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RESEARCH ARTICLE

A STUDY ON PREVALENCE OF URINARY TRACT INFECTIONS DUE TO EXTENDED SPECTRUM BETA LACTAMASE PRODUCING KLEBSIELLA SPECIES & ESCHERICHIA COLI BY PHENOTYPIC METHODS FROM CLINICAL SAMPLES IN A TERTIARY CARE HOSPITAL

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Abstract

Background: Urinary tract infections (UTIs) are the most commonly encountered bacterial infection, particularly in women. Escherichia coli and Klebsiella spp are the most common organisms causing urinary tract infection (UTI) and is responsible for Extended spectrum beta lactamases (ESBL) production. Emergence of extended spectrum beta lactamases producing strains of gram negative bacteria leads to serious infection that complicates the treatment and clinical outcome. ESBL enzymes shows increased hydrolysis of oxyimino- β lactams that have been reported increasingly in recent years and are significantly detected from various Escherichia coli & klebsiella strains. This study is conducted to know the prevalence of ESBL producing Escherichia coli & Klebsiella spp causing urinary tract infection in our health care facility.

Materials And Methods: This is a prospective study done in the Department of Microbiology, P.K Das Institute of Medical sciences, Vaniamkulam from a period of November 2022- September 2023. Urine specimens received from both In-patients and Out-patients of P.K Das Institute of Medical sciences & hospitals during the study period were subjected to culture in the bacteriology laboratory, Department of Microbiology, according to CLSI guidelines. Antibiotic susceptibility testing was done by modified Kirby-Bauer disc diffusion method on Muller-Hinton agar. ESBL producing organisms were identified using Ceftazidime disks (30 μ g) with or without Clavulanate (10 μ g) was used for phenotypic conformation of the presence of ESBL as recommended by CLSI guidelines 2022.

Results: Out of the 2065 samples processed during the period of November 2022 – September 2023, 576 samples were culture positive for Escherichia coli and Klebsiella. Out of the 576 culture positive samples 372 (64.6%) were Escherichia coli isolates & 204 were Klebsiella spp (35.4%). Out of the total 576 culture positives, 339 (59%) were females & 237 (41%) were males. Out of the total 576 culture positive Escherichia coli and klebsiella spp, 198 (34.3%) were ESBL producers, of which 122 out of 372 ESBL producers were of Escherichia coli isolates and 76 out of 204 ESBL producers were of Klebsiella spp. Among 576 culture positive isolates, 294 were obtained

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from Inpatients samples and 282 isolates were outpatient samples in the study whereas 102 out of 198 and 96 out of 198 were inpatients and outpatients respectively among the ESBL producers. In the study, 99% *Escherichia coli* and 97.8% *Klebsiella* spp which were ESBL producers were susceptible to carbapenams. The susceptibility to Piperacillin/tazobactam, cefoperazone/sulbactam, fluoroquinolones, Nitrofurantoin, Amoxicillin/clavulanic acid, ceftazidime/clavulanate, aminoglycosides were in between 50% up to 95% for isolates of both the organisms which were ESBL producers.

Conclusion: The ESBL producing *Escherichia coli* & *Klebsiella* spp are a cause of concerns to the microbiologist as well as to the clinicians, particularly the multidrug resistant strains. Screening for these resistant pathogen might eventually become necessary as ESBLs become more of an issue in hospitals and community settings especially in high risk units where infections caused by resistant organisms are more.

Conflict Of Interest: No conflict of interest.

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Introduction:-

Urinary tract Infections (UTIs) is defined as the presence of bacteria in urine along with symptoms of infection. UTIs are among the most frequent bacterial infections witnessed in outpatients as well in hospitalised patients. Antimicrobial resistance among uropathogens is increasing globally and considered to be a challenge for clinicians since there are limited treatment options. Management of UTIs in the era of antimicrobial resistance requires a systematic approach to diagnose the type of infection and to select appropriate antimicrobial agent. Misuse and overuse of antimicrobials are the main cause in the development of drug resistance. Failure to treat or frequent recurrence may lead to multiplication of pathogens which can ascend to the kidneys, causing pyelonephritis and eventually renal failure in the long term. As treatment and prevention of complications are time sensitive to diagnosis, alignment of rapid diagnosis, susceptibility testing and targeted treatment options should be integrated in the management protocol to enhance cure.

