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ANTIBIOTIC SUSCEPTIBILITY PATTERN OF URINARY TRACT INFECTION CAUSING PATHOGENS ISOLATED FROM DIABETIC PATIENTS

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ABSTRACT

Urinary tract infection is one of the most commonly occurring infections among the patients with diabetes mellitus. The present study was focused on the antibiotic susceptibility of the UTI pathogens isolated from the diabetic patients. About 936 UTI organisms were isolated from 900 culture positive urine samples collected from the diabetic patients attending the government hospital. The incidence of UTI was recorded to 82% among the diabetic patients for the study period of two years from March, 2011 to February, 2013. *Escherichia coli* was found to be the major cause of UTI. About 10 different types of organisms isolated from the UTI samples were randomly chosen to test against the UTI antibiotics of dodecadisc rings of Hi-media with codes DE004 and DEO30 .The antibiotic susceptibility pattern revealed that *Serratia marcescens* was sensitive to 91% of antibiotics tested against and was resistant to 9% of antibiotics followed by *Proteus mirabilis* (87% and 13%), *Staphylococcus aureus* (70% and 17%), *Citrobacter* sp. (70% and 30%), *Klebsiella* sp. (70% and 30%), Methicillin resistant *Staphylococcus aureus* (61% and 17%), *Enterobacter* sp. (52% and 39%) and *E. coli* (48% and 39%). Among the antibiotics tested against the isolates; Netillin, Gatifloxacin and Levofloxacin revealed a 100% sensitivity followed by other antibiotics. About 50-60% of the isolates were multi drug resistant in which *E. coli*, *Enterobacter* sp., *Klebsiella* sp. and *Citrobacter* sp. revealed resistance to 30-39% of antibiotics such as, Cefacdroxil, Cefuroxime, Cotrimoxazole, Cefaclor and Nalidixic acid. *E. coli* was found to be the most resistant organism.

INTRODUCTION

Diabetes mellitus is a metabollic syndrome characterized by an inappropriate elevation of blood glucose as a result of relative or absolute lack of insulin. Diabetes mellitus has a long term effect on genitourinary system and diabetics are more prone to urinary tract infections (UTI's) and particularly to upper UTI (Patterson and Andriole, 1997). The clinical manifestations of UTI depend on the portion of the urinary tract involved, the etiologic organisms, the severity of the infection and the patient's ability to mount an immune response to it (Foxman and Browm, 2003). It has been estimated that globally symptomatic UTIs result in as many as 7 million visits to outpatient clinics, 1 million visits to emergency departments and 100,000 hospitalizations annually (Wilson and Gaido, 2004). In the community and hospital settings, the aetiology of UTI and the antimicrobial susceptibility of the urinary pathogens have been changing over the years from place to place (Gruneberg, 1980; Gales *et al*., 2000; Saffar *et al*., 2008). Now a days it represents one of the most common diseases encountered in medical practice affecting people of all ages from the neonate to the geriatric age group (Kunin, 1994). Worldwide, about 150 million people are diagnosed with UTI each year (Gupta *et al*., 2001). As suggested by Goldman and Huskins (1997) the improper and uncontrolled use of many antibiotics resulted in the occurrence of antimicrobial resistance, which became a major health problem worldwide. In the past decades, many kinds of resistant strains have been discovered. For example, methicillin resistant *Staphylococcus aureus* (MRSA) (Wagenlehner and Naber, 2004), multidrug resistant *Psuedomonas aeruginosa* (Linuma, 2007), *Serratia marcescens* (Kim *et al*., 2006), vancomycin resistant *Enterococci* (VRE) (Gold, 2001) and extended spectrum beta lactamase (ESBL) resistant *Enterococci* (Bhattacharya, 2006). Drug resistance of pathogens is a serious medical problem, because of very fast arise and the spread of mutant strains that are insusceptible to medical treatment. Microorganisms use varied mechanisms to acquire drug resistance *viz*., horizontal age transfer (plasmids, transposons and bacteriophages),

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Table 1. Antibiotic susceptibility pattern for UTI isolates (Multi Drug Resistant)

