# THE PREVALENCE OF URINARY TRACT INFECTION IN KIDNEY TRANSPLANT RECIPIENTS AT KENYATTA NATIONAL HOSPITAL

## A DISSERTATION SUBMITTED IN PART FULFILMENT OF MASTER OF MEDICINE [M.MED] DEGREE IN INTERNAL MEDICINE

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## DECLARATION

I certify that this dissertation is my own original work and has not been presented for a degree in any other university.


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## DEDICATION

I dedicate this book to my dear friend and wife, Wambui, who has tirelessly stood with me and supported me throughout my M.Med programme and the study;

And to our fifteen month son, Joel for having entertained me every evening after school-even when I was  too tired to laugh.

## ACKNOWLEDGMENTS

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## LIST OF ABBREVIATIONS

CFU/ML          Colony forming units/millilitre

CKD             Chronic Kidney Disease

CGN             Chronic glomerulonephritis

CLSI            Clinical and Laboratory standards Institute

CMV             Cytomegalovirus

DM              Diabetes mellitus

EBV             Epstein Barr Virus

ESBL            Extended Spectrum Beta Lactamase

ESBLEC          Extended Spectrum Beta Lactamase E. coli

E. COLI         *Escherichia coli*

ESRD            End Stage Renal Disease

GNB             Gram Negative Bacilli

HBV             Hepatitis B Virus

HCV             Hepatitis C Virus

HIV             Human Immunodeficiency Virus

HIVAN           HIV Associated Nephropathy

ICD-9           International Classification of Diseases, 9th Revision

KDIGO           Kidney Disease, Improving Global Outcomes

KMLLTB          Kenya Medical Laboratory Technicians and Technologists Board

KNH             Kenyatta National Hospital

MPDB            Medical Practitioners and Dentists Board

MSSU            Mid Stream Sterile Urine

PKD             Polycystic kidney disease

SOPs            Standard Operating Procedures

TMP-SMX     Trimethoprim/sulfamethoxazole

UTI         Urinary tract infection

USRDS       United States Renal Data System

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## ABSTRACT

### Introduction

Urinary tract infections form the largest percentage of post kidney transplantation infections making up to 47% of all infections. These UTIs are more likely to be clinically asymptomatic compared to patients not on immunosuppressive therapy. UTI in this group is often associated with serious morbidity and even death. The prevalence and microbial patterns vary between centers. There is no known local data describing the prevalence and patterns in our set up.

**Objective:** To determine the prevalence of bacterial and fungal UTIs and their clinical and microbiologic patterns among kidney transplant recipients at Kenyatta National Hospital.

**Study design:** Cross sectional descriptive study

**Study population:** Kidney recipients, aged eighteen years and above, attending the follow up clinic at KNH

**Methodology:** Ninenty nine patients were recruited after an informed written consent. Clinical data was retrieved from the participants' files. Clinical assessment for UTI was carried out via history and physical examination. Microscopy, leucocyte esterase, nitrite and culture analysis was carried out on MSSU specimen. Statistical analysis was carried out using SPSS version 18.0 software.

**Results:** Twenty one percent of participants had UTI. Females were affected more than men, 38.5% and 15% respectively. 86% of the UTIs were asymptomatic. 12% of UTI were culture positive. Gram negative bacteria were the commonest, with *E. coli* making the highest percentage (58%). 40% of Gram negative bacilli were ESBL positive.

**Conclusion:** The prevalence of UTI in our population was high with a prevalence of 21%. The majority of the UTIs were asymptomatic and involved a higher percentage of females. Gram negative bacteria were the majority with *Escherichia coli* being the most isolated. Emergence of Extended Spectrum Beta Lactamase bacteria, a matter of grave concern was noted.

# 1.0    INTRODUCTION AND LITERATURE REVIEW

Chronic kidney disease (CKD) is increasingly recognized as a global public health problem.[1, 2] Worldwide, more than 2.5 million people are receiving renal replacement therapy (RRT), with incidence growing by approximately 8% annually.[3, 4] renal transplantation is superior to dialysis in terms of morbidity, survival, quality of life and cost.[5] Kidney rejection and infections are the greatest hindrances to success of allograft organ transplantation.[3]

## 1.1 Epidemiology

Infection is the most common life-threatening complication of long-term immunosuppressive therapy.[3] Kidney recipients develop urinary tract infections (UTIs) more frequently than the general population.[6] UTI is the most common infection following renal transplantation, accounting for 44–47% of the infectious complications.[7, 8] The reported incidence of post-transplantation UTI varies considerably, which is a function of variations in study design, local outbreaks, definition and diagnostic criteria.[7, 9, 10] Despite improved immunosuppressive and antimicrobial therapy UTIs continue to be a major problem.[6, 7]

Alangaden *et al* in a retrospective study in USA, in 2001-2004 involving 127 kidney recipients, observed that UTIs were the commonest infection, making 47% of all infections.[7] In a prospective study of 161 kidney recipients transplanted between July 2003 and July 2005, Valera *et al*, confirmed UTI on the forty-one patients (25%). Fifty percent of the UTI episodes occurred within 44 days of the transplant procedure.[11] In Libya, a study done in 2010 by Elkehili *et al*, showed UTI prevalence of 29.5%. [13].

## 1.2 Definitions

A urinary tract infection is defined as the presence of microorganisms in the urinary tract that cannot be accounted for by contamination. The organisms present have the potential to invade the tissues of the urinary tract and adjacent structures. Infection may be limited to the

growth of bacteria in the urine, which frequently may not produce symptoms and is described as asymptomatic bacteriuria. However, a pathological microbial invasion of urothelium that results in several clinical syndromes associated with an inflammatory response can occur and is described as symptomatic UTI. Lower tract infections include cystitis (bladder), urethritis (urethra), prostatitis (prostate gland), and epididymitis. Pyelonephritis is kidney involvement and represents upper tract infection.

## 1.3 Microbial patterns

Organisms that cause UTI after renal transplantation can be bacterial, fungal, viral, parasitic or mycobacterial.[8, 11] Bacterial causes account for the highest portion of the organism upto 97%.[9, 11] The hierarchy of bacterial UTI pathogens in transplant recipients is similar to that in the non-transplantation population, with Gram negative bacterial infections accounting for more than 70% of UTIs. *Escherichia coli, Enterococcus spp.* and *Enterobacter cloacae* are the most common enteric organisms that cause UTI in transplant recipients. Other less common bacterial causes are *Pseudomonas spp., Klebsiella spp.* and *Proteus mirabilis*. Low-virulence bacteria that would not be pathogenic in immunocompetent hosts have been implicated in post-transplantation UTI.

 *Candida albicans* is typically the fungus responsible for UTI.[7] UTIs caused by C. *albicans* are difficult to treat especially if it forms fungal aggregates that can obstruct urine outflow.[8] Diabetes is strongly associated with UTIs that are caused by fungi. Funguria could be the earliest sign of disseminated fungal infection.[12] Viral aetiolgy though minimal include BK virus, cytomegalovirus and herpes virus. BK virus can cause graft nephropathy, typically in patients on high-dose immunosuppression, and is reported to induce graft failure in 45% of cases.[13]

## 1.4 Implications of urinary tract infections in kidney recipients

UTIs in kidney recipients are more likely to be clinically asymptomatic as they do not mount the typical inflammatory response to infection as a consequence of immunosuppressive therapy. UTI in this group is often associated with acute pyelonephritis and rapidly developing bacteraemia potentially progressing to the full-blown picture of urosepsis, particularly during the early post-transplant period. Patients are at especially high risk for UTI in the first month post-transplant, where the bacteraemia-associated mortality of 11% has been reported. In the study of Chuang *et al*, nine of the ten patients who died from sepsis had post transplant UTIs.[10] Snyder *et al* in a study involving 46,471 kidney recipients showed that UTIs contributed to 15% of all admissions.[14] Wegener *et al* also found UTI as the commonest cause of bacteremia in kidney transplant recipients.[15]

Late UTIs (later than 6 months after transplantation based on ICD 9) after renal transplantation have been reported to be rather 'benign'. However, other studies suggest that many patients with late UTI's present with advanced infection. Retrospective data obtained from the United States Renal Data System (USRDS) from 28,942 patients demonstrate that UTIs occurring late after renal transplantation were independently associated with an increased risk of subsequent recipient death and graft loss.

**2.0  FACTORS ASSOCIATED WITH INCREASED RISK OF URINARY TRACT INFECTIONS IN KIDNEY RECIPIENTS**

The aetiology of UTI following renal transplantation can be examined in terms of factors that relate to the host, the graft, the anatomical features of the recipient and the infection-causing organism. Although these factors are addressed individually here, they do overlap and interact.

