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RESEARCH ARTICLE
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ANTIMICROBIAL RESISTANCE PATTERN OF *KLEBSIELLA OXYTOCA* AMONG CLINICAL SPECIMENS IN A TERTIARY CARE HOSPITAL

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Abstract

Objective: The purpose of the study was to determine Klebsiella oxytoca's pattern of antibiotic resistance among clinical specimens.

Methods:A total of 1683 clinical samples were processed**.** A modified Kirby-Bauer disc diffusion method was used to test for antibiotic sensitivity patterns. The double disc synergy test was used to confirm ESBL production among Klebsiella spp.

Results: Of the 1683 clinical samples processed, 121 isolates were Klebsiella species. Thirty-two (32.2%) of these isolates were K. oxytoca which exhibited 100% resistance to Cefoxitin followed by Ceftazidime, Ciprofloxacin, Imipenem, Meropenem and Gentamicin by 86%, 67%, 59%, 56%, and 46% respectively which is comparable to K. pneumoniae whereChloramphenicol was determined to be the most promising medication, followed by Fosfomycin. 70% of the isolates of K. oxytoca had multidrug resistance.

Conclusion: Hospitals should maintain a strict antibiotic policy in order to track the effects of growing bacterial resistance and take preventative measures against K. oxytoca.

Key words: *K. oxytoca,* Gentamicin, Antibiotic resistance, Extended spectrum beta lactamase (ESBL), Multi Drug resistant organisms (MDRO)

INTRODUCTION

During the past decade, there has been a rise in the clinical importance of nosocomial infections attributed to Staphylococcus aureus. Presently, there is also consideration given to gram-negative bacteria.(1)These bacteria's recent wide-scale outbreaks have been one of the main issues faced by both large and small hospitals. Klebsiella spp,of Enterobacteriaceae family is found on the mucosal surfaces of both humans and canines, as well as in water, food, and soil environments. It ranks as the second most common member of the Enterobacteriaceae family.(2) It has become well-known that this particular group of pathogens has the potential to seriously infect hospitalized people.(3)This organism's capacity to spread illness as a result of lengthy and intricate procedures that weaken the host's defenses.

The utilization of multiple drugs is increasing.(4)The most often prescribed and used class of antibiotics for treating bacterial infections caused by Klebsiella spp. are the β-lactam antibiotics. Unfortunately, the future of using β-lactam drugs in humans may be in risk due to the emergence of

antimicrobial resistance in Klebsiella-producing broad spectrum β-lactamases, like AmpC β-lactamases and extended-spectrum β-lactamases (ESBL) as a result of the indiscriminate use of antibiotics.

The most common antimicrobial exposure has been linked to a number of risk factors for ESBL-producing Klebsiella oxytoca infections, particularly exposure to third-generation cephalosporins, which has been linked to higher rates of morbidity, death and medical expenses. In order to prevent the development of multidrug-resistant Klebsiella spp., treatment failure attributed by Klebsiella, must be closely monitored in poor resource nations.(5)Therefore, determining the antibiotic susceptibilities of Klebsiella spp. that produce AmpC β-lactamases and ESBL is crucial for treating pathogenic infections.This study is aimed to investigate the prevalence of antimicrobial resistance mechanisms of Klebsiella strains isolated from clinically specimens in a tertiary care hospital.

MATERIAL AND METHODS

Ethical Consideration: Ethical Clearance was obtained from Institutional Ethical Committee prior to start to the study.

Study Duration: January 2023 to December 2023 (1 year)

Place of study: Department of Microbiology, Katuri Medical College and Hospital
Inclusion Criteria: Klebsiella species isolated from clinical samples
Exclusion Criteria: Any other organism isolated from clinical sample
The present study was a prospective cross sectional study with a total of 1683 clinical samples, comprising sputum, pus, blood, urine, throat swab, tissues and pleural fluids.

The patients were both male and female and ranged in age. The samples were gathered and handled in accordance with Standard operating protocols.

Samples were inoculated onto Nutrient agar, Blood agar and MacConkey agar. Large mucoid colonies were picked from MacConkey agar plate in order to isolate and identify Klebsiella.spp.
The Gram stain was used to validate the chosen colonies; biochemical assays such as oxidase test, catalase test, IMViCTest (Indole, Methyl Red, Voges Proskauer, Citrate Utilization Test), Urease Test, Mannitol motility test and Sugar fermentation test were also used.