Organism	CF	AM	NE	NO	CE	OF	CI	CX	CP	NI	NA	GE	SP	CL	AZ	ME	IM	CO	GA	LE	PO	CH	FU
E. coli	R	S	S	R	R	R	R	R	S	S	R	R	S	I	I	S	S	R	S	S	S	S	I
Citrobacter sp.	S	S	S	R	S	R	S	S	S	S	R	S	R	R	S	R	S	R	S	S	S	S	S
Klebsiella sp.	R	S	S	S	R	S	S	R	R	S	S	S	S	R	R	S	S	R	S	S	S	S	S
Enterobacter sp.	R	S	S	S	R	S	S	R	R	R	R	S	S	R	R	S	S	R	S	S	S	I	I
Serratia marcescens	S	S	S	S	S	S	S	S	S	S	S	S	S	R	S	S	R	S	S	S	S	S	S
MRSA	I	S	S	I	I	I	R	S	S	S	R	R	S	S	I	R	S	S	S	S	S	S	S
Staphylococcus aureus	S	S	S	I	R	I	R	S	S	R	R	S	I	S	S	S	S	S	S	S	S	S	S
Proteus mirabilis	S	S	S	S	S	S	S	S	S	S	R	S	S	S	S	S	S	S	S	S	R	S	R
Pseudomonas aeruginosa	R	S	S	S	R	S	S	R	S	R	I	S	S	S	S	S	S	S	S	S	R	S	R
Enterococcus feacalis	R	I	S	R	R	R	S	R	R	S	S	S	S	S	R	S	S	R	S	S	R	S	R

CF: Cefadroxil, AM: Amikacin, NE: Netillin, NO: Norfloxacin, CE: Cefaclor, OF: Ofloxacin, CI: Ciprofloxacin, CX: Cefuroxime, CP: Cefoperazone, NI: Nitrofurantoin, NA: Nalidixic acid, GE: Gentamycin, SP: Sparfloxacin, CL: Cloxacillin, AZ: Aztreonam, ME: Meropenem, IM: Imipenem, CO: Co-trimoxazole, GA: Gatifloxacin, LE: Levofloxacin, PO: Polymyxin, CH: Chloramphenicol, FU: Furazolidone

recombination of foreign DNA in bacterial chromosomes and mutations in different chromosomal locus (Klemm *et al*., 2006). It has been reported in the scientific literature on the inappropriate use of antimicrobial agents and the spread of bacterial resistance among microorganisms causing UTI (Tenever and McGowan, 1996; Hryniewicz *et al*., 2001; Kurutepe *et al*., 2005). Among uropathogens, the rate of resistance is high and frequency of resistance to antibiotics is directly linked to the consumption of antibiotics (Gossens *et al*., 1998). The changing patterns in the etiological agents of urinary tract pathogens and their sensitivities to commonly prescribed antibiotics are reported (Jacoby and Archer, 1991; Hryniewicz *et al*., 2001; Kurutepe *et al*., 2005; Mordi and Erah, 2006). The emergence of antibiotic resistance in the management of UTI is a serious public health issue, particularly in the developing world where apart from high level of proverty, ignorance and poor hygienic practices, there is also a high prevalence of fake and spurious drugs of questionable quality in circulation (Abubakar, 2009). A protocol for empirical treatment of simple lower UTI with first and second generation cephalosporins while gentamycin for the treatment of clinical pyelonephritis. The management of UTI in patients with diabetes is essentially the same as patients without diabetes. During the course of a lifetime with diabetes, UTIs would be ranked among the top 10 concurrent or complicating illness by most experts and patients (Robbins and Tucker, 1994).

MATERIALS AND METHODS

The study determines the antibiotic susceptibility of the urinary tract infection (UTI) causing organisms isolated from the diabetic patients. The study was performed on 1085 diabetic patients (429males and 656 females) with any sign and symptoms of UTI attending both outpatients and inpatient's department in the Government hospital, Mysore, Karnataka from march, 2011 to February, 2013. About 900 urine specimens (330 male, 570 females) were culture positive. The specimens were not collected from the patients whoever consumed any antibiotics in the previous 15 days of the study. The organisms were isolated and identified by standard biochemical tests (Collee *et al*., 1989). About 936 isolates were obtained from which 10 different isolates were chosen for the antimicrobial study. The antibiotic susceptibility of the isolates was performed by the disc diffusion assay on the Mullerhinton agar and Blood agar media by modified Kirby-Bauer method (WHO, SEARO, 2006). The antibiotics used to test against the isolates were UTI antibiotic dodecadisc rings of Hi-media with codes DE004 and DEO30. The interpretation of the diameter observed was recorded as sensitive (S), intermediate (I) and resistant (R) following the limits of CLSI (2006). The diameter of zone of inhibition was noted to the nearest mm of an average of three readings in all the cases.

The antibiotics tested were Cefadroxil, Amikacin, Netillin, Norfloxacin, Cefaclor, Ofloxacin, Ciprofloxacin, Cefuroxime, Cefoperazone, Nitrofurantoin, Nalidixic acid, Gentamycin, Sparfloxacin, Cloxacillin, Aztreonam, Meropenem, Imipenem, Co-trimoxazole, Gatifloxacin, Levofloxacin, Polymyxin, Chloramphenicol and Furazolidone.

