

**“A COMPARATIVE STUDY: PATTERN AND PRESENTATION OF
URINARY TRACT INFECTION IN DIABETIC AND
NON DIABETIC POPULATION”**

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Dr. UDAY KUMAR PATIL

LIST OF ABBREVIATIONS

ASB	Asymptomatic Bacteriuria
CFU	Colony Forming Units
CI	Confidence Interval
CIC	Clean Intermittent Catheterization
CLED	Cystine Lactose Electrolyte Deficient media
DM	Diabetes Mellitus
E. coli	Escherichea coli
ESBL	Extended Spectrum Beta Lactamase
FBS	Fasting Blood Sugar
HbA1c	Hemoglobin A1c(glycosylated Hb)
HLA	Human Leucocyte Antigen
K.pneumoneae	Klebsiella pneumoneae
LUTI	Lower Urinary Tract Infection
PPBS	Post Prandial Blood Sugar
S.saprophyticus	Staphylococcus.saprophyticus
UPEC	Uropathogenic E. Coli
UP1a	Uroplakin 1a
UP1b	Uroplakin 1b
UTI	Urinary Tract Infection
UUTI	Upper Urinary Tract In
XGP	Xanthogranulomatous Pyelonephritis

ABSTRACT

Background and objectives

To study the profile of UTI and to determine the etiological agents causing UTI and their antibiotic profile in Diabetics and non-Diabetics. To correlate UTI to the duration of diabetes and blood glucose control and drug therapy in the diabetic study group.

Methods

A total of 100 Diabetics and 100 Non Diabetics fulfilling the inclusion criteria, who visited Shri B M Patil medical college and hospital from January 2013 to July 2014, were included in the study. All these patients underwent a urine routine, urine culture. The profile of urine culture between the two groups was compared.

Results

In our study E.coli was the commonest organism isolated in Diabetics (60%) and Non Diabetics (69%). Rate of isolation was more in Non Diabetics. Klebsiella was the second commonest organism isolated in both groups. Staphylococcus (5%), Acinetobacter (2%) and Candida (2%) were exclusively isolated in Diabetic group (Fischers exact p test: 0.007(HS)). ESBL producers were more frequently isolated from Diabetics when compared to Non Diabetics (p value=0.041)

E.coli isolated from Diabetics was significantly less sensitive ($p < 0.05$) to Cephalosporins. Isolates of E.coli in Non Diabetics were found to be more sensitive ($p < 0.05$) to Amikacin, Piperacillin- Tazobactam, Gatifloxacin and Gentamicin in comparison to diabetic group.

On subgroup analysis we demonstrated a correlation between duration of Diabetes and organisms isolated (Fischers exact test $p = 0.015$). However there was no correlation between isolates and the glycemic control and antidiabetic medications.

Conclusion

E.coli is the commonest pathogen isolated from urine culture in both Diabetics and Non Diabetics. Isolates from Diabetics have demonstrated a higher resistance pattern to Cephalosporins and better sensitivity pattern to Nitrofurantoin, Amikacin, Piperacillin- Tazobactem, Gatifloxacin and Gentamicin. Isolation rate of Extended Spectrum Beta Lactames producing gram negative bacilli is more frequently observed in Diabetics than Non Diabetics.

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INTRODUCTION

It is a frequently stated belief that patients with Diabetes Mellitus (DM) are more prone for infection. Older studies on which this information is based derive their data from autopsy cases. Contrary to this, the association between Diabetes and infection in general is not supported by strong evidence. Many studies conducted on the same idea have also been inconclusive^{1,2}. Nevertheless, it is seen that many specific infections are more common and few occur exclusively in Diabetics. Others are associated with increased severity and complications in them. Urinary tract infection (UTI) is a frequent infection encountered in Diabetics as well as in the general population. Studies have shown that prevalence of UTI is four fold higher in diabetic women than in non-Diabetics. Complications occur more frequently in patients with DM with established UTI and upper urinary tract may be involved in 80% of these patients³.

There are many reasons why one may expect an increased prevalence of UTI in Diabetics. Several aspects of immunity are altered in patients with diabetes. Polymorphonuclear leukocyte function, Leukocyte adherence, chemotaxis, and phagocytosis may all be affected. Antioxidant systems involved in bactericidal activity may also be impaired. Moreover, glycosuria provides an excellent medium for bacterial proliferation. Diabetic autonomic dysfunction may also be a contributing factor. Even after decades of research the question remains if diabetes itself results in immunologic defects which predispose them to infection⁴.

The most common organism causing UTI in both Diabetics and non-Diabetics is *E. coli* which accounts for 80-90% of UTI cases. Other commonly encountered causative agents are *Proteus*, *Klebsiella*, *Enterobacter species* and *Enterococci faecalis*. Diabetes is a common predisposing factor for urinary tract infections caused

by fungi, particularly *Candida* species^{5,6}. Both in community and hospital settings, antimicrobial resistance among uropathogens causing UTI is also increasing and studies have shown incidence of resistance to be higher in Diabetics. This current study was undertaken to compare the presentation of UTI and pattern of causative organisms and their antibiotic profile in Diabetics and non-Diabetics and to determine any difference in them.

AIMS AND OBJECTIVES

- To study the profile of UTI in Diabetics and Non-Diabetics.
- To determine the etiological agents causing UTI and their antibiotic profile in Diabetics and Non-Diabetics.
- To correlate UTI to the duration of diabetes, blood glucose control and drug therapy in the Diabetic study group.
- To compare the incidence of complications of UTI in Diabetics and Non-Diabetics.

REVIEW OF LITERATURE

Urinary tract infection (UTI) is one of the most common infections encountered by health care personnel. UTI is the chief complaint in eight million clinic and emergency department visits and accounts for approximately 100,000 hospital admissions a year.^{5,6} Morbidity and ramification of UTI vary widely from being benign self limiting to producing life threatening sequelae. The varied presentation of UTI is related to location of infection, host co-morbidity and effectiveness of antibiotics .⁷ The infecting organisms are usually bacteria, but fungi may also contribute.

DEFINITION

Urinary Tract Infection: Presence of pathogenic microorganisms in urine or genitourinary tract, which is normally sterile.⁸

Bacteriuria: Identification of any bacteria in the urine or isolation of organism in concentrations that meet standard quantitative criteria.⁸

Significant Bacteriuria: For laboratory purposes the widely applied definition in the UK is 10^4 cfu/ml. For some specific patient groups there is evidence for lower thresholds:

1. Women with symptomatic UTI 10^2 cfu/ml
2. Men 10^3 cfu/ml (if 80% of the growth is due to a single organism).⁸

Bacteraemia: presence of bacteria in the blood diagnosed by blood culture.

Asymptomatic Bacteriuria: Urine culture meets quantitative criteria for bacteriuria without symptoms of attributable infection.^{8,9,10}

Symptomatic Bacteriuria: UTI which manifests as infection of bladder, prostate or kidney.^{8,9}

Classic Symptoms Of Urinary Tract Infection: Dysuria, frequency of urination, suprapubic tenderness, urgency, polyuria, haematuria and fever with chills.

Lower Urinary Tract Infection (LUTI): Evidence of urinary tract infection with symptoms suggestive of cystitis (dysuria or frequency without fever, chills or back pain).⁸

Upper Urinary Tract Infection (UUTI): Evidence of urinary tract infection with symptoms suggestive of pyelonephritis (loin pain, flank tenderness, fever, rigors or other manifestations of systemic inflammatory response).⁸

Haematuria: Blood in the urine either visible (macroscopic) or invisible (microscopic).^{8,10}

Long Term Catheter: An indwelling catheter left in place for over 28 days.^{8,10}

Medium Term Catheter: An indwelling catheter left in place for 7-28 days.^{8,10}

Short Term Catheter: An indwelling catheter left in place for 1-7 days.^{8,10}

Empirical Treatment: Treatment based on clinical symptoms or signs unconfirmed by urine culture.

EPIDEMIOLOGY

During the first year of life males and females have equal risk of developing UTI. In neonatal period the incidence of UTI is higher in males because male infants commonly have congenital anomalies. As females age (between 16-35 yrs), they become 40 times more likely to develop UTI when compared to age matched males. After the age of 60 yrs the difference decreases significantly when prostatic hyperplasia develops in males.^{5,6} While male infections exhibit a bimodal distribution at extremes of age, female infection displays a steady disease burden over time. Studies have shown half of all women develop UTI at least once in a lifetime and one out of three have symptomatic UTI by the age of 24 yrs.¹¹

Complicated UTI occurs in individuals with structural or functional abnormalities of the genitourinary system. Acute uncomplicated UTI rarely occurs in men; hence infection of the urinary system should be considered complicated until underlying abnormality has been ruled out. Up to 90% patients treated with appropriate antimicrobials resolve. Recurrence of UTI in women is 27-46%.^{11,12}

PATHOGENESIS:

The urine and the genitourinary tract are normally sterile except for the distal urethra. The normal floras present in the distal genitourinary tract play an important role in the defense mechanism against potential uropathogens.¹³ The normal flora includes Coagulase negative Staphylococcus, Viridans group Streptococci and Corynebacterium species. Urine is a good nutrient source for most bacterial species.¹⁴ The most important defense mechanism against infection is the unobstructed voiding. Properties of urine and uroepithelial cell components also contribute to maintaining sterile urine.

ROUTES OF INFECTION

In healthy patients most uropathogens originate from rectal flora and enter the urinary tract via the urethra into the bladder. This is known as the ascending route of infection. Uropathogens initially adhere to and colonize the epithelium of the distal urethra. In patients with soiling around the perineum, in patients with urinary catheters and in females using spermicidal agents, there is increased risk of infection via the ascending route.¹³ Any foreign body in the urinary tract such as a catheter or a stone provides an inert surface for bacterial colonization. In Patients with established cystitis, up to 50% of infections may ascend into the upper urinary tracts. Most episodes of pyelonephritis are caused by ascension of bacteria from the bladder through the ureter and into the renal pelvis. This ascent is aided by conditions such as

pregnancy and ureteral obstruction as these conditions inhibit ureteral peristalsis. Bacteria that reach the renal pelvis can penetrate the renal parenchyma through the collecting ducts and disrupt the renal tubules.

In healthy individuals infection of the kidney through the haematogenous route is uncommon. Occasionally, the renal parenchyma may be breached in patients with immunosuppressed state who are infected with *Staphylococcus aureus* bacteraemia or *Candida* fungaemia that originate from oral sources. On rare occasions bacteria from adjacent organs may penetrate the urinary tract via the lymphatics. Conditions associated with the lymphatic route are retroperitoneal abscesses and severe bowel infections.^{13,14}

Most UTI are caused by gram negative bacteria that ascend the urethra. In acute uncomplicated cystitis, *E.coli* accounts for >80% of the uropathogens. Other bacteria include *Staphylococcus saprophyticus* (5-15%), *Klebsiella*, *Proteus* (5-10%), *Enterobacter*, and *Pseudomonas*. *Candida* is the second most common cause of nosocomial UTI.¹²⁻¹⁵

URINARY PATHOGENS

In complicated UTI *E.Coli* remains the predominant organism, but other aerobic gram negative rods such as *Klebsiella*, *Proteus*, *Citrobacter*, *Acinitobacter*, *Morganella* and *Pseudomonas* species have also been isolated. Gram positive bacteria such as *Enterococcus faecalis* and *Staphylococcus saprophyticus* are causative agents for the remainder of community acquired infections. Yeasts are also important pathogens in complicated UTI.^{5,6,13,14}

BACTERIAL ADHERENCE MECHANISMS

VIRULENCE FACTORS

Bacterial virulence factors play a significant role in determining whether an organism will invade the urinary tract and the level of infection acquired. Uropathogenic *E. coli* (UPEC) is present within bowel flora and pathogenic strains of this microorganism can infect the urinary tract by expressing specific virulence factors that permit adherence and colonization of the lower urinary tract. Adherence of the micro-organism is dependent on 3 important environmental characteristics; firstly the bacteria's own adhesive characteristics, secondly the receptive features of the urothelium and finally the fluid that is present between both surfaces.

Adhesins found on the surface of the bacterial membrane are responsible for initial attachment onto urinary tract tissues. Adhesins are classified as fimbrial or afimbrial, depending on whether the adhesin is displayed as part of a rigid fimbria or pilus. Fimbriae and Pili are surface glycoproteins that function as ligands for glycolipid and glycoprotein receptors on uroepithelial cells. Bacteria may produce 100-400 pili on the same cell and other cells can produce the same pilus type. Each pilus is 5-10 μm in diameter and up to 2 μm in length. A pilus is composed of subunits referred to as pilin and they are classified as either mannose sensitive or mannose resistant, based on their ability to mediate haemagglutination of erythrocytes. The most common types of pili are types 1, P and S.^{5,13}

TYPE 1 PILI

Type 1 pili are also referred to as mannose sensitive pili and they are commonly expressed in pathogenic and non pathogenic strains of *E. coli*. An inflammatory process occurs shortly after this binding process has been initiated. This process is necessary for colonization and infection of bladder epithelium with strains

of uropathogenic *E. coli*. This specific 'adhesin-epithelial cell' binding process occurs when type 1 pili bind to bladder cell membrane proteins uroplakin 1a (UP1a) and uroplakin 1b (UP1b).⁵

After binding to the epithelial surface the activated Fim H adhesins and migrate towards deeper urothelial layers and penetrate the cell membrane. Once the uropathogen is intracellular the invasive process continues, as bacteria proliferate within the cytosol to form clusters. Eight hours after inoculation the phenotypic appearance of the bacteria changes to an engulfing 'biofilm' like structure that protects against the host's immune response and shields the uropathogen from its surrounding environment. A decrease in the rate of bacterial proliferation will allow for effective production of a 'biofilm matrix'. This matrix can prevent the host's neutrophils from penetrating its surface. The 'biofilm' concept stems from the idea that bacteria co-operate with one another to remain viable and proliferate after attaching to a suitable substrate.¹³

P FIMBRIATED PILI

P fimbriated pili or mannose resistant strains of *E. coli* are associated with uncomplicated pyelonephritis as the receptor for P fimbriae is the major glycolipid component present on renal cell membranes. They are termed mannose resistant as they are not affected by mannose during the haemagglutination process for human erythrocytes. PapG is an adhesin found at the tip of the pilus and it recognizes the - d-galctopyranosyl-(1-4)- d-galctopyranoside receptor which is found on P-blood group antigens on the host's uroepithelium. These are important in the pathogenesis of pyelonephritis.

CELL RECEPTIVITY

Epithelial cell receptivity also plays an important pathogenic role in female patients that are susceptible to recurrent UTI. The receptivity concept was established after vaginal epithelial cells were collected from patients susceptible to recurrent UTI with *E. coli* and compared with control samples that were resistant to UTI. Results from this study demonstrated that strains of *E. coli* associated with cystitis ardently adhered to vaginal epithelial cells of susceptible females. These findings indicate a genotypic trait present in females with recurrent UTIs. Further analysis of this genetic concept by assessing human leukocyte antigens (HLAs) in females with recurrent UTIs has demonstrated that HLA-A3 may be a contributing factor. It has also been shown that a greater number of uropathogens attach to epithelial cell surface in females that are greater than 65 years of age compared to premenopausal females (i.e. age 18-40).¹³

HOST SUSCEPTIBILITY FACTORS

ANATOMIC FACTORS:

Women are more susceptible to UTI due to following anatomic difference

1. Proximity of urethra to vagina and rectum.
2. Shorter urethra than men. Longer urethra in males facilitates urinary washout of ascending bacteria before they enter the bladder. ^{5,6}

BEHAVIORAL FACTORS:

This helps microbes to colonize on the female anatomic vulnerability. Several studies have shown a close association between UTI and sexual intercourse. Use of spermicide either alone or in combination with barrier contraceptives is associated with increased risk of UTI. They alter vaginal flora and facilitate periurethral colonization with uropathogens.¹⁶⁻¹⁸

GENETIC FACTORS:

Women who suffer from recurrent episodes of UTI often have maternal or family history of infections. Women with recurrent UTI have increased E.Coli binding receptor that is not limited to the vaginal and urethral mucosa. Lewis blood group antigen non secretors and recessive phenotype have increased risk of recurrent UTI. There is a observed association between HLA Ag and risk of recurrent UTI. ¹⁵

AGE SPECIFIC FACTORS:

Estrogen status is the most important age related factor. Estrogen promotes acidic vaginal pH and lactobacillus proliferation which is the greatest defense against the pathogenic organisms^{5,6,11}. In elderly, particularly if living in a health care facility UTI is common, especially asymptomatic bacteriuria¹⁵.

URINARY CATHETERISATION:

Indwelling urinary catheter and clean intermittent catheterization (CIC) is associated with high rates of bacteriuria. Incidence is found to be 3-6% /day in indwelling catheter and 1-3 % /day in CIC. Virtually all patients will develop bacteriuria at the end of 1 month.^{5,6,11}

PREGNANCY AND UTI:

It is a independent risk factor for upper UTI. Incidence of asymptomatic bacteriuria is identical in pregnant and non pregnant women. There is increased risk of upper UTI in pregnant women due to progesterone activity. 25-40% of pregnant women with untreated bacteriuria develop pyelonephritis.^{5,11,13,14}

CLINICAL MANIFESTATIONS:

The primary step in approaching a patient with UTI is to classify the clinical syndrome. This information will shape the diagnostic and therapeutic approach

ASYMPTOMATIC BACTERIURIA (ABU)

This diagnosis may be considered when patient does not have local or systemic symptoms attributable to UTI. It is a common finding particularly in women, older persons and some with persistent genitourinary abnormalities.⁹ Prevalence of ABU among sexually active young women ranges from 3%-5%, but <1% in age matched controls who are not sexually active. Bacteriuria is present in 5-10% of healthy postmenopausal women and >20% in women older than 80 yrs living in community. Among residents of nursing homes who do not have a indwelling catheter, 20-50% women and 15-40% men have bacteriuria. Prevalence among persons with chronic indwelling catheter is 100%. Prevalence of ABU is 3-7 % in pregnant women, same as age matched non pregnant women. When bacteriuria is not treated, 25-40% develop acute pyelonephritis later on in pregnancy¹⁴.