Clinically, UTIs are categorized as uncomplicated or complicated. Uncomplicated UTIs typically affect women, children and elderly patients who are otherwise healthy. Complicated UTIs are usually associated with indwelling catheters, urinary tract abnormalities, immunosuppression or exposure to antibiotics. Extended spectrum beta lactamases (ESBLs) are mutant, plasmid-mediated lactamases that confer resistance to all extended spectrum cephalosporins and aztreonam. They are also inhibited by lactamase inhibitor, but they do not exhibit any activity against cephamycins and carbapenams. Although *Escherichia coli* and *klebsiella* spp are the most frequent carriers of ESBLs, other Gram-negative bacteria have also been found to carry ESBL. Lengthy ICU stays, nursing home residency, severe sickness, and overusage of third generation cephalosporins, instrumentation or catheterization are major risk factors for colonization or infection with ESBL-producing organisms.

Methods:-

Urine specimens were received from both Out-patients and In-patients from different wards of P K Das institute of Medical sciences Vaniamkulam from a period of November 2022- September 2023. The samples were inoculated on Nutrient agar, Blood agar and MacConkey's agar and Cystine lactose electrolyte deficient agar. The plates were incubated aerobically at 37°C for 24 hrs. The organisms were identified phenotypically by Gram stain, Motility, cultural characteristics and standard biochemical tests as per CLSI guidelines. Antibiotic susceptibility testing of the isolated bacteria was done by Modified Kirby-Bauer Disc Diffusion method on Mueller Hinton agar with proper standardization using ATCC control strains. ESBL producing organisms were identified using Ceftazidime disks (30µg) with or without Clavulanate (10µg) was used for phenotypic confirmation of the presence of ESBL as recommended by CLSI guidelines. A difference of more than or equal to 5 mm between the zone diameters of Ceftazidime disks and Ceftazidime/ clavulanate disks was taken to be phenotypic confirmation of ESBL production.

Results:-

Out of 2650 urine samples processed, 576 were culture positive for *Escherichia coli* and *Klebsiella*. Out of the total 576, 372 were *Escherichia coli* (64.6%) and 204 were *Klebsiella* species (35.4%). 339 out of 576 culture positive samples were females (59%) and 237 were males (41%). A total of 198 ESBL strains were detected out of the total 576 culture positive samples for *Escherichia coli* & *Klebsiella* species.

122 out of 372 (32.7%) culture positive *Escherichia coli* were of ESBL producers and 76 out of 204 (37.2%) culture positive *Klebsiella* spp were ESBL producing. 122 out of 198 (61.7%) ESBL producers were *Escherichia coli* and 76 out of 198 (38.3%) ESBL producers were of *Klebsiella* species. Out of the total 576 culture positive isolates, 294 were obtained from Inpatients samples and 282 isolates were isolated outpatient samples in the study whereas 102 out of 198 and 96 out of 198 were inpatients and outpatients respectively among the ESBL producers.

Out of the 122 ESBL producers in *Escherichia coli*, 87.12% were susceptible to Piperacillin /tazobactam, whereas 84.88% were susceptible to the same out of the 76 ESBL producing *Klebsiella* species. The susceptibility for cefoperazone/sulbactam were 89.48% and 84.34% respectively for ESBL producers of *Escherichia coli* and *Klebsiella* species. The fluoroquinolones were 67.4% susceptible for the ESBL producers of *Escherichia coli* and 74.38% of ESBL producers of *Klebsiella* species. The susceptibility of Aminoglycosides were 79.2% for ESBL producing *Escherichia coli* and 81.4% for ESBL producers of *Klebsiella* species. 74.83% *E.coli* and 75.64% *Klebsiella* spp were sensitive to ceftazidime /clavulanate whereas 64.46% *E.coli* and 63.17% *Klebsiella* were sensitive to Amoxicillin/ clavulanic acid. The sensitivity of *E.coli* and *Klebsiella* spp were 81.78% and 64.48% respectively to Nitrofurantoin. In the study, 99% *Escherichia coli* and 97.8% *Klebsiella* spp which were ESBL producers were susceptible to carbapenams such as Meropenam and imipenam by Kirby bauer disc diffusion method.

