashibi R, Jahangirimehr F, Akbarian ZA. Study of biofilm formation, structure and antibiotic resistance in *Staphylococcus saprophyticus* strains causing urinary tract infection in women in Ahvaz, Iran. New Microbes New Infect. 2020 Dec 17;39:100831. doi: 10.1016/j.nmni.2020.100831. PMID: 33489239; PMCID: PMC7807165.
- 32. Farzam, K., & Tivakaran, V. S. (2020). StatPearls [Internet].
- 33. Silva, K. C. S., Silva, L. O. S., Silva, G. A. A., Borges, C. L., Novaes, E., Paccez, J. D., Fontes, W., Giambiagi-deMarval, M., Soares, C. M. de A., &Parente-Rocha, J. A. (2020). Staphylococcus saprophyticus Proteomic Analyses Elucidate Differences in the Protein Repertories among Clinical Strains Related to Virulence and Persistence. *Pathogens*, 9(1), 69. https://doi.org/10.3390/pathogens9010069.
- Águila-Arcos, S., Álvarez-Rodríguez, I., Garaiyurrebaso, O., Garbisu, C., Grohmann, E., &Alkorta, I. (2017). Biofilm-forming clinical Staphylococcus isolates harbor horizontal transfer and antibiotic resistance genes. *Frontiers in microbiology*, 8, 2018.
- 35. Howell L Ed. Global risks 2013:eighth edition. Geneva, World Economic Forum, 2013.
- 36. World Health Organization(2012). global strategy for the surveillance and monitoring of HIV drug resistance. Geneva.
- 37. . Wood ,A.J.(1996). Antimicrobial Drug resistance .The New England .J.Med .35:210-215.
- 38. Hugo, W. B. and Russell, A. D. (1987). Pharmaceutical microbiology. 4th ed. Churchill Livingstone. London.
- 39. Westh, H.; Knudesen, A. M.; goth, A. and Rosdah, V. T. (1991). Evaluation of Staphylococcus aureus resistance to Erythromycin in Denmark 1959 and 1988 comparison with Erythromycin susceptible strains. J. Hosp. Infect., 18: 23-34.
- 40. Chen, KJ., Sun, MH., Hou, CH. *et al.* Susceptibility of bacterial endophthalmitis isolates to vancomycin, ceftazidime, and amikacin. *Sci Rep* **11**, 15878 (2021). https://doi.org/10.1038/s41598-021-95458-w.