



## Post Renal Transplant Infections: A Six Month Follow-Up Study from a Kidney Transplant Institute of North India

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**ABSTRACT:** Transplantation returns the majority of patients to an improved life-style and an improved life expectancy, as compared to patients on dialysis. Infections are the most prevalent cause of morbidity and mortality in kidney transplant recipients, with more than 80% suffering at least one episode of infection in the first year. The method of data collection in this study was prospective hospital record analysis, all renal transplant recipients were screened pre operatively for the presence of any overt or occult infection. The predominant age group undergoing renal transplantation was between 18 - 29 yrs. Urinary tract infections were the highest and commonest infections observed. The microorganisms involved in the infections were Bacteria (36.4%), Viruses (7.6%), Fungi (3.7%) and Parasites (5.5%). In Urinary tract infection, *E. coli* followed by *Klebsiella pneumoniae* were the predominant bacterial isolates. *Candida albicans* were the commonest fungi isolated. Among the Gastrointestinal tract infections, *Cryptosporidium* was the commonest Protozoal isolate. *Cryptococcus neoformans* was isolated in two cases of meningitis. In this study the organisms causing infection during the immediate operative period have been categorized, which will give the treating physician a reasonable idea to suspect the system and cause of infection during the particular post renal transplant period. This study has focused to evaluate the spectrum of infectious complications in post renal recipients in first 6 months of follow up and evaluate the most common type of infection.

**KEYWORDS:** Immunosuppression, Renal Transplant Infections, UTI.

### INTRODUCTION

Kidney transplantation offers a healthier life over hemodialysis in patients with end-stage renal disease (ESRD). The survival following transplantation is determined by various factors, including pretransplant co-morbidities, graft type, and degree of immunosuppression (Arend *et al.*, 1997). The new developed immunosuppressive drugs has lead to the reduction in mortality of renal transplant recipients (RTRs). Nevertheless, potent immunosuppression poses an extra risk of infectious disorders in the transplant recipients. One quarter of RTR develop a serious infection in the post-transplant period that causes allograft dysfunction (Ram *et al.*, 2005). Bacterial infections are very frequent as compared to the viral infections in RTR. Nearly 13% of all patients transplanted between 1996 and 2000 in the US needed hospitalization for bacterial infections in the first 3 years compared to 6% for viral infections (Dharnidharka *et al.*, 2007).

In the period from one to six months after transplantation, infections with immunomodulating viruses, particularly cytomegalovirus, are most important. Cytomegalovirus accounts for two-thirds of febrile episodes during this period. In addition to the clinical syndromes induced by these viruses, their immunomodulating properties predispose to opportunistic infections with such organisms as *Pneumocystis carinii*, *Listeria monocytogenes*, and *Aspergillus fumigates* (Pava, 1993; Fishman, 1995; Hadley and Karchmer, 1995; vanDenBerg *et al.*, 1996). Other infections generally occurring during this period include hepatitis, Herpes zoster, Herpes simplex, *Mycobacterium tuberculosis*, and Epstein-Barr virus (EBV), which can be complicated by the development of lymphoproliferative disorders. Recurrence or relapse of urinary tract infections can also occur (Fishman and Rubin, 1998). Most infections occur early in the post-transplantation course with about two-thirds of renal transplant recipients (RTR) experiencing an infectious-related complication in the first year after transplantation (Maraha *et al.*, 2001). Approximately 70% of severe bacterial, fungal and viral infections occur within 3 months of transplantation. This study has focused to evaluate the spectrum of infectious complications in post renal recipients in first 6 months of follow up and evaluate the most common type of infection.



## MATERIALS AND METHODS

### Inclusion criteria:

1. All patients undergoing renal transplantation from 2016 to 2018.
2. All patients presenting in first 6 months with infectious complications.

### Exclusion criteria:

1. Patient who develop infectious episodes after 6 months of transplant.

**Study Design:** Prospective study.

**Method of data collection:** Prospective hospital record analysis.

The study group comprised 75 cases of renal transplant recipients, who underwent renal transplantation for end stage renal failure (ESRF) at Department of Nephrology SKIMS.

It included :

- 75 cases of live related donar renal transplantation were followed from 2016 to 2018.
- All renal transplant recipients were screened pre operatively for the presence of any overt or occult infection by

### Post operative care

Immunosuppressive protocol consisted of administration of Triple drug regime - Tacrolimus, Mycophenolate mofetil and Prednisolone. Rejection episodes were treated with Intravenous Methylprednisolone, Intravenous Dexamethasone or Oral Prednisolone or OKT3. Whenever infections occurred, samples were collected accordingly. Patients were immunized against Hepatitis B whenever possible.

### Methodology

- A. Collection of specimen.
- B. Microscopical examination.
- C. Culture procedure and identification of organisms.