E.coli is isolated from 80% of healthy females with ABU. Most of the remaining bacterial strains include Klebsiella pneumoniae, Enterococcus species and coagulase negative Staphylococcus. For men older than 65 yrs, coagulase negative Staphylococci are isolated most frequently followed by E.coli and enterococcus species E.coli. Other uropathogens in asymptomatic bacteriuria is characterized by absence of recognized virulence factors. Formation of Biofilm layer is responsible for universal development of bacteriuria with indwelling catheters. Urease producing organism such as P.mirabilis, K.pneumoniae, M.morganii and P. Stuartii are isolated from individual with chronic indwelling catheter.^{13,14}

ACUTE UNCOMPLICATED URINARY TRACT INFECTION:

CYSTITIS:

Acute uncomplicated UTI manifesting as cystitis is a common syndrome which affects otherwise healthy women. About 10 % of young, sexually active, premenopausal women experience a UTI every year. 2-5% of women experience recurrent episodes of infection. Acute uncomplicated UTI is uncommon in healthy young men with an estimated incidence of less than 0.1% per year.^{14,16}

Uropathogenic E.coli is isolated in 80%-85% of patients with cystitis. Infection occurs via ascending route after bacterial colonization of vagina and periurethral area. S.saprophyticus, a coagulase negative Staphylococcus species is an organism virtually unique to acute cystitis. It is the second most frequently isolated organism (5%-10%). K.pneumoniae is isolated in fewer than 5% of pre menopausal and 10%-15% of post menopausal women. The typical symptoms of cystitis are dysuria, urgency, frequency, nocturia and suprapubic discomfort.^{14,15}

Acute uncomplicated UTI recurs frequently. In as many as 30% of early reinfections occurring within 1 month of treatment of an episode of acute cystitis, the same strain of E.coli is isolated before and after therapy. This is attributed to failure to eliminate organisms from gut or vaginal flora.¹⁷⁻¹⁹

ACUTE NON OBSTRUCTIVE PYELONEPHRITIS:

Pyelonephritis is a less common manifestation of acute uncomplicated UTI than cystitis.² The highest incidence is among young women aged between 20 to 30 yrs. Pyelonephritis is associated with greater morbidity. Hospitalizations may be required for as many as 20 % of non pregnant women. Acute pyelonephritis complicates 1-2% of pregnancies.complications occur at end of second trimester or beginning of third trimester.²⁰

Acute non obstructive pyelonephritis rarely causes renal failure. In patients whom renal failure was reported were elderly and had co-morbid conditions such as diabetes or HIV infections.

E.coli is isolated in 85% to 90% of women who presented with uncomplicated pyelonephritis. The strains are characterized by production of P fimbriae adhesin, which plays a direct role in pathogenesis of pyelonephritis..Familial susceptibility to pyelonephritis has been reported. For premenopausal women there has been an association with frequency of sexual intercourse, history of urinary tract infection, history of UTI in patients' mother, a new sexual partner and recent spermicidal use. Diabetes mellitus is also an independent risk factor for pyelonephritis.¹⁵

Classical clinical manifestation of pyelonephritis is costovertebral angle pain or tenderness, fever, nausea, vomiting, loin pain and lower urinary tract symptoms.

Renal papillary necrosis: renal papillary necrosis should be suspected in with diabetes who have frequently relapsing or difficult-to-treat pyelonephritis. Diabetes is estimated to be present in 30 to 50% of patients with renal papillary necrosis. They may present with obstructive uropathy secondary to sloughed papillae. Symptoms of papillary necrosis include flank and abdominal pain accompanied by fever. Diagnosis is established by retrograde pyelography.²¹

PROSTATITIS

Only acute bacterial and chronic bacterial prostatitis are considered to lead to urinary tract infection and have indications for antimicrobial therapy. Acute bacterial prostatitis is a severe infection which is a urologic emergency. This syndrome is usually community acquired, although health care associated infections may occur.

Affected patients usually present with fever and marked urinary symptoms such as dysuria and frequency. Urinary obstruction and suprapubic pain are usually present.^{11,14}

E.Coli is isolated in 70% of the patients. Proteus, Klebsiella, Enterococcus, P. Aeruginosa and S. Aureus are isolated in < 10 % of the patients. Most antimicrobial agents are active in acutely inflamed prostate. A combination of Betalactam and Aminoglycoside is the first line therapy. After confirmation of the organism and the clinical response, oral antibiotic therapy is continued for 6 weeks. When there is no response to therapy and bladder drainage, CT or MRI is indicated to rule out a prostatic abscess.^{11,14,22}

Chronic bacterial prostatitis occurs in patients with persistent prostate infection. The most common manifestation is recurrent acute cystitis because of the bacteria in the prostate entering the bladder. The diagnosis requires paired cultures of mid stream and post prostatic massage urine specimens. Gram negative bacilli such as Enterobacteriaceae and P. Aeruginosa and gram positive Enterococcus species, group B streptococci are commonly isolated. Chronic bacterial prostatitis responds to antimicrobial therapy, however relapse after treatment is common. Ciprofloxacin and Levofloxacin are the first choice of antimicrobial treatment. Cure rate at 6 months after 4 weeks of antimicrobial therapy is 75-89%²².

COMPLICATED URINARY TRACT INFECTION

These include symptomatic episodes of cystitis or pyelonephritis in men or women with anatomic predilection to infection, with foreign body in the urinary tract or factors causing delayed response to therapy. Frequency of complicated UTI depends on the underlying genitourinary abnormality. Complicated urinary tract infection is a frequent cause of hospitalization. UTI is the most common cause of

community acquired bacteremia. Patients with obstruction, indwelling catheters and who have undergone recent manipulation of urinary tract are at greatest risk of septicemia and severe sepsis.^{15,22}

These patients are also at risk for local suppurative complications such as renal or perinephric abscesses, or metastatic infection after bacteremia such as septic arthritis, osteomyelitis or endocarditis. Patients at highest risk for complications are Diabetics, immunocompromised patients, or patients with chronic urologic devices and obstruction.¹⁵

Host impairment rather than virulence of organism was the major determinant for complicated UTI. E.coli remains the most frequently isolated organism. Other pathogens include Klebsiella, Enterobacter, Serratia, Citrobacter, Proteus mirabilis, Morganella morganii are common. Other gram negative organisms include pseudomonas aeruginosa and acinetobacter species. Gram positive organisms are also frequently isolated. Pathogens isolated in complicated UTI have increased antimicrobial resistance. Risk factors for resistant strains include history of recent antimicrobial therapy, health care interventions including indwelling catheter or invasive procedure.^{11,15,22}

Complicated UTI manifests across a wide clinical spectrum of signs and symptoms ranging from mild, irritative symptoms of lower urinary tract infection to pyelonephritis and bacteremia. Patients with indwelling catheter present with fever alone. Presence of costovertebral tenderness, hematuria or catheter obstruction helps in localizing source of infection to the genitourinary tract. Clinical diagnosis of symptomatic infection is problematic in older population with cognitive impairment. Since bacteriuria is very common in elderly individuals with functional impairment, nonlocalised clinical deterioration is frequently attributed to urinary tract infection

because urine culture yields positive results; non localizing clinical manifestations include fever.

URINARY TRACT INFECTION AND DIABETES:

Diabetes mellitus is the most common endocrine disease and is associated with organ complications due to microvascular and macrovascular disease. People with diabetes also suffer from simple and complicated infections, although the association between diabetes mellitus and increased susceptibility to infection has been questioned. Nevertheless many specific infections are commoner in diabetes and some occur almost exclusively in diabetic subjects. Others may occur with increased severity and may be associated with greater risk of complications. Asymptomatic bacteriuria, acute pyelonephritis and complications of UTI are reported to be more common in patients with diabetes.^{1,2,3}

ANATOMICAL SPECTRUM OF INFECTION

UTIs invariably enter via the ascending route. Several controlled studies have demonstrated a higher incidence of bacteriuria (two to four times) in diabetic women than non diabetic women, and data are less convincing for men. Upper urinary tract are involved in >80% Diabetics and they are also prone for more severe infections of the upper urinary tract.^{2,3} Clinical presentation of pyelonephritis is same in both Diabetics and non Diabetics, but Diabetics are more prone for bilateral infection. In one study by Nicolle et al¹⁴ diabetes increased the probability of acute pyelonephritis requiring hospital admission by 20–30-fold in those under 44 years of age and by three to five-fold in men and women aged 45 years and over. Poor response to antibiotic therapy suggests complications which include papillary necrosis or

perinephric abscess. Acute renal failure is twice as likely to develop in bacteraemic patients. This may be related to the additional presence of diabetic nephropathy. Metastatic Gram-negative infections are also commonly reported. Endophthalmitis, osteomyelitis, particularly of the vertebrae, septic arthritis, abscesses and bacteraemic Gram-negative pneumonia are the commonest metastatic complications arising from UTI.⁴

PATHOGENESIS

Several aspects of immunity are altered in patients with diabetes. Polymorphonuclear leukocyte function is depressed and leucocyte adherence, chemotaxis and phagocytosis may be affected. The mechanisms which potentially contribute to UTI in these patients are defects in the local urinary cytokine secretions (IL-8, IL-6), increased adherence of the microorganisms to the uroepithelial cells, partly due to a changed and lowered Tamm Horsfall protein, and granulocyte dysfunction, possibly as a result of an abnormal intracellular calcium metabolism. Antioxidant systems involved in bactericidal activity may also be impaired. On the other hand, hyperglycemia facilitates the colonization and growth of variety of organism.^{2,3}

Increased adherence of *E. coli* expressing type-1 fimbriae (a virulence factor) to uro-epithelial cells of diabetic women may play an important role in the pathogenesis of UTI, especially if diabetes is poorly controlled. Emphysematous complications in renal tissue are likely to be due to the presence of organisms that rapidly ferment glucose and produce carbon dioxide. Impaired transport of metabolic end products either due to impaired tissue perfusion or some other factor in diabetes may also contribute. Pathogenesis of acute papillary necrosis is not well understood. It is presumed to be due to a marginal change in vascular supply, which is further stressed by infection leading to infarction and sloughing of papillae^{23,24}.

Host factors associated with an increased risk for symptomatic or asymptomatic UTIs in women with DM²⁴

General

Sexual intercourse

History of (recurrent) UTIs

Obstruction, urine stasis, reflux, instrumentation of urinary tract

Associated with (complications of) DM

Peripheral neuropathy

Macroalbuminuria

Longer duration of DM

Glycosuria (in vitro)

Decreased urinary cytokine secretion

Increased adherence of E. coli to uroepithelial cells

Genetic factors

Secretor status

Blood group

History of UTIs of the mother

MICROBIOLOGICAL SPECTRUM:

UTIs in patients with diabetes are due to the same urinary pathogens as those found in the general population. Most cases occur due to colonization with E.coli or Proteus species (>80%). Hematogenous infection commonly caused by Staph.aureus, accounts for remainder of the cases. About 50–75% of emphysematous pyelonephritis cases are caused by E.coli, and majority of the rest are caused by other Gram-negative organisms. Diabetes is a common predisposing factor for urinary tract infections caused by fungi, commonly Candida species. Although the majority of fungal infections of the urinary tract are clinically insignificant, a variety of serious infections has been reported. Both Candida and T. glabrata can cause cystitis,

pyelonephritis, renal or perinephric abscesses, fungus balls, and a clinical picture identical to Gram-negative sepsis.^{26,27,31}

Fungal and bacterial infections of the urinary tract cannot be differentiated by clinical signs and symptoms. While a colony count of >100,000 colonies/ml is used to diagnose bacterial infections of the urinary tract, a colony count of 10,000 *Candida*/ml indicates a significant fungal urinary tract infection. The extent of involvement ranges from inconsequential lower urinary tract colonization to clinical cystitis, emphysematous cystitis, pyelonephritis, and renal and perinephric abscess.²⁹

CLINICAL FEATURES:

Clinical features of UTI in patients with diabetes are essentially the same as in people without diabetes. Occasionally the fever may be less apparent, particularly in individuals with diabetic metabolic decompensation. Haematuria or flank pain secondary to sloughing papillae may be noted in patients with papillary necrosis. The investigation of possible UTIs in patients with diabetes requires urinalysis and urine culture, by catheterization if necessary, prior to initiation of antimicrobial treatment. A blood culture should be routine in patients with presumed pyelonephritis. Due to increased incidence of local complications imaging is essential in patients with diabetes and acute pyelonephritis.

COMPLICATIONS:

INFECTIONS POSSIBLY RELATED TO DIABETES:

PAPILLARY NECROSIS:

Papillary necrosis is an important complication of urinary tract infections in diabetic patients. Diabetes has been present in over 50% of patients with papillary necrosis. Autopsy findings show papillary necrosis to be about five times more frequent in diabetic than Non Diabetic individuals. Patients usually complain of flank pain, chills, fever, and abdominal pain. Renal insufficiency develops in over 15% of cases. Although most patients are acutely ill, occasionally the course may be slowly progressive.²¹

E. coli or other enteric organisms cause this infection. The pathogenesis has not been determined. Presumably, infection and ischemia result in necrosis of the renal papillae.²¹

The diagnosis should be suspected in diabetic patients with urinary tract infections who respond poorly to antimicrobial therapy or develop renal insufficiency. The diagnosis may be made by retrograde pyelograms. Intravenous pyelography results in renal impairment in 50% of diabetic subjects with preexisting renal disease and should be avoided. Early radiographic findings of papillary necrosis include dilation of the calyceal fornix, irregularity of the papillary tip, and extension of the contrast material into the renal parenchyma.²²

RENAL ABSCESSSES:

Renal abscess occurs with twice the frequency in Diabetics than non Diabetics. Renal parenchymal abscess may be divided into renal carbuncle (cortical abscess) and corticomedullary abscess. More than 90 % are due to staph. aureus and

almost all result from hematogenous seeding of the kidney from a distant focus. Only rarely they occur due to ascending infection.¹⁴ Corticomedullary abscess are usually associated with underlying abnormality of the urinary tract such as reflux or obstruction and bacteriologic studies reveal involvement of enteric gram negative organism such as E.coli, Proteus and Klebsiella species. Patients with parenchymal abscess may present with flank pain, fever, chills or abdominal pain. Dysuria may be absent and urine routine may show no abnormality. A flank mass may be palpated in half the cases. CT abdomen is a useful modality for diagnosis. These abscesses may resolve with antibiotics alone. If there is no clinical improvement then a surgical drainage may be necessary.²⁵

PERINEPHRIC ABSCESES

It may be more common in diabetic patients. Diabetes is present in about one-third of patients with perinephric abscesses. It consists of collection of purulent material between Gerota fascia and capsule of the kidney and most often due to rupture of renal abscess. The onset typically is insidious. The clinical presentation is otherwise similar to that of pyelonephritis. An abdominal or a flank mass can be felt in about half the cases. Laboratory features include leukocytosis in 70%, serum creatinine elevation in 80%, and pyuria in 84% of cases. Pyelonephritis usually responds within 4-5 days of appropriate antibiotics; perinephric abscesses do not. Thus, a perinephric abscess should be suspected in patients with urinary tract infections and an abdominal or flank mass or Persistent fever after 4 days of antimicrobial therapy.²⁵

Intravenous pyelograms are abnormal in 80% of cases; however, the abnormalities are not specific. Abdominal ultrasound or computerized tomography should establish the diagnosis in most cases. E. coli or other organisms are usually

isolated, but staphylococci cause about 10% of cases. Effective treatment requires surgical drainage of the abscess in addition to specific antibiotics. The mortality is high even with proper therapy (23%).

INFECTIONS STRONGLY ASSOCIATED WITH DIABETES

EMPHYSEMATOUS PYELONEPHRITIS

It is a rare and very serious infection involving gas forming organism. It is a necrotizing infection characterized by gas production in or around the kidneys. Over 70% of reported cases have occurred in diabetic patients. It has very high mortality rate ranging from 13-50%. Imaging is diagnostic in emphysematous pyelonephritis, CT is the imaging modality of choice. Fever and flank pain are nearly always present, and a renal mass can be felt in 45% of cases. Abdominal radiographs frequently show mottled lucencies overlying the kidneys. E. coli causes about 50% of cases, the remainder being caused by other Gram-negative bacilli. Bacteremia is a frequent complication. Survival is higher in patients managed with antibiotics plus surgery (67%) than with antibiotic therapy alone. Emphysematous cystitis is less severe and is usually cured by antibiotics alone.^{14,15}

XANTHOGRANULOMATOUS PYELONEPHRITIS (XGP)

Rare and severe form of renal deterioration secondary to obstruction and infection. Most patients present with flank pain, fever and recurrent UTI with persistent bacteriuria. CT abdomen is the imaging of choice. CT reveals an enlarged, poorly functioning kidney with dilated calyces and thinned cortex. Multiple renal and perinephric abscess may be present. E.coli and Proteus species are the most common causative organism. Management include IV antibiotics and drainage procedure.¹⁴

STUDY OF UTI IN DIABETICS

O'sullivan DJ, Fitzgerald MG et al²⁸, conducted a comparative study of UTI in diabetic and non-diabetic population (1960). 150 Diabetics and 150 Non Diabetics were included in this study. Mid-stream urine sample was used for culture sensitivity. It was found that there was no significant difference between the incidence UTI in between the two groups (13.3% in case and 12% in controls). The incidence of infection was maximum for females in both the groups (of the 20 infected Diabetics 18 were women and in controls 17 were women). Incidence increased markedly after the age of 60 years and 24 out of 108 examined (22%) had UTI. E.coli and Proteus was the common organism attributed to infection.

Bonadio M et al²⁹, in a prospective study on 490 patients with proven UTI, demonstrated that 89(18.1%) had diabetes mellitus. Most Diabetics had asymptomatic bacteriuria and had undergone bladder catheterisation. Most frequent causative agent was E.coli(56.1% vs 56.8%), Proteus species(7.9 vs 7.2%), Pseudomonas(6.7 vs 8.2%), Enterococcus(6.7 vs. 7.2%). They concluded that there is no significant differences in clinical and microbiological profile in Diabetics and non Diabetics except for higher frequency of bladder catheterization.

Akbar DH et al³⁰, conducted a study to determine the clinical characteristics, risk factors, causative organisms and antimicrobial susceptibility in Diabetics and non-Diabetics. A total of 182 specimens were studied and 58 (32%) were Diabetics. Urinary catheters were present in 12 (20%) Diabetics and 31 (25%) Non Diabetics, intensive care unit admission was 40% versus 31%. Escherichia coli was isolated in 9/50 (18%) hospital acquired infections and 4/8 (50%) community acquired infections in Diabetics versus 26/106 (25%) and 8/18 (47%) in non Diabetics. Escherichia coli and Pseudomonas in both groups showed resistance to Ampicillin and sensitivity to

Aminoglycoside and Ciprofloxacin.

Bonadio et al³¹, conducted a study to evaluate the spectrum of uropathogens and the profile of antibiotic resistance in both Diabetic and Non Diabetic patients with asymptomatic urinary tract infection. Study included 346 Diabetics (229 females and 117 males) and 975 non Diabetics (679 females and 296 males) who were screened for significant bacteriuria (10^5 CFU/mL urine). The most frequent causative organisms of bacteriuria in females with and without DM were respectively: E. coli 54.1% vs 58.2% (p = NS), Enterococcus species 8.3% vs 6.5% (p = NS), Pseudomonas species 3.9 vs 4.7% (p = NS). The most frequent organisms in Diabetic and Non diabetic males were respectively E. coli 32.5% vs 31.4% (p = NS), Enterococcus species 9.4% vs 14.5% (p = NS), Pseudomonas species 8.5% vs 17.2% (p = <0.02). A similar isolation rate of E. coli, Enterococcus species and Pseudomonas species was also observed in patients with indwelling bladder catheter with and without DM. No significant differences in resistance rates to Ampicillin, Nitrofurantoin, Cotrimoxazole and Ciprofloxacin for E. coli and Enterococcus species were observed between diabetic and non diabetic patients.

