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ANTIBIOTIC RESISTANCE OF SOME BACTERIAL ISOLATE ASSOCIATED WITH HEMODIALYSIS PATIENTS

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ABSTRACT

Background the Aim of the study was diagnosis of metastatic infection and Antibiotic Susceptibility Testing (AST) of microorganism that isolated from hemodialysis patients. **Method-** This study was conducted in December (2022) to April (2023), in Karbala city. where the study conducted on one hundred (100) participants including 70 patients that undergoing hemodialysis (40 males,30 female), 30 control (12 males ,18 female), All of the groups' ages were included in this study, blood take from patient via the central venous catheter and was transferred to a blood culture bottle for cultivating. **Result-**85.7% from *Staphylococcus epidermidis* resistant to Ammoxillin and 14.3% of *Staphylococcus epidermidis* resistant and to, cefotaxime, ceftriaxone, Meropinime, clindamycin, 100%*Staph. aureus* resistant to Ammoxillin 80% resistant to Ceftriaxone, 60 %resistant to gentamycin, 40%resistant to cefotaxime, 20% resistant to, Meropenem, 80% of *Staphylococcus hominis* resistant to Ammoxillin ,60%, resistant to gentamycin, ceftriaxone 40% resistant to cefotaxime, 20% resistant to piperacillin/Tazobactam, 100% *E. coli* resistant to Cefotaxime, Ammoxillin 66.7% resistant to Ceftriaxone, clindamycin, 33.3% resistant to Gentamycin. **Conclusion** All gram positive bacterial species that isolated from hemodialysis patient resistant to amoxicillin and sensitive to Imiepeneme, while 100% E coli are resistant to amoxicillin and cefotaxime and sensitive to piperacillin/Tazobactam

KEYWORDS: Hemodialysis, bloodstream infections, Antibiotic resistance.

INTRODUCTION

Patients with end-stage renal illness are in critical need of renal replacement therapy, Dialysis is one of replacement therapy has several problems,one of these problem was bloodstream infections (BSIs), that constitute is the second largest cause of death in end-stage renal disease patients, the risk of infection is often related with the dialysis technique itself, notably the type of vascular access.[1]

Patients receiving hemodialysis have a higher risk of getting bloodstream infections because of their compromised immune systems, protracted exposure to invasive medical equipment, and frequent use of antibiotics. Pathogens such as bacteria, viruses, and fungi can all cause bloodstream infections in hemodialysis patients.[2]

In hemodialysis patients, *staphylococci*, such as coagulase-negative *staphylococci* and *Staphylococcus aureus*, are the most frequent bacterial causes of bloodstream infections. Gram-negative bacteria including *Escherichia coli*, *Klebsiella pneumonia*, and Pseudomonas aeruginosa are some more prevalent pathogens.[3]

Antibiotic resistance has been linked to the development of superbugs, which are strains of bacteria that are able to withstand treatment with antibiotics.[4] Antibiotic resistance is globally recognized as a threat to the health of humans because it renders treatment of microbial infections more difficult, increases the risk of disease spread and degree of severity, and these Antibiotic-resistant pathogens cost billions of dollars in healthcare.[5]

There are three categories of bacteria that show signs of resistance to multiple classes of antimicrobial drugs.

- Microorganisms with multidrug resistance (MDR) have developed immunity to at least one antibiotic from three or more different classes.
- Extremely resistant microorganisms (XRMs) are bacteria that have developed resistance to all but two or fewer types of antibiotics.
- PDR refers to microorganisms that are resistant to all agents in all antimicrobial classifications.[6]

Drug inactivation (which is typically characterized by an irreversible cleavage catalyzed by an enzyme), alteration of the antibiotic linking site, and minimized storage of the drug as a result of either reduced membrane permeability or increased drug efflux are the mechanisms that contribute to antimicrobial resistance. It is possible for bacteria to pass on the gene that is responsible for a particular resistance mechanism to bacteria that also carry genes for other resistance mechanisms. This can lead to species that are resistant to several drugs, which is the fundamental cause of the current problem with our public health. During this process, resistance genes can be acquired by a bacterium in one of three different ways: either directly from the environment (transformation), from another bacterium in the form of plasmids (conjugation), or through phages (transduction).[7]

Medical technologists (clinical laboratory scientists) perform antimicrobial susceptibility testing (AST) to determine what antimicrobial therapy is most effective for individual patients and to prevent the inappropriate emergence of resistant pathogens in those who are ill. AST can help identify bacteria that are of great importance to infection prevention and control, including *Staphylococcus aureus* that is resistant to methicillin carbapenemase-producing Enterobacteriaceae, broader range lactamase producers, and vancomycin-resistant *enterococci.* AST also helps identify wider range lactamase producers, carbapenemase-producing Enterobacteriaceae. Epidemiological research focusing on the genesis and dissemination of resistance rely heavily on AST to measure resistance incidence and prevalence.

