ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
Index Copernicus Value: 49. 23

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 3, Issue –2, April - 2018, Page No. : 72 - 78

A study on bacterial and fungal infections in renal transplant recipients

[1]Kandasamy Anuradha, Assistant Professor

Institute of microbiology- Madras medical college & Rajiv Gandhi government general hospital, Chennai 3

[2]Jeyachandran Dhanapriya, Assistant Professor

Department of Nephrology, Madras medical college & Rajiv Gandhi government general hospital, Chennai 3

Correspondence Author: Kandasamy Anuradha, Assistant Professor, Institute of microbiology- Madras medical college & Rajiv Gandhi government general hospital, Chennai - 3

Type of Publication: Original Research Paper

Conflicts of Interest: Nil

Abstract

The two major hurdles to successful renal transplantation are rejection and infection. Infection is the leading cause of morbidity and mortality in renal transplant recipients, with more than 80% suffering at least one episode of infection within a year. Our aim was to determine the prevalence of bacterial and fungal infections among transplant infections and their antimicrobial susceptibility pattern in renal transplant recipients. We conducted a retrospective study in 100 consecutive renal transplant recipients admitted with bacterial and fungal infections. Among 100 patients, 80 were males .The most common age group affected were 25 -35 years and the mean age was 30.5 yrs. About 72 patients had live related renal transplantation (LRRT) and 28 had deceased donor renal transplantation (DDRT). The most common symptoms were fever and burning micturition. On the whole, 74% of the transplant recipients had culture positivity and 26% were negative. Bacterial infections were in 90 and fungal in 10.Klebsiella and candida were the commonest species isolated respectively. Urinary tract infection (UTI) was the commonest infection followed by respiratory infection (RTI),skin and soft tissue infection (SSTI) and blood stream infection (BSI) /sepsis. The most common resistance pattern observed was the production of Extended Spectrum Beta Lactamases and Imipenem resistance was found to be minimal.To conclude benign UTI should not be neglected as it may progress to sepsis and graft dysfunction. Renal transplant recipients should be followed up and monitored regularly since they have increased morbidity and mortality rate due to infections.

Key-words:Anti-Microbial,Sensitivity,Bacterial,Fungal, Infection, Renal Transplant.

Introduction

Around 25% of renal transplant recipients in the tropical countries develop a serious infection at some point of their post-transplant period [1]. Peterson and colleagues found that 32% patients suffered clinically significant infections out of which 7% died and 87% of the deaths in post renal transplant are due to infection.[2] The predisposing factors include unhygienic conditions, tropical climate, overcrowding, high prevalence of endemic infections, under nutrition and extent of immunosuppression. Etiologies of these infections are diverse, including common community-acquired bacterial, viral diseases and uncommon opportunistic infections. [3] Challenges associated in early diagnosis and treatment of these infections are impaired inflammatory responses resulting in diminished clinical and radiological findings. Antimicrobial resistance is also seen increasingly in

immuno-compromised hosts and should be considered in the choice of antimicrobial regimens.

Materials and methods

We conducted a retrospective study at Institute of nephrology in which 100 consecutive renal transplant recipients admitted with bacterial/fungal infections were included. After the renal transplantation, patients were put on standard triple drug immunosuppression (Tacrolimus / azathioprine or mycophenolate mofetil /prednisolone).Induction agents used were basiliximab or anti thymocyte globulin in selected patients. Oral cotrimoxazole and anti-fungal prophylaxis (oral fluconazole 200 mg daily) were given. Data were collected regarding history, source and site of infection, clinical examination and relevant biochemical and microbiological investigations. Urine samples for culture and sensitivity were collected and plated in CLED (cystine lactose electrolyte deficient) , blood samples were incubated in BIH broth in 37 C for 5 days ,respiratory specimen were plated in crystal violet blood agar and pus samples for skin and soft tissue infections were plated in mannitol salt agar with oxacillin and blood agar.