### Collection of specimens

Urine, Drain fluid, foley catheter tip and Drain tip were collected from all cases. According to signs and symptoms, Blood, Serum, Sputum, Oral scrapings, Faeces, Pus and CSF were collected.

## OBSERVATION AND RESULTS

Infection in renal transplantation is a major and severe penalty of immunosuppression and is associated with high mortality. In order to prevent the occurrence of infection, one should know the commonest types of infection in that particular group of patients. Hence, a detailed account of post renal transplant infections was made to find out the present trend of infections and their incidence in renal transplant patients. All the details produced were based on the post renal transplant follow up of the patients which mainly explains the prevalence of infection, most common type of infection and most common organism involved.

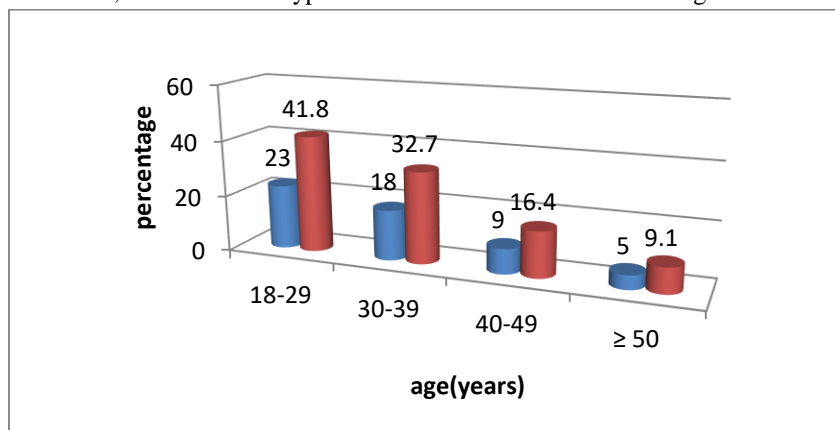


Figure- 1: Age distribution of study patients.

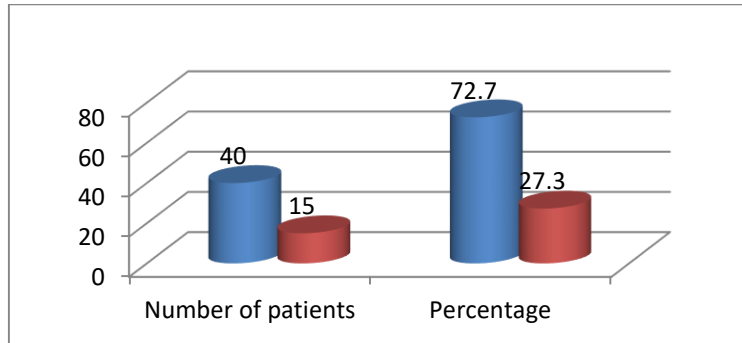


Figure- 2: Gender distribution of study patients

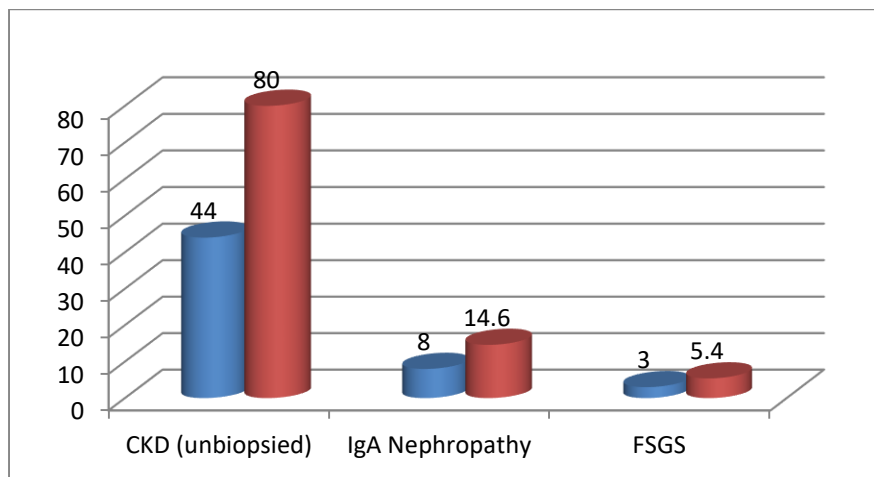


Figure-3: Basic disease in study patients.