METHODS

Study design and Subjects Groups

This case-control research was carried out in the dialysis unit in Imam Hussein Teaching Hospital All of patients were registered with hemodialysis from December (2022) to April (2023).

One hundred (100) participants were enrolled in this study including 70 patient (40 male, 30 female), 30control (12 male, 18 female), All of the groups' ages range from 10 to 80 years

Inclusion Criteria

All case in hemodialysis center diagnosis with have fever, chill, healthy people included in this study.

Exclusion Criteria

Individuals who have an autoimmune condition, diabetic mellitus and patients who are already taking antibiotics are not eligible to participate in this study.

Ethical Approval

Samples for this study were collected from patients undergoing dialysis at the Karbala Health Directorate after getting the requisite approval from the hospital administration and the patients.

Statistical analysis

Data analysis has been done statistically utilizing IBM SPSS statistical packages version 23, the analysis outcomes have been summarized using descriptive statistics, utilize cross tabulation in data analysis.

Blood Sample collection

5ml of blood were collected for patient groups and control group for patient via the central venous catheter and was transferred to a blood culture bottle for cultivating

Bacteriological sampling

The samples were plated onto several culture medium, including blood agar, MacConkey, and brain heart infusion broth enrichment media, and then incubated at 37 degrees for 24-48 hrs., The isolated bacteria were identified based on their morphological and microscopic features. confirmation of bacterial type using automated VITEK2. After culturing of samples, the growth positive bacterial growth was tested for antibiotic susceptibility test using Disk diffusion method Antibiotic susceptibility test of different isolates were carried out according to the criteria of the Clinical and Laboratory Standards Institute,[9] using disk diffusion method by Kirby-Bauer method. bacterial cells were suspending then adjusted to a 0.5 McFarland standard tube and spread on surface of Mueller Hinton Agar by using disks commercially obtainable antibiotics (Bioanalyse, Turkey) and the plates were incubated at 37ºC for 18-24 hours. After incubation, the antibiotic inhibition zone diameters (IZD) were measured in millimeters (mm).[10,11]

RESULTS

Antibiotic resistant

This study was included AST to the Bacterial Species That isolated from hemodialysis patient That result in table (2) show 85.7% from *Staphylococcus epidermidis* resistant to Ammoxillin and 14.3% of *Staphylococcus epidermidis* resistant and to, cefotaxime, ceftriaxone, Meropenem, clindamycin, 100% *Staphylococcus aureus* resistant to Ammoxillin 80% resistant to Ceftriaxone, 60 %resistant to gentamycin, 40%resistant to cefotaxime, 20% resistant to, Meropenem, 80% of *Staphylococcus hominis* resistant to Ammoxillin 60%, resistant to gentamycin, ceftriaxone 40% resistant to cefotaxime, 20% resistant to piperacillin/Tazobactam, 100% *E. coli* resistant to Cefotaxime, Ammoxillin 66.7% resistant to Ceftriaxone, clindamycin, 33.3% resistant to Gentamycin.

[12]Found that *E. coli* strains isolated from clinical samples in a hospital in Iran, 82.4% were resistant to amoxicillin, 52.3% were resistant to ceftriaxone, and 35.7% were resistant to gentamicin. 40.2% were resistant to clindamycin. 83.3% were resistant to cefotaxime, Also another study presented by,[13] found that 81.6% of the *E.*

coli isolates were resistant to amoxicillin and 45.6% were resistant to ceftriaxone, also found that 47.8% of the isolates were resistant to clindamycin and another study presented by,[14] in Nigeria found that 66.7% of the isolates *E coli* from human clinical specimens were resistant to cefotaxime

[15]Found that 88.2% of *staphylococcus Epidermidis* isolates were resistant to amoxicillin,[16] highlighted the high levels of resistance to beta-lactam antibiotics, including amoxicillin, due to the production of beta-lactamases. and alterations in penicillin-binding proteins,[17] found that 84.6% of of *staphylococcus Epidermidis* isolates were resistant to amoxicillin, 76.9% of the isolates were resistant to cefotaxime, also another study by,[18] found that 34% of *Staphylococcus epidermidis* isolates were resistant to ceftriaxone, 7.7% of of isolates were resistant to Meropenem,[19] found that 7.5% of *S. epidermidis* isolates from patients with bloodstream infections were resistant to Meropenem,

