Original Research Article

Microbiological profile of transplant recipients in a tertiary care hospital in South India

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Abstract

Introduction: Infections are the leading cause of morbidity and mortality in transplant recipients. Advances in transplantation biology, organ procurement, surgical techniques, and immunosuppressive therapy have made organ transplantation an effective option for the management of organ failure, with a 1-year survival >60%-80%. However, infection remains one of the most challenging complications of transplantation**. Materials & Methods**: A total of 1156 clinical specimens from 300 patients who under-went solid organ (renal, liver, heart) & HSCT at Nizams Institute of Medical Sciences over a period of one year were included in the study. The specimens were investigated for microbiological staining, culture, antimicrobial susceptibility testing (AST) and Galactomannan (GM). Samples were processed as per the standard procedures. **Results:** Of the 1156 specimens received from Solid Organ Transplant/ Haematopoietic Stem Cell Transplant recipients, the majority were fromRenal transplant recipients (n= 1107, 95.76%) followed by HSCT (n=38, 3.28%). The rest were from recipients of liver (n=8), heart (n= 2) and heart- lung (n=1). About 63 showed growth on bacterial or fungal culture. **SOT** - 60 were culture positive, all were from renal transplant recipients. Most were UTI (n= 32, 53.3%) followed by Blood Stream Infection (n= 13, 21.6%). The other infections seen were pneumonia, wound infection.Of the bacterial isolates (n=49) gram negative- 40 (81.6%) gram positive- 9 (18.4%). *E.coli* was the predominant isolate (21, 52.5%). Drug resistance was seen in 19 isolates (38.77%), of which 6 were ESBL (31.5%), 13 multi drug resistant (68.4%). Mycobacteria- detected in 9 (n= 52 samples) of which 8 showed *M. tuberculosis* and one *M. abscessus*. MDRTB detected in 1 case. 9 patients were diagnosed with Probable Invasive Aspergillosis. *Candida parapsilosis reported* from a patient with sepsis.GMS stain showed *P. carinii* in one patient. **HSCT**-3 bacterial isolates were reported of which one strain was resistant to carbapenems. One Probable case of Invasive Aspergillosis reported. **Conclusion**: Urinary tract infections were predominant with most isolates multi drug resistance. Infection control measures should be used to decrease the incidence and bacterial resistance of infections.

Keywords: Solid organ, Haematopoieticstem cell, Transplant, Infections, Resistance

Introduction

Organ transplantation was made an effective option for the management of organ failure with advances intransplantation biology, organ procurement, surgical techniques, and immunosuppressive therapy, with a 1-year survival >60%-80%. However, infection remains one of the most challenging complications of solid organ transplantation [1,2]. Infections are a common cause of morbidity and mortality after transplantation, and infections rank second as the cause of death in patients with allograft function [3].

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Infections after transplantation are influenced by the level of immunosuppression. Therefore, infectious agents and their distribution vary with respect to the period after transplantation. In the first month-the perioperative period-wound, pulmonary, and urinary tract bacterial infections are more likely to occur [4].

The greatest risk for life-threatening infection occurs between 1- and 6-months post transplantation because of the peak anti-rejection immunosuppressive therapy [4]. This study was done to knowthe spectrum of bacterial, mycobacterial and fungal infections in recipients of Solid organ Transplant (SOT) and

Haematopoietic Stem cell transplant (HSCT) and to assess the antimicrobial susceptibility profile of the bacterial isolates.

Materials & Methods

A total of 1156 clinical samples received in the Microbiology over a period of one year from January 2017 to December 2017 were included in the study. These samples were received from 300 patients who underwent SOT (renal, liver, heart) & HSCT at Nizam's Institute of Medical Sciences.

Institutional ethical committee clearance was taken. An informed consent was obtained from all the subjects. The specimens were investigated for –

Bacterial– All the samples were subjected to Gram stain, aerobic culture on blood agar, chrome agar (Biomeriux). All the isolates were identified by Vitek 2 IDGN, IDGP and antimicrobial susceptibility was performed by Vitek2 N280, N281 for gram negative bacteria and P628 for Gram Positive bacteria.

Fungal- All the samples were subjected to KOH mount, Calcoflour mount, Gomori Methanamine Silver (GMS) culture was performed on SDA, blood agar. All the yeasts were identified by Vitek 2 IDY and antifungal susceptibility was performed by Vitek2 YST. All the serum and bronchial wash specimens were subjected to galactomannan.

Mycobacterial- All the samples were subjected to auramine rhodamine stain, culture (Bac T ALERT, Solid culture- LJ), Gene Xpert. All the positive flagged MP bottles were identified by acid fast stain. Further characterization was done by MPT 64 Ag and biochemical tests. Samples were processed as per the standard procedures [5].