Antimicrobial susceptibility testing was done in accordance with Clinical and Laboratory Standards Institute (CLSI) guidelines. Using a modified Kirby-Bauer disc diffusion method, the susceptibility of bacterial isolates to several antibacterial drugs was ascertained on Mueller-Hinton agar using lawn culture of 0.5 McFarland bacterial suspension. The plates were incubated at 37°C for 16 – 18hours and the zone of inhibition was determined as per CLSI guidelines.Antibiotics used were Ceftazidime (30 mg), Ceftazidime +clavulanic acid (30 µg/ 10), Gentamicin (10 mg), Amikacin (30 mg) Ciprofloxacin (5mg), Imipenem (10mg), Meropenem (10mg), Piperacillin and tazobactam (10mg), Co-trimoxazole (2µg), Cefoxitin (30 µg), Chloramphenicol(30 mg) Nitrofurantoin(10mg), Fosfomycin (200µg).

ESBL Detection:
Double disc synergy test: Ceftazidime (30 mg) and ceftazidime–clavulanic acid (30 mg/10 mg) discs were used for confirmatory tests.
ESBL Positive: zone difference of ≥5 mm between Ceftazidime and ceftazidime–clavulanic acid.
Escherichia coli ATCC 25922 and K. pneumoniae ATCC 700603 were used as positive and negative controls, respectively.

RESULTS

A total of 1683 samples were processed at the hospitallaboratory during the study period. Klebsiella was isolated from 121 of these clinical samples. Out of these Klebsiella species, 82 (67.7%) were K. pneumoniae and 39 (32.2%) were K. oxytoca.

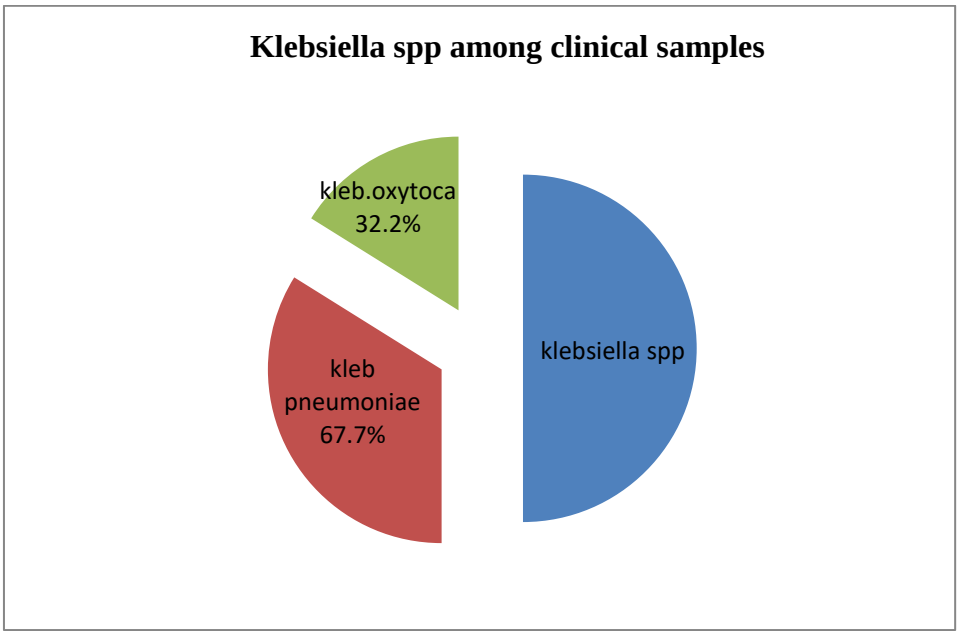

Fig1:Klebsiella species among clinical samples.