Alimohammadi et al³², conducted a study in 2007 comparing UTI in Diabetics and non Diabetics and antibiotic sensitivity pattern in the isolated organisms. A total of 1510 patients were included among which 452 were Diabetics. Among the 452 subjects, 102(22.5%) had UTI and 72 (70.5%) were females. He concluded that most of the UTI in Diabetics especially females was asymptomatic. Organism isolated in nosocomial UTI in Diabetics showed significant growth of Klebsiella species (41%) compared to non diabetic

Krenke DS et al³³, conducted a study in 2007 on UTI in diabetic and non diabetic patients and evaluated the prevalence of broad spectrum beta lactamase pathogens and

quinolone resistance. The study population consisted of 494 patients and it included 210 Diabetics and 284 non Diabetics. They concluded that E.coli was the most commonly isolated pathogen in Diabetics and Non Diabetics. Broad spectrum Beta Lactames production was more frequent in Klebsiella and it was more frequently observed in Diabetics(12%) than Non Diabetics(4%).Quinalone resistance was more common in Diabetics(40%) than non Diabetics(4%)

Baqai R, Aziz M et al³⁴ conducted a study in 2008 to determine the etiological agents of urinary tract infection and their antibiotic sensitivity patterns. Formation of biofilm pattern among pathogens was also evaluated. A total of 100 urine samples were collected from diabetic patients attending the outpatient department. Among 100 samples there was significant growth in 21% of samples. E.coli (50%) was the predominant organism, followed by staphylococcus aureus (20%),staphylococcus Saprophyticus(20%), Proteus species and Enterococcus fecalis. Candida was isolated in 10.2% of patients. Biofilm production of uropathogens was detected in 75% of the cases indicating their role in persistence of infection and drug resistance.

Saber MH, Barai L et al³⁵ conducted a study in 2010 to determine the etiologic agents and their antibiotic sensitivity pattern in both diabetic and non-diabetic patients with urinary tract infection (UTI). Among the study cases, 43.8% diabetic patients and 42.9% non-diabetic patients had positive growth from urine. Majority of culture positive patients were females. Rate of isolation of Escherichia coli in diabetic was less (61.8%) compared to non-diabetic (77.8%). Rate of isolation of Pseudomonas species in Diabetic male and Enterococcus in diabetic female was higher than in non-diabetic patients. E coli isolated from diabetic patient was significantly ($p<0.05$) less sensitive to Ceftriaxone, Ceftazidime, Cefuroxime, Netilmicin, Gentamicin, Ciprofloxacin and Nitrofurantoin than that of non-diabetic patients. In addition,

isolation rate of the Extended Spectrum Beta Lactamase producing gram negative bacilli was found higher among diabetic population (47.8%) compared to the non-Diabetics (9.1%).

STUDY ON UTI IN DIABETIC WOMEN

Bonadia M, Boldreni E et al³⁶ screened 228 women with diabetes for bacteriuria during the period of January 1997 through December 2000 at Pisa General Hospital (Pisa, Italy). A control group of 146 women without diabetes were also evaluated. The frequency of significant bacteriuria was 17.5% (40 of 228) among women with diabetes and 18.5% (27 of 146) among women in the control group. Seven (13.5%) of 52 and 33 (18.8%) of 176 women with type 1 and in type 2 diabetes, respectively, had significant bacteriuria. The presence of higher glycated hemoglobin levels was the only significant risk factor for significant bacteriuria in women with type 2 diabetes. A similar frequency of bacteriuria in women with and women without diabetes was found.

Geerlings SE, Stolk RP et al³⁷(2001) conducted a multicenter study to compare women with DM with and without ASB for the development of symptomatic urinary tract infections, renal function, and secondary complications of DM during an 18-month follow-up period. At least 1 uncontaminated urine culture was available from 636 women (258 with type 1 DM and 378 with type 2 DM). The prevalence of ABU at baseline was 26% (21% for those with type 1 DM and 29% for those with type 2 DM). Follow-up results were available for 589 (93%) of the 636 women. Of these 589 women, 115 (20%) (14% with type 1 DM and 23% with type 2 DM) developed a symptomatic UTI. Women with type 2 DM and ASB at baseline had an increased risk of developing a UTI during the 18-month follow-up (19% without ASB vs 34% with ASB, $P = .006$). In contrast, there was no difference in the incidence of symptomatic

UTI between women with type 1 DM and ASB and those without ASB. They concluded that Women with type 2 DM and ASB have an increased risk of developing a symptomatic UTI than those without ASB.

Meiland R, Geerlings SE¹⁹ (2006) conducted a prospective study among women with type 1 or type 2 DM to study the long-term consequences of asymptomatic bacteriuria (ASB) on renal function in women with diabetes mellitus (DM). Women with ABU (diagnosis based on findings from 1 urine culture specimen) were compared with women without ASB for differences in renal function development and incidence of hypertension. Total of 644 women were included in the study (296 with type 1 DM and 348 with type 2 DM) and followed up for a mean (SD) duration of 6.1 (1.9) years. The prevalence of ABU was 17%. In women with DM and ASB, the creatinine clearance decreased from 87 mL/min (1.45 mL/s) at baseline to 76 mL/min (1.27 mL/s) at study end point; in women with DM without ABU the creatinine clearance decreased from 97 to 88 mL/min (from 1.62 to 1.47 mL/s). In the multivariate analyses, adjusted for age, length of follow-up, duration of DM, and microalbuminuria at baseline, no association was found between ABU and the relative or the absolute decrease in creatinine clearance.

UTI AND HbA1c LEVEL

Boyko EJ, Fihn SD et al³⁸, conducted a (1998–2002) prospective study on 218 diabetic and 799 non-diabetic women aged 55–75 years for UTI and Asymptomatic Bacteriuria (ABU). The baseline examination and two annual follow-up examinations included urine culture, measurement of Hemoglobin A1c (HbA1c) and post void residual bladder volume, and a survey of diabetes and other characteristics. UTI incidence was 12.2 for diabetic women and 6.7 for non-diabetic women per 100 person-years (relative risk (RR) = 1.8, 95% confidence interval (CI): 1.2, 2.7). ASB

incidence per 100 person-years was 6.7 for diabetic women and 3.0 for non-diabetic women (RR = 2.3, 95% CI: 1.3, 3.9). Increased UTI risk occurred mainly in women taking insulin (RR = 3.7, 95% CI: 1.8, 7.3) and women with a longer diabetes duration (> 10 years; RR = 2.6, 95% CI: 1.3, 5.1) compared with non-diabetic women. No clear linear trend between HbA1c and UTI or ASB risk was seen. However another study by Bonadio et al⁸, showed high levels of HbA1c represented a significant risk factor for bacteriuria in diabetic women.

INDIAN STUDIES

Saleem M, Daniel B³⁹, Conducted a study to evaluate the incidence of UTI in patients with DM in Bangalore. Between July 2005 - 2009, 1000 diabetic and non-diabetic urine samples were collected and processed in the lab following standard laboratory protocol. Prevalence of UTI was higher in diabetic patients belonging to the lower socioeconomic status (56.4). Commonly recovered UTI isolates were E.coli, Enterococcus faecalis, Pseudomonas aeruginosa, and Staphylococcus aureus. In type 1 diabetic patients E.coli (44%) was the most prevalent cause of UTI.

Eshwarappa, et al⁴⁰, conducted a prospective observational study in Bangalore between Jan and Dec 2008. A total of 5564 subjects suspected to have UTI were screened among whom 510 patients showed growth on culture. Most of cases were recorded in elderly age group (50 -79 years) and fever and dysuria was most common clinical presentation. Diabetes (42.6%) was the most common factor associated with complicated UTI. E.coli (66.9%) was the most common organism causing community acquired UTI with extended spectrum Beta Lactamase (ESBL) seen in 2/3 rd cases. A high resistance rate to Fluoroquinolones (74.1%) was noted.

Thair N et al⁴¹ conducted a study to determine the frequency of urinary tract infection (UTI) in diabetic females. Out of 100 female diabetic patients (80 type 2

DM & 20 type1 DM) Leukocyturia >5/hpf was present in 33/100 (33%) cases. Out of these 33 cases, positive urine culture report was seen only in 23 (69.7%) cases. Overall frequency of UTI was 23% and the commonest organism isolated was E. coli in 16 urine cultures. In type 2 DM patients, Leukocyturia >5/hpf was present in 27/80 (33.75%) cases and positive urine culture was found in 19/27.(70.4%) cases. In type 1 DM patients, Leukocyturia >5/hpf was present in 6/20 (30%) and positive urine culture was found in 4/6 (66.7%) cases. E.coli was isolated from 16 (69.6%) urine cultures. Enterobacteriaceae from 3(13.04%) , Pseudomonas from 2 (8.7%) and Staphylococcus from 1 (4.35%) positive cultures and C.albicans was isolated in 1 (4.35%) positive culture.

Janifer J, Geethalakshmi S et al⁴²(2009) conducted a study to determine the prevalence of lower urinary tract infection (UTI), the causative pathogens, their antimicrobial pattern, and the recurrence of infection in type 2 diabetic subjects. A total of 1157 (M: F 428: 729) type 2 diabetic subjects were selected for this study. A significant colony count was seen in 495 (42.8%) subjects and an insignificant count in 350 (30.3%) subjects. Women (47.9%) had a significantly higher prevalence of UTI than men (34.1%) which was statistically significant. Except for BMI, UTI was significantly associated with age, duration of diabetes, and poor glycemic control in both sexes. Escherichea coli (E. coli) was the most commonly found organism. Gram negative pathogens were found to be highly sensitive To Sulbactem / Cefoperazone and Piperacillin / Tazobactum.

Arul Prakasam K C Etal,⁴³ conducted a cross sectional study to determine the prevalence of UTI and their antibiotic utilization pattern. In this study young married female were at more risk of getting UTI . Diabetes mellitus appeared to be a significant risk factor of UTI.Dysuria and fever were the most common clinical

presentation. E. coli was the predominant organism isolated showing maximum susceptibility to Meropenem and Amikacin. The isolated organisms showed resistance to Fluroquinolones and Cephalosporins.

Mehvish Saleem , Betty Daniel ⁴⁴ conducted the study of UTI among diabetes patients in Bangalore city, E. coli were the most common organism isolated from the urine culture followed by enterococcus , Pseudomonas and Staphylococcus. UTI was most commonly seen in the patients from lower socioeconomic class.

Amongst catheterised patients also, E. coli was the most frequent isolate ⁴⁵

A study at AIIMS in 2001 on prevalence of UTI and renal scars on 155 patients with Diabetes and healthy controls concluded a 10 fold increased risk of UTI and 3 fold risk of renal scarring. E. coli again was the most common isolate (64.3%) followed by Staph. aureus (21.4%) & Klebsiella (14.3%).⁴⁶

Abhilash et al ⁴⁷ studied the epidemiology and outcome of bacteremia caused by extended spectrum B-lactamase (ESBL) producing E. coli & Klebsiella sp. in a tertiary care hospital in South India amongst 131 bacteremic patients & concluded a very high ESBL production & resistance to multiple classes of antibiotics. The most common co-morbid condition was type 2 Diabetes mellitus, seen in 42.7% patients.

Ramana B V and Chaudhury A ⁴⁸, in their study on the Prevalence of uropathogens in diabetic patients and their resistance pattern at a tertiary care centre in south India, found that Escherichia coli are the most common bacterial pathogen causing urinary infection in diabetics, other organisms being Klebsiella pneumoniae , Proteus mirabilis and Pseudomonas aeruginosa. Among the 1200 diabetic patients, a total of 630 pathogens were isolated. Gram negative bacilli were found to be more sensitive than gram positive cocci to amikacin (65vs29%). Gram positive cocci (67%) were found to be more sensitive to cefotaxime than gram negative bacilli (55%), whereas

gram negative bacilli (65%) were more sensitive than gram positive cocci (49%) to ceftizoxime. *Escherichia coli* was commonly isolated; the gram negative pathogens were highly sensitive to sulbactam / cefoperazone and piperacillin / tazobactam.

Pargavi B et al⁴⁹, in the study done on prevalence of of Urinary Tract Infection (UTI) among Diabetics patients in Vandavasi, Tamil Nadu, found that overall prevalence of UTI was 37%, female preponderance was higher 43% and male was 30%. The urinary tract infections were found to be common in age group between 41-50 yrs. The most predominant bacterial isolates were *Escherichia coli*, *Klebsiella pneumoniae* and *Proteus mirabilis*. Invitro antibiotic susceptibility tests revealed that Nalidixic acid; Ofloxacin and Ciprofloxacin were more effective against *E. coli*, *K. pneumoniae* and *P. mirabilis* respectively. Ampicillin, Carbenicillin and Gentamicin were poorly effective, with urinary isolates.

Ranganath vasudevan⁵⁰ in the study Urinary Tract Infection: An Overview of the Infection and the Associated Risk Factors, found that both males and females. Despite the fact, that both the genders are susceptible to the infection, women are mostly vulnerable due to their anatomy and reproductive physiology. Among the bacterial species *Escherichia coli* account to 80% to 85% of the infection followed by *Staphylococcus* species that constitutes to 10% to 15%. In addition, bacterial species *Klebsiella*, *Pseudomonas*, *Proteus* and *Enterococcus* species plays a minor role in conferring the infection.

Arun Hari⁵¹, in the study titled Asymptomatic bacteriuria in patients with diabetes attending a tertiary care level ,a descriptive study done showed that,42% of the people had asymptomatic bacteriuria. the occurrence of asymptomatic bacteriuria among female diabetics in the study group was 54%, as opposed to 30% in male.

Ankur Goyal et al⁵² in the study Prevalence and antimicrobial sensitivity pattern of

asymptomatic bacteriuria in type 2 diabetes mellitus patients presenting in tertiary care hospital of Agra, North India, found that total of 23.7% patients were having asymptomatic bacteriuria (ASB). The mean age of these patients was 59.22 ± 9.76 years and mean duration of diabetes was 7.33 ± 6.42 years. it was noteworthy that females in 40- 50 years age group had significantly more ASB as compared to their male counterparts. the most frequent causative agent of asymptomatic bacteriuria was *E. coli* (27.8%) followed by *Staphylococcus* (22.2%), *Enterococcus* (22.2%), *Candida* (22.2%) and *Streptococcus* (5.6%). All strains (100%) of *E. coli* were sensitive to imipenem, meropenem and piperacillin/tazobactam and resistant to ampicillin and cephalothin. 80% *E. coli* strains were ESBL (Extended spectrum beta lactamase) producer, however amikacin (80%) and chloramphenicol (80%) showed good sensitivity against these isolates.

Aswani Srinivas Mareddy et al⁵³, in the study clinical profile of urinary tract infections in diabetics and non-diabetics, showed that Almost 30% of the patients (both diabetics and non diabetics) presented with asymptomatic bacteriuria and the prevalence of pyelonephritis was significantly higher (p-0.04) in diabetics compared to non-diabetic patients. Majority of the diabetics with UTI (87.14 %) had HbA1c > 6.5 % with $p < 0.001$. The isolation rate of *Escherichia coli* from urine culture was higher (64.60%) among diabetic patients followed by *Klebsiella* (12.10%) and *Enterococcus* (9.90%). The prevalence of extended-spectrum beta-lactamase (ESBL) producing *E.coli* was significantly higher in diabetics (p- value 0.001) compared to non-diabetics. *E.coli* showed maximum sensitivity to carbapenems in both diabetic and non-diabetic subjects and susceptibility to ampicillin.

Mahesh E et al⁵⁴ in the study done on Community-acquired urinary tract infection in the elderly in Bangalore, found that Diabetes mellitus (DM) and recent

uro-genital instrumentation were the most common risk factors associated with UTI in the present study . E. coli (138/194 - 71.1%) was the most commonly isolated pathogen responsible for UTI in the present study . 56.2% of the total infection was caused by ESBL positive organisms. The antimicrobial potency and spectrum for nine selected antimicrobial agents (Imepenem, Meropenem, Ciprofloxacin, Norfloxacin, Ofloxacin, Gentamicin, Amikacin, Nitrofurantoin and Cotrimoxazole) against the uropathogens were studied. The highest and least antibiotic resistance was noted against fluoroquinolones (79.9%) and carbapenems (3.61%) respectively.

MATERIALS AND METHODS

STUDY DESIGN: case- control, prospective study.

STUDY DURATION: the study was conducted over a period of one and half years from January 2013 to June 2014 after obtaining ethical clearance.

STUDY SITE: The study was conducted at.

STUDY SIZE: A sample size of 100 was taken in each group.

STUDY POPULATION: Study population was divided into 2 groups

Group A (case) consisted of all Diabetics (>18 yrs of age) attending the in-patient and outpatient department who have been diagnosed as having urinary tract infection irrespective of the reason for visit.

According to the WHO criteria Diabetes Mellitus will be defined as Fasting Blood Sugar (FBS) more than 126mg/dl or a 2 h Post Prandial Blood Sugars (PPBS) of > 200 mg/dl or the use of glucose-lowering medication (tablets or insulin).

Group B (control): consisted of all Non-Diabetics (>18 yrs of age) attending the in-patient and outpatient department who have been diagnosed as having urinary tract infection irrespective of the reason for visit.

The criterion used for defining UTI (bacteriuria) is the presence of at least 10^5 colony forming units/ml (CFU/ml) in one culture of clean-voided mid-stream urine specimen⁶.

Symptoms clinically suggestive of UTI with a colony count of 10^3 to 10^5 will were considered as UTI for the study.

Patients in whom urine culture was positive even after taking antibiotic therapy from outside were included in the study.

EXCLUSION CRITERIA:

1. Urine routine showing pus cells but negative urine culture.
2. History of receiving antibiotics within 2 weeks prior to culture (except patients whose urine culture positive even after antibiotic therapy).
3. Urine culture showing contamination (Presence of at least two different microorganisms in a urine specimen).
4. Patients in whom ultrasound abdomen is not available.
5. Patient on continuous indwelling catheter.
6. Menstruating and pregnant women.
7. Uncooperative patients and patients not consenting.

A Specially designed questionnaire was used to collect demographic and clinical information including age, sex, address, occupation and antibiotic use, symptoms of UTI and their complication. A detailed examination of all systems with emphasis on temperature, pulse rate, blood pressure, suprapubic tenderness, costovertebral angle tenderness, mass on deep palpation was done.

SPECIMEN COLLECTION

A Mid-stream urine sample was collected for culture sensitivity. A urinary specimen was also collected for routine urinalysis and microscopic examination. Urine thus collected was immediately transported to the microbiology laboratory and processed within 1 h.

URINE CULTURE

Urine sample collected was inoculated on MacConkey's agar, blood agar, and Cystine Lactose Electrolyte Deficient (CLED) medium with a calibrated loop to determine CFU and incubated at 37⁰ C for 24-48 hours. Identification of isolates was done based on colony morphology, gram staining and standard biochemical tests.

Significant bacteriuria was defined as the presence of at least 10^5 CFU/ml of one bacterial species in a culture of clean-voided midstream urine. Presence of at least two different microorganisms in a urine specimen was considered as contamination. Urine samples was inoculated on Sabouraud's agar for the detection of fungus, and identification was done by colony morphology and staining.

URINE ANTIBIOTIC SENSITIVITY

Antimicrobial susceptibility testing was done by Kirby Bauer's disc diffusion agar method and reported accordingly.