**2.1 Host factors**

Females, advanced age, pre-transplant UTIs, diabetes mellitus, prolonged dialysis before transplantation and net immunosuppression have been shown to raise the risk of UTI. Shorter urethra in females and relative proximity of the urethra to the perirectal area raise the risk of UTI compared to men.[16, 17] Chuang *et al* showed that 55% of the patients who were 65 years of age or older at kidney transplantation developed post-transplant UTIs compared to 30% of patients who were younger than 30 years.[10] Higher risk is attributed to impaired mobility, poor hygiene in institutionalized individuals, reduced native immunity, higher rate of urinary retention secondary to prostatism and bladder atrophy. Untreated or partially treated pre-transplant UTIs pose a risk of progression or reactivation after transplantation. Immunosuppression places the transplant recipient at risk of all types of infections, including UTI. The net state of immunosuppression is the result of a complex interaction among multiple factors, including immunosuppressive therapy (drug, dose and duration), underlying immune deficiency, autoimmune disease, functional immune deficits, neutropenia, lymphopenia, uremia, malnutrition, DM and infection with immunomodulating viruses including CMV, EBV, HBV, HCV, HIV.[3]

## 2.2 Surgical factors

Urethral catheter which is a routine placement is likely to be related to early post transplantation UTI even when sterile technique is used. In the general population, the risk of bacteriuria increases by 5% with each day that a catheter is in situ; this increased risk is likely to apply to transplant recipients. Prompt catheter removal has been associated with a drop in UTI rates.[18] Ureteric stents inserted at the time of transplantation to prevent leakage from the vesicoureteric anastomosis are associated with a 1.5-times increased relative risk of UTI.[19] Vesicoureteral reflux disease increased the relative risk for development of a UTI up to 3 times. [10] Retransplantation quadruples the risk of UTI.[7]

## 2.3 Allograft factors

Infected donor organ can turn out to be a source of infection.[3, 14] The infection may progress or get reactivated. Transplantation of cadaveric kidney increases the incidence of UTI by about 20%.[14] The use of organs from living donors leads to lower rates of UTI, because these kidneys are subjected to shorter periods of cold ischemia and less-severe ischemic–reperfusion injury. Deceased-donor kidney recipients have more delayed graft dysfunction and acute rejection, and likely receive more immunosuppression making them more susceptible.

## 2.4 Anatomical factors

Urinary stasis, reflux or stones raise the risk of UTI development. These features are more prominent in the renal transplant population. Stasis can develop in response to obstruction of the pelviureteric or vesicoureteric junctions, bladder dysfunction or outflow obstruction, and urethral disease. Reflux can affect both the native and the transplanted kidneys. Native kidneys, polycystic kidneys and ureteric stumps that remain after native nephrectomy can act as a reservoir for pathogens.[8, 20]

## 2.5 Organism factors

The hierarchy of UTI pathogens in transplant recipients is close but not similar to non-transplantation population. Bacterial pathogens form the majority causes with Gram negative bacterial infections accounting for more than 70% of UTIs. Most common organisms have virulence factors that enable them to colonize and invade urothelium e.g. *E. coli* expresses type 1 or P fimbriae, which increase the bacterium's pathogenicity in the urothelium.[20] Low-virulence bacteria that would not be pathogenic in immunocompetent have been implicated in post-transplantation UTI. Organism virulence can be increased by immunosuppressant drugs, which facilitates bacterial–urothelial adherence.[21]

## 3.0    METHODS APPLIED IN URINARY TRACT INFECTIONS DETECTION

Excluding specimen contamination, bacteriuria indicates either urinary colonization (replication of bacteria in urine without evidence of tissue invasion) or urinary tract infection (bacteriuria associated with clinical, histologic or immunologic evidence of host injury.

### 3.1 Specimen collection

Clean-catch midstream technique involves allowing the first part of the urine stream to pass out and collect urine from the midstream. It is simple, inexpensive, can be performed in almost any clinical setting, and has no risk of introducing bacteria into the bladder. Its drawback includes risk of urine contamination on passing through distal urethra, difficulties with proper collection of samples from elderly and patients with physical or mental impairments. Other methods include suprapubic aspiration and straight catheter technique. While they are the best methods for avoiding specimen contamination they are invasive, uncomfortable, costly and labor intensive. Colony counts from urine specimens collected by MSSU correlate well with those of specimens collected via suprapubic aspiration or straight catheterization.

### 3.2 Detection of pyuria

**Microscopy:** Involve counting urine leukocytes with a neubauer chamber; simple and inexpensive. Counts of $\geq 10$ WBC/mm$^3$ correlates with growths of $10^5$ cfu/mL on culture for both transplant and non transplant groups. Its advantages are that leukocytes, leukocyte casts, and other cellular elements are observed directly. It has sensitivity of up to 96% and specificity of 71%. One disadvantage is that leukocytes deteriorate quickly in urine that is not fresh or poorly preserved.

**Leukocyte esterase test:** it's based on the hydrolysis of ester substrates by proteins with esterolytic activity released from human neutrophils. These proteins react with ester

substrates to produce alcohols and acids that then react with other chemicals to produce a color change that is proportional to the amount of esterase in the specimen[32]. It has the advantage of detecting both esterases in intact leukocytes and esterases released after cell lysis; therefore, even specimens that have not been preserved properly may yield a positive test result. Its sensitivity and specificity is up to 68% and 82% respectively.

### 3.3 Detection of bacteriuria

**Nitrite test** uses biochemical reaction associated with members of the family Enterobacteriaceae. They reduce nitrates in urine to nitrites. Its drawback include nitrite production is not associated with urinary-tract pathogens such as S. saprophyticus, Pseudomonas species, or enterococci and it requires testing a specimen of the first urine produced in the morning, as 4 hours are required for bacteria to convert nitrate to nitrite at levels that are reliably detectable. It has low sensitivity of 45-60% but high specificity of over 95%.

Other methods include direct observation of wet preparation of uncetrifuged urine whereby shapes and number of microorganisms and cells per field are recorded.[36] Gram stain of uncentrifuged urine which has the advantage of providing immediate information as to the nature of the infecting organism. Its drawbacks include being insensitive and labor intensive.

### 3.4 Simultaneous detection of bacteriuria and pyuria

The two tests, when used together, perform better than either test performs when used alone. Taken together, the performance characteristics of these tests make them useful as a way to rule out bacteriuria on the basis of a negative test result. The sensitivity is raised to 67-100% and specificity to 67-98%. [22]

**3.5 Cultures in the diagnosis of UTI**

Urine cultures are necessary for identification of the infecting microorganism(s) and for antimicrobial susceptibility testing. Cultures are recommended for patients with infections that do not respond to therapy, patients who have recurrent UTIs, patients who have anatomic or functional abnormalities of the urinary tract, or patients who continue to have unexplained abnormal urinalysis findings.

Each laboratory should have guidelines by which pathogens are tested for antimicrobial susceptibility. These guidelines should be developed and reported according to the most recent version of the CLSI guidelines.[22]

## 4.0    JUSTIFICATION

Infections after renal transplantation are common and come second to organ rejection as causes of graft loss. Urinary tract infections form the largest percentage of post transplantation infections. These UTIs are more likely to be clinically asymptomatic. UTI in this group is often associated with acute pyelonephritis and rapidly developing bacteraemia, progressing to urosepsis and death. Therefore, careful surveillance is necessary to identify and eliminate these infections.

Kidney recipients are usually on prophylactic antibiotic mainly cotrimoxazole and receive frequent empirical antibiotic treatments due to recurrent episodes of infection, both urinary and non urinary related. This may alter presentation of UTIs in post-transplant recipients and their likely microbial sensitivity patterns.

Appropriate treatment can be accorded to the patients if the microorganisms causing infections are known. Understanding the sensitivity patterns of commonly used antimicrobials would enable planning of a good empirical treatment strategy for UTIs and possible prevention of later complications. This would ensure reduction in morbidity, mortality, treatment costs and subsequently improve quality of life for the recipient.

It is likely that the organism and the strain that cause most post-transplantation UTIs vary between centers, depending on local immunosuppressive and antimicrobial protocols. There is no local published data on prevalence of UTIs or microbiological patterns on this group of patients. This study therefore sought to establish the microbiological patterns and antimicrobial sensitivity in our setup.

## 5.0    RESEARCH QUESTION

What is the prevalence of urinary tract infections and their clinical and microbiologic patterns

in kidney transplant recipients at Kenyatta National Hospital?

**6.0    OBJECTIVES**

**6.1 Broad Objective**

To determine the prevalence of urinary tract infections and their clinical and microbiologic patterns in kidney transplant recipients at Kenyatta National Hospital.