RESULTS AND DISCUSSION

Of the 10 different UTI isolates tested against 23 types of UTI antibiotics, *E. coli*, *Enterococcus feacalis* and *Enterobacter* sp. played a predominant role in being resistant to 9 types of UTI antibiotics and sensitive to 11 types of antibiotics (48%), 10 and 12 (44% and 52%), 9 and 12 (39% and 52%) (Table 1). *Serratia marcescens* was the most sensitive to 21 types of antibiotics (91%) and was resistant to only 2 types of antibiotics (9%) followed by *Proteus mirabilis* 20 and 3 (87% and 13%), *Pseudomonas aeruginosa*

16 and 7 (70% and 30%), *Klebsiella* sp. 16 and 7 (70% and 30%), *Staphylococcus aureus* 16 and 4 (70% and 17%) and Methicillin resistant *Staphylococcus aureus* (MRSA) 14 and 4 (61% and 17%) (Table 2). Among the 23 types of antibiotics tested Netillin, Gatifloxacin and Levofloxacin showed 100% positive result against all the isolates. About 90% of isolates were sensitive against Amikacin, Chloramphenicol and Impenem and 80% of isolates were sensitive to Gentamycin, Sparfloxacin and Meropenom followed by 70% of isolates against Ciprofoxacin, Cefoperazone, Nitrofurantoin and rest of the antibiotics fall below 50% of isolates against them (Table 3).

Table 2. Susceptibility percentage of the UTI isolates

Organism	Sensitivity	Intermediate	Resistant
Serratia marcescens (Fig 1)	21 (91%)	0	2 (9%)
MRSA (Fig 2)	14 (61%)	5 (22%)	4 (17%)
E. coli (Fig 3)	11 (48%)	3 (13%)	9 (39%)
Citrobacter sp. (Fig 4)	16 (70%)	0	7 (30%)
Pseudomonas aeruginosa (Fig 5)	16 (70%)	1 (4%)	6 (26%)
Klebsiella sp. (Fig 6)	16 (70%)	0	7 (30%)
Staphylococcus aureus (Fig 7)	16 (70%)	3 (13%)	4 (17%)
Enterobacter sp. (Fig 8)	12 (52%)	2 (9%)	9 (39%)
Proteus mirabilis (Fig 9)	20 (87%)	0	3 (13%)
Enterococcus feacalis (Fig 10)	12 (52%)	1 (4%)	10 (44%)

Table 3: Resistance pattern against antibiotics

Antibiotics	Sensitivity	Intermediate	Resistant
Cefadroxil	4 (40%)	1 (10%)	5 (50%)
Amikacin	9 (90%)	1 (10%)	0
Netillin	10 (100%)	0	0
Norfloxacin	5 (50%)	2 (20%)	3 (30%)
Cefaclor	3 (30%)	1 (10%)	6 (60%)
Ofloxacin	5 (50%)	2 (20%)	3 (30%)
Ciprofloxacin	7 (70%)	0	3 (30%)
Cefuroxime	5 (50%)	0	5 (50%)
Cefoperazone	7 (70%)	0	3 (30%)
Nitrofurantoin	7 (70%)	0	3 (30%)
Nalidixic acid	3 (30%)	1 (10%)	6 (60%)
Gentamycin	8 (80%)	0	2 (20%)
Sparfloxacin	8 (80%)	1 (10%)	1 (10%)
Cloxacillin	5 (50%)	1 (10%)	4 (40%)
Aztreonam	5 (50%)	2 (20%)	3 (30%)
Meropenem	8 (80%)	0	2 (20%)
Imipenem	9 (90%)	0	1 (10%)
Co-trimoxazole	5 (50%)	0	5 (50%)
Gatifloxacin	10 (100%)	0	0
Levofloxacin	10 (100%)	0	0
Polymyxin B	7 (70%)	0 ()	3 (30%)
Chloramphenicol	9 (90%)	1 (10%)	0
Furazolidone	5 (50%)	2 (20%)	3 (30%)