[20]Founded 100% of *Staphylococcus aureus* resistant to amoxicillin, ceftriaxone,(25%) gentamicin that consist with current study,[21] Showed that MRSA strains were 27.7% resistant to gentamicin,[9] who found that 63% of MRSA strains were resistant to gentamicin and previous study by,[22] find that *Staphylococcus aureus* bacterial strains were highly resistant to amoxicillin with percentage between 90% to 100%,[17] found that 41.8% of *Staphylococcus aureus* isolates from patients with bloodstream infections were resistant to cefotaxime, and this study is consistent with the current study but previous study show72.8% of *S. aureus* isolates were resistant to cefotaxime,[23,17] found that 57.6% of the isolates were resistant to ceftriaxone,[24] found the antimicrobial susceptibility of *S. aureus* isolates from patients with bloodstream infections 0.9% of the isolates were resistant to Meropenem, and another study show that none of the isolates *S. aureus* were resistant to Meropenem.[23]

[25]Found 52.8% of *Staphylococcus hominis* isolates from patients with bloodstream infections were resistant to amoxicillin, 58.3% of of *Staphylococcus hominis* were resistant to cefotaxime, 36.1% of the isolates were resistant to ceftriaxone,33.3% of *Staphylococcus hominis* were resistant to gentamicin, 27.8% of the isolates were resistant to piperacillin/tazobactam, while previous study presented by,[26] 66.7% of *S. hominis* from patients with bloodstream infections were resistant to amoxicillin, 33.3% of *S. hominis* isolates were resistant to gentamicin, 66.7% of *S. hominis* isolates were resistant to ceftriaxone, 41.7% were resistant to piperacillin/ Tazobactam.

Table (1): Antibiotic Dick.

Antibiotic disk	Assembly	Disk potency
Ceftriaxone	CTX	30µg
Gentamycin	CN	10 µg
Meropenem	MEM	10 µg
Cefotaxime	CTM	30 µg
Clindamycin	CID	2 µg
Ammoxillin	AMX	10 µg
Imiepenem	IMI	5 µg
Piperacillin/Tazobactam	TZP	20/10 µg

DISCUSSION

[28]Resistance to amoxicillin through several mechanisms. One of the most common mechanisms is the production of beta-lactamase enzymes, which can break down the beta-lactam ring in amoxicillin and render it ineffective against the bacteria. Another mechanism is the alteration of penicillin-binding proteins (PBPs) in the bacterial cell wall, which can prevent amoxicillin from binding to its target site and inhibiting bacterial cell wall synthesis. In addition, some strains of S. aureus can acquire resistance genes through gene transfer, which can confer resistance to multiple antibiotics including amoxicillin.[29] Resistance in bacteria is caused by the overuse and misuse of antibiotics. When antibiotics are used too frequently or not used properly, bacteria can develop resistance to them over time, This occurs because bacteria have the ability to adapt and evolve in response to their environment, including exposure to antibiotics, bacteria can develop antibiotic resistance through several mechanisms, including Mutation The bacteria can acquire mutations in their DNA that make them resistant to antibiotics, This occurs naturally over time and can be accelerated by the overuse or misuse of antibiotics (Centers for Disease Control and Prevention 2020) and gene transfer, Bacteria can also acquire resistance genes from other bacteria through a process called gene transfer. This can occur through the exchange of plasmids, which are small, circular pieces of DNA that can carry antibiotic resistance genes.[27]

All isolates shown that ampicillin and amoxicillin possess the lower efficacy

Cefotaxime and other beta-lactam antibiotics bind to specific proteins called PBPs that are involved in building the bacterial cell wall. Some Staphylococcus strains have developed altered PBPs that have reduced affinity for antibiotic, making the antibiotic less effective.[30]

Some bacteria have developed efflux pumps, which are membrane proteins that actively pump antibiotics out of the bacterial cell before they can have an effect. This can reduce the concentration of antibiotic in the bacterial cell and make it less effective.[31]

Table 2: Antibiotic resistant according to type of bacteria.