Table 4: Blood and urine culture in study patients.

| Culture                      |          | Number of patients | Percentage |
|------------------------------|----------|--------------------|------------|
| Blood Culture (total no. 38) | Positive | 2                  | 5.2        |
|                              | Negative | 36                 | 94.8       |
| Urine Culture (total no. 30) | Positive | 17                 | 56.7       |
|                              | Negative | 13                 | 43.3       |

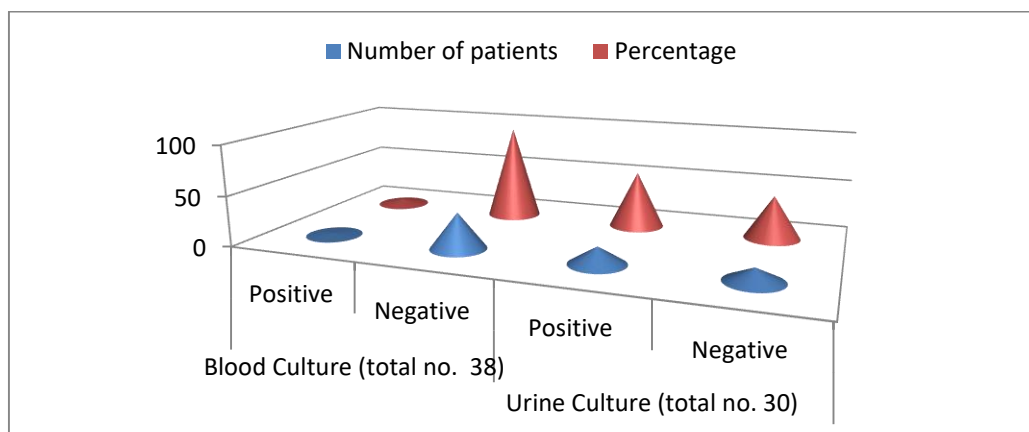
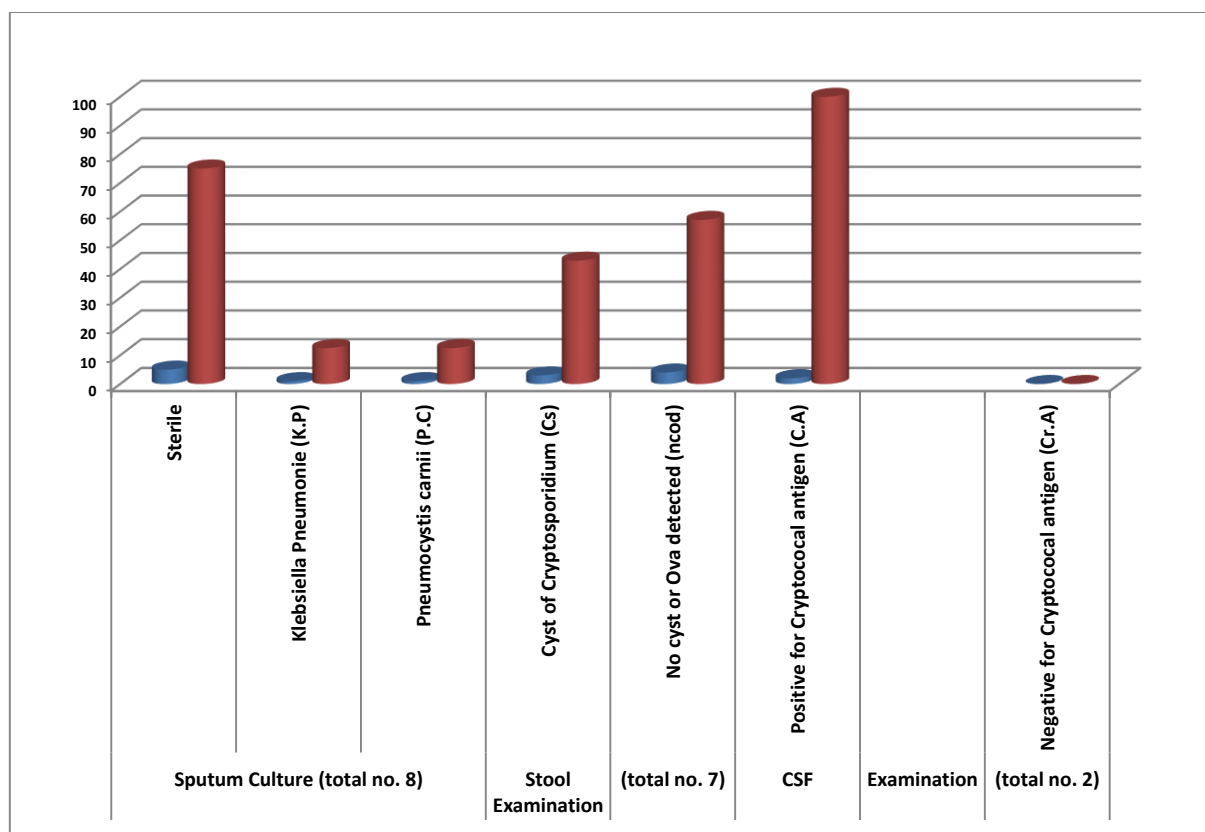