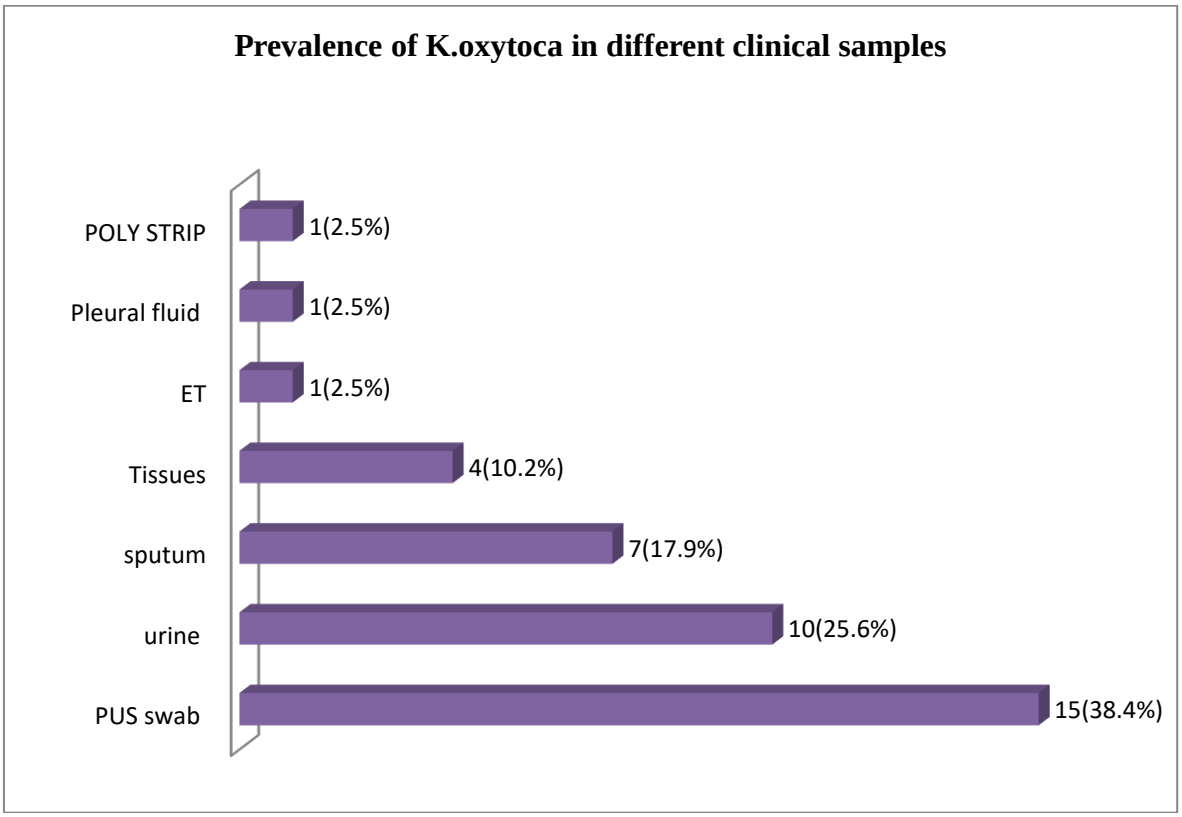

Fig2:Prevalence of K.oxytoca in different clinical samples

Pus swab samples had the highest prevalence (66%), which was followed by urine samples (25.6%), sputum (17.9%), and tissues (10.2%).Compared to females, males were more affected by Klebsiella spp., 26 (66.7%) versus 13 (33.3%).