Results

Total of 100 patients were included.80% were males and 20% were females The most common age group affected were 25 -35 years and the mean age was 30.5 yrs. About 72 patients had LRRT and the remaining had DDRT. The most common symptoms observed were fever and burning micturition. 74% of the transplant recipients reported culture positive and 26% were negative. In our study it was observed that live related transplants had lesser incidence of infections. Out of the 26 patients, who had culture negative samples, 24 of them had live related transplants.

Out of the 235 samples received, 97 (41%) showed culture positivity which was predominantly bacterial (90%) followed by fungus (10%). Most common bacteria isolated was klebsiella pneumoniae and fungal was candida spp. Early post transplant period (<1 month) showed less incidence (20%) due to vigorous antibiotic.There was high incidence (48%) of infections between 1-6 months which may be due to graft dysfunction and rejection. Repeat sampling was done for many patients, if the same organism isolated in the same sample it is not taken in to account for sensitivity.

Table 1 gives details about number of samples and culture positivity of four type of infection namely urinary tract infection(UTI),respiratory infection (RTI),skin and subcutaneous tissue infection (SSSTI) and BSI/sepsis encountered in 100 renal transplant recipients.

Urinary tract infection was the most common infection affecting the renal transplant recipients Around 140 urine samples were received from 73 patients, 62 were culture positive.56 patients had multiple episodes of urinary tract infections. The organisms isolated were Klebsiella spp in 19 patients followed by pseudomonas spp and E.coli .For respiratory tract infections ,23 samples were received from 20 patients.The commonest oraganisms being klebsiella followed by E.coli and Aspergillus fumigatus. Out of the 19 samples obtained surgical site infection include 14 and the other samples are from various sites of the body like thigh, gluteal abscess and peri-anal abscess .Staphylococcus was the commonest organism isolated. As with other types of surgery, the main risk factors for postoperative complications are obesity, reoperation, and increased age. About 20 samples were collected for blood culture and sensitivity from patients who were suspected to have septicaemia and those who had persistent bacteriuria. Three were culture positive (staph aureus in 2 and pseudomonas in 1). The sensitivity and resistant pattern of UTI, RTI, SSTI and sepsis for microbials were given in table 2,3,4 & 5 respectively.

Discussion

Infections are the major cause of morbidity and mortality in kidney transplant recipients.[4] Abbott et al found that kidney transplant recipients have an adjusted incidence ratio of hospitalizations for septicemia of 41.52 compared to that of the general population.[5] The rate of first infections in the initial 3 years after kidney transplantation is 45 per 100 patient-years of follow-up, as estimated by the U.S. Renal Data System.[6] The usual clinical manifestation of infection in the post-transplant period are masked by immunosuppressants. Post-transplant infections can be classified by the organisms, the system involved or by the time of appearance in relation to transplant. Rubin categorized infections as those occurring within the first month after transplantation, 1 to 6 months and thereafter.[7] More than 90% of infections occurring in the first month are the nosocomial bacterial or candida infections.[8] UTIs are the most common bacterial infections requiring hospitalization in renal transplant recipients, followed by pneumonia, postoperative infections, and septicemia. [9] In a study from India.the most common infections were those of urinary tract (34.5%), followedby viral (31.2%), sepsis (15.2%), mycobacterial (9.7%), and fungal (6.2%) [10]

The risk factors of UTI include female gender, DDRT, kidney-pancreas transplantation with bladder drainage, prolonged catheterization, uretero-vesical stents, and increased immuno-suppressed state.[11] UTI are common but frequently asymptomatic and 60 % of bacteraemia are originated from a urinary source .[12] In our study the incidence was 44% as compared to 30 - 40 % in other studies.[13-15] Although different studies reported widely variable incidence rate, the majority of the organisms cultured were gram negative bacilli (65%) with Klebsiella spp being the most common organism (27%) followed by E.coli (13%).Some patients had persistent urinary tract infection, with asymptomatic bacteriuria and they were left untreated.In our study one patient died of candidemia with ascending urinary tract infection.Vesico urethral reflux can allow the bacteria direct access to the kidney, resulting in increased risk of pyelonephritis.[16] In our study, 4 transplant recipients had VUR with UTI.