**6.2 Specific Objectives**

a) To determine the prevalence of bacterial and fungal urinary tract infections in kidney transplant recipients attending the follow up clinic at Kenyatta National Hospital.

b) To describe the bacterial causative organisms and their antimicrobial sensitivity patterns in kidney transplant recipients attending the follow up clinic at Kenyatta National Hospital.

## 7.0    METHODOLOGY

### 7.1 Study design

The study was a cross-sectional descriptive study

### 7.2 Study site

The study was carried out at the kidney transplant follow up outpatient clinic at Kenyatta

National hospital.

### 7.3 Study population

Kidney recipients, aged eighteen years and above, who attended the follow up clinic at KNH.

At least 7 days were allowed to elapse after the transplantation. This allowed a transition

period from admission to follow up in the clinic

### 7.4 Sample size determination

Using the Daniel's formula below, the minimal sample needed was calculated to 98 patients.

$$n = \frac{Nz^2Pq}{\{E^2 (N-1) + (z^2Pq)\}}$$

Where:

n = Minimum sample size

N=Total population of kidney recipients on follow up in our transplant clinic= 140

Z= Normal standard deviation 95% confidence interval (Z = 1.96)

P= Prevalence of the disease (29.5% based on; Elkehili *et al*, Libya, 2010)[23]

q= 1 – Prevalence

E= Margin of error (0.05)

**7.5 Sampling**

Consecutive sampling was done i.e. **every** subject who attended the clinic and fulfilled the inclusion criteria was requested to participate in the study and subsequently recruited on giving consent.

**7.6 Inclusion criteria**

Any kidney recipient 18 years and above and willing to participate

**7.7 Exclusion criteria**

Kidney recipient who was below 18 years or who declined to give consent

**7.8 Case Definition**

A UTI is diagnosed based upon **any** one of the following:

1. Pyuria≥10 WBC/mL of uncentrifuged urine
2. Urinary Leukocyte esterase positive
3. Nitrites positivity
4. Positive Urine Culture $\geq 10^5$ CFU/mL)

Each case will be defined as either symptomatic or asymptomatic.

**Symptomatic:** Any symptom or sign

    **Symptom:** Frequency and/or Dysuria and/or Urgency

    **Sign:** any of the following

    Temp ≥38.3C

    Tender suprapubic

    Tender renal angle

    Tender area over graft

**Asymptomatic:**

Absence of **any** above features

**7.9 Time line**

The study was carried out from November 2013 to March 2014

**7.10 Recruitment**

On presenting for the routine kidney transplant follow up clinic, every kidney transplant recipient was informed about the study. Informed, written consent was obtained. At this point the patient was considered recruited (consecutive sampling). Socio-demographics data was collected including age, gender and level of education. Further details were retrieved from the file including cause of ESRD, how long the patient had dialysed before transplantation, date when the transplantation was done, current immunosuppresives and their doses, (See Appendix 1). Evidence of prior UTI was assessed in the file using the study criteria of UTI. History and physical examination was conducted with emphasis on the urinary system. The history focused on the symptomatology of the UTI (e.g. frequency, dysuria, and urgency) and usage of antibiotics one month prior. Abdominal exam was done focusing on suprapubic, graft and renal angle tenderness. See figure 1 below
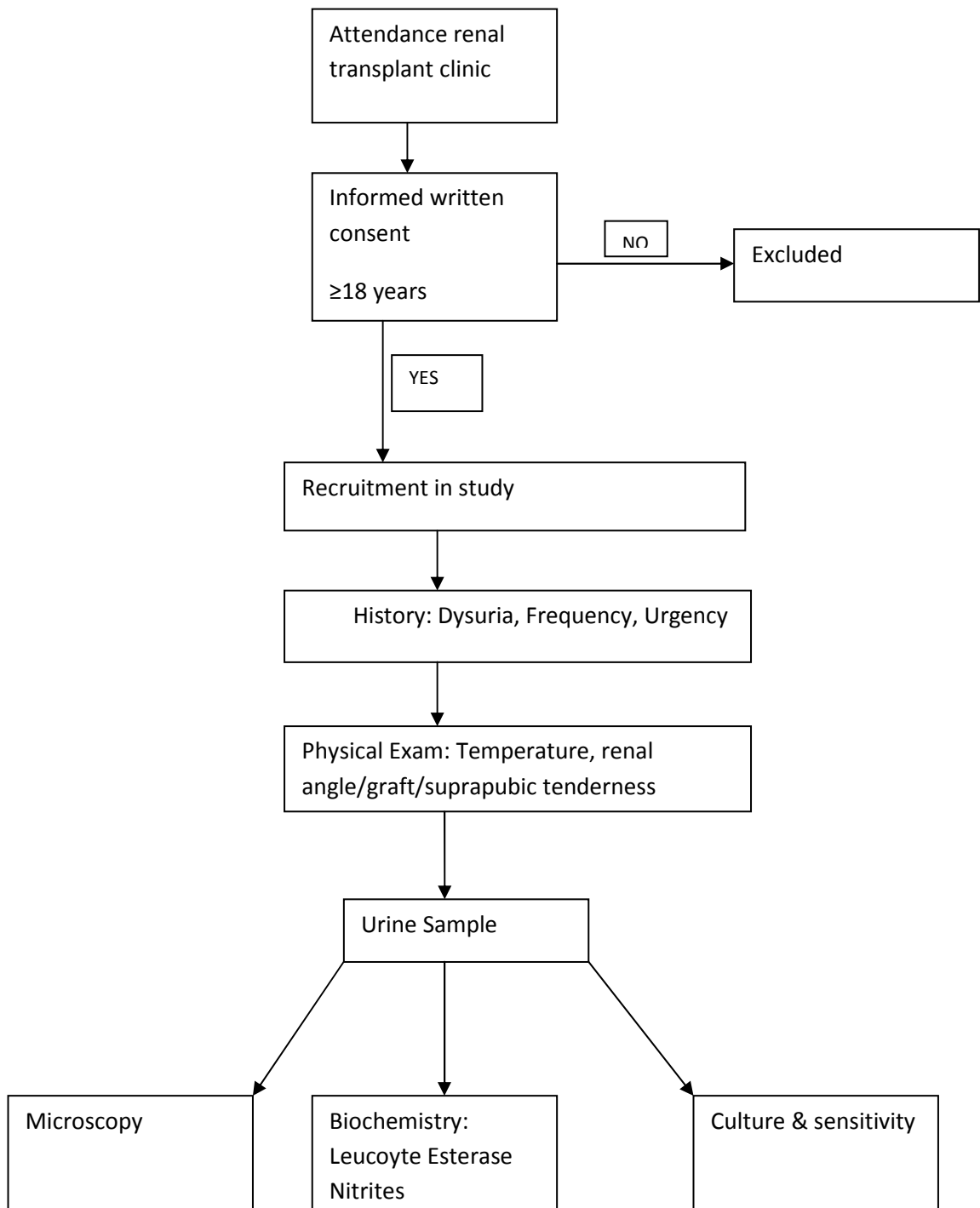
**Figure 1:Flow Chart Representing a Summary of the Study**

**7.11 Specimen Collection and processing**

10ml of clean catch mid-stream (appendix 4), urine was collected in a sterile container. Urinalysis, microscopy and culture was done for **all** recruited. Urine specimens were stored in a refrigerator in Renal Unit at 4°C for two to three hours then transported in cooler box with ice packs to the Lancet pathologists' laboratory.[24, 25]

**Procedure for processing urine specimens**

Microscopy of uncetrifuged urine was carried out in a neubar chamber. Analysis for nitrites and leucocyte esterase followed. Then 0.001ml loop was used to plate specimens for culture on Blood agar, MacConkey's agar and CLED (cysteine Lactose Electrolyte Deficient) media. Incubation was done for 24 hours at 35°C–37°C in ambient air before being read. When growth was observed, identification of the organisms was carried out. Antimicrobial sensitivity was done for each organism depending on standard set of antibiotics as per CLSI guidelines. Most pathogenic yeasts grow well on blood agar plates, hence, no selective fungal media for cultures was used. The samples were used only for this study and were discarded immediately after each test.

**7.12 Study variables**

The dependent variable was presence or absence of UTI. The independent variables were age, gender, level of education, presumptive cause of ESRD, duration of dialysis before transplantation, time since transplantation, number of transplantation(s) and current immunosuppressive therapy.