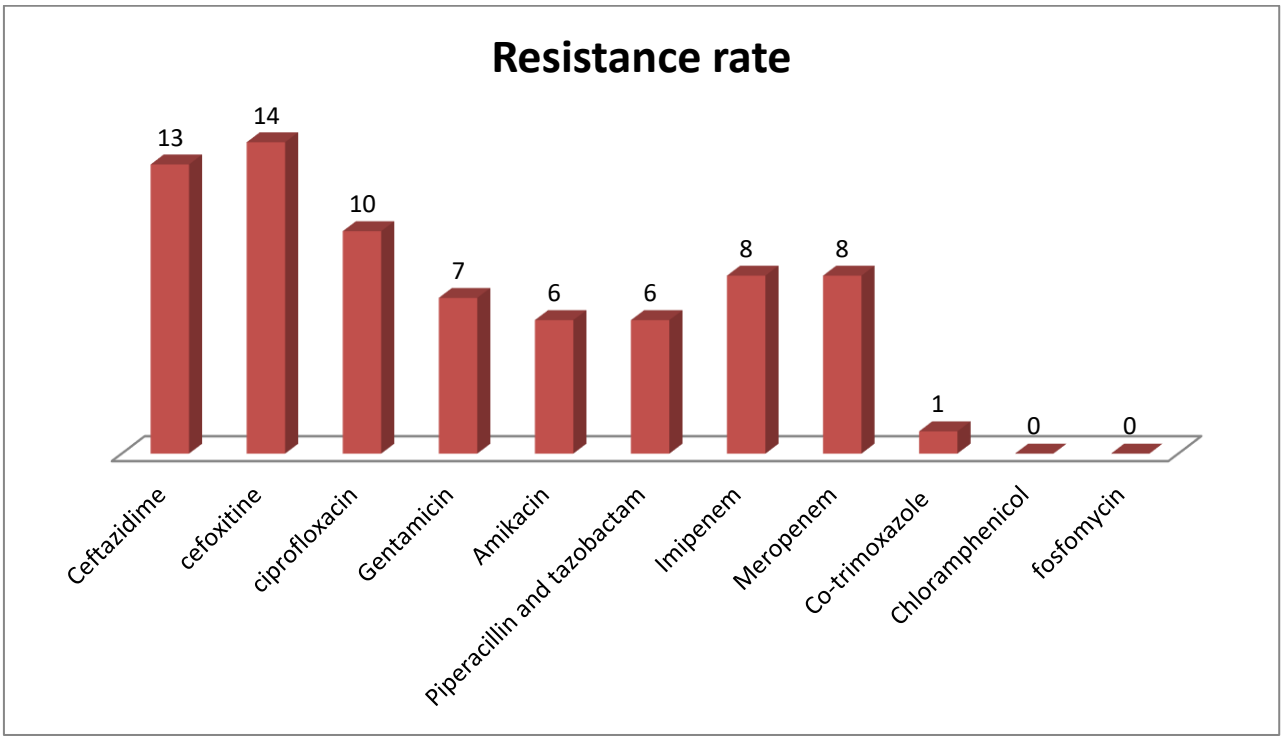

Fig3: Resistance rate of K.oxytoca in pus swab

In this study, there were 11 different antimicrobials. Based on the results,14 (93%) isolates exhibited a high resistance rate to cefoxitin, followed by ceftazidime(n=13, 86.6%) and Ciprofloxacin (n=10, 66.6%). Furthermore, the *K. oxytoca* was affected by Imipenem and (n=8, 53.3%) and Meropenem (n=8, 53.3%).

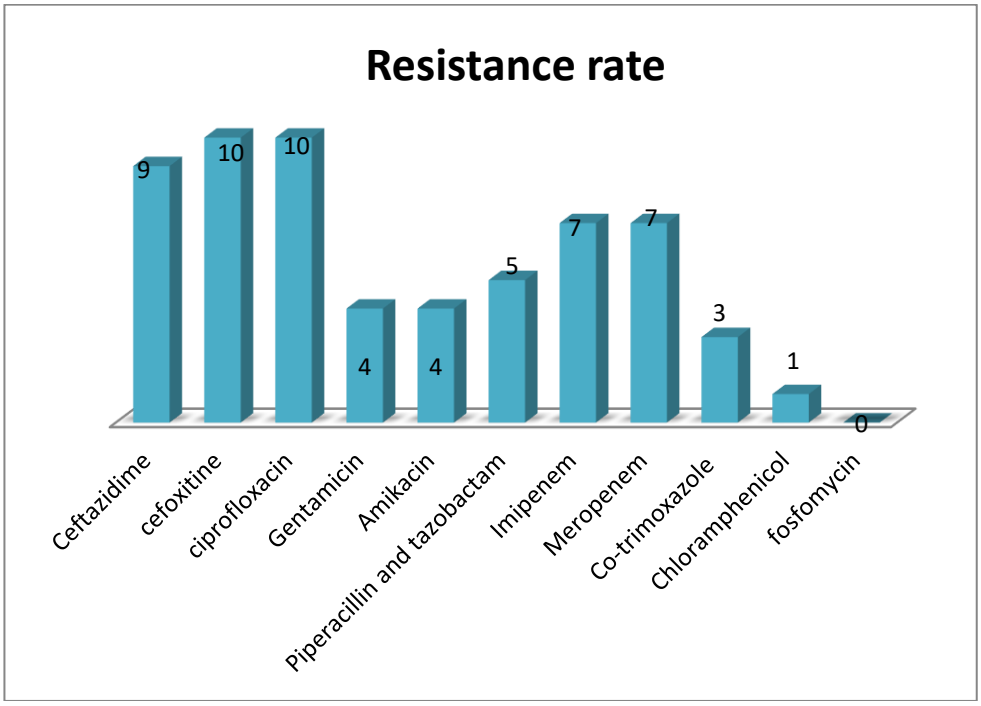

Fig4: Resistance rate of K.oxytoca in urine sample

Among urine samples, following cefoxitin (n=10, 100%) and ciprofloxacin (n=10,100%), the isolates with the highest rates of resistance. Furthermore, imipenem and meropenem (n=7, 63.6%) and (n=7, 63.6%) had an impact on K. *oxytoca.*