Discussion:-

The present study was done in the Department of Microbiology, P.K Das Institute of Medical sciences, Vaniamkulam from a period of November 2022- September 2023. The most common infectious diseases encountered in the community in all age group is Urinary tract infection (UTIs) and usually empirical antibiotic therapy is given depending upon the common causative agent and their susceptibility to commonly used antibiotic. But because of the increasing prevalence of bacterial resistance to a wide range of antibiotics, these microorganisms pose a major public health issue.

More than 70% of the UTIs are caused by Enterobacteriaceae group, of which *Escherichia coli* and *Klebsiella* accounts for majority of cases (Dhruba Hari chandi, Nandkishor Bankar, et al study). Multidrug resistant (MDR) and the generation of the Extended spectrum beta lactamases (ESBLs) by gram negative bacilli especially *Escherichia coli* and *Klebsiella* species in hospitals are always a concern due to the failure in treatment. 294 out of 576 culture positive samples were Inpatient samples and 282 samples were outpatient samples. 102 out of 198 Extended Spectrum beta lactamase producers were Inpatient samples and 96 out of 198 were outpatient samples which correlates with Sofia Patel and Sunayana M jangla et al study. In the present study, out of 576 culture positive samples for *Escherichia coli* and *Klebsiella* 372 were positive for *Escherichia coli* that is 64.6% which correlates with Prabhat Sharma, Kirti Malpekar et al, and 204 were positive for *Klebsiella* that is 35.4% which correlates with Shrabanti Barua, Saikat Barua et al. The present study shows, out of the total 198 ESBL producers, 122 were of *E.coli* (61.6%) which correlates with studies of Poornima venugopal and Carol sara cherian et al and 76 (38.3%) were of *Klebsiella* which correlates with studies of kuldeep yadav and Nikitha Sharma et al. Urinary tract infections (UTIs) classified as urethritis (an infection of the urethra), cystitis (inflammation of the bladder) or pyelonephritis (infection of the kidneys) or may develop in to blood stream infections as urosepsis. In the Enterobacteriaceae family *E.coli* and *Klebsiella* were identified as major ESBL producing organisms which cause UTI. This enzyme is also effectively produced by other members of the Enterobacteriaceae and certainly by non fermenting Gram negative bacteria. The concern towards ESBL producing *Klebsiella* has been increased after emergence of plamid mediated resistance to ESBL reported in India. Urinary tract infections caused by ESBL-producing *E.coli* and *Klebsiella* spp are of great concern because of the lesser availability of last line treatment options. The present study shows there were a total of 198 culture positive *Escherichia coli* and *Klebsiella* species, out of which 339 were females and 237 were males. Out of the total 198 ESBL producers males were 117 (59%) and females were (41%) which correlates with the study of Dhruba harichandi, Nandkishore Bankar et al. Urinary tract infection is one of the most common infections afflicting women often accompanies vaginal infections. This can be

mainly due to short urethra which reduces the distance for bacterial ingress and also it opens into the vulvar vestibule. On the other hand, the proximity of the anus facilitates the colonization of both the reproductive organs and distal parts of the urinary tract by E.coli and other bacteria. Pelvic prolapse and urinary incontinence also contribute to frequent UTIs.