Figure- 4: Blood and urine culture in study patients

**Table-5:** Sputum culture, stool examination, CSF and PCR in study patients.

|                                 |  | Number of patients | Percentage |
|---------------------------------|--|--------------------|------------|
| Sputum Culture (total no. 8)    | Sterile                                  | 5                  | 75         |
|                                 | Klebsiella Pneumonie (K.P)               | 1                  | 12.5       |
|                                 | Pneumocystis carinii (P.C)               | 1                  | 12.5       |
| Stool Examination (total no. 7) | Cyst of Cryptosporidium (Cs)             | 3                  | 42.9       |
|                                 | No cyst or Ova detected (ncod)           | 4                  | 57.1       |
| CSF Examination (total no. 2)   | Positive for Cryptococcal antigen (C.A)  | 2                  | 100        |
|                                 | Negative for Cryptococcal antigen (Cr.A) | 0                  | 0          |



**Figure- 5:** Sputum culture, stool examination, CSF and PCR in study patients.

**Table 6:** PCR of study patients.

|                                 | Number of patients | percentage |
|---------------------------------|--------------------|------------|
| Herpes simplex positive (H.S.P) | 1                  | 33.3       |
| BK virus                        | 1                  | 33.3       |
| CMV virus                       | 1                  | 33.3       |

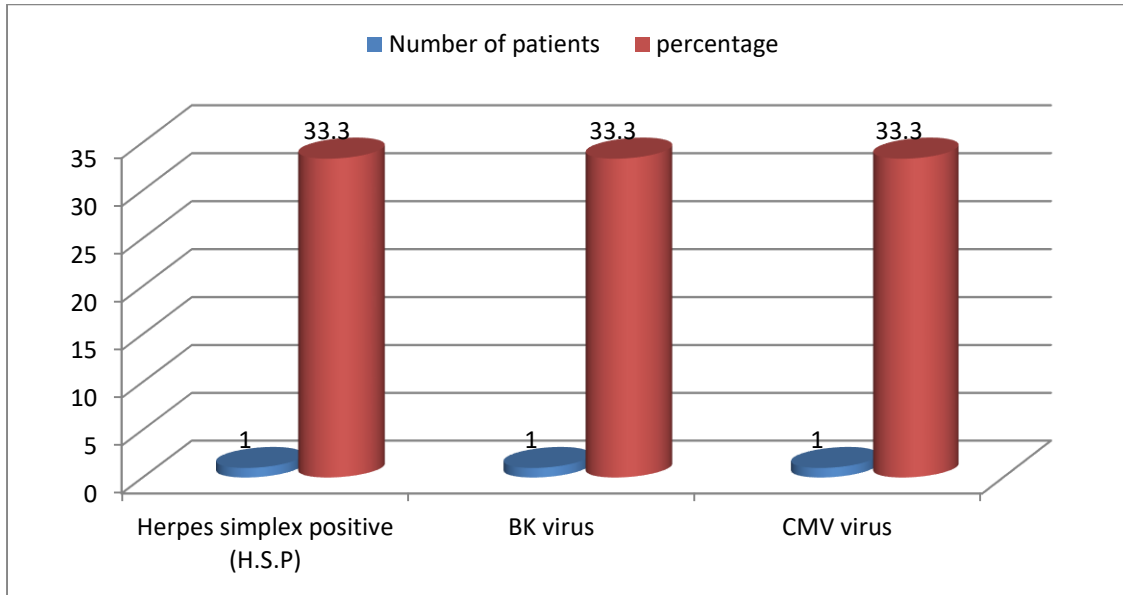


Figure 6: PCR of study patients (total no. 3)

Table 7: Repeat urine culture in study patients

| Urine culture | Number of frequency | Percentage |
|---------------|---------------------|------------|
| Positive      | 1                   | 5.9        |
| Negative      | 16                  | 94.1       |