Statistical analysis- Values were expressed as the mean (standard deviation) or median (interquartile range) for continuous variables depending on the distribution or as a mean (percent) for binary variables. The variables between groups were comparedusing the Student's t-test, chi-square, tests as appropriate. All data were analyzed using MS EXCEL 2007 (Microsoft).

Results

Of the 1156 specimens received from SOT/HSCT recipients during the study period, the majority were from Renal transplant recipients (n= 1107, 95.76%) followed by HSCT (n=38, 3.28%) (Table1). About 63 showed growth on bacterial, Mycobacterial or Fungal culture.

Table-1: Distribution of clinical samples.

test	Renal		BMT		liver	heart
	Number	positives	Number	positives		
Blood culture	250	13	25	3	3	1
exudates	296	4	7	0	1	0
urine	456	32	3	0	3	1
BW- fungalculture	27	2	2	0	1	0
BW & serumGAL	27	9	1	1	0	0
BW,sputum-TB culture	51	9	0	0	1	0
total	1107	69	38	4	9	2

Note: BMT- Bone marrow transplant, BW- Bronchial wash

SOT

About 60 culture positives were reported from renal transplant cases. Most common infections were UTI (32, 53.3%) followed by BSI (n=13, 21.6%). The other infections seen were pneumonia, wound infection. Of the bacterial isolates (n=49), Gram negative – 40 (81.6% & Gram positive – 9(18.4%). *E.coli* was the predominant gram-negative isolate (21, 52.5%) followed by *Klebsiell*a (10, 25%). *E.faecium* was the predominant among gram positives. Most of the renal transplant were early infections. Both cadaveric and live donors were in equal proportion. All were subjected to triple immunosuppression with tacrolimus, mycophenolate and steroids.

Drug resistance was seen in 19 isolates (31.7%) of which 13 were ESBL producers(21.6%) & 6 carbapenem resistant (10%). All ESBL were reported in *E.coli*. Among the carbapenem resistant strains,Enterobacteriaceae producers were 11(84.6%) of which *Klebsiell*a was the predominant resistant strain.

Mycobacteria - was detected in 9 (17.3%, n= 52 samples) of which 8 showed *M. tuberculosis (15.3%)* and one *M. abscessus* (2%). Multi drug resistant TB (MDRTB) was detected in 1 case.

Fungal– based on growth of *Aspergillus* in culture &/ positive galactomannan test, 9 were (33.3%, n=27) diagnosed with probable invasive aspergillosis as per EORTC criteria. Blood culture showed growth of *C. parapsilosis* from a patient with sepsis. GMS stain showed *P. carinii* in one patient.

HSCT

3 bacterial isolates (Enterobacter, Pseudomonas, Staphylococcus haemolyticus) were reported of which Enterobacter was resistant to carbapenems and one probable case of invasive aspergillosis was reported