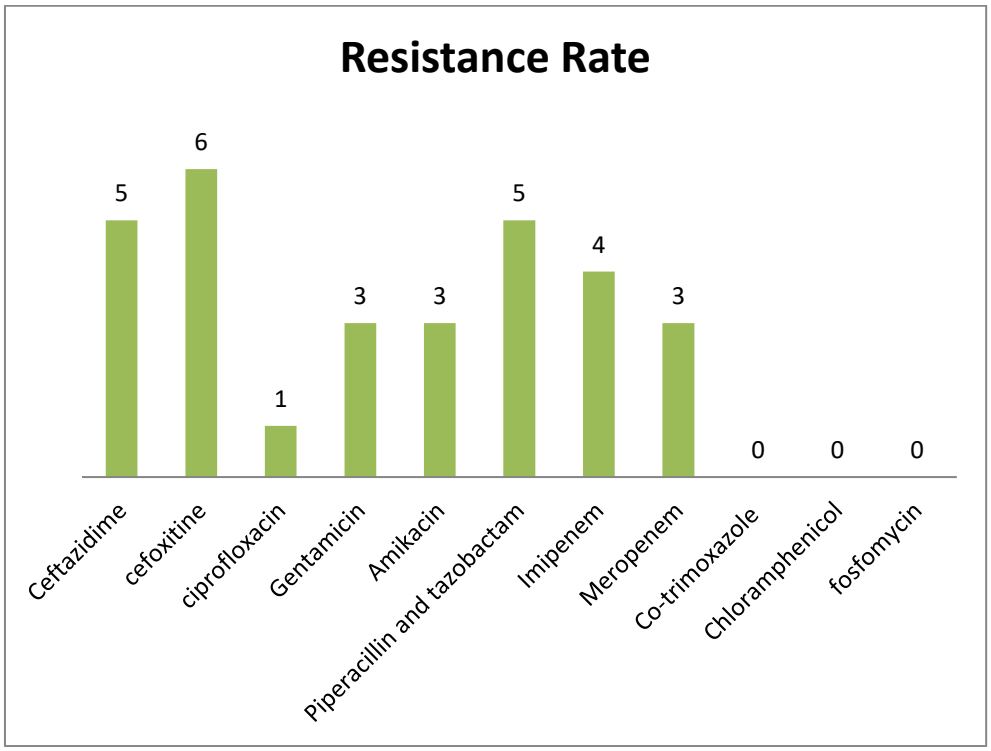

Fig5: Resistance rate of K.oxytoca in Sputum sample

Among sputum samples, following Cefoxitin (n=6, 85.7%) the isolates with the highest rates of resistance. Furthermore, ceftazidime (n=5,71.4%) and Piperacillin and tazobactam (n=5, 71.4%) had an impact on K. *oxytoca.*