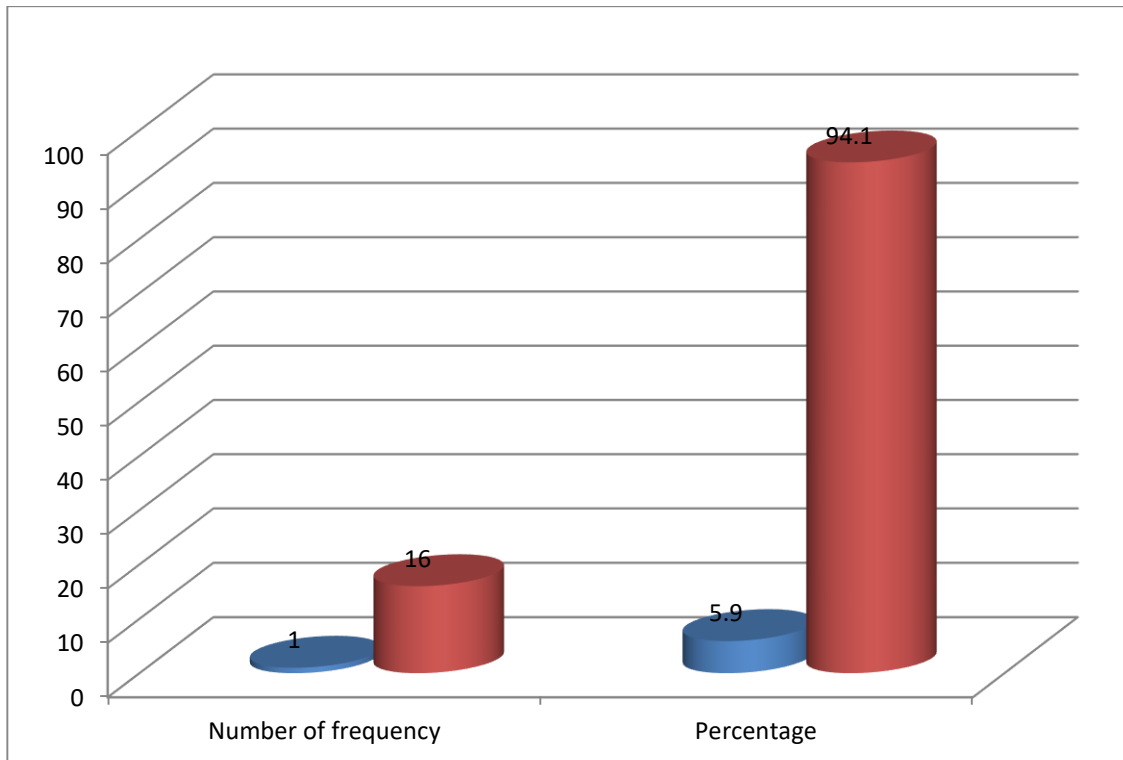
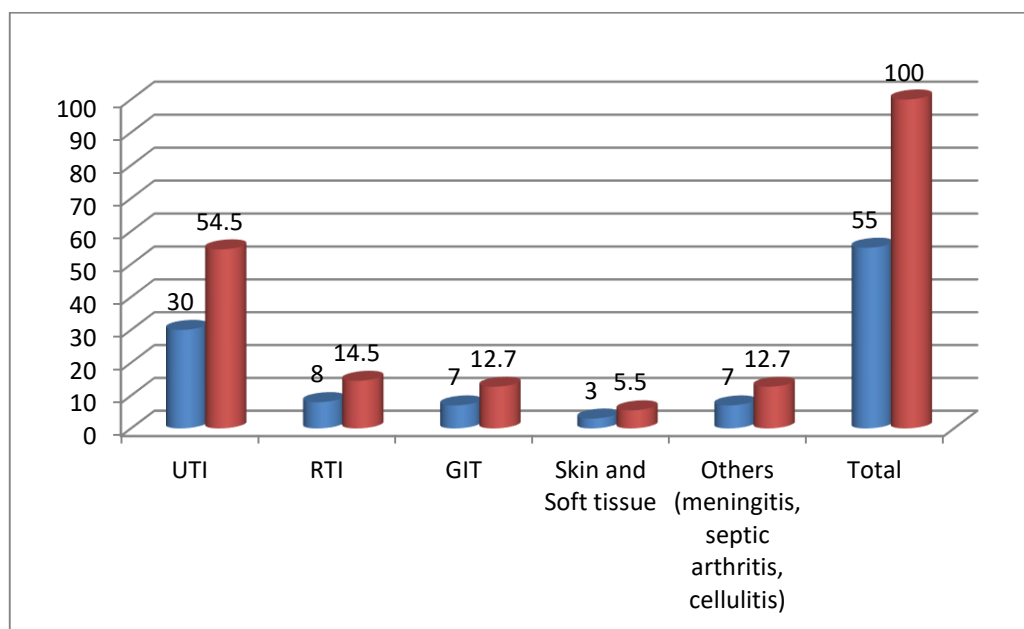


