

**A STUDY ON INCIDENCE OF BETA LACTAMASE AND METHICILLIN  
RESISTANT STAPHYLOCOCCUS AUREUS IN URINARY TRACT INFECTIONS**

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**ABSTRACT**

Urinary tract infections are serious health problems affecting millions of people every year. Women are especially more prone to UTI for reasons not very well understood but most likely it is because of close proximation of urethral vaginal and anal openings. One woman in five develops UTI during her lifetime. UTI in men are not as common as in women but can be very serious when they do occur. Normally urine is sterile. It is free from bacteria, viruses and fungi but does contain fluids, salts and waste Products. An infection occurs when living organisms usually bacteria from digestive tract adhere to the opening of urethra and begin to multiply. The urethra is the tube that carries urine from bladder to outside the body. Most infections occur from one type of bacteria i.e. *E. coli* which normally lives in colon. In many cases bacteria first travel to urethra, multiply and cause urethritis. If they move to bladder and multiply it is called cystitis. If infection is not treated promptly they may travel up to involve kidney and is known as pyelonephritis. Microorganism called *Chlamydia* and *Mycoplasma* may also cause UTI in both men and women but these infections tend to remain limited to urethra unlikely *E-coli*, *mycoplasma*, may be transmitted sexually and infections require treatment of both partners.

## INTRODUCTION AND HISTORY

Urinary tract infections are serious health problems affecting millions of people every year. Women are especially more prone to UTI for reasons not very well understood but most likely it is because of close proximation of urethral vaginal and anal openings. One woman in five develops UTI during her lifetime. UTI in men are not as common as in women but can be very serious when they do occur. Normally urine is sterile. It is free from bacteria, viruses and fungi but does contain fluids, salts and waste Products. An infection occurs when living organisms usually bacteria from digestive tract adhere to the opening of urethra and begin to multiply. The urethra is the tube that carries urine from bladder to outside the body. Most infections occur from one type of bacteria i.e. *E. coli* which normally lives in colon.

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Microorganism called *Chlamydia* and *Mycoplasma* may also cause UTI in both men and women but these infections tend to remain limited to urethra unlikely *E-coli*, *mycoplasma*, may be transmitted sexually and infections require treatment of both partners.

*E.coli* and *Klebsiella* isolates are equally resistant to Ampicillin (76% and 75% respectively) while for cotrimoxazole, *E. coli* is more resistant (75%) than *Klebsiella* (53%). Indian isolates showed higher resistance against ampicillin and cotrimoxazole than the isolates from USA (39.1% and 18.6% respectively and Europe 29.8 % and 14.1% respectively. On the other hand, rate of resistance against these antibiotics in countries like Senegal (77% and 55%), Spain (65% and 33%) Taiwan (80% and 56%) and Israel (66% and 26%) is comparable with Indian isolates.

In a study conducted by Microbiology Department JN Medical College Aligarh. the *E coli* and *Klebsiella* isolates are highly resistant against nitrofurantoin (80 % and 76% resistant respectively) whereas this drug exhibited low resistant rate in the major part of the world (0- 54 %), despite of its being used for many years<sup>78</sup>. This is probably due to the fact that this antibiotic has been widely used in treating community acquired UTIs over the past decade in this region. The resistance rate of *E. coli* to extended spectrum cephalosporins range from 55% to 85%, which is contrary to the other community acquired UTI studies in Europe, Israel and US. Higher resistance rate to all the antibiotics with the exception of amikacin and Imipenem may be explained as uncontrolled consumption of these antibiotics during the past decade. In the study conducted by Microbiology Department JN Medical College Aligarh the overall imipenem resistance was 12% for *Klebsiella pneumoniae*, whereas, other isolates of uropathogens were found to be resistant to imipenem. It is highly stable against beta lactamase and has an unusual property of causing post antibiotic effect on gram negative bacteria. Due to its small molecular size, it can overcome the poor permeability of beta lactams for *Pseudomonas* by efficient penetration through Porins, OMPD. Extended spectrum cephalosporins showed remarkable rates of resistance against *E. coli*, *K. pneumoniae*, *Staphylococcus aureus*, *Acinetobacter* and *P. aeruginosa*. All *Staphylococcus aureus* isolates were susceptible to third generation cephalosporins i.e. cefotaxime and ceftriaxone, whereas among *P.aeruginosa* all isolates showed resistance to cefpodoxime and the same study 42% of uropathogens were found to produce ESBLs. High prevalence rate of ESBL producing strains have also been reported earlier in *K. pneumoniae*. This is consistent with other drug resistant groups in

India (48.3%). A 34.42% of *E. coli* isolates were ESBL producers, followed by 27.3% of *K. pneumoniae*. It might be possible that the high level of multidrug resistance was most probably due to production of extended spectrum beta lactamases in these isolates.<sup>88</sup>

The role of third generation cephalosporins in the treatment of *K. pneumoniae* is limited as ESBL mediated resistance is on the increase in the last decade. In a study from South India ESBL mediated resistance was 25.8 % and in another study a very low prevalence of 6% was reported. This very low prevalence in their study may be due to the fact that isolates were from infections in children and this may be the reason for disparity. However there are various reports where incidence is reported to be 23 % in hospital isolates and 84 % of epidemic isolates. Farhat ullah *et al* found in his study that *E. coli* (33.9%) was the commonest organism isolated from urine samples. More isolates were received from females as compared to males. The ratio was 3:1. Middle aged patients that 22-45 years accounted for 54.3 % of infections while second predominant group was children (24%). Among beta lactams the most effective antibiotic was Imipenem with 98.3 % of isolates susceptible to this agent followed by meropenem with 97.4 % of the isolates being susceptible. Among cephalosporins 62 % resistance was reported to cefotaxime, 65% to cefaclor and ceftazidime both and 72 % to cepharidine while the highest resistance was reported to penicillin group (ampicillin) i.e. 89%. Among aminoglycosides, 48% isolates were susceptible to gentamicin and 43% to amikacin. In their study 56.9% *E. coli* were found to produce ESBL.