## 7.13 Data management and analysis

Data were collected into a questionnaire (See appendix 1). Data entry, checking and validation were done. This was then cleaned and transferred into MS Excel and finally analysed by SPSS software version 18.0. Continuous data e.g. age, duration of dialysis and time after transplantation was summarized into means, standard deviation, modes, median, and range. Categorical data e.g. gender, education, immunosuppressive therapy was summarized into proportions and percentage. Prevalence was calculated as percentage of the whole study sample. Results were presented as tables, bar charts, line graphs and pie charts.


## 7.14 Ethical consideration

The study was undertaken after approval by the Department of Clinical Medicine and Therapeutics and the Kenyatta National Hospital / University of Nairobi Ethics and Research Committee. Enrolment into the study was voluntary after obtaining written informed consent. (See appendix 2 and 3). The study did not involve the performance of invasive procedures that would expose the participant to risks. Information gathered from the subjects including data forms has been kept confidential. Those patients diagnosed to have UTI were informed and a copy of their results were attached to the file after informing the primary clinician working in the transplantation clinic for appropriate care. Participants were free to withdraw from the study at any time without jeopardizing their care. No participant bore any cost of the urine studies.

## 8.0    RESULTS

The data was collected over four months; from November 2013 to March 2014. 107 consecutive patients attending the kidney transplant clinic were screened. Eight kidney recipients were excluded, the reasons being; five were less than 18years, one declined consent and two had failed grafts. Ninety nine participants were therefore recruited, fulfilling the target minimum sample size of 98. This is represented in figure 2 below.

```
┌─────────────────────┐
│    107 screened     │
└─────────────────────┘
           │                                        ┌──────────────────────┐
           │      8 Excluded from study             │ 5 < 18years          │
           │ ─────────────────────────────────────► │ 1 declined consent   │
           ▼                                         │ 2 failed graft       │
┌─────────────────────┐                              └──────────────────────┘
│    99 recruited     │
└─────────────────────┘
           │
           ▼
┌──────────────────────────────┐
│  History and Physical exam   │
└──────────────────────────────┘
           │
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┌──────────────────────────────┐
│    MSSU urine collection     │
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│ Urine analysis: urinalysis, microscopy, culture   │
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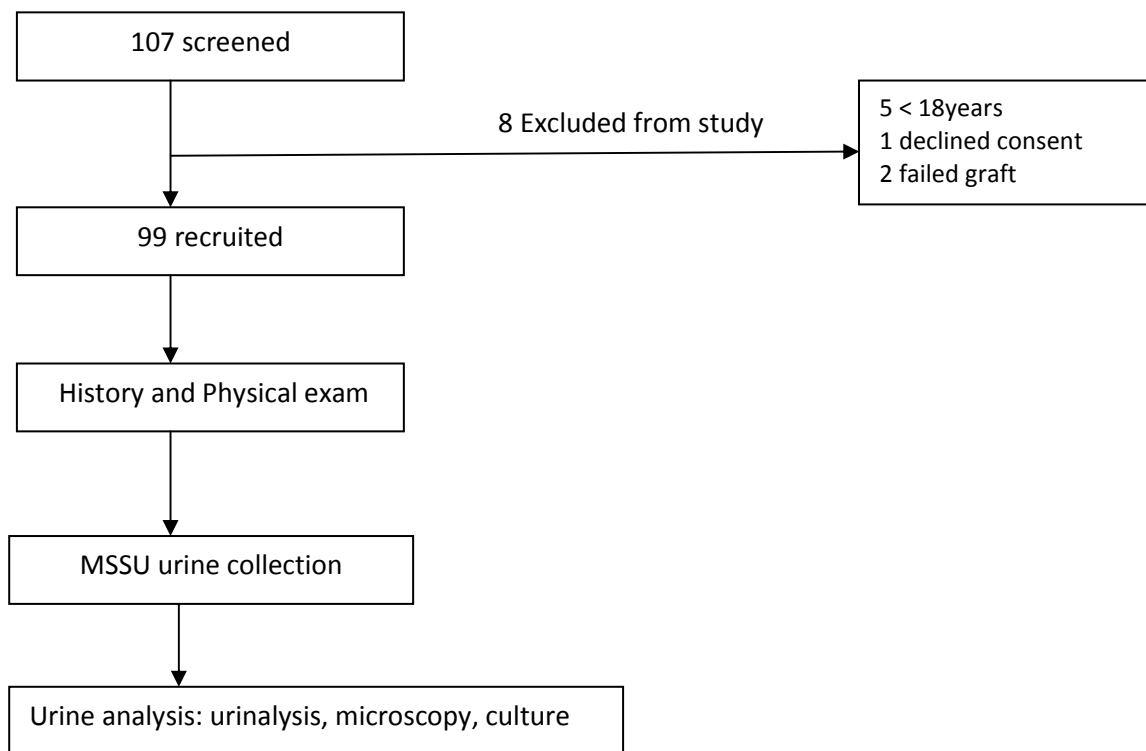
**Figure 2: Flow Chart Representing Participants Recruitment**

### 8.1    Characteristics of study participants

The average age of the participants was 42.5 ±13.4 years and ranging between 18 years to 72 years. The median age was 42 years. Majority of the participants were male 73 (73.7%) as compared to the female participants who were 26 (26.3%). The sociodemographic and clinical characteristics of the study participants are summarized in table 1 below.

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**Table 1; Sociodemographic and Clinical Characteristics in Kidney Recipients (N=99)**

| Characteristic | Value |
|---|---|
| Age in years | |
|     Mean, SD | 42.5 ±13.4 |
|     Min-Max | 18-72 |
| Male (%) | 73 (73.7) |
| Number with post primary education | 84 (84.8) |
| Cause of ESRD (%) | |
|     Chronic Glomerulonephritis | 49 (49.5) |
|     Diabetes Mellitus | 20 (20.2) |
|     Systemic hypertension | 19 (19.2) |
|     Bladder Outlet Obstruction | 3 (3.0) |
|     Polycystic kidney disease | 3 (3.0) |
|     Other | 5 (5.2) |
| Duration of dialysis in months | |
|     Mean | 22.7 ±22.6 |
|     Min-Max | 0-156 |
| Average time since transplantation in months | |
|     Mean | 33.5±48 |
|     Min-Max | 0.3-268 |
| Number of kidney transplantation (s) (%) | |
|     One transplantation | 98 (98.9) |
|     Two transplantations | 1 (1.0) |
| Current immunosuppressive therapy (%) | |
|     Prednisolone+Mycophonolate+Cyclosporine | 51(51.5) |
|     Prednisolone+Mycophenolate+ Tacrolimus | 43 (43.4) |
|     Prednisolone+Azathioprine | 5 (5.1) |
| Number on Cotrimoxazole prophylaxis (%) | 15(15.2) |
| Number with History of antibiotic use  one month prior | 20(20.2) |
| Prevalence of UTI | 21(21.2) |
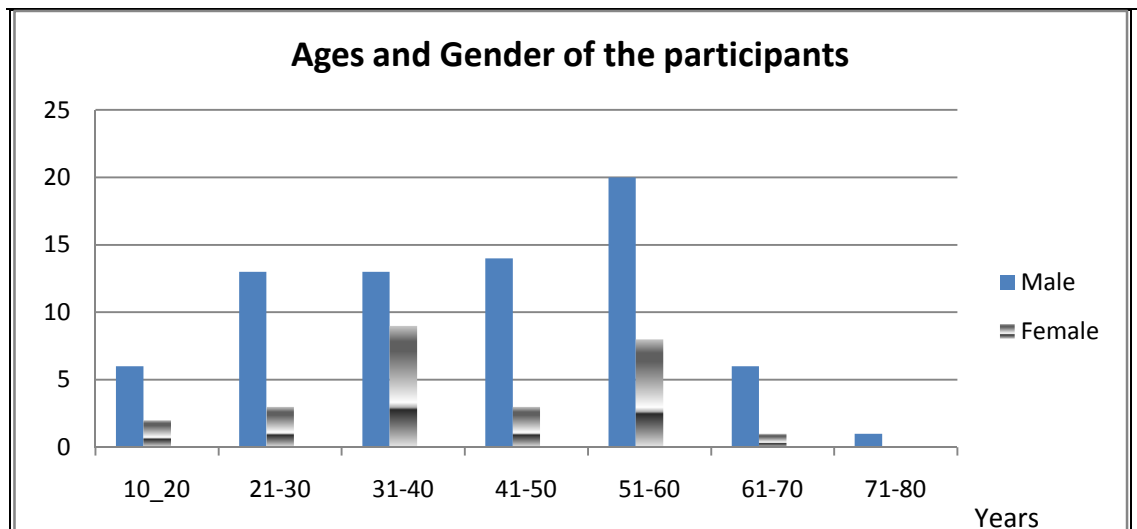
**Figure 3: The Ages and Gender among Kidney Recipients**

The ages and gender of the participants are represented in figure 3 above. The causes of the ESRD as were indicated in the pre-transplantation work up and checklist in the participants are summarized in the table 1 above. Five participants categorized under the subgroup 'others' had ESRD from HIVAN, systemic lupus erythematosus and eclampsia. Fourteen participants with hypertension also had either diabetes mellitus (7 patients) or CGN (7 patients). These fourteen have not been reclassified under hypertension.

The average duration of dialysis before transplantation was 22.7 ±22.8 months. The participant with the longest period of dialysis was 156 months and the participant who had dialysed for the shortest period of time was 0 months i.e. had preemptive kidney transplant. This is represented in figure 4 below.
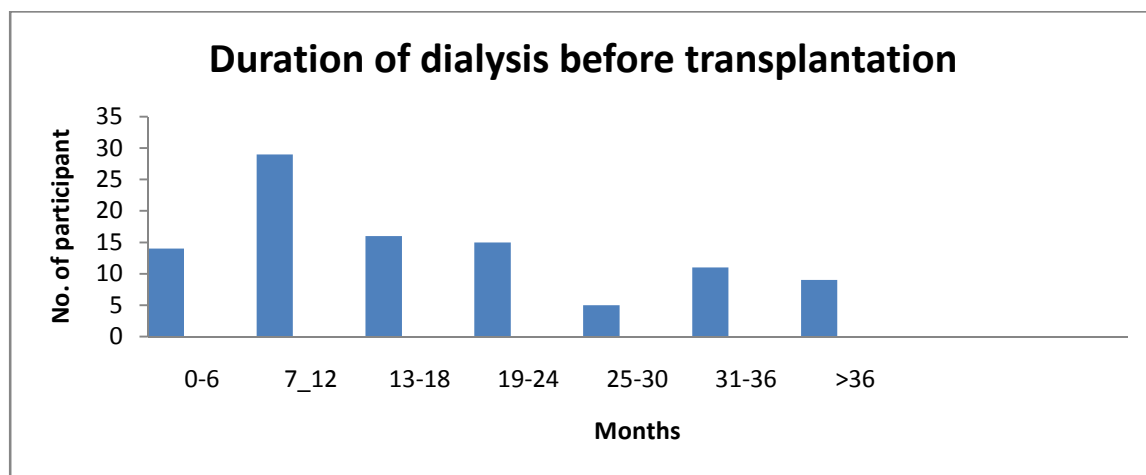
**Figure 4: Duration of Dialysis before Transplantation**

## 8.2 Prevalence of Urinary Tract Infections

After analysis of all urine specimens collected during this study, 21 (21.2%) participants met the criteria for UTI. Males were 11 and females 10. This then translates into 15% and 38.5% of all (n=99) males and females respectively. Majority (86%) of these participants were asymptomatic. The causes of ESRD in the patients with UTI were; 13 chronic glomerulonephritis, 4 diabetes mellitus, 2 systemic hypertension, 1 bladder outlet obstruction, 1 HIV and none had polycystic kidney disease. It's observed that out of each category of causes; hypertension, diabetes mellitus, CGN and bladder outlet obstruction caused 10.5%, 20%, 26.5%, and 33.3% respectively. The mean duration of dialysis was 33± 41 months, a range of 3 months to 13 years and a mode of 1 year. There were three major combination of immunosuppressive therapy as shown in table 2 below. The range of time since transplantation was one month to fourteen years with an average of 3.2± 4 years. While in the whole study 20% participants had used antibiotic one month prior, only 3 (14.3%) participants had used antibiotic prior to the study and had UTI.

**Table 2: Clinical Characteristics for Kidney Recipients with UTI (N=21)**

| Characteristic | Value |
|---|---|
| Age in years | |