Fig. 1. Sensitivity test of *Serratia marcescens* against antibiotics

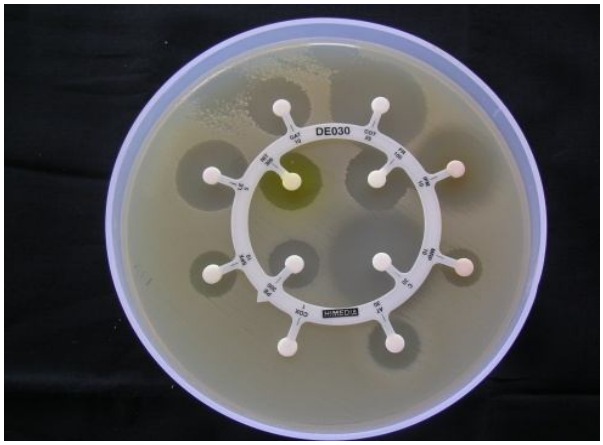


Fig. 2. Sensitivity test of MRSA against antibiotics

Fig. 3. Sensitivity test of *E. coli* against antibiotics

Fig. 4. Sensitivity test of *Citrobacter* sp. against antibiotics

Fig. 5. Sensitivity test of *Pseudomonas aeruginosa* against antibiotics

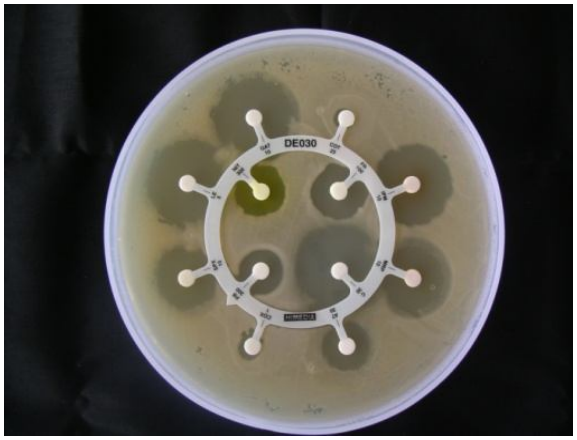


Fig. 6. Sensitivity test of *Klebsiella* sp. against antibiotics

Fig. 7. Sensitivity test of *Staphylococcus aureus* against antibiotics

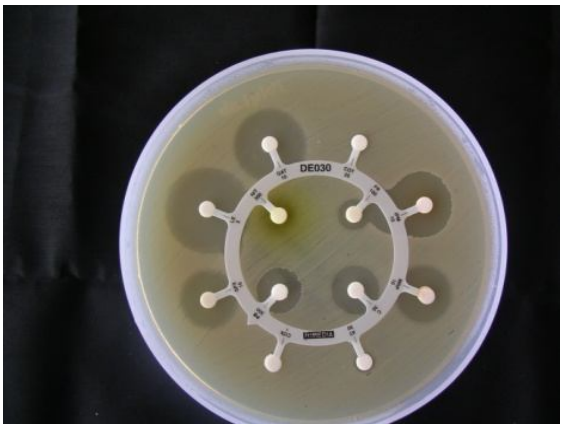
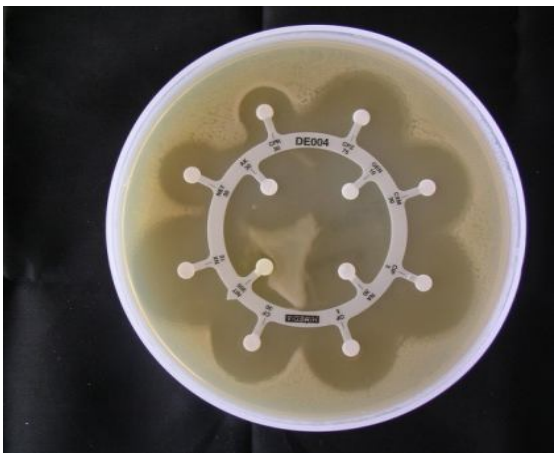


Fig.8. Sensitivity test of *Enterobacter* sp. against antibiotics



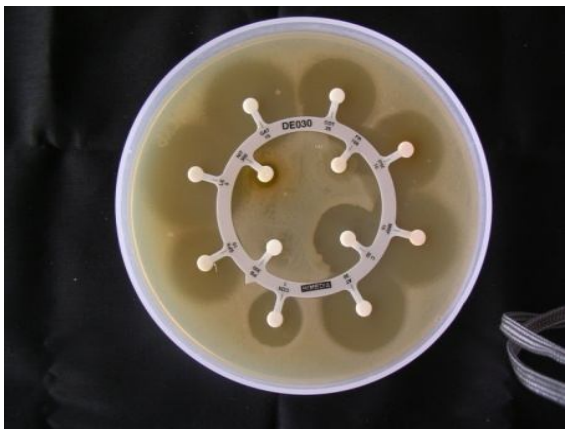
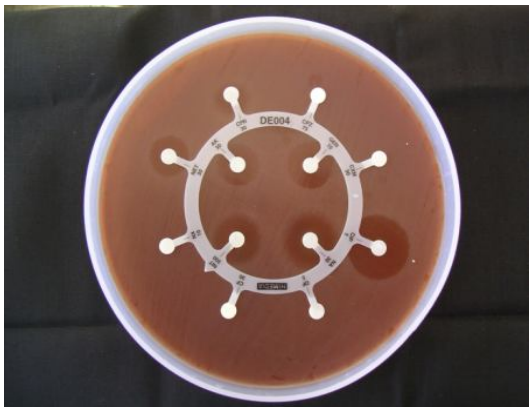