The incidence of respiratory tract infections in our study was 39%. Most of the samples received are sputum, followed by tracheal swab and bronchoalveolar lavage. Klebsiella spp was found to be more common (66%) followed by E.coli. Fungal respiratory tract infections were minimal, only 2 cases of Aspergillus fumigatus were reported .The most common bacteria causing pulmonary infections include streptococcus pneumonia, staphylococcus, Gram Negative Bacteria, Mycobacteria, Legionella and Nocardia.Transplant recipients are also at the risk of atypical mycobacterial infection like M.kansasi, M.cheloneuii and M.marinum, M.xenopii and M.avium intracellulare.[17,18] Fungal respiratory infections include candida and aspergillus species.[19]

The incidence of surgical site and wound infections depends on the technical skill of the surgeon. Multiple factors which predispose to wound infections are, juvenile diabetes, cadaver donor, acute tubular necrosis, hematoma, urinary fistula.The most common organism isolated was E.coli. Out of 37 patients, 41 samples are collected, which showed culture positivity of 18 (42%). In our study three patients(9%) died during the period of study. The reported incidence of wound infection after renal transplantation has ranged from 2 % to 56%. The most important sources of infection are wound hematoma as secondary to inadequate haemostasis, urinary leaks and development of lymphocele.[20]Perioperative antibiotics are an important cornerstone in the prevention of wound infection in renal transplant recipients.The most common isolate is Staphylococcus aureus, but infections with Gram

Negative enteric Bacteria, Staphylococcus epidermidis, Candida spp and Mycoplasma hominis may also be seen[21].Among the fungal agents candida albicans remains the most common cause for wound infection followed by Aspergillus species.[22]

Blood stream infections are frequently associated with urinary tract infection, with a high prevalence of Gram Negative Bacilli. [23]E.coli was reported to be the most common organism causing post transplant BSI. In our study,staphylococcus aureus was isolated frequently. About 40% of the Gram Negative Bacilli were found to produce Extended Spectrum Beta Lactamase enzyme which confers resistance to most of the third generation cephalosporins.Similarly the Metallo Beta Lactamase production was 1% and Amp C beta Lactamase production was 6%.This stress upon the need for culture and sensitivity and switch over to appropriate narrow spectrum antibiotic for prolonged therapy[24].Among the staphyloccus species, Methicillin Resistance was found in 48% and one strain of S.aureus was found to be vancomycin resistant.

To conclude , the risk of infection in renal transplant is patient is determined by three factors: the presence of technical abnormalities,the epidemiological exposure that the patient experiences and the net state of immunosuppression. So the selection of antibiotics should be appropriate.The role of medical microbiologist is crucial and immense, to help the physician in diagnosing the cause of infection and to select the antimicrobial agents.

References

1.John GT. Infections after renal transplantation in India.Transplant Rev. 1999;13:183–91.

2.Peterson PK, Anderson RC.Infection in renal transplant recipients. Current approaches to diagnosis, therapy, and prevention. Am J Med. 1986 ;81:2-10.

3. Fishman JA: Infection in solid-organ transplant recipients.N Engl J Med .2007;357:2601–14.

4. Tolkoff-Rubin NE, Rubin RH: Opportunistic fungal and bacterial infection in the renal transplant recipient. J Am Soc Nephrol. 1992: S264–S269.

5. Abbott KC, Swanson SJ, Richter ER, Bohen EM, Agodoa LY, Peters TG, Barbour G, Lipnick R, Cruess DF: Late urinary tract infection after renal transplantation in the United States. Am J Kidney Dis.2004; 44: 353–62.

6. Snyder JJ, Israni AK, Peng Y, Zhang L, Simon TA, Kasiske BL: Rates of first infection following kidney transplant in the United States.Kidney Int.2009; 75: 317–26.