|     Mean, SD | 41.8 ±15.5 |
|     Min-Max | 18-72 |
| Number of male (%) | 11 (52.4) |
| Cause of ESRD (%) | |
|     Chronic Glomerulonephritis | 13 (61.9) |
|     Diabetes Mellitus | 4 (19.0) |
|     Systemic hypertension | 2 (9.5) |
|     Bladder Outlet Obstruction | 1 (4.8) |
|     HIV | 1 (4.8) |
| Duration of dialysis in months | |
|     Mean | 22.7 ±22.6 |
|     Min-Max | 3-156 |
| Average time since transplantation in months | |
|     Mean | 38.4±48 |
|     Min-Max | 1-170 |
| Number of kidney transplantation (%) | |
|     1 | 20 (95.2) |
|     2 | 1 (4.8) |
| Current immunosuppressive therapy (%) | |
|     Prednisolone+Mycophonolate+Ciclosporine | 10 (47.6) |
|     Prednisolone+Mycophenolate+ Tacrolimus | 10 (47.6) |
|     Prednisolone+Azathioprine | 1 (4.8) |
| Number with symptomatic UTI[a] (%) | 3 (14.3) |
| Number on Cotrimoxazole prophylaxis (%) | 6 (28.6) |
| Number who used antibiotic one month prior[b] (%) | 3(14.3) |

a: Symptomatic UTI= History :( frequency /dysuria / urgency) or Exam (Temp ≥38.3C/ Tender suprapubic/Tender renal angle/ Tender area over graft)     b: all had used ciprofloxacin

Positive cultures were obtained from seventeen specimens. Five did not meet the colony threshold of $100000(10^5)$ CFU/ml. One had $10^3$ cfu/ml while the other four had $10^4$ cfu/ml. Out of the twelve remaining growth, one grew fungal (*Candida spp.*) and the rest were bacterial in origin. Figure 5 summarizes this.
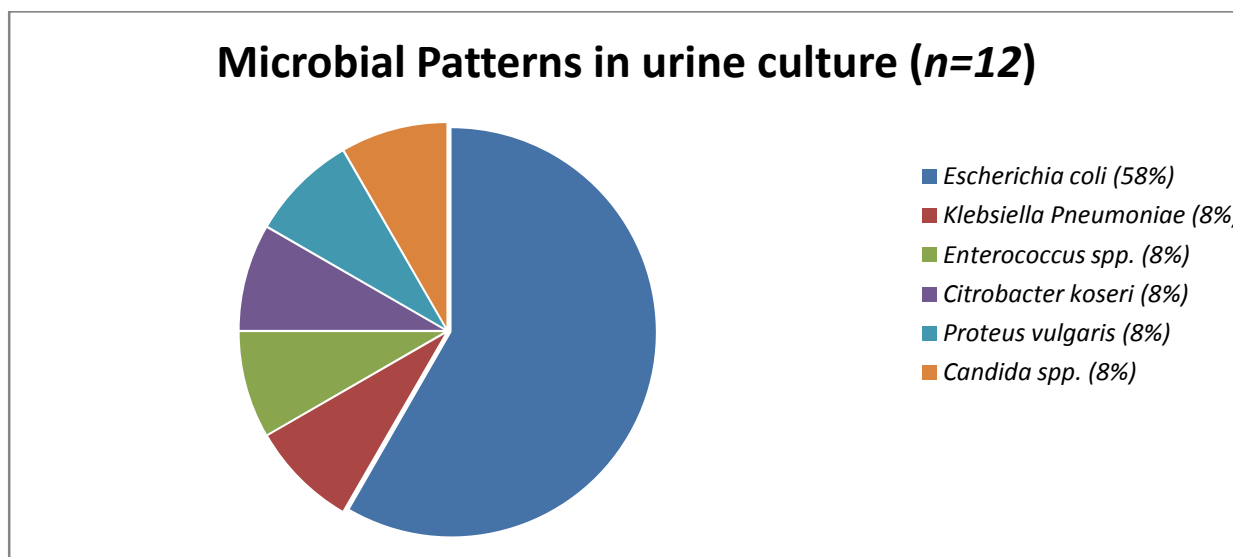
**Figure 5: Microbial Patterns in Urine Culture in Kidney Recipients**

*Escherichia coli* formed the majority 58% of the microbes that were isolated on culture. The other organisms were equal at 8%.

Antimicrobial sensitivity according to CLSI guidelines was done to all significant cultures except for the fungal isolation. Sensitivity was done for fifteen antimicrobials and this is depicted by the table 3 and 4 below.

**Table 3; Antimicrobial Sensitivity in Kidney Recipients, in Percentage (N=11)**

| Organism | N | TMP-SMX | | Ciproflo | | Amox-Clav | | Ceftriaxone | | Cefotaxime | | Ampiclox | | Gentamycin | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | S | R | S | R | S | R | S | R | S | R | S | R | S | R |
| *E. coli* | 7 | 0 | 100 | 14 | 86 | 57 | 43 | 57 | 43 | 57 | 43 | 0 | 100 | 29 | 71 |
| *Proteus* | 1 | 0 | 100 | 100 | 0 | 100 | 0 | 100 | 0 | 100 | 0 | 0 | 100 | 100 | 0 |
| *Klebsiella* | 1 | 0 | 100 | 0 | 100 | 0 | 100 | 0 | 100 | 0 | 100 | 0 | 100 | 0 | 100 |
| *Enterococcus* | 1 | N | N | N | N | 100 | 0 | N | N | N | N | 100 | 0 | N | N |
| *Citrobacter* | 1 | 0 | 100 | 100 | 0 | 0 | 100 | 100 | 0 | 100 | 0 | 0 | 100 | 100 | 0 |

S=Sensitive       R=Resistant       N=Not tested

Table 4; Antimicrobial Sensitivity in Percentage (N=11)

| Organism | N | Amikaci | | Nitrofurantoin | | Cefuroxime | | Nalidixic | | Tetracyclin | | Fosfomyci | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | S | R | S | R | S | R | S | R | S | R | S | R |
| *E. coli* | 7 | 100 | 0 | 57 | 43 | 57 | 43 | 14 | 86 | 0 | 100 | 86 | 14 |
| *Proteus* | 1 | 100 | 0 | 0 | 100 | 100 | | 100 | 0 | 0 | 100 | | |
| *Klebsiella* | 1 | 100 | 0 | 0 | 100 | 100 | 0 | 0 | 100 | 100 | 0 | | |
| *Enterococcus* | 1 | N | N | 100 | 0 | N | N | N | N | 100 | 0 | 100 | 0 |
| *Citrobacter* | 1 | 100 | 0 | 100 | 0 | 100 | 0 | 0 | 100 | 100 | | 100 | 0 |

S=Sensitive     R=Resistant     N=Not tested

* *Susceptibility to carbapenems (meropenem, imipinem & ertapenem) was only done to ESBL positive cultures and they were all sensitive.

None of the bacterial cultures isolated were susceptible to cotrimoxazole. Only 3 (27%) out of 11 were sensitive to ciprofloxacin. Only about half (54.5%) of cultures were sensitive to Amoxiclav (6 out of 11). Ceftriaxone had a relatively good (60%) sensitivity of six out of ten cultures tested. Amikacin had the best (100%) antimicrobial activity, however only four out of ten cultures were sensitive to gentamycin (40%). Susceptibility to carbapenems (meropenem, imipinem & ertapenem) was only done to ESBL positive cultures and they were all susceptible. The presence of Extended Spectrum Beta Lactamase (ESBL) was sought in the bacterial culture. The outcome is summarized in the table 5 below.

Table 5; Presence of ESBL Among Kidney Recipients (N=11)

| | Bacteria | EBSL Positive | EBSL Negative |
|---|---|---|---|
| 1 | *Escherichia coli* | 3 | 4 |
| 2 | *Klebsiella Pneumoniae* | 1 | 0 |
| 3 | *Enterococcus spp.* | 0 | 0 |
| 4 | *Citrobacter koseri* | 0 | 1 |
| 5 | *Proteus vulgaris* | 0 | 1 |

ESBL=Extended Spectrum Beta Lactamase

## 8.3    History and Trend of previous Urinary Tract Infections

Review through the participants files revealed occurrence of at least one UTI (Leucocyte Esterase positive or Nitrite positive or culture) in 33 patients (33.3%). Twenty two were males and eleven were females. There were 88 counts of UTIs from the participants' records. Half of the UTIs occurred within the first 6 months of transplantation and 73% within one year. The number reduced with time and was remarkably low by the end of 24 months after transplantation. See figure 6 below.



**UTI Trend after renal transplantation**

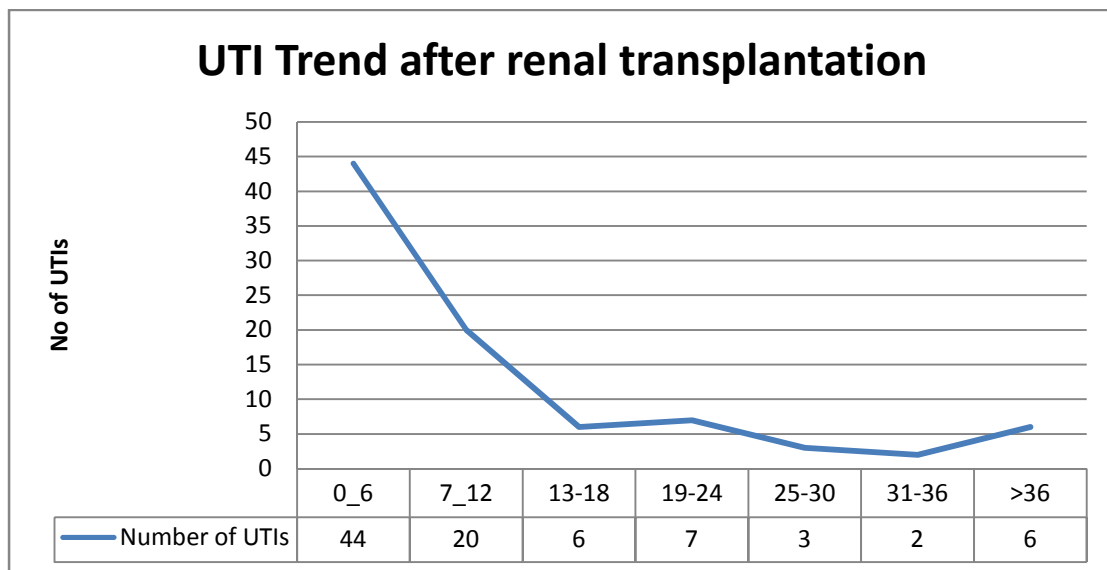| | 0_6 | 7_12 | 13-18 | 19-24 | 25-30 | 31-36 | >36 |
|---|---|---|---|---|---|---|---|
| Number of UTIs | 44 | 20 | 6 | 7 | 3 | 2 | 6 |

**Figure 6; History and Trend of previous UTIs in the Kidney Recipients (N=99)**

## DISCUSSION

The average age of the participants was 42.5± 13.41 years, with a range between 18 years to 72 years and a median of 42 years. This reflects a generally younger population with ESRD. This compares with the age group shown by Elkihili *et al* in Libya, whose mean age was 43 years with a range of 20-63 years and also by Chuang *et al* in USA whose mean age was 43 years at transplantation, range 18–79 years.[10, 23] This reflects that CKD mainly affects economically productive young society between the ages of 20 and 50 years. It's not usual to transplant elderly patients KNH. The 72 year old participant was transplanted two and half years prior to the study.

The majority of the participants were male 73.7%, revealing a sharp gender imbalance. A recent studies in KNH by Ngigi *et al* showed that prevalence of CKD including ESRD is comparable in males and females.[26] Therefore high prevalence of CKD in males cannot explain the difference. Perhaps, ability to secure kidney donor and financial capacity to cater for the transplantation favours males. However, this finding is similar to what Elkihili and Chuang  found in Libya and USA respectively suggesting a factor that is widely distributed.[10, 23]

 Eighty five percent of the participants had post primary education. This shows majority are able to understand and follow the important pre and post transplant counseling and care. Moreover, it may suggest the well educated section of the population is more informed about transplantation as a mode of renal replacement therapy.  It could also reflect financial ability to undergo the rigorous pretransplant preparation and still afford the costly daily dose of immunosuppresives.