OTHER INVESTIGATION

Haemoglobin, Total Leucocyte Count, Differential count, ESR, Urine for proteins, sugar, ph., specific gravity, and microscopic examination. Blood sugar was done for all patients.

RESULTS

Table 1: Baseline characters of study population

	DIABETIC			NON DIABETIC			P VALUE
	N	MEAN	STD DEVIATION	N	MEAN	STD DEVIATION	
AGE	100	55.34	11.15	100	49.48	15.49	0.0024
Hemoglobin(g/ dl)	100	10.40	1.85	100	11.18	1.83	0.0031
Total count (cells/cumm)	100	12097	2884.36	100	10520	3165.85	0.0003
ESR	100	59.16	12.2	100	46	11.16	0.0001
RBS(Mg/dl)	100	246.9	26.05	100	109.82	9.48	0.0001
Urine routine							
ph	100	6.04	0.13	100	6.01	0.11	0.079
Specific gravity	100	1.0141	0.006	100	1.0137	0.004	1.000

Comparison of baseline characters showed that Group A had a lower hemoglobin (p=0.00), higher ESR (p=0.035) and higher total count(0.0003) and blood sugars (p=0.00).Other baseline characters were not statistically significant.

Table 2: Urine routine examination in Diabetics And Non Diabetics

Variables	Value	DIABETIC	NON DIABETIC	total	P value
SUGAR	NIL	43	91	134	0.000
	Blue	8	8	16	
	Yellow	29	1	30	
	Orange	16	0	16	
	Red	4	0	4	
WBC	<10cells/cumm	20	24	44	0.733
	10-20 cells/cumm	25	26	51	
	>20cells/cumm	55	50	105	
RBC	nil	20	30	50	0.202
	1-10cells/cumm	65	60	125	
	>10 cells/cumm	15	10	25	
Epithelial	<5 cells/cumm	96	97	193	0.682 (FISHER'S TEST)
	6-10 cells/cumm	4	2	6	
	>10cells/cumm	0	1	1	
Casts	yes	10	12	22	0.651
	No	90	88	178	
Bacteria	Yes	35	42	77	0.309
	No	65	58	123	

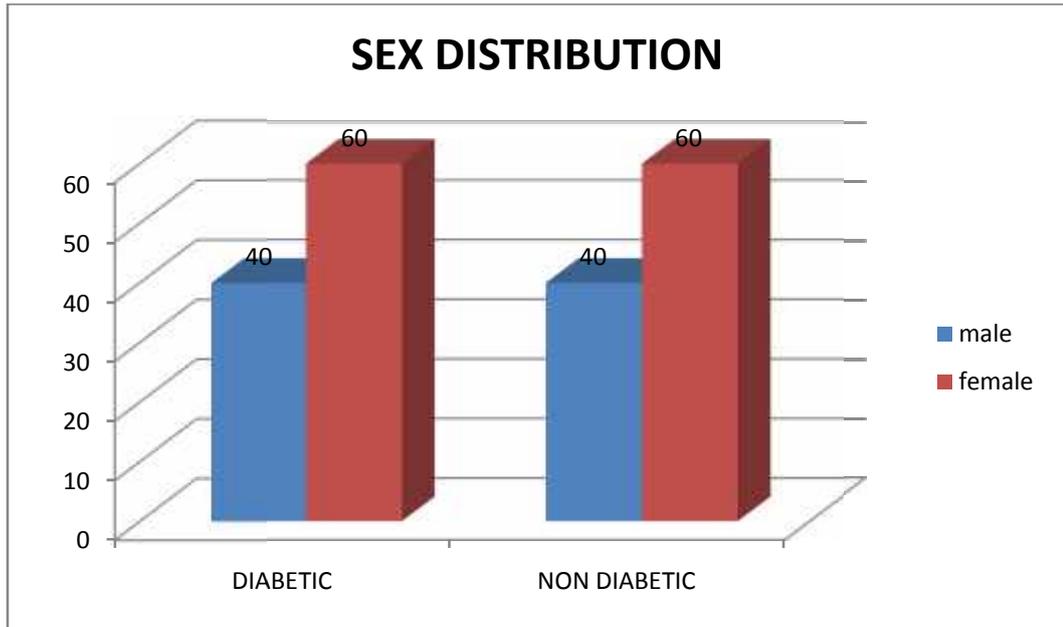


Figure 1: Gender distribution of the study population

- A total number of 200 subjects were included in the study and the study group was divided into Group A- 100 Diabetics (40 males and 60 females) and Group B -100 Non Diabetics (40 males and 60 females).

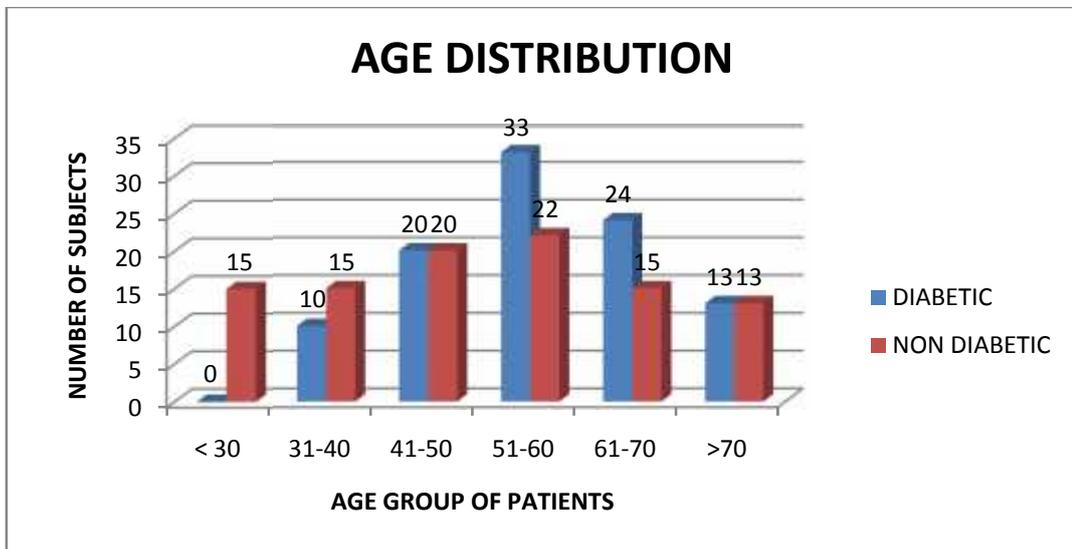


Figure 2: Age distribution of the study population

- Subjects were older In the Diabetic group, majority of the population being between the age group of 51 to 60 yrs(p value 0.001 HS).The Mean Age in Diabetics was 55.34 yrs and Non Diabetics was 49.48 yrs.

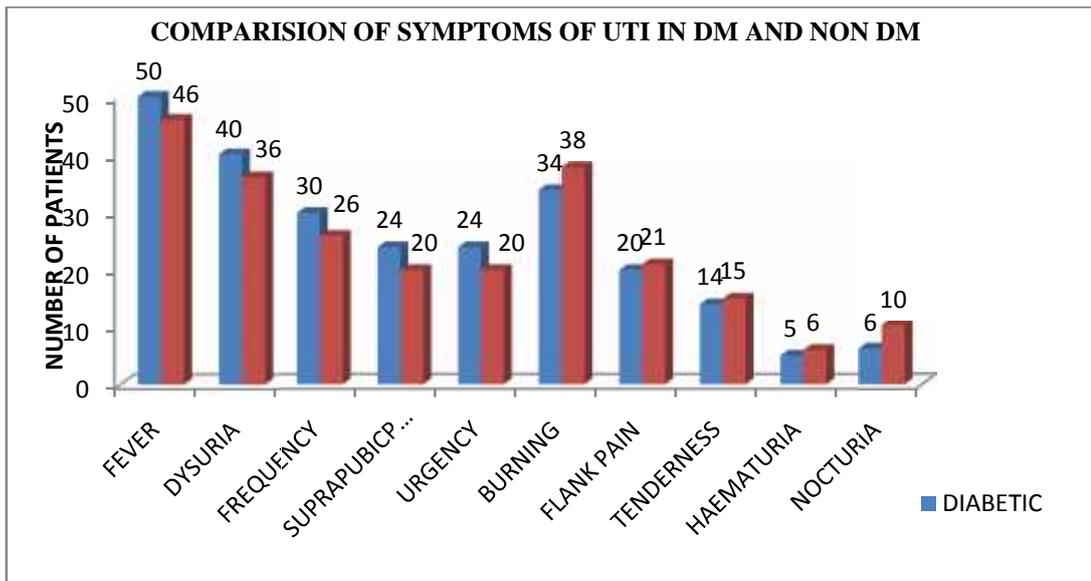


Figure 3: Comparison of symptoms of UTI in Diabetics And Non Diabetics

- The presentation of UTI was similar in Diabetics and non Diabetics (P =not significant). The most common presenting complaint was fever followed by dysuria and burning micturition.

ANALYSIS OF GROUP A

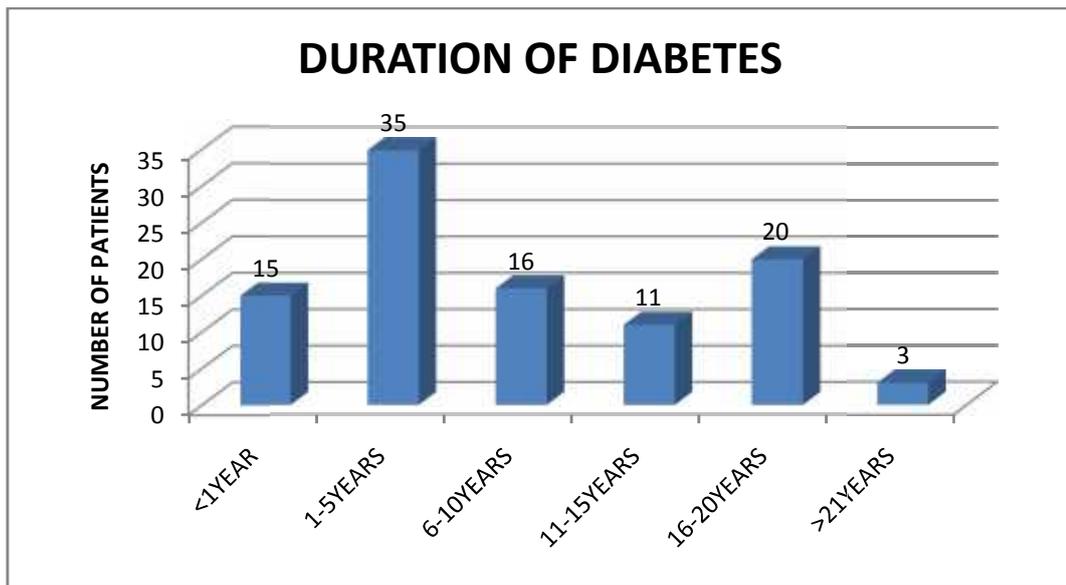


Figure 4: Duration of Diabetes

- The mean duration of diabetes was 8.75 yrs. Duration of Diabetes was less than 1 year in 15 patients and >21 yrs duration in 3 patients.

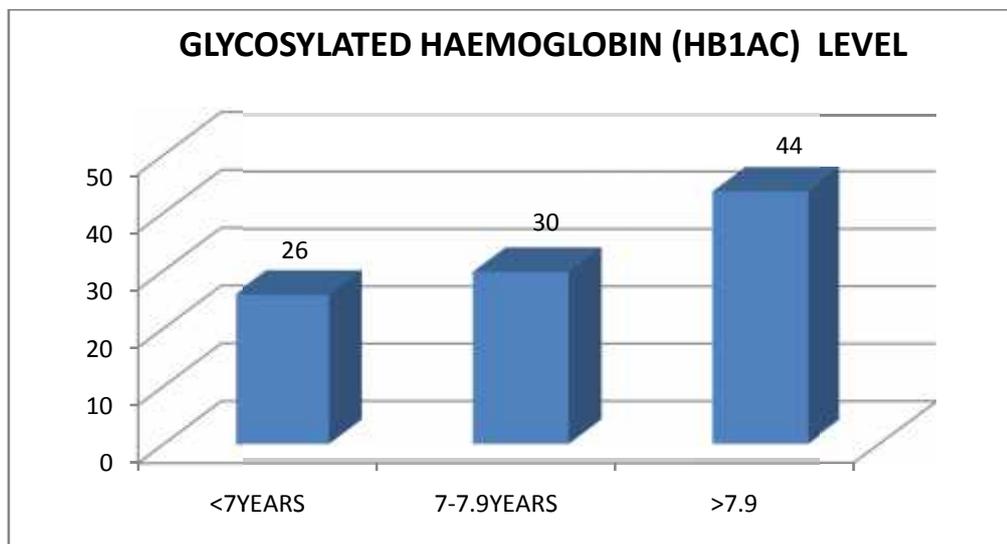


Figure 5: Glycosylated Hemoglobin (HbA1c) Level

- 71 subjects in group A had uncontrolled blood sugars. A total of 30 subjects had an HbA1c level of 7 to 7.9 and 44 subjects had a HbA1c of >7.9.

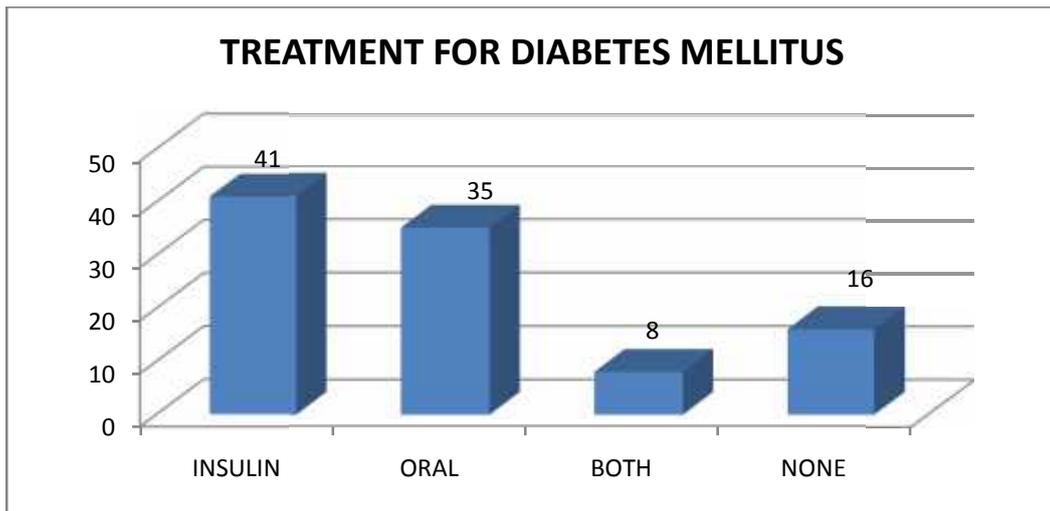


Figure 6: Treatment for Diabetes Mellitus

- Total Number Of Diabetics:100
- Total Number Of Patients On Oral Hypoglycemic Therapy :35
- Total Number Of Patients On Insulin Therapy :41
- Total Number Of Patients On Both :8
- Total Number Of Patients On None: 16

Among the 16 patients who were not on any medications for diabetes, 6 patients had been detected to have diabetes during the present admission. Among the 10 patients, 2 were not on medications due to poor drug compliance and 6 were detected to have associated nephropathy and had low insulin requirements and hence were continued on diabetic diet.

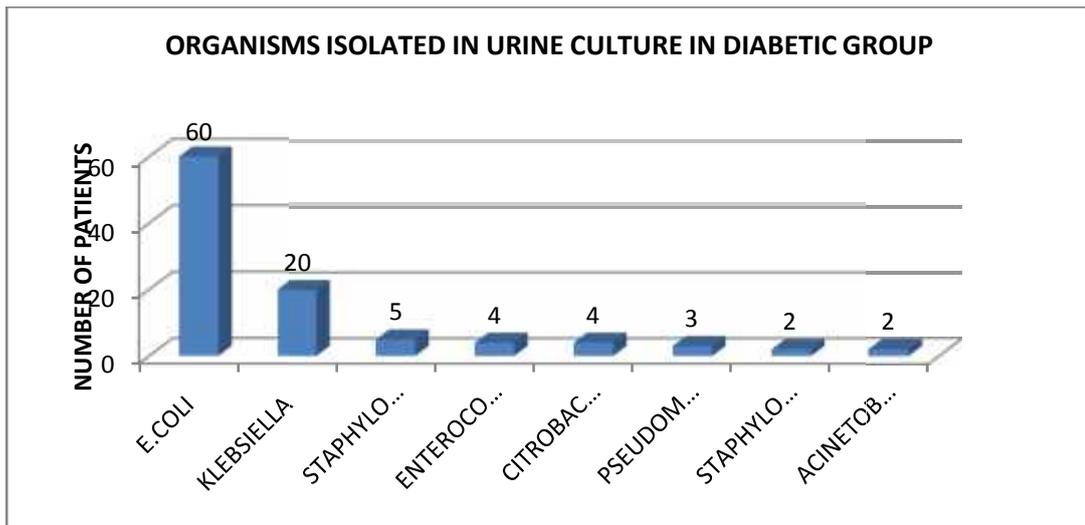


Figure 7: Organism isolated in urine culture in group A

E.coli was the commonest organism isolated in Diabetics (60%) Klebsiella was the second commonest organism isolated (20%). Other organisms isolated included Pseudomonas (3%), Enterococcus(4%), Acinitobacter(2%), and Citrobacter(4%). Staphylococcus (5%) and Candida (2%) were exclusively isolated in diabetic group (Fischers exact p test:0.007(HS)).

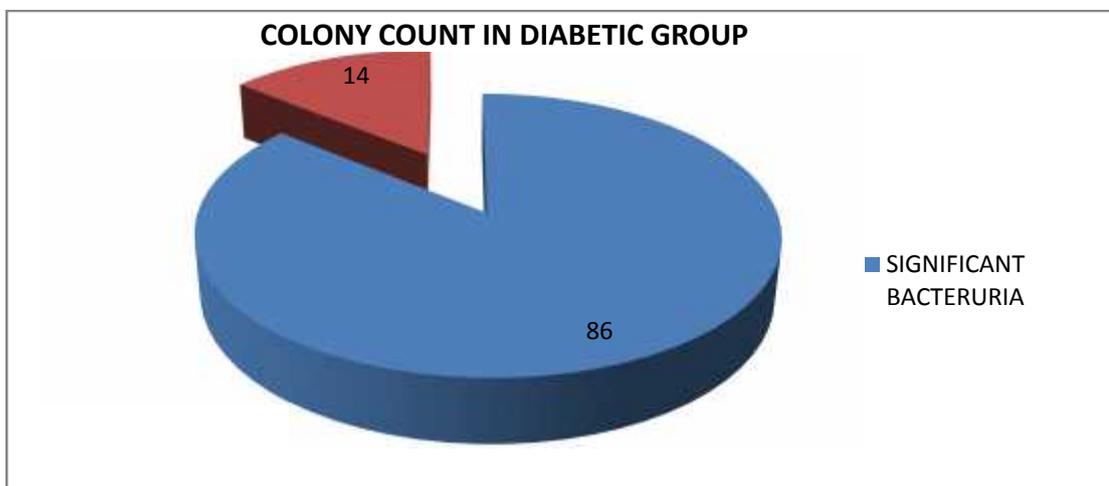


Figure 8: Colony count in group A

A total of 86 patients in Group A had significant bacteriuria, with colony count of >10⁵ on urine culture.