Recent studies on ESBL production in members of enterobacteriaceae isolated from clinical specimens showed 9-50% ESBL. A study from north india on ESBL production in uropathogens showed 26.6 % ESBL producers which belonged to *Klebsiella*, *E. coli*, *Enterobacter*, *Proteus* and *Citrobacter* sp

### **FINDINGIS OF THE STUDY**

Urinary tract infection is one of the most common infections diagnosed in outpatient and as well as in hospitalized patients. . Current knowledge on antimicrobial susceptibility pattern is mendatory for appropriate therapy. Extended spectrum beta lactamases (ESBL) hydrolyse extended spectrum cephalosporins like Ceftazidime, Cefaclor, Cefuroxime and cefotaxime which are used in the treatment of UTI. ESBL producing bacteria may not be detectable by routine disc diffusion

susceptibility test leading to inappropriate use of antibiotics and treatment failure. Not much information on ESBL producing organism causing urinary tract infection is available from India. An effort is therefore made to study the ESBL producing pathogens and also the susceptibility pattern of ESBL and non ESBL producer organisms.

A number of reports have demonstrated the emergence of ESBL in the community in long care facility and ambulatory patients with chronic conditions. These reservoirs add to the pool of hospital environment. Community acquired infections are defined as individuals who did not have history of hospitalization in the preceding three months and who were either outpatient or admitted patients who had their first positive culture from samples obtained within 48 hrs of hospital admission. Other hospitalized patients and those hospitalized within three months were deemed to have nosocomial infections<sup>3</sup>.

The development of antibiotics has contributed to reducing mortality caused by infections but as the use of antibiotics became generalized the vicious circle of development of new antibiotics and emergence of resistant bacteria develops. This has to be stopped. In fact according to epidemiological study conducted by National Nosocomial infections surveillance (NNIS). The resistance rate of most bacteria to antibiotics has increased.

The current situation of resistance to antibiotics has reached a serious level in urinary tract infection. And presently multidrug resistant bacteria can be readily encountered in clinics. Antibiotics that can be used for the treatment of multidrug resistant bacteria including ESBL producing bacteria in urinary tract infections are limited.

factors for the emergence of ESBL producing bacteria. This explains very high incidence of ESBL positivity in our study (Table-6). Table 4 & 5 shows that prevalence of ESBL positivity is more in female gender. This suggests that blocking of infection within the hospital could reduce the prevalence of ESBL producing bacteria and could lower the spread to communities. Thus efforts to reduce the opportunities for inpatient infection with ESBL producing bacteria should be considered very important. Siegel *et al* recommended that to block the spread of multidrug resistant bacteria within the hospitals , hospitals should restrict contact with patients infected with multidrug resistant bacteria internally and provide detergents containing alcohol in the area. In addition they mentioned that hand hygiene education for the medical staff and guardians should be required. Furthermore Siegel *et al* emphasized the need to monitor the trend of multidrug resistant bacteria by routine bacterial culture and also to establish organized report systems.

Calber *et al* reported that exposure to second generation cephalosporins particularly cefaclor and cefuroxime are also important risk factors for emergence of ESBL producing bacteria . Goossens *et al* explained the association of the level of use of antibiotics with bacteria acquiring the resistance and emphasized the adequate use of antibiotics. Infact it has been reported that the appropriate use of antibiotics against gram negative bacteria decreases the frequency of multidrug resistant bacteria. On the other hand. in clinics, prescription of antibiotics empirically for pyuria in asymptomatic bacteriuria patients or catheterized patients is seen occasionally and the IDSA

In our country, second generation oral cephalosporins like cefaclor and cefuroxime are extensively used by general practitioners, unqualified doctors and chemists and that too in inadequate doses and duration to treat not only urinary tract infections but all kind of infectious diseases. This may be one of the most important reasons of high prevalence of ESBL producing organisms. Therefore to prevent the emergence of multidrug resistant bacteria in urinary tract infections , efforts should be made to strictly observe the indications for the administration of antibiotics and to use antibiotics appropriately for minimal period through culture for cases requiring antibiotics.

Foley catheterization is well known to be a risk factor for urinary tract infection . About 20% of urinary tract infections are associated with foley catheterization due to unskilled sterilization techniques during insertion of the catheter. Infection may occur due to contamination of the collecting specimen through the lumen of the catheter ,Other cases have been reported to occur through the biofilm formed between catheter and urethral mucosa. Therefore unnecessary foley catheterization should be avoided in patients with urinary tract infections to prevent emergence of ESBL producing bacteria.

Despite worldwide use of beta lactum antibiotics the distribution of the enzymes responsible for resistance to oxyimino cephalosporins and carbapenems is not uniform. Some hospitals have no ESBLs while in others there is very high prevalence of ESBLs. ESBLs are mostly found in *E. coli* and *Klebsiella* but have also been reported in *Citrobacter*, *Enterobacter*,

*Proteus* and other genera of enteric and in some non enteric organisms such as *Acinetobacter* and *Pseudomonas aeruginosa*.

Risk factors for colonization and infections by ESBL producing organisms are little different from the risk factors for other nosocomial infections. Reported risks, many of which are linked , include an increased length of stay in the hospital , an increased length of stay in the intensive. Among the beta lactams tested. the carbapenems have the widest spectrum of activity. Imipenem was the most active antimicrobial agent having approximately 95 to 98 % activity. Imipenem was followed by meropenem with 85 to 95 % activity.



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