Chronic glomerulonephritis made up half of the causes of ESRD, reflecting bacterial, viral, and parasitic infections are still the commonest cause of CKD in our population.[27] Our study findings contrast Abbot *et al* who found the commonest cause of ESRD in developed countries is diabetic nephropathy.[16] However, our study concurs with Elkihili[13], Chuang[11] and Puourand[42] *et al* in three separate studies who found out the three commonest cause of ESRD worldwide is chronic glomerulonephritis, diabetes and hypertension.[10, 23, 28]

The average duration of dialysis before transplantation was 22.7± 22.8 months. This is a long duration and increases the recipients' risk of development of UTI. Alangaden *et al* in USA in a predominantly cadaveric study found a mean duration of 60± 45.6 months. Arnol *et al* in Slovenia in a deceased donor study found a median of 56 months. The concern in these finding is the higher risk of UTI associated with longer dialysis duration as suggested by Munoz.[7, 20, 29]

Twenty one participants (21.2%) had a diagnosis of current UTI. This finding is significantly high. Elkehili in Libya found a prevalence of 29.5% in his predominantly living related donor retrospective study and Pourmand *et al* in Iran found 41.5% in a predominantly living unrelated donor prospective study with one year follow up. Maraha *et al* in Netherlands found a prevalence of 54%. This high figure could have been contributed by his flexible criteria that not only included the criteria used in our study but also clinical judgment to diagnose a UTI. In addition his population did not receive routine cotrimoxazole prophylaxis. Our cross sectional study design with no follow up period could have contributed to our lower figure. Furthermore 24.2% of our sample population had used an antibiotic within the month they took part in the study, which could have resulted to diagnosis of fewer UTIs. Of all patients with UTI only 3 (14.3%) had used antibiotic within the month of the study.[9, 23]

Eighty six percent of the UTIs were asymptomatic. This is not unusual as revealed by Maraha. Underlying diseases such as advanced diabetic neuropathy, combined with denervation of the allograft and immunosuppressive medications, especially corticosteroids, affect the reliability of clinical symptoms. This population is not only more prone to complications of UTI because of an incidence of reflux as high as 50%, but acute pyelonephritis also represents a risk factor for long-term impairment of allograft function. Moreover, asymptomatic bacteriuria itself has been suggested to cause subclinical damage to the allograft due to inflammation, as increased IL-8 levels have been measured during such episodes. While treatment of these UTIs has been contested by Emanuelle *et al* and Moradi *et al*, there are still no randomized studies or international guidelines that indicate it's safe to leave the UTIs untreated especially in the first six to twelve months.[9, 30, 31]

Fifteen percent of males and 38.5 % females in our sample population had UTI. Twenty percent of all diabetics who participated in the study had UTI. Females and diabetes mellitus have been associated higher risk and incidence of UTIs. The shorter urethra and relative proximity of the urethra to the perirectum contribute to an increased risk of UTI in females compared with men. Diabetes mellitus puts a patient at risk of UTI by lowering their immunity. Many studies have been done to assess these factors but they have had conflicting results. Elkehili *et al* only found a positive association in prevalence of UTI and females but no other factors. Chuang *et al* in a two centre study, found a positive association between UTI and females, vesicoureteric reflux, advanced age (>65 years) and cadaveric kidney. Perhaps, his large population (n=500) and long review period (7 years) enabled him to gather sufficient data to make these associations. However, he did not find any association with diabetes mellitus possibly due to the overall high incidence of UTIs in their population, as well as the frequent development of post-transplant diabetes mellitus in many of these

patients, of which they did not control for in their study. Alangaden *et al* noted that ureteral stenting, diabetes mellitus and retransplantation as strong predictors of UTI. Maraha *et al* found an association between females and late catheter removal with UTI, but none with age, DM, cadaveric kidneys and recurrent transplantation.

Twelve positive cultures were found.  One was fungal (*Candida spp.*) and the rest were bacterial in origin. The organisms grown were *Escherichia coli, Klebsiella pneumoniae, Enterococcus spp., Citrobacter koseri, Proteus vulgaris and Candida spp.*. Most of these causative microorganisms were gram negative (84%), similarly observed at 65% and 53% by Elkihili and Chuang respectively. *E. coli* made up the majority (58%) of the organisms grown, which is higher than what was shown by Elkihili (25.8%) and Chuang (29%) but lower than Senger (61%).[10, 23, 32]

In the general population *E. coli* causes 80-90% of UTIs. However, in renal transplantation population, despite being the commonest organism isolated, its relative contribution is less, revealing a change in microbiological pattern that has a bigger contribution from other organisms. *Escherichia coli* expresses type 1 or P fimbriae, which increase the bacterium's pathogenicity in the urothelium. *E. coli* that express P fimbriae that decrease IgA transport into the urine resulting in a reduction of local host defence. In addition, fimbriated *E. coli* may invade the uroepithelium enabling the development of pathogenicity islands within the urinary tract.  It has hemolysin that enable cellular lysis and multiple mechanisms e.g. siderophones for competing for iron and other nutrients. Its capsular polysaccharide enables it to avoid host bactericidal activity. Development of B lactamases especially the newer ones have made it resistant to many antimicrobials.[33] Thus, use of usual antimicrobial therapy may lead to partial response or treatment failure. The hierarchy of bacterial UTI pathogens in

transplant recipients is similar to that in the non-transplantation population, with Gram negative bacterial infections accounting for most of UTIs. Low-virulence bacteria that would not be pathogenic in immunocompetent hosts have been implicated in post-transplantation UTI. [33, 34]

While in our study only 8% of culture-positive UTIs were caused by gram positive bacteria, other studies have shown higher relative frequencies of up to 40%. Alangaden, Maraha and Roberto *et al*, in three separate studies have noted Enterococcus spp. as an emerging bacterium.[7, 9, 10, 12]