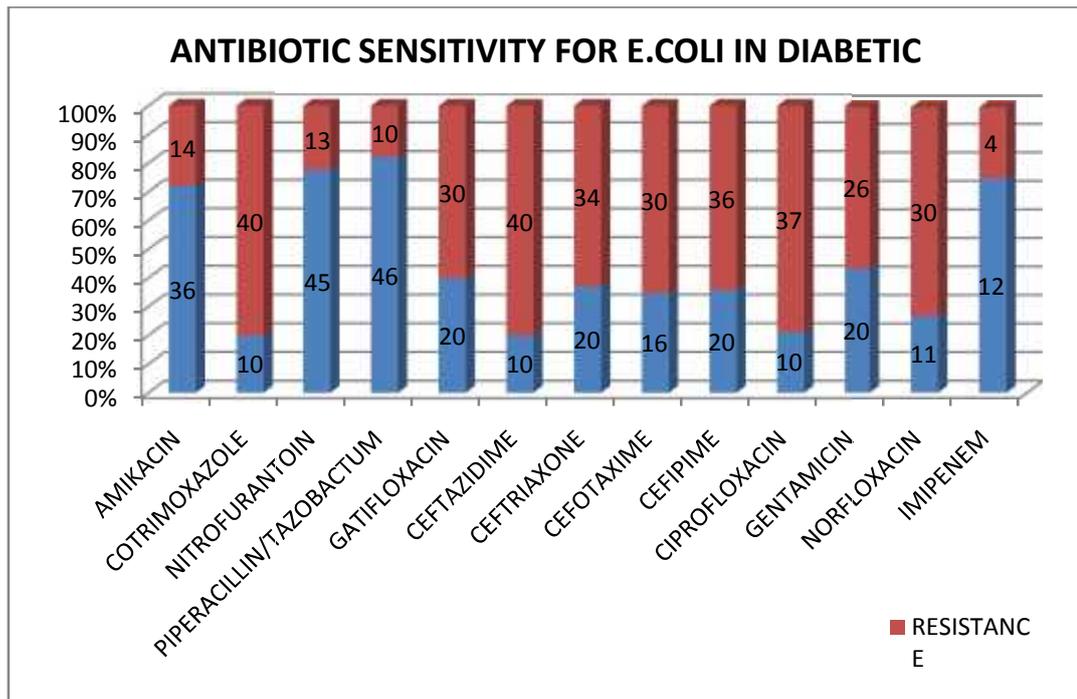


Figure 9: Antibiotic sensitivity for E.coli in Group A

- E.coli isolated from group A was found to be highly resistant to Cotrimoxazole (80%), Cephalosporin (72% to 74%) and Fluoroquinolones (Ciprofloxacin-78%,Norfloxacin-73% , Gatifloxacin-60%).
- Most of the isolates were sensitive to Nitrofurantoin(78%), Amikacin (72%), Piperacillin –Tazobactem (82%).

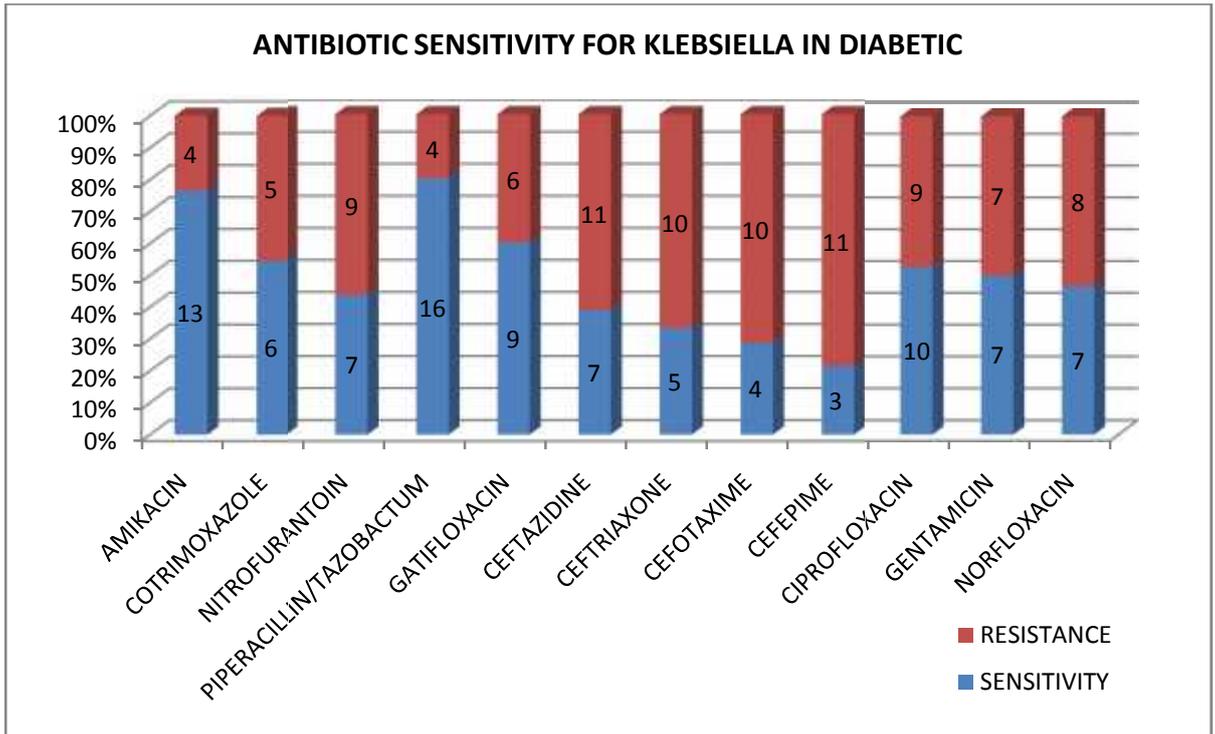


Figure 10: Antibiotic sensitivity for Klebsiella in group A

Klebsiella isolated from Group A were more resistant to Cephalosporins(80%-82%) and Nitrofurantoin(78%) and sensitive to Amikacin(72%), Piperacillin – Tazobactem(82%).

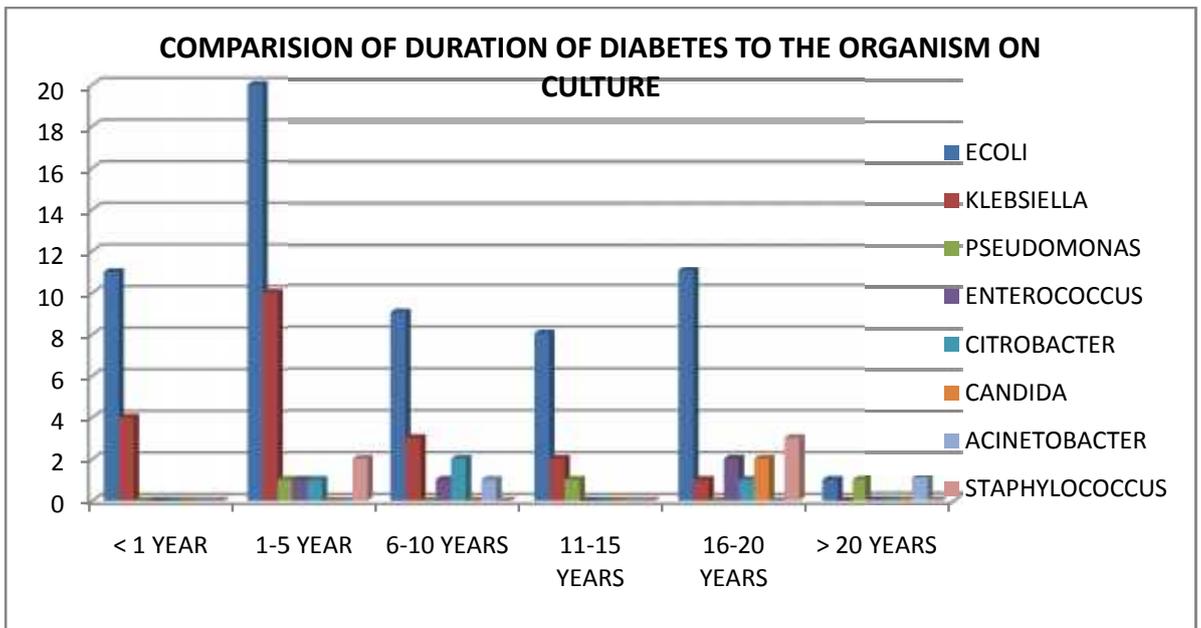


Figure 11: Comparison between Duration of Diabetes and Organism Isolated In Group A

- In group A, duration of diabetes was associated with the organism isolated (Fischers exact test p=0.015)
- A total of 40 patients (67%) who grew E.coli in culture had < 10 yrs duration of diabetes.
- However isolates such as Citrobacter, Staphylococcus and Candida were more common among subjects with history of Diabetes of >6 yrs duration.

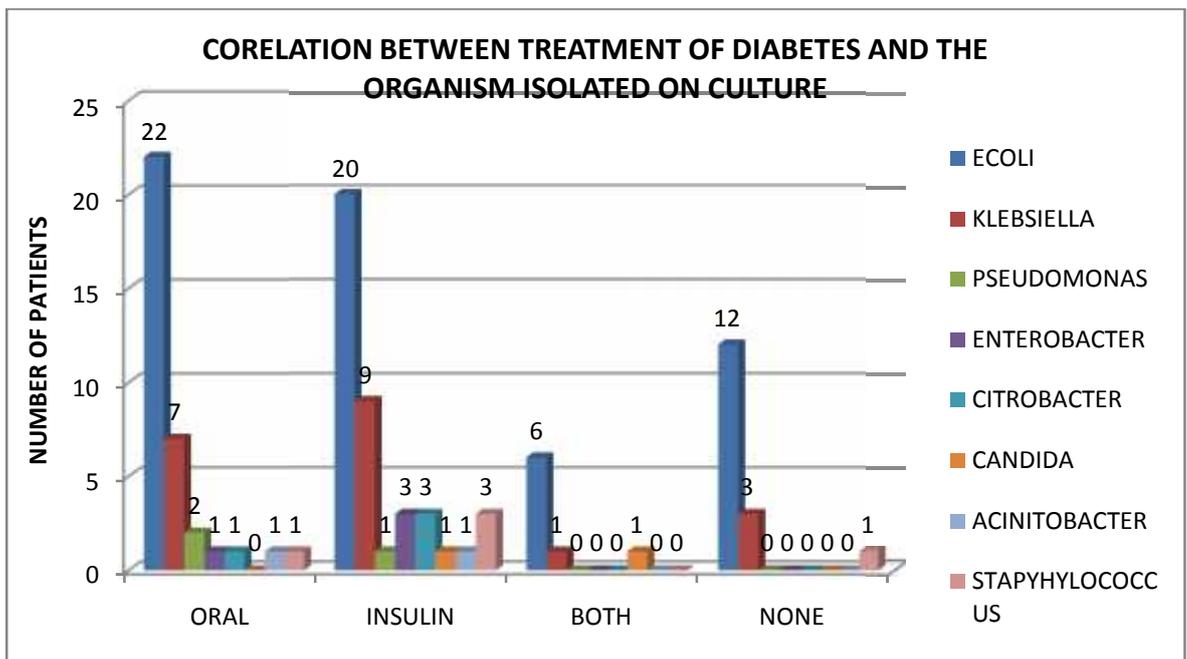


Figure 12: Correlation between Treatment of Diabetes and the Organism Isolated In Group A

- There is no statistical correlation between the organism isolated and the treatment received for Diabetes.

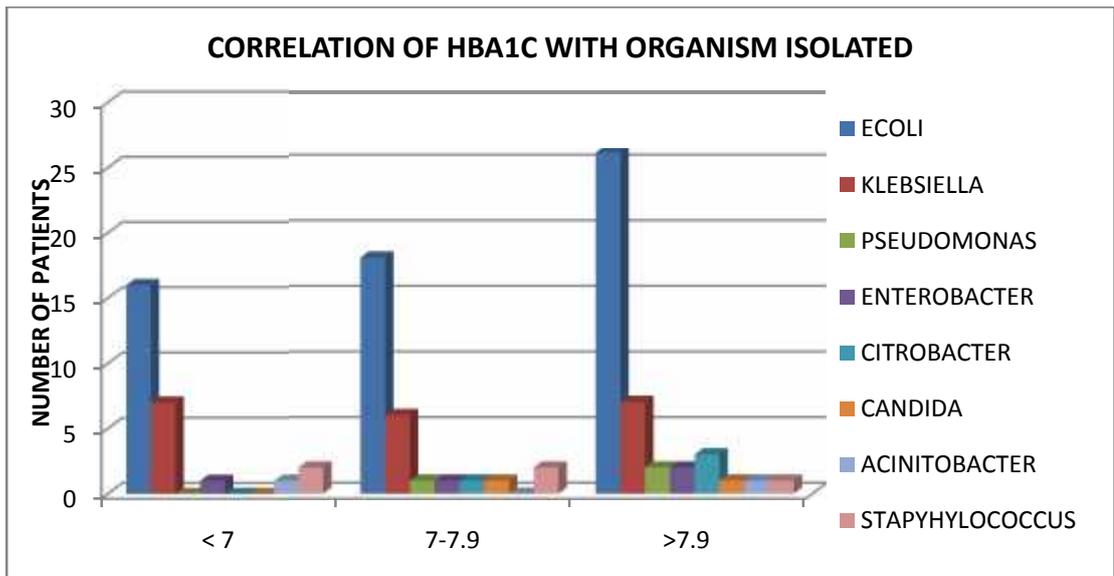


Figure 13: Correlation between HbA1c Level and Organism Isolated In Group A

- There is no correlation between the organism isolated and the HbA1c level.

ANALYSIS OF NON DIABETIC

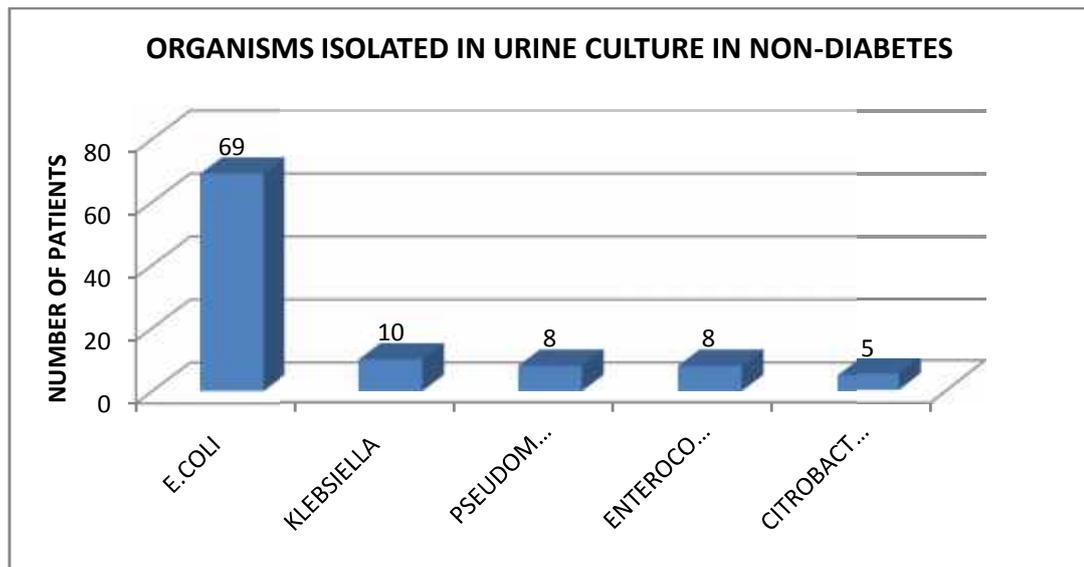


Figure 14: Organisms Isolated In Urine Culture in Group B

- E.coli was the commonest organism isolated in non Diabetics (69%). Rate of isolation was more in Non Diabetics than Diabetics. Klebsiella was the second commonest organism isolated (10%).

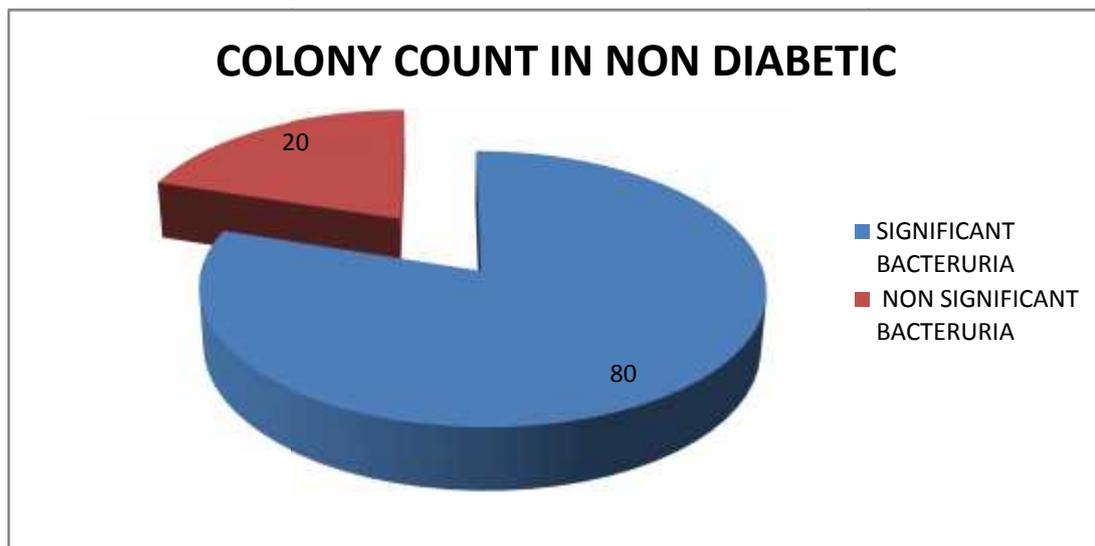


Figure 15: Colony count in group B

A total of 80 patients in Group B had significant bacteriuria, with colony count of $>10^5$ colony count on urine culture.