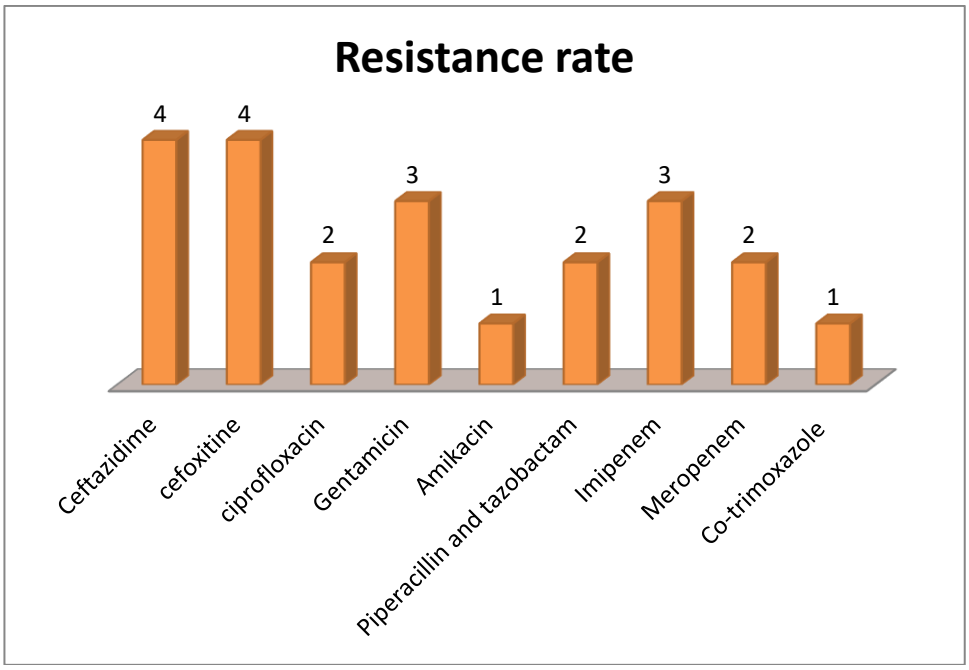

Fig 6: Resistance rate of *K.oxytoca* in tissues

In this study, there were 12 different antimicrobials. Based on the results, 4(100%) isolates exhibited a high resistance rate to Ceftazidime and Cefoxitin, followed by Gentamicin (n=3, 75%) as well as Imipenem and gentamicin (n=3, 75%). Furthermore, the *K. oxytoca* was affected by ciprofloxacin and Meropenem (n=2, 50%) and (n=2, 50%).

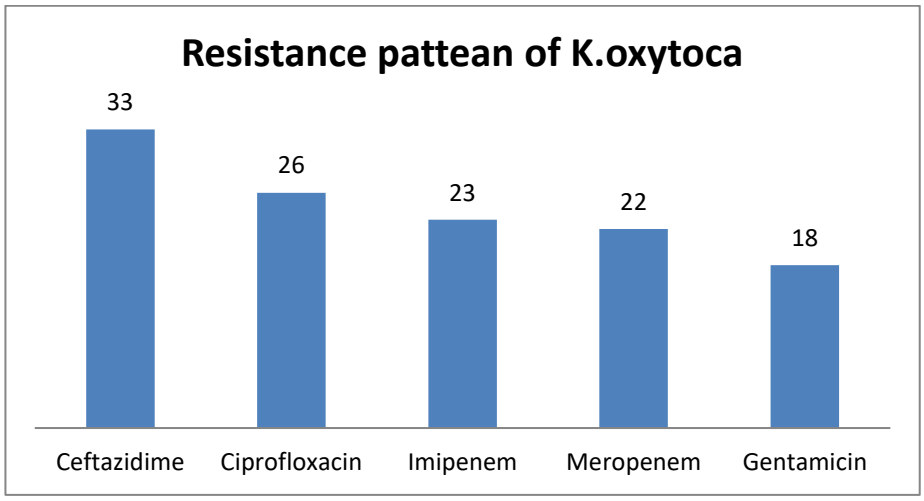

Fig7:Total antibiotic resistance pattern of K.oxytoca

Based on our data, K.oxytoca exhibited 100% resistance to Cefoxitin,which is comparable to K. pneumoniae Chloramphenicol was found to be the most promising medication, followed by Fosfomycin, in contrast to K. oxytoca, which showed resistance to Ceftazidime, Ciprofloxacin, Imipenem, Meropenem, and Gentamicin by 86%, 67%, 59%, 56%, and 46%. Seventy percentof the isolates of K. oxytoca had multidrug resistance.

Discussion

In the last year, Klebsiella species, opportunistic bacteria that cause serious infectious diseases in hospital settings, have developed a fast multidrug resistance. In the present study, 32% prevalence rate of *Klebsiella oxytoca* was observed among clinical patients from which is alarming since less prevalence rate (24%) was observed previously in north eastern part of Bangladesh by Sourav Chakraborty et al.,2016.This difference in prevalence rate may be acceptable because the prevalence of *Klebsiella* infections varies in different geographical locations .(6)

The capacity to synthesize indole from tryptophan allowed *K. pneumonia* and *K. oxytoca*, two species of clinical relevance, to be distinguished from one another. Thirty two percent of the isolates in this investigation were *K.oxytoca*, which is consistent with earlier findings. However, male samples had a greater frequency of species than did the female ones. It was shown that women in the age range of 40 to 50 and over 60 were more susceptible to infections linked to Klebsiella, while men in the age group of over 65 had the highest prevalence of infections. This is correlated with Akter J, et al study(7) Female in the age group of 31-40 years and greater than 50 years of age was shown to be extremely susceptible to Klebsiella-associated infections, whereas males had the greatest frequency of infection in the age group over fiffty.