Figure-7: Repeated urine culture in study patients

**Table 8:** Showing prevalence of infections in study patients

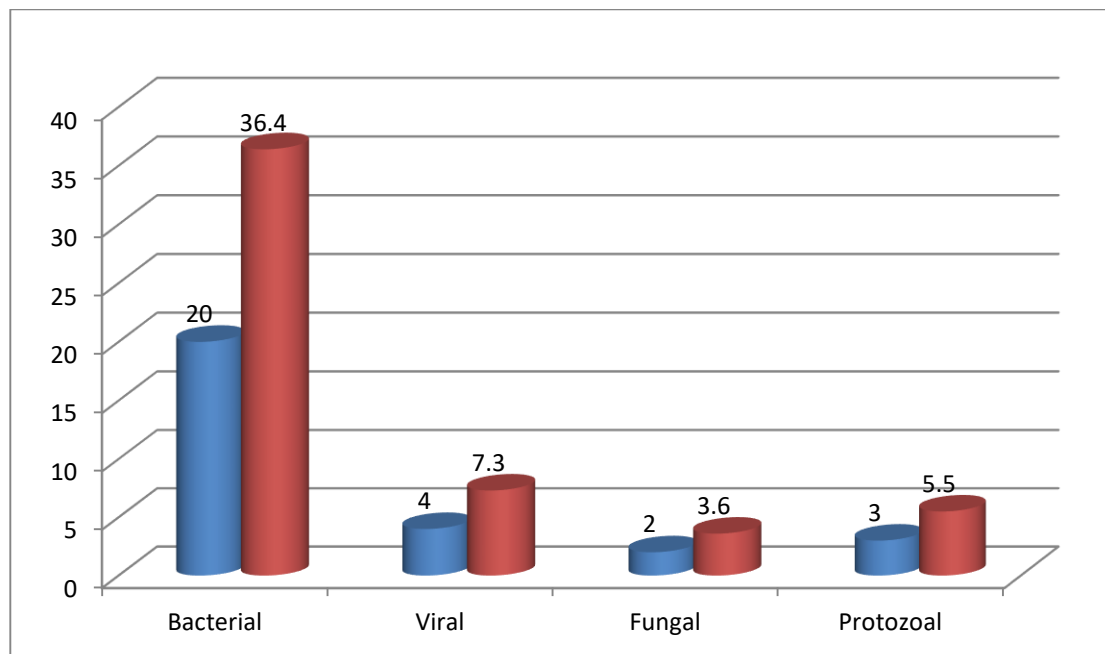
| Type of infections                                | Number of patients | Percentage |
|---|--------------------|------------|
| UTI   | 30                 | 54.5       |
| RTI   | 8                  | 14.5       |
| GIT   | 7                  | 12.7       |
| Skin and Soft tissue                              | 3                  | 5.5        |
| Others (meningitis, septic arthritis, cellulitis) | 7                  | 12.7       |
| Total   | 55                 | 100        |



**Figure-8:** Showing prevalence of infections in study patients

**Table 9:** Showing nature of infections (culture positive) in study patients.

| Nature of infections | Number of patients | Percentage |
|----------------------|--------------------|------------|
| Bacterial            | 20                 | 36.4       |
| Viral                | 4                  | 7.3        |
| Fungal               | 2                  | 3.6        |
| Protozoal            | 3                  | 5.5        |



**Figure-9:** Showing nature of infections (culture positive) in study patients

**Table 10:** Organism involved in study patients

| Organism Involved      | < 1 Month | 1-6 Months |
|------------------------|-----------|------------|
| E. coli                | 0         | 8          |
| Kliebsiella            | 0         | 7          |
| Pseudomonos            | 0         | 5          |
| Sttaphylococcus aureus | 0         | 2          |
| CONS                   | 0         | 1          |
| Acinetobacter Boumani  | 0         | 1          |
| CMV                    | 1         | 0          |
| BK Virus               | 1         | 0          |
| Herpes Virus           | 1         | 1          |
| Candida albicans       | 0         | 1          |
| Cryptosporidium parvum | 0         | 3          |