Fungal UTI from *Candida spp*. made up a relative frequency of 8% and 1% of all the study participants. This matches several others studies.[7, 10, 11] The pathogenesis of candiduria involves several factors including germ tube and hypha formation, adhesion factors, phenotypic switching, slime formation and production of different enzymes. However, these factors have less virulence compared to bacteria hence contributing a much less percentage of UTIs. *Candida* UTIs can have serious consequences and may cause ascending infection and/or obstructing fungal balls at the ureterovesical junction. Therefore, treatment of candiduria (even if asymptomatic) is recommended in renal transplant recipients. [6, 20] This view is supported by IDSA 2009 guidelines. Our patient was treated with systemic antifungal for ten days.

The antibiogram developed in our study revealed good, intermediate and poor antimicrobial sensitivity pattern. Drugs with relatively good sensitivity included amikacin and fosfomycin. Intermediate activity with amoxclav, ceftriaxone, cefotaxime, cefuroxime and nitrofurantoin. Poor activity was registered by cotrimoxazole, ciprofloxacin, ampiclox and nalidixic acid.

This study found 100% resistance to Trimethoprim/sulfamethoxazole (TMP-SMX). Similar finding was reported by Senger *et al*. TMP-SMX is used as prophylactic agent against pneumocystis, UTI, toxoplasmosis, Nocardia, and Listeria. TMP/SMX prophylaxis could induce and result in the emergence of resistant species and failure of the employed prophylaxis in preventing UTI development in individual patients. This does not negate role of TMP/SMX as a prophylactic agent. Work by Fox *et al* in a double blinded randomized controlled trial showed TMP-SMX prophylaxis was associated with fewer febrile hospital days, reduction of UTIs and other bacterial infections compared with placebo. KDIGO 2009 guidelines still recommend prophylaxis with cotrimoxazole.[35, 36]

Ciprofloxacin was found to have resistance of 70% to the gram negative bacilli, similarly observed by Senger at 75%. However, Elkehili and Greskas, in two separate studies, found lower resistance at 48% and 46% respectively.[37] Ciprofloxacin is one of the commonest oral antibiotics used for UTI treatment. Revathi *et al*, in Nairobi, Kenya, analysed 178 non transplant patients with UTI. 10% (seventeen) were resistant to both ciprofloxacin and levofloxacin. Out of the 17, fifteen were community acquired and on outpatient follow up. In his work in South Africa, Fredricka *et al*, found 11% and 41 % resistance to ciprofloxacin in uncomplicated and complicated non transplant UTIs respectively**.** Our population which has complicated UTIs, frequent contact with health facilities, is on immunosuppresives and anatomical abnormalities from transplantation may be predicted to have higher resistance pattern. Indeed, Elkihili, Senger, Greska and our study confirm this.[38, 39]

Out of eleven isolations of GNB, 60% were susceptible to ceftriaxone. The remaining 40% were all ESBL positive. Similar pattern was noted for cefuroxime and cefotaxime. Rivera-Sanchez *et al* reported intermediate resistance to cephalosporin; whereas, Lazinzka *et al* in Poland reported that 90% of Gram-negative strains isolated were susceptible to ceftriaxone and ceftazidime. [12, 40]

Amikacin had the best (100%) antimicrobial activity. Fosfomycin closely followed at 89% antimicrobial susceptibility. Despite good antimicrobial cover, amikacin is used with caution due to risk of nephrotoxicity. Fosfomycin is not recommended in complicated UTIs.[41] The rare use of these two antibiotics may have preserved them from the high resistance pattern noted with other antibiotics.[41]

Three out of seven *Escherichia coli* isolated were ESBL positive, and the *only Klebsiella pneumoniae* isolated was ESBL positive. This makes 42.9% and 40% of all *E. coli* and GNB ESBL positive respectively. In their work Valera *et al* found that *E. coli* as the principal isolated agent (71%) and ESBLEC made up 24%. Risk factors for ESBL development in general population include increased length of stay in ICU, Increased severity of illness, use of a central venous/ arterial catheter, Use of a urinary catheter, hemodialysis and administration of any antibiotic especially oxyimino-b-lactams cephalosporins like ceftriaxone or ceftazidime. Majority of these factors affect the renal transplantation population especially immediately after transplantation. Infections caused by ESBL producers are associated with increased mortality, length of stay and increased cost. An inadequate empirical therapy for serious infections caused by these organisms is independently associated with increased mortality. Monitoring of ESBL production and antimicrobial susceptibility testing are necessary to avoid treatment failure in management of UTI. As noted in our study, presence of ESBL bacteria has grave implication, as they were only sensitive to carbapemems-rare and expensive drugs. In addition, carbapenem resistant B-lactamases have been reported. [33, 42]

Review through all the participants' files and records revealed a 50% and 73% UTI occurrence in the first six months and one year respectively after transplantation. The number reduced with time and was remarkably low by the end of 24 months. This early post kidney

transplant time correlates with the period of the highest immunosuppresion, recent hospitalization and recent injury to tissues during procedures like surgery, urinary catheterization among others. In addition, reactivation of latent or partially treated pre transplant UTIs may contribute to the high prevalence. Valera *et al*, found 50% of UTI occurred in first 44 days while Elkihili *et al* found 72% of UTI occurred in first 3 months post transplantation emphasizing our observation. UTIs presenting in the first 6 months post transplantation are associated with overt pyelonephritis, bacteremia and high rate of relapse when treated with a conventional course of antibiotics. Need for heightened surveillance and high index of suspicion cannot therefore be overemphasized.[43]

**CONCLUSIONS**

1. UTI prevalence in our population was high with a prevalence of 21%. Majority of the UTIs were asymptomatic. A higher percentage of females were involved.

2. Gram negative bacteria caused the majority (83%) of UTIs with *Escherichia coli* being the most (58%) isolated.

3. Emergence of Extended Spectrum Beta Lactamase bacteria a matter of grave concern was noted.

# LIMITATIONS AND RECOMMENDATIONS

## 11.1 Limitations

1. Absence of routine urine cultures on the transplant recipients on follow up at KNH. If present it would have added more information on the previous causative microorganisms and which antimicrobials they responded to.

## 11.2 Recommendations

1. Routine urine cultures especially in the first six to twelve months after kidney transplantation for recipients on follow up at KNH. Every visit (monthly). This would allow choosing of antimicrobial agent(s) tailored on culture and sensitivity.