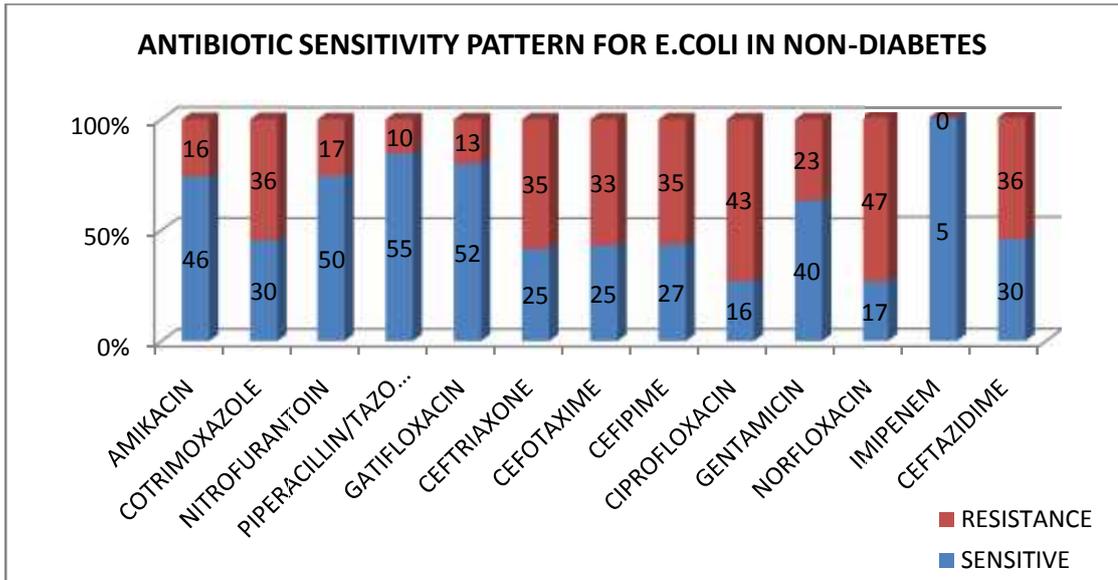


Figure 16: Antibiotic sensitivity pattern for E.coli in group B

- E.coli isolated from group B was found to be resistant mainly to Fluoroquinolones (Ciproflox-73%, Norflox-73%)
- Most of the isolates were sensitive to Nitrofurantoin(75%), Amikacin (88%), Piperacillin –Tazobactem (84.6%)

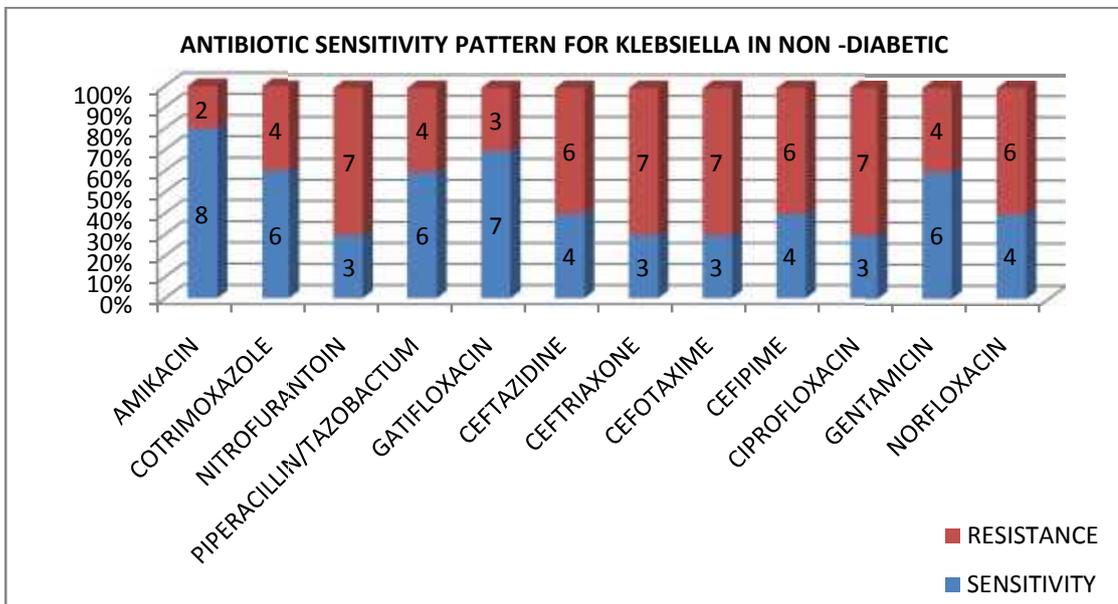


Figure 17: Antibiotic sensitivity pattern for Klebsiella in Group B

Klebsiella isolated from Group B were more resistant to cephalosporins(60%) and Nitrofurantoin(70%) and sensitive to Amikacin(80%).

COMPARISON OF BETWEEN GROUP A AND GROUP B

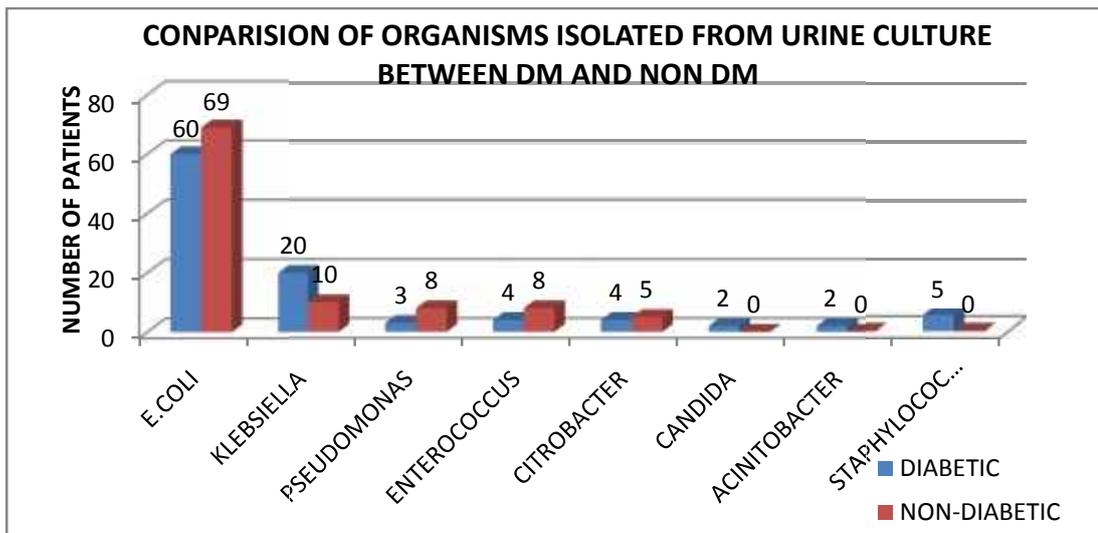


Figure 18: Comparison of organisms isolated from urine culture between group A & Group B

- E.coli was the commonest organism isolated in Diabetics (60%) and Non Diabetics (69%).Rate of isolation was more in Non Diabetics. Klebsiella was the second commonest organism isolated in both groups (Diabetics: 20%, Non Diabetics: 10%).
- Other organisms isolated included Pseudomonas (Diabetics: 3%, non diabetics: 8%), Enterococcus (Diabetics: 4%,non Diabetics:8%). and Citrobacter (Diabetics: 4%, Non Diabetics: 5%)..
- Staphylococcus (5%),acinitobacter(2%) and Candida (2%) were exclusively isolated in diabetic group (Fischers exact p test: 0.007(HS))..

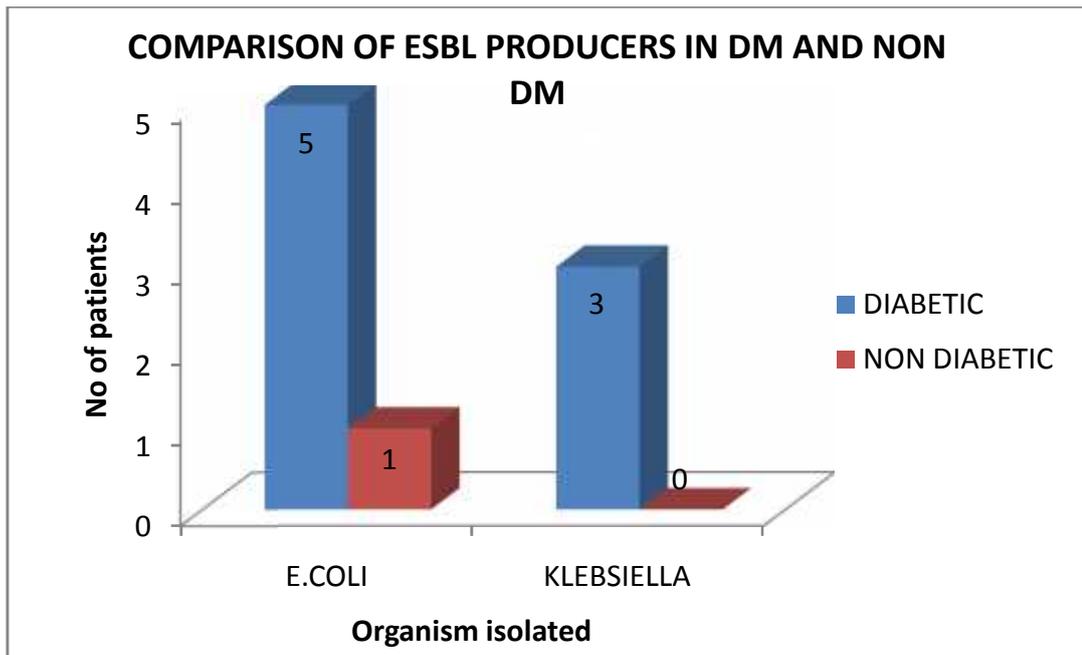


Figure 19: Comparison of ESBL producers in Group A and Group B

Isolation rate of Extended Spectrum Beta Lactames producing gram negative bacilli was observed in 9 patients with UTI. It was more frequently observed in Diabetics (8%) than Non Diabetics (1%) (P value=0.041 for E.coli, p=0.099 for Klebsiella).

Candida was isolated exclusively from urine culture of two (2%) diabetic subjects. These organisms were found to be sensitive to Nystatin, Fluconazole, Ketoconazole, Clotrimazole and Amphotericin B

DISCUSSION

Urinary tract infection is one of the commonest infections encountered in general population. The incidence and complications of UTI have been demonstrated to be higher in Diabetics in comparison with non Diabetics. Urine culture and sensitivity is the investigation of choice for demonstrating organism in urine. In the present study which included 100 Diabetics and 100 non Diabetics, the pattern of UTI, etiological agents causing UTI and their antibiotic profile in Diabetics and Non-Diabetics was compared.

Age and UTI

In our study the Mean Age in Diabetics was 55.34 yrs and non Diabetics was 49.48 yrs. Subjects were older In the Diabetic group, majority of the population being between the age group of 51 to 60 yrs (p value 0.001 HS). Of the total population in each group, 40% were females.

In a study by **O'sullivan DJ** et al²⁸, Incidence of UTI increased markedly after the age of 60 years and 24 out of 108 examined (22%) had UTI. The incidence of infection was maximum for females in both diabetics and non diabetics. **Bonadio M et al**²⁹ in his study demonstrated a mean age of $.9 \pm 13.2$ (SD) and 54.4 ± 23.3 years in diabetics and non Diabetics was respectively.

Organism isolated from urine

In our study, E.coli was the commonest organism isolated in Diabetics (60%) and non Diabetics (69%). Rate of isolation was more in Non Diabetics. Klebsiella was the second commonest organism isolated in both groups. Other organisms isolated in diabetics vs non diabetics included Pseudomonas (3% vs 8%), Enterococcus (4% vs 8%) and Citrobacter (4% vs 5%). Broad spectrum Beta Lactames production was more frequently observed in E.coli. Among the ESBL producers, it was more frequently

observed in Diabetics (8%) than Non Diabetics (1%) (p value=0.041)

Bonadio M et al²⁹, reported E.coli (56.1% vs. 56.8%) as the most frequent causative agent for UTI in diabetics and non diabetics, followed by Proteus species (7.9 vs 7.2%), Pseudomonas (6.7 vs 8.2%). **Krenke DS et al**³³, also concluded that E.coli was the most commonly isolated pathogen in Diabetics and Non Diabetics. Broad spectrum Beta Lactames production was more frequent in Klebsiella and it was more frequently observed in Diabetics(12%) than non Diabetics(4%). In a study conducted by **Saber MH et al**³⁵, rate of isolation of Escherichia coli in diabetic was less (61.8%) compared to non-diabetic(77.8%) which was consistent with our study findings. Rate of isolation of pseudomonas species in diabetic male and Enterococcus in diabetic females was higher than in non-diabetic patients. The same could not be concluded in our study. Isolation rate of the Extended Spectrum Beta Lactamase producing gram negative bacilli was found higher among diabetic population (47.8%) compared to the non-Diabetics (9.1%).

In our study, Staphylococcus (5%) and Candida (2%) were exclusively isolated in diabetic group (Fischers exact p test: 0.007(HS)). Two patients in whom staphylococcus was isolated in urine also demonstrated the same in the blood culture. All patients responded to antibiotics as per culture sensitivity report. In a study by **Baqai R et al**³⁴ E.coli(50%) was the predominant organism isolated from diabetic patients with UTI, followed by Staphylococcus aureus (20%), Staphylococcus saprophyticus(20%) Proteus species and Enterococcus faecalis. Candida was isolated in 10.2% of patients. Our study and reference data support the theory that staphylococcus and candida infection are common isolates in diabetic patients.

Antibiotic sensitivity pattern

In our study, Antibiotic sensitivity pattern in E.coli was compared between Diabetics and Non Diabetics and we demonstrated a high resistance pattern of E.coli to Cephalosporins, Fluoroquinolones in both the groups. There was statistically significant difference in the resistance pattern for cephalosporin. E.coli isolated from Diabetics was significantly less sensitive ($p<0.05$) to Ceftazidime, Ceftriaxone, Cefotaxim and Cotrimoxazole. E.coli in Non Diabetics were found to be more sensitive ($p<0.05$) to Amikacin, Piperacillin- Tazobactem, Gatifloxacin and Gentamicin. There is no statistical significant difference in the resistance pattern to Norfloxacin and Ciprofloxacin.

When antibiotic sensitivity pattern for Klebsiella was compared among the two groups, there was no statistical significant difference in the sensitivity pattern.

In a study conducted by **Akbar DH et al**³⁰ Escherichia coli and Pseudomonas in both diabetics and non diabetics showed resistance to Ampicillin and sensitivity to Aminoglycoside and Ciprofloxacin. **Bonadio et al**³¹, demonstrated no significant differences in resistance rates to Ampicillin, Nitrofurantoin, Cotrimoxazole and Ciprofloxacin for E. coli and Enterococcus species were observed between diabetic and non diabetic patients. **Saber MH, Barai L et al**³⁵ observed that, E. coli isolated from diabetic patient was significantly ($p<0.05$) less sensitive to Ceftriaxone, Ceftazidime, Cefuroxime, Netilmicin, Gentamicin, Ciprofloxacin and Nitrofurantoin than that of non-diabetic patients. **Krenke DS et al**³³, demonstrated Quinalone resistance was more common in Diabetics (40%) than non Diabetics (4%) which was not demonstrated in our study. **Janifer J, et al**^{42s} demonstrated that Escherichea coli (E. coli) was the most commonly found organism. Gram negative pathogens were found to be highly sensitive To Sulbactum / Cefoperazone and Piperacillin / Tazobactum.

In our study all the gram negative isolates were relatively sensitive to Amikacin and Gentamicin. This did not correlate with **Eshwarappa et al.** who reported nearly half of uropathogens showing resistance to Amikacin and Gentamicin.

In our study as the population included only urine culture positive subjects, the duration, therapy and HbA1c level could not be correlated with risk of culture positive UTI . Hence we demonstrated correlation with the organisms isolated. On subgroup analysis we demonstrated a correlation between duration of diabetes and organisms isolated. However there was no correlation between isolates and the glycemic control and antidiabetic medications.

Boyko EJ, Fihn SD et al³⁸ showed a increased risk of UTI mainly in women taking insulin (RR = 3.7, 95% CI: 1.8, 7.3) and women with a longer diabetes duration (10 years; RR = 2.6, 95% CI: 1.3, 5.1) compared with non-diabetic women. No clear linear trend between HbA1c and UTI or ASB risk was seen. However another study by **Bonadio M et al**⁸, showed high levels of HbA1c represented a significant risk factor for bacteriuria in diabetic women

Janifer J et al⁴² demonstrated that UTI was significantly associated with age, duration of diabetes, and poor glycemic control in both sexes.

CONCLUSION

- Pattern of presentation of UTI is the same in both Diabetics and non Diabetics. The usual symptom during presentation is Fever, dysuria and burning micturition.
- E.coli is the commonest pathogen causing UTI in both Diabetics and non Diabetics, followed by Klebsiella. Other organisms isolated includes Pseudomonas, Enterococcus and Citrobacter .
- Rate of isolation of Staphylococcus,acinitobacter and Candida is higher in Diabetic group.
- Gram negative bacteria isolated from Diabetics and non Diabetics were found to be resistant to Cephalosporins and Fluoroquinolones.
- Isolates from Diabetics have demonstrated a higher resistance pattern to Cephalosporins and better sensitivity pattern to Nitrofurantoin, Amikacin, Piperacillin- Tazobactem, Gatifloxacin and Gentamicin.
- Isolation rate of Extended Spectrum Beta Lactames producing gram negative bacilli is more frequently observed in Diabetics than Non Diabetics.
- There is no significant difference in the complication rate between Diabetics and non Diabetics
- There is no correlation between organism causing UTI and the glycemic control and antidiabetic medications in diabetic patients.

SUMMARY

This study was conducted at Shri B M Patil Medical between January 2013 and June 2014. A total of 200 patients were included in the study and the study group was divided in 100 Diabetics and 100 Non Diabetics. Urine examination, urine culture sensitivity was done for all patients

Out of the 100 subjects studied in each group, 40 were males and 60 were females. Majority of subjects in both the groups were in the age group of 51-60 years (33% of Diabetics and 22% of non Diabetics). Subjects were older in the Diabetic group. The mean age in Diabetics was 55.34 yrs and non Diabetics was 49.48 yrs. Comparison of other baseline characters showed that Diabetics with UTI had a lower hemoglobin($p=0.00$), higher ESR ($p=0.035$)

Duration of diabetes in 67 subjects in group A was < 10 yrs .A total of 74 subjects in group A had uncontrolled blood sugars with HbA1c of >7 , among whom 30 subjects had an HbA1c of 7 to 7.9 and 44 subjects had a HbA1c of >7.9 .A total of 35 subjects were on oral hypoglycemic therapy, 41 subjects on insulin therapy and 8 subjects on both.

There was no statistical significant difference in the presentation of UTI in Diabetics and Non Diabetics. E.coli was the commonest organism isolated in Diabetics (60%) and non Diabetics (69%).Rate of isolation was more in Non Diabetics. Klebsiella was the second commonest organism isolated in both groups. Other organisms isolated included Pseudomonas, Enterococcus, Acinitobacter and Citro bacter. Staphylococcus (5%) and Candida (2%) were exclusively isolated in diabetic group(Fischers exact p test:0.007(HS)). Among the ESBL producers, 8 were isolated from Diabetics and 1 from non Diabetics (p value=0.041)

E.coli isolated from Diabetics was more resistant to Cotrimoxazole,

Cephalosporin ($p < 0.05$) and Fluoroquinolones when compared to non Diabetics. Most of the isolates were sensitive to Nitrofurantoin, Amikacin, Piperacillin –Tazobactam, and Ertapenem in both groups. Klebsiella isolated from both groups were more resistant to Cephalosporins and Nitrofurantoin and sensitive to Amikacin, Piperacillin – Tazobactam. When antibiotic sensitivity was compared between Diabetic and non Diabetics, it was observed that isolates from group B were more sensitive to Cephalosporin, Gatifloxacin and Gentamicin($p < 0.05$)

There was no significant difference in the complication rate in diabetics and non diabetics

On subgroup analysis, duration of diabetes was associated with the organism isolated (Fischers exact test $p = 0.015$). However there is no correlation between the organism isolated and the HbA1c level and the treatment received for diabetes

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ANNEXURE-I

ETHICAL CLEARANCE



B.L.D.E. UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 18-10-2012 at 3-30 pm to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.