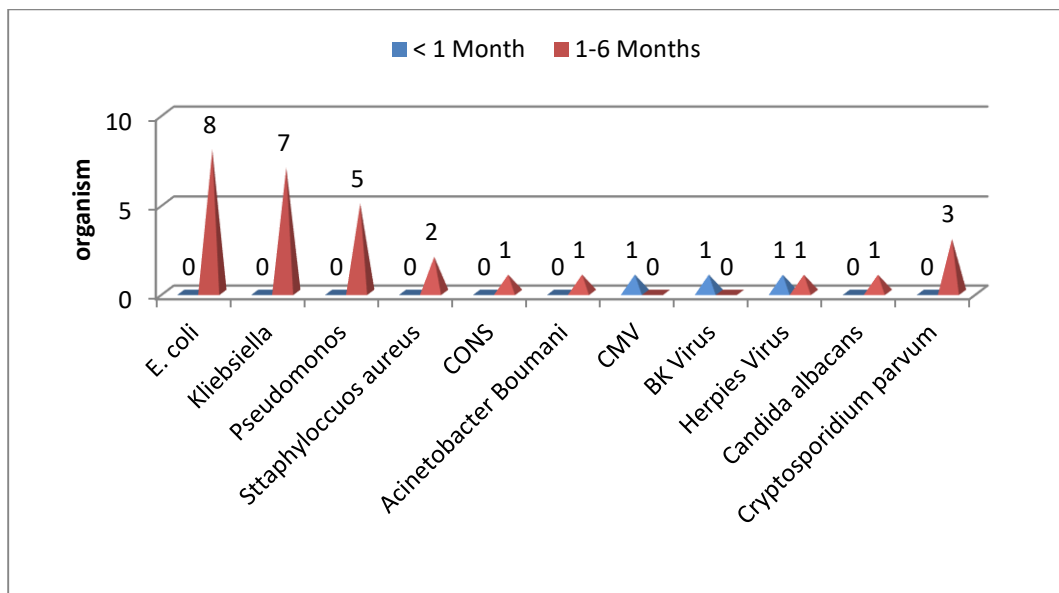


Figure-10: Organism involved in study patients

**DISCUSSION**

The current study group comprised of 53 male recipients and 22 of female recipients, male to female ratio being 2.4:1. However, Ravikumar (1992),<sup>140</sup> has reported predominance of male population (82.5%) and male to female ratio of 4.7:1. Ram, R. *et al.*, (2005) reported that out of 169 renal transplant patients 136 (80.4%) patients were males and 33 (19.5%) were females in this population. Kumar *et al.*, (2016) revealed the study population renal transplant patients (n = 45, 35 male and 10 female) had a mean age of 35.5 ± 10.4 years and follow-up after transplant was 2.1 ± 1.7 years. The predominant age group in this study was between 18 - 29 years (Table-1).

All 75 cases underwent live related donor transplantation and no case underwent Cadaver transplantation. Urinary tract infections were commonest followed by respiratory tract infections (Table-8). Bacterial infections were the most common infections in the post transplant period (Table-9).

**URINARY TRACT INFECTION**

Urinary tract infections (UTIs) are the most common bacterial infections requiring hospitalization in kidney transplant recipients, followed by pneumonia, postoperative infections, and septicemia. Women are at greatest risk for UTIs; other risk factors include deceased-donor transplant, kidney-pancreas transplantation with bladder drainage, prolonged catheterization, uretero-vesical stents, and increased immunosuppressed state (Lorenz EC and Cosio FG., 2010).<sup>155</sup> Urinary tract infections were the single most common infection occurring in renal transplant recipients, as noted in the present study and also reported by Rubin, *et al.*, (1981)<sup>141</sup> and Jadav, *et al.*, (1992).<sup>142</sup> Urinary tract infection constituted 54.5% (Table-8) of the total infections in this study. Umesh *et al.*, (2007) has reported 31.1% of UTI incidence in transplant recipient. Jadav, *et al.*, (1992) observed the incidence of 53% which were in congruence with the present study. Krieger JN, *et al.* [1977] observed 61% , the reports of Leigh, D.A. (1970) and Chan, P.C. (1990) varies from 30-79%, 31% incidences based on study by Chan PC, *et al.* [1990]. The incidences of 51% reported by Ravi kumar (1998) were in proximity with current investigation. A study of 28,942 primary renal transplant recipients from the U.S. has revealed a cumulative UTI incidence of 17% during the first 6 months after transplantation; at 3 years the incidence were 60% for women and 47% for men (Abbott KC. *et al.*, 2004). Kumar, A. *et al.*, (2016) reported UTI as most common infection, out of 45 patients 15 cases were of UTI. UTI occurred in transplant recipient was found as 72.7% Sujit *et al.*, (2016) .

Most of the infectious occur during early months of transplantation and the most common organism are *E. coli* and *Klesiella*. The aetiological agents causing urinary tract infection in the present study were Bacteria and Fungi. The bacterial isolates included *E. coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Pseudomonas aeruginosa*, *Staph aureus*, *Acinetobacter baumannii* and





*Enterococcus faecalis*. Similar organisms were also isolated by Paul, D. Ellner (1987). *E. coli* followed by *Klebsiella pneumoniae* were the most frequently isolated organism in this study. Takai *et al.*, (1998) found that *E. coli* was the commonest organism causing urinary tract infection. Gram negative bacilli of Enterobacteriaceae family were most frequently isolated in urinary tract infections in a study by Morz, E. *et al.*, (1993). 3.3% of the urinary tract infections were due to fungi of which all were caused by *Candida albicans*. Funguria has been attributed in part to the widespread use of broad spectrum antibiotics, Corticosteroid, antineoplastic agents, immunosuppressive agents and urinary catheterization. Fluconazole is the drug of choice for susceptible *Candida* species; other azoles and echinocandins are not concentrated in the urinary tract and thus are less likely to be effective if infection is confined to the urinary tract (Pappas PG. *et al.*, 2004; 2009).