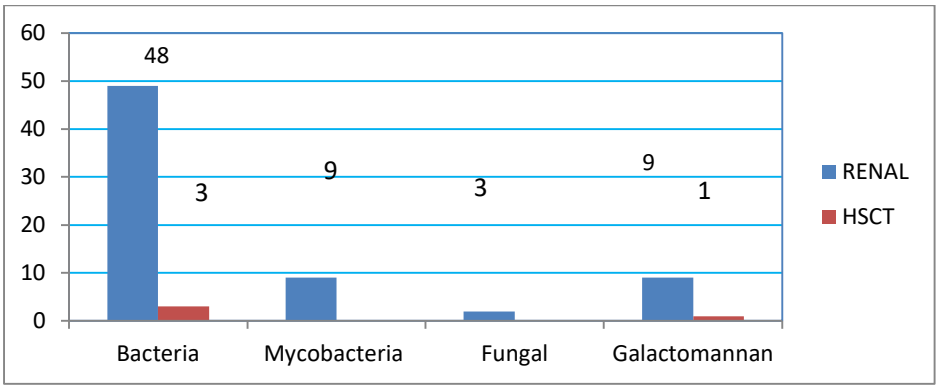

Fig-1: Microbiological profile in transplant patients

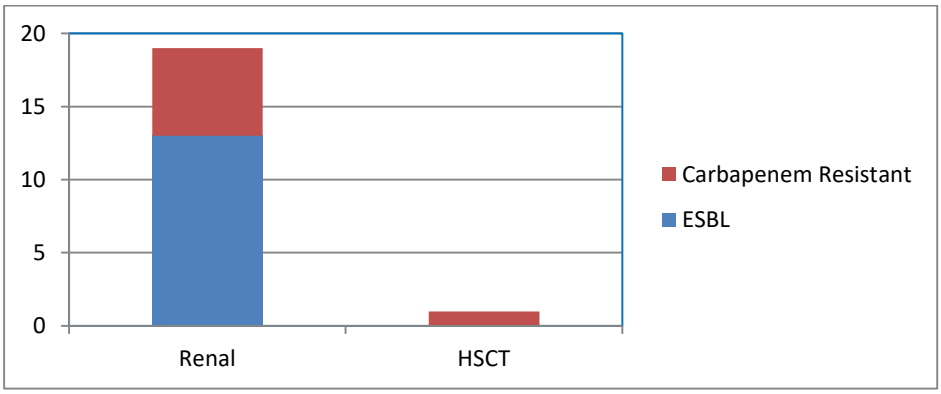

Fig-2: Drug resistance pattern of Gram negative isolates

Discussion

The factors whichinfluence the development of infection in transplant patients are postoperative medical care, immunosuppressive status, epidemiologic contact, hygienic conditions, and socio-economic factors [6]. Several studies have reported post transplantation infections incidences ranging from 49% to 81% [7-9]. The difference in incidences and infection patterns may be due to environmental, social, and economic factors [7]. While in developing countries the greater infectious complications might be due to lower standards of hygiene and Epidemiological exposure [2,10]. The incidence of infection has recently decreased because of improvements in surgical technique and in immunosuppressive regimens [2,10].

Urinary tract infections are the most common infections which range from 35% -79% in frequency [7,9]. In our study, urinary tract infections were reported in 53.3% of renal transplant patients. *E.coli* (52.5%), *Klebsiella* spp. (25%) were the most commonly isolated micro-organisms. Studies performed by Oguz et al, Senger et al, also reported *E. coli* to be the most common agent [11,12]. Whereas, Alangaden et al found *Enterococcus* spp; and Pourmand et al, *Klebsiella* spp as the most common urinary pathogens with increased antibiotic resistance [2,7]. In our study, 31.5% of our *E. coli*. isolates produced ESBL, while it was 53% in study conducted by O.A Ketal [13]. In our study 68.4% of the strains were multi drug resistant. All isolates were

consistently susceptible to amikacin. The prevailing problem in kidney transplant recipients are infections [14]. About, 80% of patients suffer froma bacterial infection in the first year after transplantation. Immunosuppressive therapy, necessary to avoid acute and chronic rejection, exposes patients to a higher rate of infectious complications [15]. Bacterial infections constitute 47% of all infections in renal transplant recipients and, according to Snydman, in the first month after transplantation they are related to surgical complications, and include wound infections, UTI, pneumonia, IV catheter sepsis, Clostridumdifficile, and others [16,17]. Many authors observed that UTI are the most frequent infection after renal transplantation, and may be followed by bloodstream infections, which are reported to worsen graft function and shorten patients' survival [18].

In our study Mycobacteria was detected in 17.3% of cases; Mycobacterial diseases are serious infections, especially in developing countries. Its incidence varies widelyfrom less than 1% in the United States to 15% in India [7,19]. M. tuberculosis was detected in 15.38% cases while M. abscessus in 2% of cases. MDRTB was detected in one case. TB has been transmitted through kidney, lung, and liver grafts [20]. Latent infection with M. tuberculosis in the donor could be reactivated in the transplant recipient. Therefore, all living donors should undergo PPD skin testing. If the result is positive, active TB should be ruled out [21]. The situations are more complex in cadaveric donors, because there is often not enough information to rule out the existence of latent TB infection or active TB. Therefore, in principle, not only active TB, but also a well-founded suspicion of it should contraindicate SOT [21].

Biopsy samples must be obtained, and cultures must be performed at the time of transplantation to rule out active TB in the donor. *M. abscessus*, a ubiquitous potential opportunistic microorganism, is resistant to chlorine, disinfectants, classic anti-tuberculosis drugs, and many other antibiotics. It can colonize organic surfaces and is especially pathogenic inimmuno-suppressed patients [22]. There is no efficient prophylaxis for this disease, so early diagnosis and oriented therapy is important.

In our study probable invasive aspergillosis were reported in 9 renal transplant cases and one HSCT case. Hamanandi et al reported 41(8.4%) fungal strains out of which Candida and Aspergillus were the most common ones isolated [23]. Troullihet et al reported fungal infections in 13% of cases, three episodes caused by Candida albicans (two urinary infections and one intrabdominal) and two invasive aspergillosis [24].

The symptoms of systemic fungal infections are non-specific and early detection of fungal infections and proper therapy are important in improving survival and reducing mortality. Preventive measures should be taken using sensitive assays (e.g. antigen detection and molecular assays) to monitor patients at given interval and stop progression to invasive disease. A positive assay will require initiation of therapy and reduction in the anti-suppression medication, with frequent monitoring of the patient [25].