7. Rubin RH. Infectious disease complications of renal transplantation.Kidney Int. 1993; 44 : 221‑36.

8. Alangaden GJ, Thyagarajan R, Gruber SA, Morawski K, Garnick J, El‑Amm JM, *et al.* Infectious complications after kidney transplantation: Current epidemiology and associated risk factors. Clin Transplant.2006;20:401‑9.

9. Lorenz EC, Cosio FG: The impact of urinary tract infections in renal transplant recipients. Kidney Int 78: 719–721, 2010

10. Sriperumbuduri S,Kalidindi K,Guditi S,Taduri G.Declining trend of infections in renal transplant recipients in a tertiary care hospital from India.Indian J Transplant.2017;11:143-8.

11. Khanna P, Abraham G, Mohamed Ali AA, Miriam PE, Mathew M, Lalitha MK, *et al.* Urinary tract infections in the era of newer immunosuppressant agents: A tertiary care

center study. Saudi J Kidney Dis Transpl. 2010;21:876‑80.

12.Moradi M, Abbasi M, Moradi A, Boskabadi A, Jalali A: Effect of antibiotic therapy on asymptomatic

bacteriuria in kidney transplant recipients. Urol J .2005;2: 32–5.

13.Tolkoff-RubinNE, Cosimi AB, Russell PS, Rubin RH: A controlled study of trimethoprim-sulfamethoxazole prophylaxis of urinary tract infection in renal transplant recipients. Rev Infect Dis .1982;4: 614–8.

14.Rathnamalala NK. Urinary tract infection in the kidney allograft recipients. Saudi J Kidney Dis Transpl.2012;23:832‑3.

15.de Souza RM , Olsburgh J . Urinary tract infection in the renal transplant patient . *Nat Clin Pract* 2008 ; 4 :252 – 264 .

16 Pelle G , Vimont S , Levy PP *et al.* Acute pyelonephritis represents a risk factor impairing long-term kidney graft function . *Am J Transplant.*2007 ; **7** : 899 – 907 .

17. Hoyo I, Linares L, Cervera C, Almela M, Marcos MA, Sanclemente G, *et al.* Epidemiology of pneumonia in kidney transplantation. Transplant Proc. 2010;42:2938‑40.

18.Shirazi M, Ranjbar R, Hemati F, Sadeghifard N. Bacterial infections in renal transplant recipients. Iranian Journal of Public Health. 2005; 34:62–6.

19. Jayakumar M, Gopalakrishnan N, Vijayakumar R, Rajendran S, Muthusethupathi MA. Systemic fungalinfections in renal transplant recipients at Chennai, India. Transplant Proc. 1998;30:31-5.

20. Umesh L, Mahesh E, Kumar A, Punith K, Lalitha K, Suman G. Infections in renal transplant recipients. J Indian Acad Clin Med 2007;8:316‑23.

21. Ram R, Murty KV, Prased N. Time table of infections after renal transplantation – South Indian experience. Indian J Nephrol 2005;15 Suppl 2:S14‑21.

22.Pappas PG, Rex JH, Sobel JD, Filler SG, Dismukes WE,Walsh TJ, Edwards JE; Infectious Diseases Society of America: Guidelines for treatment of candidiasis. Clin Infect Dis . 2004; 38 : 161–89.

23. McClean K, Kneteman N, Taylor G. Comparative risk of bloodstream infection in organ transplant recipients. Infect Control Hosp Epidemiol.1994;15:582‑4.

24.Fishman JA, Rubin RH. Infection in organ-transplant recipients. N Engl J Med. 1998; 338:1741-51.

List of Table.