Uncontrolled Diabetes mellitus is also a major risk factor for recurrent UTIs in both males and females. The main risk factors for ESBL producing UTIs are older age, previous history of UTI, diabetes mellitus, renal diseases, chronic obstructive pulmonary disease, malignancies, improper usage of antibiotics, immunosuppressive medications; kuldeep yadav and Nitika Sharma et al. Maintaining proper personal hygiene, and usage of antibiotics only with proper prescription is necessary in these circumstances. The study shows 87.12% Escherichia coli (E.coli) were sensitive to Piperacillin and tazobactam whereas 84.88% klebsiella spp were sensitive to the same. 89.48% E.coli were sensitive to Cefaperazone and sulbactam, and 84.34% klebsiella were sensitive to the same. The sensitivity of fluoroquinolones were 67.4% and 74.38% to E.coli and klebsiella spp respectively. The sensitivity of aminoglycosides were 79.2% and 81.4% for E.coli and klebsiella respectively. This study correlates with Prabhat Sharma and kirti malpekar et al study. 74.83% of E.coli and 75.64% of klebsiella were sensitive to ceftazidime /clavulanate and 64.46% of E.coli and 63.17% of klebsiella were sensitive to Amoxicillin /clavulanic acid which correlates with the study of Dr Shreeram Astic and Dr Divya M B et al study. The sensitivity of Nitrofurantoin was 81.78% for E.coli and 64.48% for Klebsiella spp which correlates with the Sohni naem, Hazrat bilal et al study. 99% of E.coli and 97.8% Klebsiella were sensitive to carbapenams which correlates with Shrabanti barua and Saikat barua et al study.

Table 1:- Culture Positivity for Escherichia coli & Klebsiella species.

Total number of culture positive for Escherichia coli & klebsiella	Total number of Escherichia coli isolated from culture	Percentage of Escherichia coli isolated from culture	Total number of Klebsiella isolated from culture	Percentage of Klebsiella isolated from culture
576	372	64.6%	204	35.4%

Figure No 1:- Culture Positivity & ESBL producers for Escherichia coli & Klebsiella species.

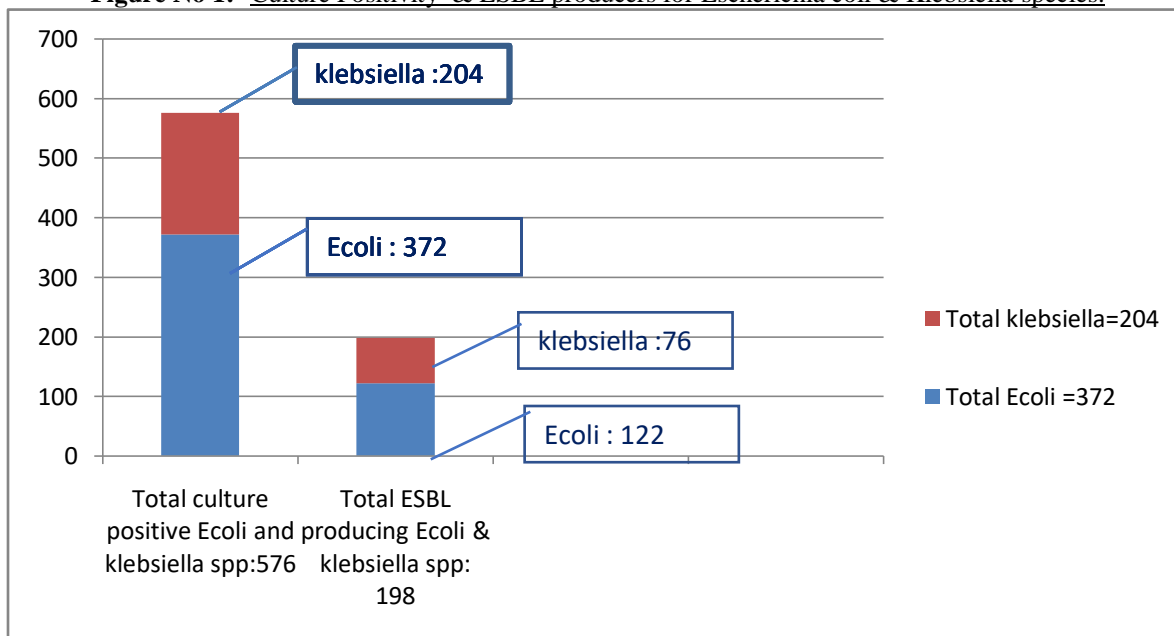


Table No 2:- Prevalence Of Total ESBL Producers.

Total No of Culture positives for E. coli & Klebsiella spp	Total Number of ESBL producers	Percentage of ESBL producers
576	198	34.3%

Table No 2A:- Prevalence Of ESBL Producing Escherichia Coli & Klebsiella Spp In Percentage.