The current investigation found a substantial increase in the percentage of *K. oxytoca* isolates from inpatients as opposed to outpatients, and this finding is associated with Montecino-Rodriguez E. et al(8).According to these results, prolonged hospital stays and decreased immunity from ageing may be risk factors for K. oxytoca infections.

According to the present investigation, urine accounted for 10 (25.6%) of the K. oxytoca infections, whereas pus swabs accounted for 15 (38.04%). Other investigations by G. Sibi, P. Kumari, et al.(9) revealed that *K. oxytoca* was the most prevalent bacterial cause of UTIs in pregnant women, but their findings varied. It has been demonstrated that the prolonged use of catheters, particularly in hospital settings, contributes to the occurrence of *K.oxytoca* in urine at a higher rate than other causes and can also result in urinary tract infections (UTTIs) in older female patients.

High resistance to various commonly used antibiotics was revealed by the results of the antibiotic susceptibility test to eleven different antibiotics. Enzymes called beta lactamases are a global problem that have been linked to medication resistance in several Enterobacteriaceae(10).

For this kind of multidrug-resistant bacteria, the antibiotic of choice may be determined mostly by the resistance pattern. Treatment should be guided by the antimicrobial susceptibility profiles of

individual isolates.(11)Further research, which is connected to the Yahya Abdulla, N. et al.(12)study, has revealed that ampicillin is no longer effective against urinary tract infections.
To be clear, K. oxytoca infections are commonly treated with second- and third-generation cephalosporins. Because of their low susceptibility to cephalosporins, antibiotics like ceftazidime and cefoxitin are widely accessible without a prescription and can be purchased at any local drugstore for relatively low prices. This suggests that the resistance rate to these drugs was 90% in the current study, which is consistent with the findings of the study conducted by Chayakulkeeree and Junsriwong(13).
The study conducted by Razzaque(14) and Pérez-Vazquez, Oteo-Iglesias, found that the rates of resistance to Imipenem and Meropenem were 53.3% and 63.6%, respectively, in pus and urine samples(15).In certain circumstances, there may be variations between the findings of this study and those found in other papers. This might be a testing error; the disc, kind, and depth of the culture media all play significant roles in influencing the outcome. The medium has a normal depth of 4 mm; a thinner depth might make antibiotics more sensitive.

Conclusion

The K. oxytoca isolates that were isolated from clinical samples in this area became highly resistant to cephalosporins, and carbapenem resistance has also been observed. Tight antibiotic policies should be upheld in hospitals in order to track the effects of growing bacterial resistance and implement preventative measures. Strict antibiotic policies along with traditional antibiograms, when combined with ongoing ESBL monitoring, would significantly reduce bacterial resistance to antibiotics and facilitate the development of effective treatment alternatives for Klebsiella infections.

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AUTHORS' CONTRIBUTIONS

Sandhya RaniThotaworked as principal investigator and contributed to the conduction of the experiment,drafting the proposal,and acquiring approval for conducting the study.K. Saileela contributed as a coinvestigator and played a key role in the study conception, revise it critically for important intellectual content.M. Shabnum assisted in the study by reviewing the content,data collection, interpretation,analyzing the data, and draft manuscript preparation to be published. All authors have read and approved the final manuscript.

COMPETING INTERSTS

None

AUTHORS' FUNDING

None

REFERENCES

1. Pouladfar G, Basiratnia M, Anvarinejad M, Abbasi P, Amirmoezi F, Zare S. The antibiotic susceptibility patterns of uropathogens among children with urinary tract infectionin Shiraz. Medicine(Baltimore).2017Sep;96(37):e7834.PMID:2890636,PMCID: PMC5604634DOI: 10.1097/MD.0000000000007834
2. Nordmann P, Cuzon G, Naas T. The real threat of Klebsiella pneumoniae carbapenemase-producing bacteria. 2009 Apr;9(4):228-36. doi: 10.1016/S1473-3099(09)70054-4.
3. Gomez-Simmonds A, Greenman M, Sullivan SB, Tanner JP, Sowash MG, Whittier S, et al. Population Structure of Klebsiella pneumoniae Causing Bloodstream Infections at a New York City Tertiary Care Hospital: Diversification of Multidrug-Resistant Isolates. Journal of Clinical Microbiology. 2015 Jul;53(7):2060-7. doi: 10.1128/JCM.03455-14.