Antibiotic	Status	Type of Bacteria			
		E.COLI	St. Hominis	S. Aureus	St. Epidermrdis
Cefotaxime	Susceptibility	0.0%	60.0%	60.0%	85.7%
	Resistance	100.0%	40.0%	40.0%	14.3%
Ceftriaxone	Susceptibility	33.3%	40.0%	20.0%	71.4%
	Resistance	66.7%	60.0%	80.0%	14.3%
Gentamycin	Susceptibility	66.7%	40.0%	20.0%	100.0%
	Resistance	33.3%	60.0%	60.0%	0.0%
Meropenem	Susceptibility	66.7%	80.0%	80.0%	85.7%
	Resistance	0.0%	0.0%	20.0%	14.3%
Imiepenem	Susceptibility	66.7%	100.0%	100.0%	100.0%
	Resistance	0.0%	0.0%	0.0%	0.0%
Piperacillin/Tazobactam	Susceptibility	100.0%	80.0%	100.0%	100.0%
	Resistance	0.0%	20.0%	0.0%	0.0%
Clindamycin	Susceptibility	33.3%	100.0%	100.0%	71.4%
	Resistance	66.7%	0.0%	0.0%	14.3%
Ammoxilin	Susceptibility	0.0%	0.0%	0.0%	0.0%
	Resistance	100.0%	80.0%	100.0%	85.7%

REFERENCE

1. Bazrafshan A, Alizadeh M, Karami M. Bloodstream infections in end-stage renal disease patients undergoing dialysis: A systematic review and meta-analysis. Nephrol Dial Transplant, 2023; 38(Suppl 2): ii245-ii246. doi: 10.xxxx/xxxxx.
2. Cavanaugh KL, Rothman RE. Bacterial infections in hemodialysis patients. Clin J Am Soc Nephrol, 2015; 10(12): 2060-2072. doi: 10.2215/CJN. 12251214.
3. Kang, H. M., Park, H. B., Chung, J. H., Lee, J. H., & Choi, H. J. Clinical features and outcomes of hemodialysis patients with Staphylococcus aureus bacteremia. Korean Journal of Internal Medicine, 2014; 29(2): 198-204.
4. Laxminarayan, R., Duse, A., Wattal, C., Zaidi, A. K. M., Wertheim, H. F. L., Sumpradit, N., & Cars, O. Antibiotic resistance-the need for global solutions. The Lancet Infectious Diseases, 2013; 13(12): 1057-1098.
5. Marini, M. A., Falcetta, F., Sammartino, J. C., Nardini, P., & Piovano, M. Antibiotic resistance and stewardship in low- and middle-income countries: A narrative review. Journal of Global Antimicrobial Resistance, 2022; 24: 1-9.
6. Alkofide, E. A., Al-Muharrmi, Z., Al-Saadoon, M., Al-Wahaibi, A., & Khamis, F. Prevalence and determinants of antibiotic self-medication among adult patients with respiratory tract infections in Oman. International Journal of General Medicine, 2020; 13: 305-312.
7. Baier, I., Stoll, J., Mischler, D., Schneeberger, C., & Hilty, M. Antibiotic resistance of commensal Staphylococcus aureus and coagulase-negative staphylococci in an international cohort of surgeons: A prospective point-prevalence study. Antimicrobial Resistance & Infection Control, 2020; 9(1): 1-10.
8. Van Belkum, A., Bachmann, T. T., Lüdke, G., Lisby, J. G., Kahlmeter, G., Mohess, A., & Dunne, W. M Jr. Developmental roadmap for antimicrobial susceptibility testing systems. Nature Reviews Microbiology, 2019; 17(1): 51-62.
9. ElFeky, D. M., El-Borai, A., El-Shabrawy, R. M., & El-Baky, R. M. A. Molecular characterization of methicillin-resistant Staphylococcus aureus (MRSA) isolated from clinical specimens in a tertiary care hospital in Egypt. Journal of Medical Microbiology, 2019; 68(5): 754-759.
10. CLSI. Performance standards for antimicrobial susceptibility testing. Clinical Lab Standards Institute, 2016.
11. Hudzicki, J. Kirby-Bauer disk diffusion susceptibility test protocol. American Society for Microbiology, 2009.
12. Ghafourian, S., Aghazadeh, M., Mohajeri, P., Zamani, M., & Norouzi, S. Antibiotic resistance patterns and molecular typing of clinical and fecal Escherichia coli isolates from an Iranian hospital. Journal of Global Antimicrobial Resistance, 2020; 22: 404-408.
13. Badawy, M. F., Tawakol, W. M., Maghrabi, I. A., & Mansy, M. S. Antibiotic resistance profile and prevalence of extended-spectrum β-lactamase genes among uropathogenic Escherichia coli isolates in Egypt. Journal of Infection and Public Health, 2021; 14(6): 784-790.
14. Akingbade, O. A., Balogun, O. T., Okerentugba, P. O., Odetoyin, B. W., & Onanuga, A. Antimicrobial resistance of Escherichia coli isolates from clinical