Total No of ESBL producers out of 576 culture positive E coli & Klebsiella spp	Total No of ESBL producing E coli	Percentage of ESBL producing E coli	Total No of ESBL producing Klebsiella spp	Percentage of ESBL producing Klebsiella spp
198	122	61.6%	76	38.3%

Figure No 2:- Total ESBL Producing Ecoli And Klebsiella SPP.

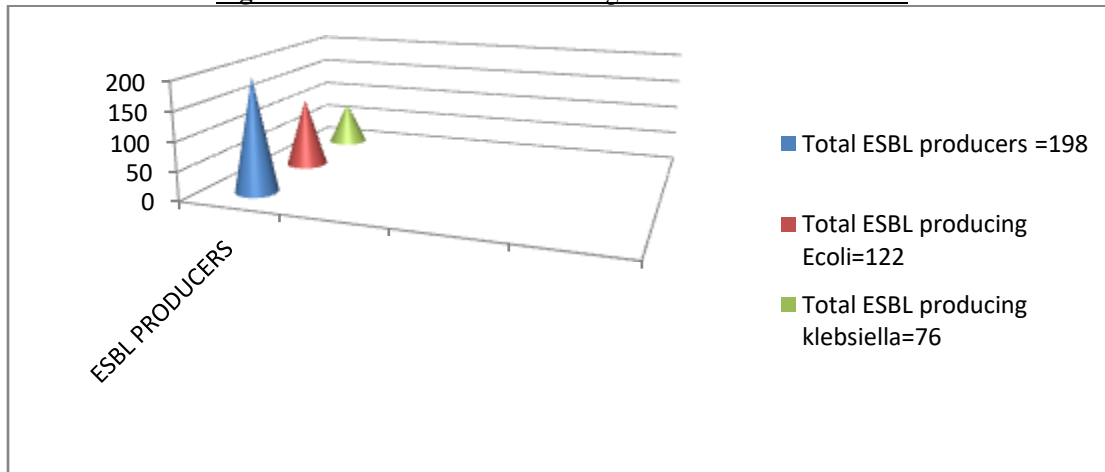


Figure No 2A:- Percentage Of Esbl Producing Ecoli & Klebsiella SPP.