2. There is need to develop a dynamic antibiogram that is regularly reviewed by the transplantation team. This would inform a better empirical therapy as the clinicians await culture results.

3. Further studies with longer observation time to evaluate the clinical course of UTIs and graft function and mortality.

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## APPENDIX 1: URINARY TRACT INFECTIONS IN KIDNEY TRANSPLANT RECIPIENT'S QUESTIONNAIRE

### I.   GENERAL DATA

Study number_____                     Study date__/____/___

Sex_____                                  Date of birth__/____/_____

Highest Educational Attainment: _____

1= No formal Education; 2= Primary; 3= High School; 4= College / University

### II.   PAST MEDICAL HISTORY

1. Etiology of the kidney disease_____
   ____ Chronic glomerulonephritis
   ____ Diabetic nephropathy
   ____ Hypertensive renal disease
   ____ Obstructive uropathy
   ____ Polycystic kidney disease
   ____ Others

2. Date of starting dialysis: __/____/_____

3. Date of transplantation: __/____/_____

4. Timing of urinary catheter removal     ___early(within 7 days)     _____Late(> 7 days)

5. Source of kidney:     ____Living        ___cadaveric

6. How many times have you been transplanted     ____

7. Occurrence of UTI in the past transplantation as evidenced by:

   Leukocyte Esterase (LE): ___ Nitrites (N): ___

___6months ___12 months ___18 months ___24 months ____30 months____36months___ >36 Months

### III. CURRENT MEDICAL HISTORY

1. History:
   o Frequency _____
   o Dysuria _____
   o Urgency _____

2. Exam:
   o Temp $\geq$38.3C _____
   o Tender suprapubic _____
   o Tender renal angle _____
   o Tender area over graft _____

3. Current immunosuppresives and their dosages

   DRUG      DOSE    FREQUENCY
   a. Prednisolone _____/_____/_____
   b. Cyclosporine _____/_____/_____
   c. Tacrolimus _____/_____/_____
   d. Mycophenolate_____/_____/_____
   e. Sirolimus _____/_____/_____
   f. Others _____/_____/_____

4. Have you received any antibiotics in the last 1 month?

   Yes____   No____

   If yes, which one(s):_____

5. Presence of JJ stents? Y/N

**APPENDIX 2: RESEARCH CONSENT EXPLANATION FORM**

 **Title of the Study:** Prevalence of urinary tract infections in post kidney transplant patients in Kenyatta National Hospital

**Principal Investigator:** Dr. Njogu Maina (Phone: 0723 254 850)

**Description of the research:** You are invited to participate in a research whose aim is to find out how common is urinary tract infection in people who are kidney transplant recipients. This study is being done on all people male and female who have been transplanted and are willing to participate in the study.

**What will my participation involve?** If you decide to participate in this research you will be requested to answer a few questions about yourself, about any treatment that you could be on and finally be requested to give a urine specimen.

**Are there any risks to me?** There are no risks associated with participation in this study.

**Are there any costs to me?** There are no costs to you associated with this study.

**Are there any benefits to me?** Yes. The benefits are that if you are found to have urine infection you will be referred to the right doctor for treatment.  Even if your urine test is normal, the results of this study may help in coming up with recommendations that may reduce the occurrence and complications related to these infections. You will receive no money for participating in this study.

**How will my confidentiality be protected?** Information related to you will be treated in strict confidence to the extent provided by law.  Your identity will be coded and will not be associated with any published results. While there will probably be a publication as a result of this study, your name will not be used.

**Whom should I contact if I have questions?** You may ask any questions about the research at any time. If you have any questions to ask about the study, you can contact Dr. Njogu: 0723254850.

**What are the terms of my participation?** Your participation is completely voluntary. If you decide not to participate or to withdraw from the study, that decision will have no effect on any services or treatment you are currently receiving. You can withdraw from the study at any stage without prejudicing any services you may be receiving.

## APPENDIX 3: VOLUNTARY CONSENT FORM

I certify that the nature and purpose, the potential benefits and possible risks associated with participation in this research study have been explained to the above individual and that any questions about this information have been answered.

Signature of PI:…………………………………………

Date: ……………………………

Having got explanation about the nature and purpose of this study, the procedures, the potential benefits and risks associated in participating in this study, I hereby voluntarily agree to participate in the study by appending my signature.

Name of

Participant: .....................................................Sign……………………. Date……….

## IDHINI

Mimi……………………………………………………………………………………………

…...

Natoa idhini mwenyewe bila aina yoyote ya kushurutishwa au kulazimishwa kushiriki katika utafiti uliotajwa hapa kuhusu utafiti wa shida ya mkojo kwa wagonjwa waliopandikizwa figo. Nimeelezewa kikamilifu kuhusu madhumuni na hali yake na naelewa kuwa nitaulizwa maswali kadhaa na nipimiwe mkojo. Pia naelewa kuwa naweza kujiondoa wakati wowote iwapo nitabadilisha mawazo.

Sahihi ya Mtafiti Mkuu ……………… Tarehe……………………

Sahihi ya mshiriki……………………..Tarehe……………………

## APPENDIX 4: CLEAN CATCH URINE SPECIMEN COLLECTION[31]

**Male**

(1) Before beginning the procedure, the patient should wash his hands with soap

(2) Instruct the uncircumcised patient to withdraw the foreskin to expose the urethral meatus.

(3) With a sterile cleansing towelette , cleanse the glans, beginning at the urethra and working away from it.

(4) Have the patient begin urination, passing the first portion into the bedpan or toilet. Collect the midportion in the appropriate urine specimen container without contaminating the container. Any excess urine can pass into the toilet.

(5) Offer assistance if the patient is unable to carry out the recommended procedure. Sterile gloves should be worn by the assistant.

**Female**

(1) Before beginning the procedure, the patient should wash her hands with soap

(2) Instruct the patient to squat over the bedpan or toilet (or stand with legs apart).

(3) With a sterile cleansing towelette, cleanse the urethral meatus and surrounding area.

(4) Have the patient begin urination, passing the first portion into the bedpan or toilet. The midportion should be collected in the appropriate container without contaminating the container. Any excess urine can pass into the bedpan or toilet.

(5) Offer assistance if the patient is unable to carry out the recommended procedure. Sterile gloves should be worn by the assistant.