4. Moayednia R, Shokri D, Mobasherizadeh S, Baradaran A, Fatemi SM, Merrikhi A. Frequency assessment of β-lactamase enzymes in Escherichia coli and Klebsiella isolates in patients with urinary tract infection. Journal of Research Medical Sciences. 2014 Mar; 19(Suppl 1):S41-45.PMCID: PMC4078376, PMID: 25002893.
5. LEE S O, LEE E S, PARK S Y, KIM S Y, SEO Y H, CHO Y K 2004 Reduced use of third-generation cephalosporins decreases the acquisition of extended spectrum *b*-lactamases producing *Klebsiella pneumoniae*. *Infect Control Hosp Epidemiol* 25: 832-837,http://dx.doi.org/10.1086/502304
6. S.Chakraborty *et al.* Prevalence, antibiotic susceptibility profiles and ESBL production in *Klebsiella pneumoniae* and *Klebsiella oxytoca* among hospitalized patients. PERIODICUM BIOLOGORUM UDC 2016 57:61 VOL. 118, No 1, 53–58, CODEN PDBIAD DOI: 10.18054/pb.2016.118.1.3160.
7. AKTER J, CHOWDHURY A M M A, FORKAN M A 2014 Study on prevalence and antibiotic resistance pattern of *Klebsiella* isolated from clinical samples in south east region of Bangladesh. *Am J Drug Disc Dev* 4: 73-79. http://dx.doi.org/10.3923/ajdd. 2014.73.79
8. Montecino-Rodriguez E., Berent-Maoz B., Dorshkind K. Causes, consequences, and reversal of immune system aging. *J. Clin. Investig.* 2013;123:958–965. doi:10.1172/JCI64096
9. G. Sibi, P. Kumari, and N. Kabungulundabungi. Antibiotic sensitivity pattern from pregnant women with urinary tract infection in Bangalore, india. Asian Pac J Trop Med. 2014 Sep: 7S1:S116-20. doi: 10.1016/S1995-7645(14)60216-9
10. AL-Khikani FHO, Abadi RM, Ayit AS. Emerging carbapenemase Klebsiella oxytoca with multidrug resistance implicated in urinary tract infection. Biomed Biotechnol Res J. 2020;4(2):148-51,doi:: 10.4103/bbrj.bbrj_165_19
11. Neog N, Phukan U, Puzari M, Sharma M, Chetia P. Klebsiella oxytoca and Emerging Nosocomial Infections. Curr Microbiol. 2021 Apr;78(4):1115-1123. doi: 10.1007/s00284-021-02402-2
12. Yahya Abdulla, N1, Abduljabbar JaloobAljanaby, I2 Assessment of ß-lactams and Carbapenems Antimicrobials Resistance in Klebsiella Oxytoca Isolated from Patients with Urinary Tract Infections in Najaf, Iraq Archives of Razi Institute. Vol. 77, No. 2 (2022); 669-673.doi: 10.22092/ARI.2022.356957.1947
13. Chayakulkeeree M, Junsriwong P Keerasuntonpong A, Tribuddharat C, Thamlikitkul V. Epidemiology of extended-spectrum beta-lactamase producing gram-negative bacilli at Siriraj Hospital, Thailand, 2003.Southeast Asian J Trop Med Public Health. 2005 Nov;36(6):1503-9.PMID: 16610653
14. Razzaque S. A cross sectional study highlighting the sensitivity patterns and incidence of extended spectrum beta lactamase producing Klebsiella oxytoca in patients with urinary tract infection. Int J Pulmonol Infect Dis. 2017; 1:1-5. dio:10.15226/2637-6121/1/1/00102
15. Pérez-Vazquez M, Oteo-Iglesias J, Sola-Campoy PJ, Carrizo-Manzoni H, Bautista V, Lara N, et al. Characterization of carbapenemase-producing Klebsiella oxytoca in Spain, 2016–2017. Antimicrob Agents Chemother. 2019;63(6):02529-18. doi: 10.1128/AAC.02529-18