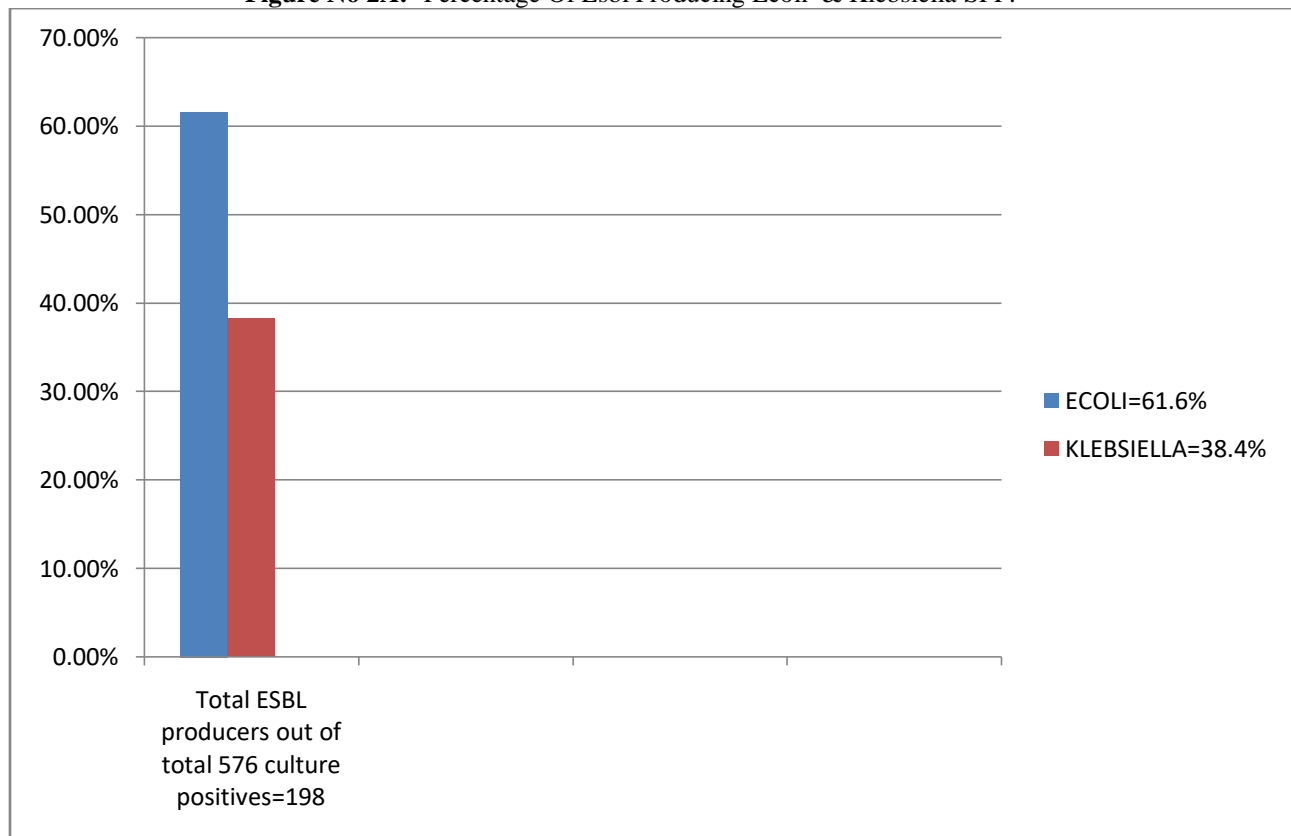


Table 3:- Culture Positive Male and Female ratio.

Total No of Culture Positive samples for Escherichia coli & Klebsiella species	Total number of Males of culture positive for Escherichia coli & Klebsiella species	Total number of Females of culture positive for Escherichia coli & Klebsiella species	Total number of ESBL producers	Total No of Males patient samples which were Positive	Total No of Females patient samples which were ESBL Positive
576	237 (41.2%)	339 (58.8%)	198	117(59%)	81(41%)

Figure No. 3:- Percentage of Male & Female samples which are ESBL producers.