## RESPIRATORY TRACT INFECTION

Respiratory tract infection occurred in 16.3% of the transplant recipient in comparison with 33% based on the study by the Jha R, *et al.* [1999].

Respiratory tract infection constituted about 14.5% of the total infections which was second most prevalent infection in the current study (Table-8). These reported incidence showed proximity with some of the previous studies whereas some reports showed a significant variation: 8% of incidences were observed by Moore, F.D *et al.*, (1983), 15% by Giri (1992) which is approximately same as reported by present study, 12.6% by Ravi kumar (1998), 33% by Jha R, *et al.* [1999]. Maraha, B. *et al.*, (2001) reported 8% of RTI incidences as second most prevalent infection in renal transplant patients following UTI. Organisms causing bacterial infection were *E. coli*, Gee-Chen Chang (2004), mention which organism was involved in current study.

## GASTROINTESTINAL TRACT INFECTION

Infections of the Gastrointestinal tract occurred in 12.7% of the total infectious patients (Table-8), which were not in view with previous Incidence. Giri, (1992) reported 5% incidences and 17.2% of were reported by Attoparmark, M R. *et al.*, (2002) and the most common organism was *Candida*. The causative organisms isolated was *Cryptosporidium*. Majority of the GIT infections occurred between 3-6 months post transplant duration.

## SKIN AND SOFT TISSUE INFECTION

Skin and soft tissue infection accounted for 5.5 % of the infections (Table-10). Among the infections *Staph aureus-1 Herpies-2 and Histoplasma-1*.

## CYTOMEGALO VIRAL INFECTION

*Cytomegalovirus* infection is a recognized problem of the early post transplant period in renal transplant recipients (Boehter A., 1994). In the present study, one patients (1.8%) developed *cytomegalovirus* infection which was detected in the first month of transplant (Table ). Kumar, A. *et al* (2016) reported *cytomegalovirus* infected six out of forty-five patients and Maraha, B. *et al.*, (2001) reported 8% of *cytomegalovirus* infections.

## CENTRAL NERVOUS SYSTEM INFECTION

Two patients were observed to develop meningitis which constituted 3.6% of the total infectious. Giri, (1992) has reported the incidence of 0.7% in his study. The causative organism was found to be *Cryptococcus neoformans*. Both patients developed meningitis in the 6th month post transplant. Ravi kumar (1998) has also reported two cases of *Cryptococcus neoformans* meningitis in his study. It has been mentioned that *Cryptococcus neoformans*, the single most common cause of central nervous system infection in the renal transplant patients, occurs almost exclusively in the late post transplant period (more than six months after transplant ) Robert H. Rubin, (1993).

In the present study it was noted that infections in renal transplant patients were commonly caused by Bacteria (36.4%) followed by Viruses (7.3%), Fungi(3.6%) and Protozoal (5.5%). However, Alangaden *et al.*, (2006) has reported viral infections (17%), pneumonia (8%), and surgical wound infections (7%), *Enterococcus* spp. (33%) and *Escherichia coli* (21%) were the most prevalent uropathogens. Wang X. *et al.*, (2014) studied Pulmonary infections after renal transplantation. Infections more likely to occur within 6 months after transplantation, and the peak being at about 3 months. Mixed infections (62.1%) were the common



types, followed by virus infection (24.1%) and bacterial infection (13.8%). In 10 patients taken chest radiographs with pulmonary infections after renal transplantation, patchy shadow and/or increased lung markings were showed in 7 cases (70%).<sup>166</sup>

## CONCLUSION

Infections are the major bane of renal transplants, and the leading cause of hospitalization and also leads to considerable morbidity and mortality. The predominant age group undergoing renal transplantation was between 18 - 29 yrs. The male prevalence more, Urinary tract infections were the highest and commonest infection observed. The microorganisms involved in the infections were Bacteria (36.4%), Fungi (3.7%), Viruses (7.6%) and Parasites (5.5%). In Urinary tract infection, *E. coli* followed by *Klebsiella pneumoniae* were the predominant bacterial isolates. *Candida albicans* were the commonest fungus isolated. Among the Gastrointestinal tract infections, *Cryptosporidium* was the commonest Protozoal isolate. *Cryptococcus neoformans* was isolated in two cases of meningitis. It is clearly emphasized that early and correct recognition of infectious agents in renal transplant recipients during immediate transplant period will improve the outcome of the patients. In this study the organisms causing infection during the immediate operative period has been categorized, which will give the treating physician a reasonable idea to suspect the system and cause of infection during the particular post renal transplant period.

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