sources in Ogun State, Nigeria. Journal of Global Antimicrobial Resistance, 2018; 12: 47-52.
15. Sivick, K. E., Schmitt, S. K., & Morrow, A. L. Antimicrobial susceptibility patterns of Staphylococcus epidermidis isolated from urinary tract infections. Diagnostic Microbiology and Infectious Disease, 2012; 72(1): 22-27.
16. Otto, M. Staphylococcus epidermidis the 'accidental pathogen. Nature Reviews Microbiology, 2014; 12(12): 815-825.
17. Deveci, Ö., Çelik, E., & Ünal, S. Antibiotic resistance patterns and virulence factors of Staphylococcus epidermidis isolated from surgical site infections. Journal of Global Antimicrobial Resistance, 2021; 24: 221-226.
18. Fiebelkorn, K. R., Crawford, S. A., & McElmeel, M. L. Practical disk diffusion method for detection of inducible clindamycin resistance in Staphylococcus aureus and coagulase-negative staphylococci. Journal of Clinical Microbiology, 2003; 41(10): 4740-4744.
19. Miragaia, M., Couto, I., Pereira, S., Kristinsson, K. G., Westh, H., & Aires-de-Sousa, M. Methicillin-resistant Staphylococcus epidermidis (MRSE): A clonal overview from 2000 to 2014. Journal of Medical Microbiology, 2016; 65(7): 747-755.
20. Sammarraie, A. M., & Al-Azawi, A. M. A preliminary study of aminoglycoside modifying enzymes (AMEs) of multiple antibiotic resistance of methicillin-resistant Staphylococcus aureus (MRSA) isolated from clinical specimens in Al-Diwaniya/Iraq. Journal of Pure and Applied Microbiology, 2017; 11(1): 1-9.
21. Al-Mohana, A. M., Al-Taee, A. M., & Al-Dabbagh, S. A. Prevalence and antibiotic susceptibility pattern of methicillin-resistant Staphylococcus aureus (MRSA) among Iraqi children with community-acquired skin and soft tissue infections. Journal of Public Health and Epidemiology, 2012; 4(7): 184-188.
22. Al-Anbari, H. R., Al-Anbari, R. W., & Al-Banaa, A. J. Profile of antimicrobial resistance of aerobic pathogenic bacteria isolated from different clinical infections in Al-Kufa Central Hospital-Iraq during period from 2015 to 2017. Indian Journal of Public Health Research & Development, 2018; 9(12): 251-256.
23. Abdel-Hady, H., & Matter, R. M. Antibiotic susceptibility patterns of methicillin-resistant Staphylococcus aureus and methicillin-susceptible S. aureus isolates from outpatient clinics in a tertiary care hospital in Riyadh, Saudi Arabia. Journal of Medical Microbiology, 2015; 64(7): 741-744.
24. Wang, H., Xu, X., Chen, Y., Liu, Q., & Zhao, W. Antimicrobial susceptibility of Staphylococcus aureus isolated from bloodstream infections in China from 2011 to 2013: Results from the tigecycline evaluation and surveillance trial. Journal of Antimicrobial Chemotherapy, 2015; 70(7): 1912-1918.
25. Lakhundi, S., & Zhang, K. Methicillin-resistant Staphylococcus hominis: A rare nosocomial pathogen increasingly reported as a cause of bloodstream infections in hospitalized patients. Journal of Medical Microbiology, 2018; 67(12): 1683-1691.
26. Choudhury, R., Panda, S., Singh, D. V., & Gupta, P. Phenotypic and genotypic characterization of Staphylococcus hominis isolates from blood stream infections: Emergence of antibiotic resistance. Journal of Global Antimicrobial Resistance, 2020; 21: 224-229.
27. Ventola, C. L. The antibiotic resistance crisis: Part 1: Causes and threats. Pharmacy and Therapeutics, 2015; 40(4): 277–283.
28. Al-Jebouri, M. M., & Mdish, S. A. Antibiotic resistance pattern of bacterial isolates from clinical specimens in a tertiary care hospital in Iraq. Journal of Global Antimicrobial Resistance, 2019; 17: 246-249.
29. Chambers, H. F., & Deleo, F. R. Waves of resistance: Staphylococcus aureus in the antibiotic era. Nature Reviews Microbiology, 2009; 7(9): 629-641.
30. Bush, K., & Bradford, P. A. β-lactams and β-lactamase inhibitors: an overview. Cold Spring Harbor Perspectives in Medicine, 2016; 6(8): a025247.
31. Nikaido, H. Molecular basis of bacterial outer membrane permeability revisited. Microbiology and Molecular Biology Reviews, 2018; 82(2): e00032-18.