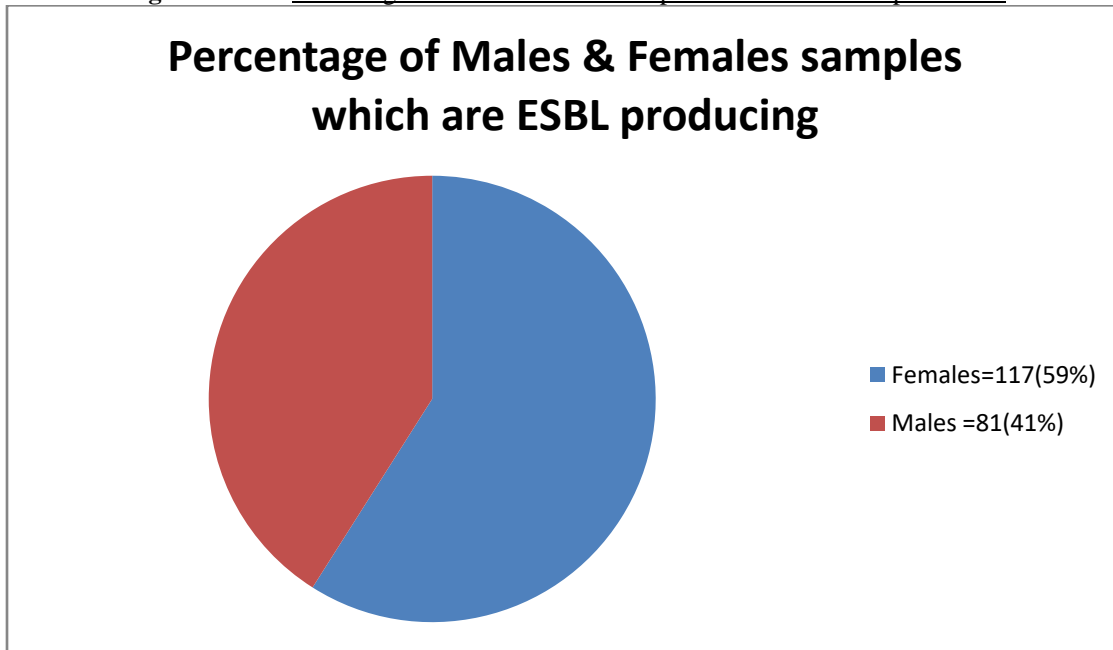
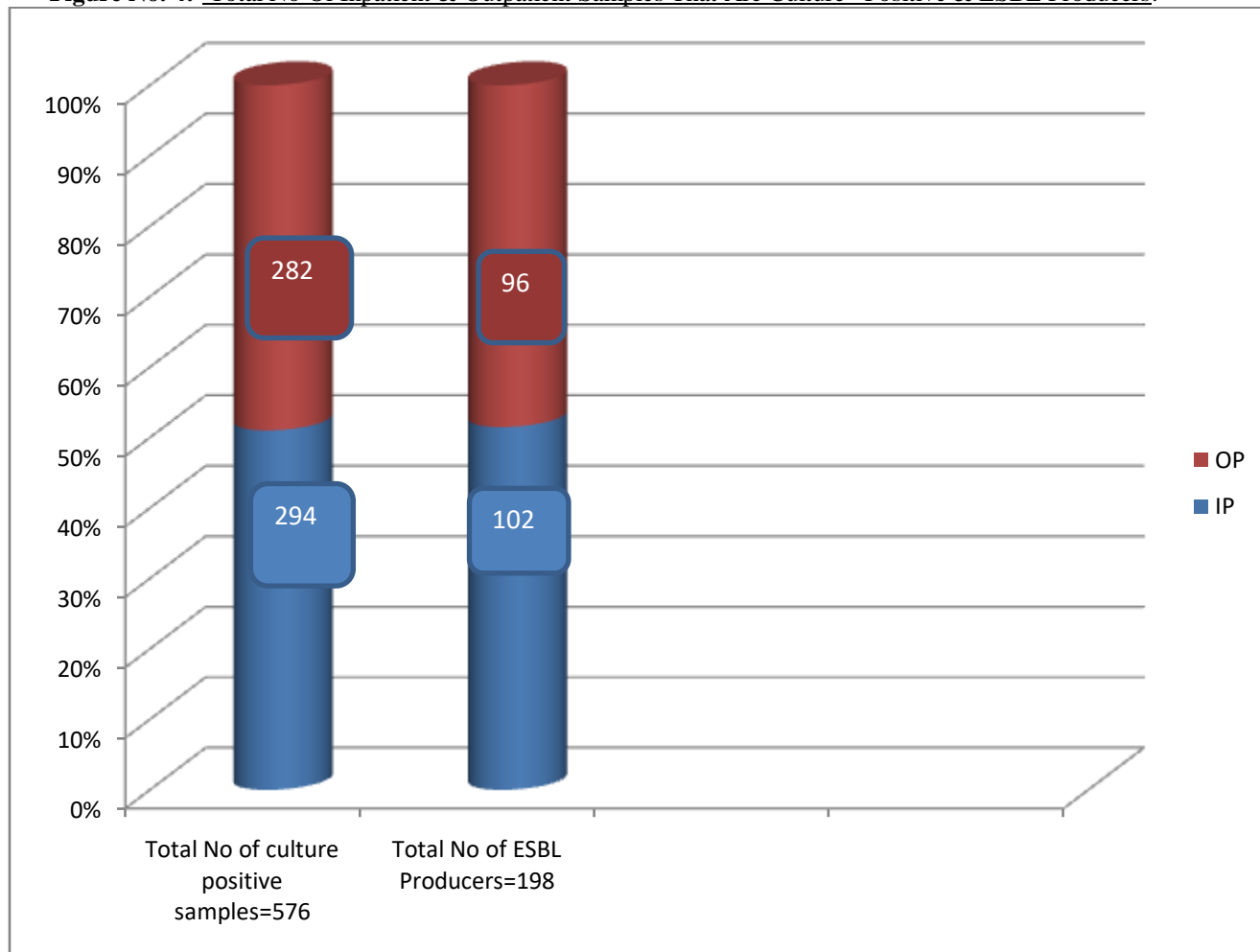
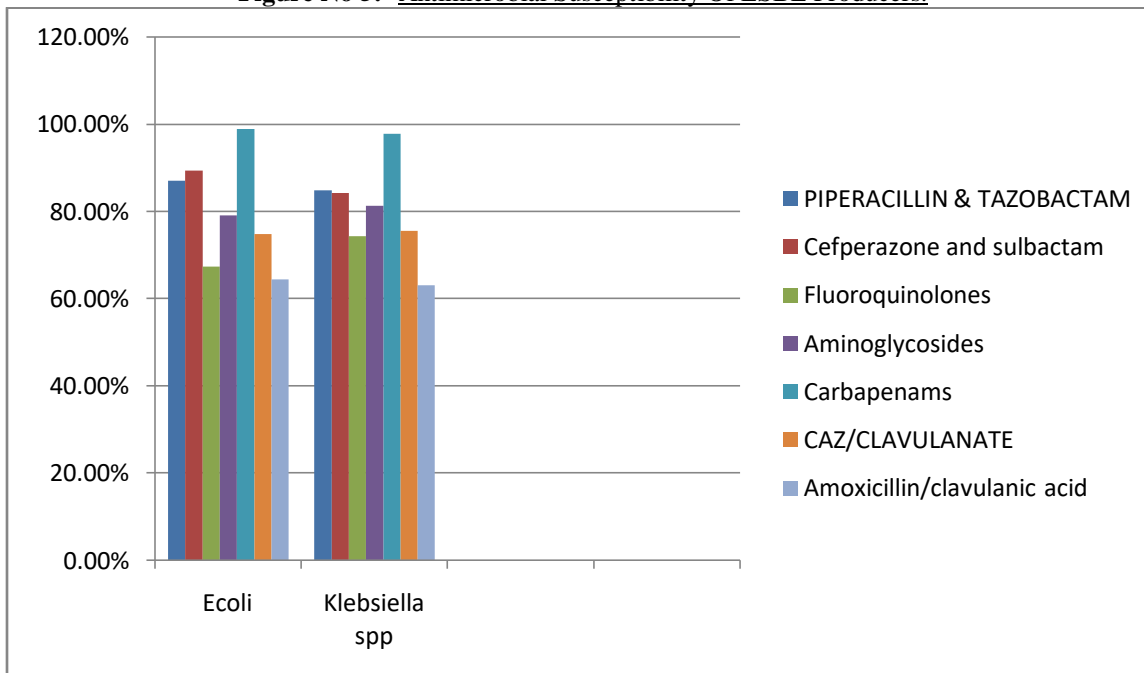