Fig. 9. Sensitivity test of *Proteus mirabilis* against antibiotics



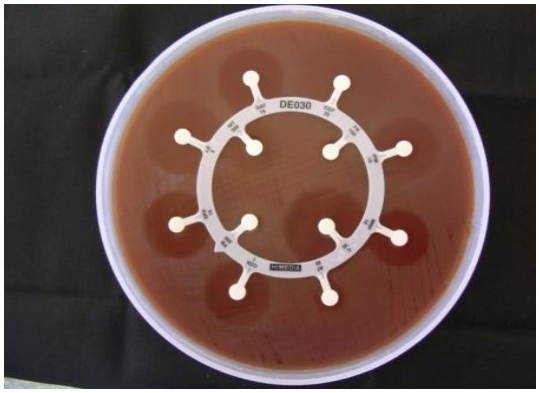


Fig. 10. Sensitivity test of *Enterococcus feacalis* against antibiotics

The present the study reveals the antibiotic resistant profile of the most common UTI causing organisms. Among the uropathogens, the rate of resistance is high and frequency of resistance to antibiotics and drugs is directly linked to consumption of antibiotics (Goossens and Sprenger, 1998). In this investigation, the organisms isolated from the UTI samples of diabetic patients were most resistant to many antibiotics. The poor susceptibility of *E. coli* to Nalidixic acid and Gentamycin gives less support to the previous work (Uwaezuoke and Ogbulie, 2006; Aboderin *et al*., 2009). According to Mandal *et al*. (2001) reports from India, *E. coli* as the commonest cause of UTI and antibiotic resistance was high among the strains, which emphasize the need for judicious use of antibiotics. *Staphylococcus aureus* and MRSA revealed to be resistant to 17% of antibiotics.

According to Tomasz gram positive bacteria are the most common cause of nosocomial infections and difficult to treat because of their frequency of drug resistance. No single antibiotic is bactericidal for vancomycin resistant *Enterococci* (VRE) and MRSA and combination therapy is mandatory (Michel and Gutmann, 1997). In this study, the isolates showed resistance to either single or multiple antibiotics. It has been argued that there is a direct relation between the antibiotics used and the frequency and kinds of antibiotic resistance strains in human beings. Epidemiological studies have suggested that antibiotic resistance genes emerge in microbial populations within 5 years of the therapeutic introduction of antibiotics (Web and Davis, 1992). The study shows that Ciprofloxacin was active against 70% and resistant against 30% of UTI isolates. It has been studied that Ciprofloxacin is highly active against UTI pathogens (Farrell *et al.*, 2003) and maintain excellent level of susceptibility among common UTI pathogens (Gupta *et al*., 1999). Due to

frequent use, susceptibility to Ciprofloxcacin decreases in a stepwise manner (Karlowsky *et al*., 2003) and resistance rate increasing among UTI isolates (Gales *et al*., 2002). So a wide spread empirical use of fluoroquinolones should be discouraged because of potential promotion of resistance (Nicolle, 2003). The results of this study coincide with the findings of Shittu and Mandere (1999) that *S. aureus* strains were highly resistant to naladixic acid. Brown *et al.* (2003) have reported that horizontal gene transfer is a factor in the occurrence of antibiotic resistance in clinical isolates and suggested that the high prevalence of resistance to a particular antibiotic does not always reflect antibiotic consumption as previously suggested by Nwanze *et al.* (2007).

Conclusion

UTI causing organisms are more sensitive to Netillin, Gatifloxacin, Levofloxacin and resistant to other antibiotics such as Nalidixic acid, Cefaclor, Cefadroxil, Cefuroxime and Cotrimoxazole which is most commonly prescribed antibiotics and may lead to the inaffective treatment of UTI. The continuous use of antibiotics without any test or knowledge of antibiotic sensitivities should be discouraged. The study confirms that there are still some uropathogens present which are multi drug resistant.

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