Table 1: Type of infection and specimen collected

Type Of Infection	Type of specimen for culture	No of samples	Culture positive
UTI	urine	140	62(44%)
RTI	Sputum/BAL	30	12(40%)
SSTI	Drain/pus	41	18(44%)
BSI	Blood	20	3(15%)

TABLE 2: Sensitivity and resistance pattern of urinary tract infection

	SENSITIVITY PATTERN						RESISTANCE PATTERN		
GRAM -VE	AMIKACIN	OFLOX	CEFOTOX	CS	COTRI	IMI	ESBL	MBL	AMPC
K.PNEUMONIAE(12)	7(58%)	6(50%)	4(33%)	11(92%)	-	12(100%)	8	-	1
K.OXYTOCA(7)	1(14%)	1(14%)	1(14%)	7(100%)	-	7(100%)	6	-	-
E.COLI(8)	6(75%)	6(75%)	6(75%)	8(100%)	-	8(100%)	2	-	-
P.MIRABILIS(6)	5(83%)	4(66%)	3(50%)	4(67%)	-	6(100%)	3	-	2
P.VULGARIS(2)	2(100%)	2(100%)	2(100%)	2(100%)	-	2(100%)	-	-	-
PSEUDOMONAS AERUGINOSA(8)	6(75%)	6(75%)	6(75%0	7(87%)	-	7(87%)	-	1	-
GRAM +VE	MSSA	MRSA	-	-	-	-	-	-	-
S.AUREUS(8)	5	3	-	-	5	-	-	-	-
S.SAPROPHYTICUS(2)	1	1	-	-	1	-	-	-	-
S.EPIDERMIDIS(1)	1	-	-	-	1	-	-	-	-
E.FECALIS(20	2	-	-	-	-	-	-	-	-

Table 3:Sensitivity and resistance pattern of respiratory tract infection isolates

	SENSITIVITY PATTERN							RESISTANCE PATTERN		
Organism	Amikacin	Oflox	Cefatoxime	CS	Penicillin	Cotri	Imipenem	ESBL	MBL	AMP C
K.pneumoniae (5)	4(80%)	-	3(60%)	3(100%)	-	4(80%)	5(100%)	**2(40%)**	-	**1(20%)**
K.oxytoca (1)	1(100%)	1(100%)	1(100%)	1(100%)	-	1(100%)	1(100%)	-	-	-
E.Coli (2)	2(100%)	2(100%)	2(100%)	2(100%)	-	2(100%)	2(100%)	-	-	-
Pseudomonas (1)	1(100%)	1(100%)	1(100%)	1(100%)	-	1(100%)	1(100%)	-	-	-
S.pneumonia (1) Optochin - S	-	-	-	-	1(100%)	-	-	-	-	-

TABLE 4: Sensitivity and resistance pattern of skin and soft tissue infection isolates

Sensitivity pattern								Resistance pattern		
Gram – ve organism	**Amikacin**	**Ofloxacin**	**Cefatoxim**	**CS**	**Penicillin**	**Cotri**	**Imipenem**	**ESBL**	**MBL**	**AMP C**
E.Coli (4)	2(50%)	2(50%)	2(50%)	4(100%)	-	-	4(100%)	2	-	-
C.freundii (1)	1(100%)	1(100%)	1(100%)	1(100%)	-	-	1(100%)	-	-	-
A.baumanii (1)	1(100%)	1(100%)	1(100%)	1(100%)	-	-	1(100%)	1	-	-
Proteus mirabilis(2)	1(50%)	1(50%)	1(50%)	2(100%)	-		2(100%)	1	-	-
Gram + ve								**MR**	**VR**	**-**
S.aureus (5)	4(100%)	-	4(100%)	-	4(100%)	4(100%)	-	1	1	-
S.epidermidis(1)	1(100%)	-	1(100%)	-	1(100%)	1(100%)	-	-	-	-

TABLE -5 Sensitivity and resistance pattern of isolates in blood stream infection/sepsis patients

SENSTIVITY PATTERN				RESISTANCE PATTERN		
Organism	**Amikacin**	**oflox**	**Cefatox**	**ESBL**	**MBL**	**AMP C**
Pseudomonas aerugenosa 1	1(100%)	1(100%)	1(100%)	-	-	-
S.aureus 2	1(50%)	1(50%)	2(100%)	-	-	-