Table No 4:- Total No Of Inpatient & Outpatient Samples That Are Culture Positive & ESBL Producers.

Total No of IP Samples that are culture positive	Total No of OP Samples that are culture positive	Total No of IP Samples that are ESBL producers	Total No of OP Samples that are ESBL producers
294	282	102	96

Figure No. 4:- Total No Of Inpatient & Outpatient Samples That Are Culture Positive & ESBL Producers.**Table No. 5:- Antimicrobial Susceptibility Of ESBL Producers.**

Antimicrobials	Percentage of sensitivity of Ecoli	Percentage of sensitivity of Klebsiella spp
Piperacillin and Tazobactam	87.12%	84.88%
Cefoperazone and sulbactam	89.48%	84.34%
Ceftazidime /clavulanate	74.83%	75.64%
Amoxicillin /clavulanic acid	64.46%	63.18%
Nitrofurantoin	81.78%	64.17%
Fluroquinolones	67.4%	74.38%
Aminoglycosides	79.2%	81.4%
Carbapenams	99%	97.8%

Figure No 5:- Antimicrobial Susceptibility Of ESBL Producers.**Conclusion:-**

Urinary tract infection is a significant health burden impacting the global community. Tackling the major risk entities and drug resistance is fundamental for management. Early diagnosis and periodic local surveillance of the antibiotic spectrum has a pivotal role in mitigating serious sequelae. It is also important to monitor and optimize antibiotic use through antibiotic stewardship programmes. The collaboration of Microbiologists and clinicians is also necessary for the effective management of infections especially due to ESBL producing organisms.

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