Title "A Comparative Study of urinary tract infection in diabetic and non-diabetic population"

Name of P.G. student Dr. Eday Kumar patil
Medicine

Name of Guide/Co-investigator Dr. M.S. Mulimani
prof & HOD. Medicine

DR. TEJASWINI VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization

- 1) Copy of Synopsis/Research project.
- 2) Copy of informed consent form
- 3) Any other relevant documents.

Drug history: Insulin/oral/none

Regular/Irregular

Examination

Pallor /Icterus/Clubbing/Cyanosis /Lymphadenopathy/Pedal oedema

Pulse:

BP:

Temperature:

Respiratory Rate:

Systemic Examination:

Abdomen: suprapubic tenderness

Costovertebral angle tenderness

Mass/tenderness on palpation

Respiratory System:

Cardiovascular System:

Central Nervous system:

Investigations:

Hb: URINE: Albumin: pH:

TC: sugar: specific gravity:

DC: microscopy:

ESR:

HbA1c (diabetic):

Urine culture and sensitivity:

Organism isolated:

Sensitive to:

Resistant to:

INFORMED CONSENT FORM

I exercising free power of choice hereby give my written consent to be included as a subject in the study “A COMPARATIVE STUDY: PATTERN AND PRESENTATION OF URINARY TRACT INFECTION IN DIABETIC AND NON DIABETIC POPULATION” conducted by and undergo the necessary investigations required for this study and I fully consent for the same.

I am over 18 yrs of age and I have been explained to my satisfaction by the attending Physician, in the language I understand, about the purpose of the study .I have also understood that the investigator will maintain confidentiality regarding my identity.

SIGNATURE OF DOCTOR

SIGNATURE OF PATIENT/RELATIVE

NAME OF THE DOCTOR

NAME OF PATIENT/RELATIVE

RELATIONSHIP (IF RELATIVE)

DATE:

KEY TO MASTER CHART

Sl No	Variables	Coding
1	Sex	1-Male 2-Female
1	Patients	1-Diabetic 2-Non -diabetic
2	Duration of Diabetic	1-<1 year 2-1-5 years 3-6-10 years 4-11-15 years 5-16-20 years 6->20 years
4	Symptoms of UTI	1-Dysuria 2-Frequency 3-Haematuria 4-Suprapubic Pain 5-fever 6-urgency 7-nocturia 8-Flank pain 9-Burning micturition 10-Tenderness
5	Drug History	1-Oral 2-Insulin 3-Both 4-None
6	Urine Sugar	1-Null 2-Blue 3-Yellow 4-Orange 5-Red
7	Urine WBC	1-<10cell/cumm 2-10-20 cell/cumm

		3->20 cell/cumm
8	Urine RBC	1-Nil 2-1-10 cell/cumm 3->10 cell/cumm
9	Urine Epithelial Cell	1-<5 cell/cumm 2-6-10 cell/cumm 3->10 cells/cumm
10	Urinary Casts	1-Yes 2-No
11	Urinary Bacteria	1-Yes 2-No
12	Organisms isolated	1-Ecoli 2-Klebsiella 3-Pseudomonas 4-Enterococcus 5-Citrobacter 6-Candida 7-Acinitibacter 8-Staphylococcus
13	Antibiotic Sensitivity and Resistance for Organisms isolated in Diabetic And Non Diabetic Ptients for Ecoli And Klebsiella.	1-Amikacin 2-Co-trimoxazole 3-Nitrofurantoin 4-Piperacillin/Tazobactam 5-Gatifloxacin 6-Ceftazidime 7-Ceftriaxone 8-Cefotaxime 9-Cefipime 10-Ciprofloxacin 11-Gentamycin 12-Norfloxacin 13-Imipemem

MASTER CHART

sno	age	sex	h/o of DM	duration	symptoms	drug h/o	Hb	TLC	ESR	RBS	HB1Ac	urine ph	urine gravity	urine sugar	Urine WBC	Urine RBC	Urine epi cell	urine casts	urine bacteria	organism isolated	senitive to	resistant to
1	57	f	1	2	5,1,2,9	1	10.5	9,300	68	258	6.8	6.12	1.02	1	3	1	1	2	2	1	3,4,6,7,9,11	2,5,8,10,12
2	59	f	1	4	1,6,4,2	2	11	12,500	38	321	8.9	6.25	1.003	3	1	3	1	1	1	1	1,3,5,11	2,5,6,7,8,9
3	33	f	1	1	5,6,1,9	4	13.4	13,568	70	256	7.5	6.3	1.003	2	3	2	1	2	2	1	3,6,8,11,12	2,4,5,7,10
4	44	f	1	2	8,2,9,1	2	7.4	11,786	84	243	8	6	1.005	1	3	2	2	2	1	1	3,4,11	1,2,7,8,10,12
5	35	f	1	2	1,4,6,10	1	8.6	12,430	64	258	7.2	5.8	1.01	2	1	2	1	1	1	2	1,7,8,10,12	1,3,4,6,9
6	76	f	1	3	5,1,9	1	13	14,000	76	250	8.3	6.2	1.008	3	3	1	1	2	2	1	3,5,6,8,9	2,4,7,10,11,12
7	56	f	1	4	1,9,5,2	2	9.3	11,400	46	208	6.7	6.02	1.02	1	2	2	1	2	1	1	4,11,12	3,5,6,7,8,9,10
8	45	f	1	4	5,8,9,4	4	10	7,450	58	278	7.3	6.03	1.004	1	3	2	1	2	1	1	1,6,8,9,11	2,3,4,5,7,12
9	35	f	1	1	1,5,6,10	2	12	4,865	90	250	8.2	6.04	1.002	3	1	2	1	2	2	1	3,8,9,11,12	1,2,4,5,7,10
10	67	f	1	6	7	4	13	14,580	43	245	8.1	6.06	1.02	2	3	1	1	2	2	1	4,5,7,8,9	1,2,6,10,11,12
11	47	f	1	3	8,6,5	1	8.9	15,000	56	265	7.5	6.08	1.012	5	2	3	1	2	2	2	3,5,10,12	1,4,6,7,8,9
12	78	f	1	5	4,1,9,10	2	9	13,800	60	248	8.1	5.8	1.016	1	3	2	1	2	2	1	1,4,8,9,11	2,3,6,7,12
13	64	f	1	5	5,4,10,8	3	10	14,000	35	275	6.9	6.3	1.016	3	1	1	1	2	1	1	1,3,4,6,11	2,5,8,9,10,12
14	37	f	1	2	1,2,8,4	2	7	6,800	75	248	8.2	6.02	1.014	2	3	2	1	2	1	8	4,12	1,6,7,8
15	47	f	1	3	1,2,5,9	1	11	17,840	36	280	7.6	6.06	1.016	1	2	2	1	2	1	1	3,5,7,8,9	2,4,10,11,12
16	42	f	1	2	5,4,9,1	3	6.8	15,840	70	205	6.4	6.23	1.01	3	1	1	1	2	1	1	1,4,8,10	3,5,6,9,12
17	37	f	1	2	1,2,5,10	2	9	8,500	65	208	6.8	6.3	1.012	2	1	2	1	2	2	2	3,5,8,12	2,4,7,9,11
18	56	f	1	3	4,2,5,6,8	4	8.6	18,500	45	264	7.8	6.1	1.012	1	3	2	1	1	2	1	1,4,8,10,11	1,5,6,8,9,10
19	59	f	1	4	9,2,1,5	1	13	13,500	58	248	8.1	6.2	1.018	3	3	1	1	2	2	2	1,4,11,12	1,3,6,7,10
20	51	f	1	3	6,8,10	2	10.2	12,500	70	208	6.9	6.06	1.02	4	1	2	1	2	1	7	3,12	2
21	41	f	1	2	1,2,4,5,8	4	11	8,650	48	273	8.2	6.08	1.016	1	3	3	1	2	1	1	3,4,5,6,8	1,2,7,9,11
22	57	f	1	5	1,5,9	1	8.8	12,560	60	236	7.6	5.9	1.012	4	3	2	1	2	2	1	1,9,11	3,4,5,6,7,8,12
23	43	f	1	3	6,8,10	2	6.6	13,800	78	248	8.1	6	1.012	3	1	1	1	2	2	1	3,4,11,12	2,5,7,8,9,10
24	55	f	1	5	2,4,6,8	4	9	15,850	50	195	6.9	6.05	1.04	1	3	2	1	2	1	8	3	1,10,12
25	34	f	1	2	9,6,2,1	2	14	13,500	45	275	8.5	6.09	1.04	4	3	2	1	2	1	1	3,5,7,8,9	1,2,4,6,11,12
26	76	f	1	5	1,2,5,9	1	10	12,560	65	249	7.5	6.04	1.016	3	2	1	1	2	2	1	1,3,9,11,12	2,4,5,6,7,8,10
27	65	f	1	4	6,8,9	2	10	12,500	58	263	8.2	6.04	1.015	1	1	2	1	2	1	1	1,3,4,8	2,5,6,7,9,11
28	45	f	1	3	1,2,5,9,10	4	9	13,850	75	225	6.7	6.1	1.015	4	3	1	1	2	2	2	1,4,11	3,6,7,10,12
29	54	f	1	5	3,10,8	2	11	8,690	60	236	7.4	6.2	1.018	3	1	2	1	2	2	8	3,5,7,8,9	2,4
30	53	f	1	4	1,2,5,9	3	8	5,900	54	225	7.2	6.04	1.013	1	3	2	1	1	2	1	3,4,8,12	1,2,5,6,9,11
31	52	f	1	3	4,5,8	1	12	12,590	60	274	8.3	6.04	1.019	3	3	1	1	2	1	1	1,3,9	2,4,5,7,8,10
32	58	f	1	5	1,2,9	2	10	11,570	60	293	8.7	6.06	1.017	5	3	2	1	2	2	1	1,3,4	5,6,8,9,10,12
33	62	f	1	4	3,6,5,10	3	9	14,000	54	214	6.6	6.09	1.008	4	2	3	1	2	1	1	3,6,7,8,9	1,2,4,5,10,11
34	71	f	1	5	3	2	13	13,780	66	236	7.1	6.08	1.009	1	1	2	1	2	2	2	1,2,4,10,12	3,6,7,8,9
35	55	f	1	4	1,2,5,9	1	12	12,560	35	273	8.5	6.04	1.017	3	3	1	1	2	2	3	3,11	2,4,7,8,9
36	49	f	1	3	1,2,5,9	2	7.7	13,450	68	304	8.5	5.9	1.016	2	3	2	1	2	2	5	3,11	1,12
37	52	f	1	2	6,8,10	4	8	12,780	54	196	6.6	6	1.016	4	2	3	1	2	2	2	1,2,4,11,12	1,3,9,10
38	63	f	1	2	1,4,5,9	1	10	9,800	48	206	7.2	6.12	1.012	1	1	2	2	2	1	8	3,4,7,8,9	2,5,6
39	62	f	1	2	2,4,5,6	2	10	8,750	52	234	7.5	6.2	1.009	3	3	1	1	2	2	1	1,4,9	3,5,7,10,11
40	44	f	1	2	9,10,1	2	11	11,860	55	246	8.3	6.04	1.013	2	3	2	1	2	2	2	3,4,6,8,10	1,5,7,9,11
41	66	f	1	4	4,5,6,9	1	13	16,500	58	253	8.1	6.04	1.017	4	3	3	1	2	1	1	3,4,8,9	1,2,5,6,7,10

42	72	f	1	4	1,2,5,4	4	8	9,560	68	260	8.2	6.08	1.019	1	1	2	1	2	2	2	1,4,5,6,11	3,8,9,10,12
43	64	f	1	5	5,9,2	2	9	7,840	72	244	7.6	6.04	1.012	1	2	1	1	2	2	1	3,4,12	1,5,6,7,8,9,10
44	56	f	1	3	7,5,9	4	6.8	14,700	68	264	8.1	6.2	1.017	3	3	2	1	2	2	1	1,3,4,7	2,6,8,9,10,12
45	53	f	1	2	5,2	1	12	9,500	94	224	6.5	6.07	1.008	1	3	2	1	2	1	1	1,4,10	3,5,6,7,8,9,11
46	66	f	1	1	3	2	13	11,680	62	226	6.5	6	1.005	4	1	2	1	2	2	1	1,3,4,13	2,7,8,9,10,11
47	61	f	1	4	1,9	4	10	14,580	46	244	8.2	6.12	1.016	1	3	3	1	2	2	1	3,5,7,8,9	1,2,4,6,10,12
48	45	f	1	3	1,5,9	2	9.4	8,950	60	206	6.8	6.12	1.02	1	2	1	1	2	2	2	1,4,6,7,8,10	2,5,9,11,12
49	44	f	1	2	7	1	14	7,850	45	248	7.5	6.01	1.002	3	3	3	1	2	1	1	1,3,4,11	2,6,8,9,10,12
50	54	f	1	1	6,9	4	10	16,740	68	240	8.1	6.08	1.014	1	1	2	1	2	2	1	3,4,13	2,5,6,7,8,9,10
51	62	f	1	5	1,2,4	2	11	13,850	35	230	6.7	6.08	1.012	2	3	2	1	1	2	8	1,3,8	9,10,11
52	42	f	1	3	4,9	2	12	9,670	73	225	7.3	6.1	1.02	1	3	1	1	2	2	1	1,2,3,4,11	5,6,7,8,9,10
53	72	f	1	6	3	1	14	15,304	43	260	8.3	6.12	1.014	4	2	2	1	2	1	7	4,5,7,8,9	2,10,11
54	54	f	1	3	2	4	9	9,802	54	244	7.3	6.01	1.013	3	3	2	1	2	2	1	1,3,4,8,11	2,5,6,7,9,10
55	61	f	1	2	5,7	2	8	11,680	54	284	8.2	6.1	1.017	1	1	1	1	2	1	2	1,4,5,7,9	3,6,8,10,12
56	63	f	1	3	5,1,9	1	12	14,580	50	254	6.8	5.6	1.012	5	3	2	1	2	2	1	3,4,6,7,11	1,2,5,8,9,10
57	42	f	1	1	4	2	13	13,870	62	239	7.3	6.01	1.017	3	3	2	1	2	2	2	3,4,5,6,12	8,10,11
58	62	f	1	5	8,9	3	10	15,830	54	305	8.6	6.12	1.013	1	2	2	1	2	2	1	1,3,4,7,13	2,5,6,8,9,10
59	46	f	1	3	1,5	1	11	9,460	60	214	6.5	6	1.018	1	3	2	1	2	1	4	2,5	3,10,11
60	64	f	1	5	7	2	13	14,370	65	274	8.2	6.11	1.013	4	3	3	1	2	2	4	3,11	2,5,8,9
61	43	m	1	2	4	4	9	13,690	50	246	7.4	6.06	1.017	3	2	2	1	2	2	1	1,3,4,13	2,6,7,9,10,12
62	38	m	1	1	1,5	2	9.4	14,584	70	204	6.6	6	1.012	1	2	2	1	2	2	1	3,4,11,13	2,5,6,7,8,9,10
63	73	m	1	6	6	1	12	8,940	56	258	8.1	6.1	1.004	1	3	1	1	2	2	3	4,5	3,9,10
64	62	m	1	3	9,5	2	11	11,680	75	248	8.2	6.12	1.002	4	2	2	1	2	2	5	1	2,5,7,8
65	56	m	1	2	5	2	12	12,680	68	230	6.5	5.8	1.02	1	1	2	1	2	1	1	1,2,4,6,13	3,5,7,8,9,11
66	47	m	1	1	1	4	13	12,600	40	275	8.1	6.11	1.016	1	3	2	1	2	2	1	1,3,4,5,7	2,8,9,10,11
67	56	m	1	5	2	1	14	9,800	50	222	6.6	5.8	1.012	3	3	2	1	2	2	1	1,3,4,13	2,5,6,7,8,9,12
68	64	m	1	5	1,9	2	12	7,850	64	246	7.3	6	1.013	1	2	3	1	2	1	6	3,11	2,7,10
69	62	m	1	5	5,6	4	7.6	15,380	45	256	7.7	6.11	1.017	4	2	1	1	1	2	1	1,2,4,13	3,5,6,7,8,9,12
70	42	m	1	2	4	2	13	13,750	63	274	8.3	6.11	1.02	5	3	2	1	2	2	2	1,2,4,5,10	2,6,7,8,9,12
71	37	m	1	2	1	1	14	14,680	58	186	6.5	5.8	1.021	1	3	3	1	2	2	1	1,4,6,7,9	3,5,10,11,12
72	72	m	1	5	5,2	2	9	15,980	55	204	6.5	5.6	1.017	4	1	2	1	2	2	1	2,3,4,5,11	1,6,9,12,13
73	71	m	1	5	6	2	10	13,680	68	260	7.8	6.11	1.012	3	2	2	1	2	1	4	1,11	2,5,6,7,9
74	54	m	1	2	5,10	1	12	14,680	40	284	8.5	6.11	1.021	1	3	2	1	2	2	5	1,4	10,11
75	63	m	1	5	4,8	2	11	7,800	57	250	7.4	6.04	1.014	1	2	2	1	2	2	5	3,10	2,5,6,8
76	45	m	1	2	10	3	10	5,980	45	236	6.6	5.8	1.021	4	3	2	1	2	2	2	1,4,5,7,9	6,10,11,12
77	58	m	1	2	1	1	12	14,380	60	274	8.2	6.11	1.007	1	2	2	1	2	2	1	3,4,10,11	2,5,6,7,9,13
78	63	m	1	5	2	2	10	12,674	66	234	7.4	6.11	1.023	3	3	3	1	2	1	1	1,3,5,10,13	4,6,7,9,11
79	32	m	1	1	5,4	1	11	15,890	74	254	7.5	6.01	1.009	4	3	2	1	2	2	2	1,3,4,6,11	5,8,9,10
80	56	m	1	2	7	2	10	14,680	76	263	8.4	6.06	1.003	1	1	2	1	2	2	2	2,3,4,10,11	5,6,8,12
81	63	m	1	5	6,5	3	9	13,680	53	273	8.1	6.06	1.002	3	3	2	1	2	2	6	4	10,11
82	57	m	1	2	1,9	1	10	11,590	68	230	6.6	5.8	1.014	1	2	1	1	1	1	1	1,3,4,10,12	2,6,7,8,9,11
83	74	m	1	1	2	1	11	13,680	65	245	8.3	6.1	1.012	1	3	2	1	2	1	1	1,2,3,4,5,7	6,8,9,10,11
84	63	m	1	2	5,1	2	12	12,450	35	260	8.1	6.1	1.019	3	3	2	1	2	2	2	2,3,5,7,10	4,6,8,9,11
85	56	m	1	1	1,6	1	12	7,850	75	235	6.5	5.7	1.015	1	2	2	1	2	1	2	1,4,6,10,12	2,5,7,8,11

86	36	m	1	1	5,9	2	9	7,850	56	258	8.2	6.04	1.017	3	3	3	1	2	2	1	1,3,4,5,10	2,6,7,8,9,11
87	73	m	1	2	8	1	11	9,580	48	263	8.5	6.11	1.025	1	3	2	1	2	2	1	2,3,4,5,7,9	1,6,10,11,12
88	62	m	1	1	5,2	1	9	13,950	56	234	7.3	6	1.021	1	2	2	1	1	1	1	1,3,4,5,7,13	2,6,8,9,11
89	56	m	1	1	4	2	8.9	7,850	74	273	8.2	6.2	1.017	3	3	2	1	2	2	1	1,2,3,4,5,7	6,8,9,10,11
90	42	m	1	1	5,6	1	10	11,450	64	204	6.8	5.8	1.014	3	2	2	1	2	2	2	2,4,10,11	3,5,6,7,12
91	71	m	1	2	1	1	11	14,580	60	235	7.3	6.03	1.023	1	3	2	1	2	1	2	1,4,5,6,9	2,3,7,10
92	62	m	1	2	5	2	9	13,470	54	294	8.3	6.12	1.012	3	2	3	1	2	2	4	2,4	10,11
93	54	m	1	2	6	1	10	9,450	46	230	8	6.04	1.014	4	3	2	1	2	2	1	1,4,5,10,13	2,3,6,7,9,12
94	72	m	1	2	8	1	11	7,850	75	204	6.7	5.9	1.021	1	3	2	2	1	1	1	3,4,5,7,9,12	2,6,10,11,13
95	54	m	1	1	2	2	7	9,430	57	236	7.4	6.01	1.021	3	2	2	1	2	2	1	1,2,3,4,5,7,10	6,9,11,12,12
96	56	m	1	2	5,4	1	9	8,450	60	274	8.2	6.1	1.002	1	3	2	1	2	2	1	1,2,4,5,10,12	3,6,7,9,11
97	62	m	1	2	5	2	10	11,450	52	248	7.8	6.12	1.009	3	3	2	1	2	1	3	3,4,10	2,6,9
98	55	m	1	2	6,5	3	11	13,580	70	250	7.7	6.11	1.005	1	3	2	1	2	2	1	1,3,4,9,13	2,6,7,10,11
99	52	m	1	2	6	1	10.2	12,750	65	240	8.1	6.11	1.006	3	2	1	1	2	2	1	1,2,4,5,7,10	3,6,9,11
100	55	m	1	2	5,8	1	8.8	13,890	60	243	6.5	5.7	1.007	1	1	3	2	1	1	1	1,4,5,7,9,12	2,3,6,10

Sl No	Age	Sex	H/o of dm	Duration	Symptoms	Hb	Tlc	Esr	Rbs	Urine ph	Urine gravity	Urine sugar	Urine wbc	Urine rbc	Urine epi cell	Urine casts	Urine Bacteria	Organism isolated	Senitive to	Resistant to
101	56	f	2	0	1,9,5	11	9,570	46	102	6.01	1.013	1	2	1	1	2	1	1	1,3,4,5,8,12	2,6,9,10,11
102	44	f	2	0	4,8,6	10.6	14,600	50	130	6.02	1.016	1	3	2	1	2	2	1	2,4,5,9,11	1,3,6,7,12
103	42	f	2	0	5,9,1,2	8.4	8,640	38	95	5.7	1.013	1	2	3	1	1	2	1	4,5,13,11,12	2,3,9
104	34	f	2	0	4	9	7,840	40	94	6.1	1.014	1	1	1	1	2	2	4		
105	32	f	2	0	9,8,10	11.4	8,590	79	108	5.8	1.012	1	3	2	1	2	1	1	1,2,4,9,11	3,7,10,12
106	73	f	2	0	1,2,5,6	6.8	7,540	39	104	5.7	1.014	1	2	2	1	2	2	1	1,3,5,6,11,13	2,9,10,12
107	62	f	2	0	1,5,9	7.9	13,780	60	93	6.1	1.016	1	1	2	1	1	2	1	2,3,5,6,9,11	1,4,7,12
108	44	f	2	0	2,4,6	13.6	6,840	50	100	6.11	1.016	1	3	1	1	2	1	2	1,2,4,7,8,10	3,5,6,9,11,12
109	56	f	2	0	3	11.4	13,590	47	126	6.08	1.006	1	2	2	1	2	2	1	1,3,4,5,8,12	2,6,9,10,11
110	52	f	2	0	6,8,10	13.9	14,680	58	114	6.11	1.013	1	3	3	1	2	2	1	1,2,3,5,8,13	4,6,7,10,12
111	46	f	2	0	5,1,6	8.9	12,560	69	99	6.03	1.014	1	1	2	1	2	2	1	3,4,5,7,9,12	1,2,6,11
112	62	f	2	0	2	11.4	11,680	50	106	6.07	1.012	1	3	1	1	2	1	4		
113	71	f	2	0	4,6,8	11.2	8,950	38	115	6.08	1.02	1	2	2	1	2	2	1	1,2,4,5,6,11	3,7,8,10,12
114	25	f	2	0	5,9	9.6	9,560	49	124	6.09	1.03	2	3	3	1	2	2	1	1,3,4,5,8,13	2,6,7,9,11,12
115	38	f	2	0	7	13.4	12,580	70	124	6.1	1.014	1	1	2	1	2	2	1	2,3,5,7,9,12	1,4,6,10
116	42	f	2	0	1,2,5,9	11	11,780	40	102	6.16	1.008	1	3	1	1	2	2	1	1,3,4,5,9,13	2,6,7,8,11,12
117	56	f	2	0	1,6,9	10	12,450	59	100	6.2	1.013	1	2	2	1	2	2	1	1,2,4,5,8,12	3,6,7,9,10
118	63	f	2	0	2,4,8	9.3	9,540	57	94	6.06	1.012	1	3	2	1	1	1	1	2,3,4,5,9,12	1,7,8,10
119	56	f	2	0	7	7.9	7,890	38	103	6.08	1.016	1	1	2	1	2	2	1	1,3,4,5,6,11	2,7,8,9,12
120	74	f	2	0	3	9.8	12,890	60	102	6.09	1.007	1	2	1	2	2	2	4		
121	65	f	2	0	1,5,9	14	13,860	50	100	6.03	1.015	1	3	2	1	2	2	1	1,2,4,5,8,12	3,6,7,9,10,11
122	45	f	2	0	6	11.9	8,590	48	93	6.09	1.013	1	1	2	1	2	1	1	3,4,5,7,9,12	1,2,6,8,10,11
123	32	f	2	0	5,8	13	7,840	70	124	6.08	1.014	1	2	2	1	2	2	2	2,3,5,9,11,12	1,4,6,7,8,10
124	24	f	2	0	1,5,9	10	14,904	48	111	6.09	1.018	1	3	2	1	2	2	1	1,3,4,5,8,12	2,6,9,10,11
125	52	f	2	0	8,6,2	13	16,840	37	99	6.01	1.012	1	1	1	1	2	2	1	1,2,4,5,8,11	6,7,8,10,11
126	45	f	2	0	1,5,4	12	8,450	47	118	6.03	1.017	1	3	2	1	2	1	1	1,3,4,5,9,13	2,6,7,10,11,12
127	36	f	2	0	2,6	10.2	7,489	38	114	6.04	1.014	1	2	2	1	2	1	1	1,3,4,7,10,12	2,6,8,11
128	29	f	2	0	9	9.4	8,439	40	94	6.11	1.016	2	3	2	1	2	2	1	1,3,4,5,6,11	7,8,9,10,12
129	46	f	2	0	5,1,2	11	12,650	50	94	6.07	1.004	1	1	2	1	2	2	5		
130	53	f	2	0	1,9	10.3	8,950	38	113	6.08	1.003	1	3	1	1	1	1	1	2,3,4,6,8,9,12	5,7,10,11
131	57	f	2	0	3	9.3	13,780	40	102	6.05	1.009	1	2	2	1	2	2	1	1,3,4,5,7,12	2,6,8,9,10
132	63	f	2	0	4,8	9.4	8,680	30	120	6.09	1.015	1	3	2	1	2	1	2	1,4,5,7,8,11	2,3,6,9,10,12
133	71	f	2	0	5,9	8.4	13,680	47	111	6.08	1.015	1	1	2	1	2	1	1	1,3,4,5,6,9	7,8,10,11,12
134	57	f	2	0	8,10	11	8,390	28	109	6.04	1.019	1	2	2	1	2	1	1	2,3,4,5,8,13	1,6,9,10,11,12
135	37	f	2	0	1,2	10.3	8,690	46	110	6.03	1.018	1	3	1	1	2	2	1	1,3,4,5,6,13	2,8,9,11,12
136	25	f	2	0	5,7	11.2	3,864	38	103	6.1	1.03	1	1	2	1	2	2	1	1,3,4,6,9,13	2,5,8,11,12
137	36	f	2	0	4,8	14	15,940	28	100	6.01	1.017	1	2	2	1	2	1	1	2,3,4,5,6,11	1,7,8,10,12
138	41	f	2	0	1,9	9.3	8,490	39	103	5.9	1.016	2	3	2	1	2	1	1	1,3,4,5,6,10	2,7,9,11,12
139	53	f	2	0	2,4	8.5	13,680	40	98	5.7	1.015	1	3	2	1	2	2	1	1,2,4,5,8,11	3,6,7,8,9,10,12
140	62	f	2	0	9,10	13.5	8,348	35	120	6.02	1.013	1	2	1	1	1	2	1	1,3,4,5,6,9,12	2,7,8,10
141	73	f	2	0	6,5	11	10,380	50	103	6.07	1.014	1	1	2	1	2	1	2	1,2,4,6,10,12	3,5,7,8,9,11
142	46	f	2	0	1,5	10	11,290	25	114	5.8	1.005	1	3	2	1	2	2	5		

143	57	f	2	0	1	12	8,945	38	117	5.9	1.003	1	2	2	1	2	1	1	2,3,4,5,8,12	1,6,8,10,11
144	36	f	2	0	9	9.3	15,234	50	90	6.2	1.018	1	3	1	1	2	1	1	1,3,4,5,6,13	2,8,9,10,11,12
145	27	f	2	0	5	10	14,326	46	116	5.9	1.017	1	1	2	1	2	2	1	1,2,4,9,10,12	5,6,7,10,12
146	29	f	2	0	1	11	8,649	60	104	6.05	1.018	1	2	2	1	2	1	1	2,3,4,5,11	1,7,8,10,12
147	76	f	2	0	10	14	9,536	35	119	6.07	1.016	1	3	3	1	2	2	4		
148	64	f	2	0	1,5	11	1,274	40	114	6.09	1.015	1	3	2	1	2	2	2	1,3,4,5,7,8	2,6,9,10,11,12
149	53	f	2	0	2,4,5	10.2	8,594	60	113	6.03	1.015	1	2	1	1	2	1	1	1,2,3,5,6,8,10	4,7,9,11,12
150	59	f	2	0	1,3,9	13	9,578	50	120	5.9	1.019	1	3	1	2	2	2	1	1,3,4,5,6,9,11	2,7,8,10,12
151	63	f	2	0	5,6,8	12	15,368	35	106	6.03	1.012	1	3	2	1	2	2	3		
152	47	f	2	0	2,5,9	11	9,574	28	107	6.07	1.012	1	2	2	1	2	1	1	2,3,4,7,10,11	1,5,6,8,9
153	28	f	2	0	1,4,6	9.1	14,253	15	115	6.03	1.013	1	3	2	1	1	2	5		
154	23	f	2	0	2,8	8.2	7,428	60	118	5.9	1.009	1	3	1	1	2	1	1	1,3,4,5,6,8,11	2,9,10,12
155	32	f	2	0	5,9,10	9	15,368	50	94	6	1.016	2	3	2	1	2	2	1	1,2,4,5,9,11	3,6,7,8,10
156	26	f	2	0	4,5,9	7.4	8,569	40	120	5.9	1.009	1	2	2	1	2	2	1	3,4,5,7,10,11	1,2,6,8,9
157	36	f	2	0	1,6,9	9.5	9,464	25	118	5.8	1.019	1	3	2	1	2	1	2	1,2,5,6,11	3,4,7,8,9,10,12
158	47	f	2	0	5,7	11.6	12,540	36	108	6.05	1.013	1	1	1	1	2	2	3		
159	23	f	2	0	5,8	13	9,560	50	120	6.07	1.012	1	3	3	1	2	2	1	1,2,4,8,10,11	3,5,6,7,9
160	54	f	2	0	1,9,10	9.3	15,367	35	119	6.03	1.012	1	2	2	1	2	1	1	1,3,4,8,9,11	2,5,6,7,10,12
161	72	m	2	0	2,3,6	10	8,690	50	113	6.01	1.016	1	3	1	1	2	2	1	3,5,6,10,11,13	1,4,9,12
162	46	m	2	0	5,9	11	4,738	45	106	5.92	1.013	1	3	2	1	2	1	1	1,3,4,7,10,11	2,5,6,8,9,12
163	32	m	2	0	1,6,10	8.4	7,468	38	112	5.7	1.017	1	3	1	1	2	2	2	2,3,4,5,10	1,6,7,8,9,11,12
164	47	m	2	0	2,8	13.5	15,248	35	119	6.12	1.018	1	2	2	1	1	2	3		
165	67	m	2	0	5,7,9	10.8	9,965	48	105	6.02	1.012	2	3	2	1	2	1	1	1,3,4,5,6,8,11	2,7,9,10,12
166	57	m	2	0	1,9	11.3	4,638	50	103	5.86	1.013	1	1	1	1	2	2	4		
167	26	m	2	0	5,10	12	11,540	60	115	6.12	1.013	1	3	1	1	2	2	1	2,3,4,5,9,11	1,6,8,10,11
168	58	m	2	0	5,9	13	11,769	70	120	6.09	1.018	1	2	2	1	2	2	1	1,3,4,5,10,11	2,6,7,8,9,11
169	61	m	2	0	1,4,6	11.2	5,780	30	120	5.9	1.018	1	3	2	1	2	1	1	1,2,4,5,6,8,11	3,9,10,12
170	75	m	2	0	3,5,10	14.5	16,805	60	124	6.05	1.014	1	3	3	1	2	2	1	1,3,4,5,8,11	2,6,8,9,12
171	47	m	2	0	1,4,7	11	8,590	50	111	6.07	1.012	1	2	1	1	2	2	2	1,5,6,11,12	2,3,4,7,8,9,10
172	36	m	2	0	5,9	13.6	5,740	40	110	5.9	1.017	1	3	1	1	2	1	1	2,3,4,5,9,11	1,6,7,8,10,12
173	48	m	2	0	1,10	12.6	16,380	44	108	6	1.012	1	1	2	1	2	2	1	1,3,4,6,8,11,13	2,5,9,10,12
174	64	m	2	0	2,4,9	10.5	13,569	48	108	6.07	1.016	1	2	2	1	2	1	1	1,2,4,5,6,8,12	3,7,9,10
175	75	m	2	0	5,7	11	6,480	50	117	6.09	1.013	1	1	2	1	2	2	2	1,2,6,9,11	3,4,5,7,8,10,12
176	57	m	2	0	1,8,10	13.5	16,829	60	124	5.9	1.015	1	3	1	1	2	1	3		
177	65	m	2	0	5,9	11.8	10,480	64	111	6.03	1.012	2	2	2	1	2	2	1	3,4,5,6,10,13	1,2,8,11,12
178	32	m	2	0	1,7	14	8,490	44	120	6.02	1.018	1	3	2	1	1	2	5		
179	27	m	2	0	5,9	10.4	7,650	45	108	6.04	1.014	1	2	3	3	2	1	1	1,2,4,5,6,11	3,7,8,9,12
180	78	m	2	0	2,8,10	13.8	7,890	60	103	6.01	1.012	1	3	2	1	1	2	1	3,4,5,7,9,11	2,6,8,10,12
181	43	m	2	0	1,5,6	10.4	11,680	35	98	5.9	1.009	1	1	1	1	2	1	4		
182	35	m	2	0	4,5,9	12.5	9,820	25	120	6.1	1.012	1	3	1	1	2	2	1	1,3,7,8,10,11	2,5,6,12
183	26	m	2	0	5,8	8.8	7,390	60	120	6.03	1.012	1	2	2	1	2	1	2	1,4,5,9,11,12	2,3,6,7,8,10
184	67	m	2	0	1,2,7,8	11	9,380	44	114	6.04	1.013	1	3	2	1	2	1	1	3,4,5,7,10,12	2,6,8,9,11
185	73	m	2	0	4,5	13	12,890	46	123	6.05	1.007	1	1	1	1	2	2	1	1,2,7,8,9,11	3,4,5,6,10

186	36	m	2	0	1,4,9	12	9,580	50	121	5.79	1.006	1	3	2	1	2	1	1	3,4,6,8,9,13	2,5,10,11,12
187	48	m	2	0	5,8,9	14	13,780	48	110	6	1.007	1	3	1	1	2	1	3		
188	67	m	2	0	2,6,9	14	8,670	36	89	6.02	1.015	1	1	3	1	2	2	1	1,3,5,7,10,11	2,4,6,8,9,12
189	25	m	2	0	5,9	13	9,340	26	113	6	1.012	2	3	1	1	1	1	1	2,5,7,9,11,13	3,8,10,12
190	71	m	2	0	1,8	14.6	13,790	50	104	6.09	1.013	1	3	2	1	2	2	4		
191	54	m	2	0	5,9,10	13.5	9,340	46	102	5.9	1.011	3	1	2	1	2	1	3		
192	59	m	2	0	2,4,5	10.3	8,450	50	118	6.05	1.016	1	3	1	1	1	2	1	1,7,8,9,10,11	2,3,4,6,12
193	27	m	2	0	1,9,10	11.8	9,420	44	124	6.03	1.012	2	3	2	1	2	1	1	1,2,4,6,8,11	3,5,7,10,12
194	46	m	2	0	2,4	13	10,260	48	103	6.03	1.016	1	1	3	1	2	2	5		
195	54	m	2	0	5,9	12.4	9,400	35	102	5.9	1.012	1	3	2	1	2	1	1	1,3,5,6,8,11	2,4,7,9,12
196	64	m	2	0	1,2,6	10.8	13,490	60	105	5.7	1.012	1	1	1	1	2	2	3		
197	55	m	2	0	5,7	14	12,483	50	108	5.93	1.013	1	3	2	1	2	1	1	4,6,7,9,11	3,8,10,12
198	45	m	2	0	2,5,9	12.5	7,840	60	110	6.03	1.017	1	1	3	1	1	1	4		
199	75	m	2	0	1,8	10.4	13,904	50	114	6.23	1.019	1	3	2	1	2	2	1	1,3,6,8,9,10,11	2,4,5,9,12
200	52	m	2	0	2,5	11	9,956	44	121	6.1	1.012	1	1	1	1	2	1	3		