Conclusion

Urinary tract infections were predominant with most isolates resistant to extended spectrum antibiotics. Bacteria are accountable for majority of infections, especially the MDR Gram-negative Enterobacteriaceae. Infection control measures should be used to decrease the incidence and bacterial resistance of infections. There is a need for proper surveillance to detect these infections early and institute appropriatemeasures to avoid complications and mortality.

Findings: Nil; **Conflict of Interest**: None initiated
Permission from IRB: Yes

References

1. Russell DL, Flood A, Zaroda TE, et al. Outcomes of colonization with MRSA and VRE among liver transplant candidates and recipients. Am J Transplant. 2008Aug;8(8):1737-43. doi:10.1111/j.1600-6143. 2008. 02304.x.Epub 2008 Jun 28.

2. Moreno A, Cervera C, Gavaldá J, et al. Bloodstream infections among transplant recipients: results of a nationwide surveillance in Spain. Am J Transplant. 2007 Nov;7(11):2579-86. Epub 2007 Sep 14.

3. Ko KS, Cho DO, Ahn JH, Lee TW, Ihm CG, Chang SG, Chai SE, Park HC, Hong SH, Joo HZ, et al: Infections after renal transplantation. Transplant Proc 1994;26: 2072–2074

4. Charfeddine K, Zaghden S, Kharrat M, Kamoun K, Jarraya F, Hachicha J. Infectious complications in kidney transplant recipients: a single center experience. *Transplant Proc.* 2005;37:2823– 2825.

5. Collee JG, Miles RB, Watt B. Mackie and McCartney Practical Medical Microbiology. 14th ed. Churchill Livingstone; 1996. Test for identification of bacteria. In: Collee JG, Fraser AG, Marimion BP, Simmons A, editors; pp. 131–49. (reprinted 2008)

6. Splendiani G, Cipriani S, Tisone G, Iorio B, Condo S, VegaA, et al. Infectious complications in renal transplant recipients. Transplant Proc. 2005;37(6): 2497–2499.

7. Pourmand G, Salem S, Mehrsai A, et al. Infectious complications after kidney transplantation: a single-center experience. Transpl Infect Dis. 2007 Dec; 9 (4): 302-9. Epub 2007 May 19.

8. Maraha B, Bonten H, van Hooff H, et al. Infectious complications and antibiotic use in renal transplant recipients during a 1-year follow-up. Clin Microbiol Infect. 2001 Nov;7(11):619-25.

9. Ferraresso M, Berardinelli L. Nosocomial infection in kidney transplant recipients: a retrospective analysis of a single-center experience. Transplant Proc. 2005 Jul-Aug; 37(6): 2495-6. DOI:10.1016/j.transproceed. 2005. 06.029

10. Fishman JA, Issa NC. Infection in organ transplantation: risk factors and evolving patterns of infection. Infect Dis Clin North Am. 2010 Jun; 24 (2): 273-83. doi: 10.1016/j.idc.2010.01.005.

11. Oguz Y, Doganci L, Bulucu F, et al. Acute pyelonephritis causing acute renal allograft dysfunction. Int Urol Nephrol. 2002;34(3):299-301.

12. Senger SS, Arslan H, Azap OK, Timurkaynak F, Çag˘irÜ, Haberal M. Urinary tract Infections in renal transplant recipients. Transplant Proc. 2007; 39 (4): 1016 –1017.

13. Ak O, Yildirim M, Kucuk HF, et al. Infections in renal transplant patients: risk factors and infectious agents. Transplant Proc. 2013 Apr; 45 (3):944-8. doi: 10.1016/j.transproceed.2013.02.080.

14. Berry CL. Transplantation pathology. New york city: Springer science and business media; 1999;19-31

15. Veroux M, Giuffrida G, Corona D, et al. Infective complications in renal allograft recipients: epidemiology and outcome. Transplant Proc. 2008 Jul-Aug; 40(6):1873-6.doi:10.1016/j.transproceed. 2008. 05.065.

16. Patel R, Paya CV. Infections in solid-organ transplant recipients. Clin Microbiol Rev. 1997 Jan;10 (1): 86-124.

17. Snydman DR. Epidemiology of infections after solid-organ transplantation. Clin Infect Dis. 2001 Jul 1;33 Suppl 1:S5-8. DOI:10.1086/320897

18. Daskalaki E, Koukoulaki M, Bakalis A, et al. Blood stream infections in renal transplant recipients: a single-center study. Transplant Proc. 2014 Nov;46(9):3191-3. doi: 10.1016/j.transproceed.2014.10.033.

19. Singh N, Paterson DL. Mycobacterium tuberculosis infection in solid-organ transplant recipients: impact and implications for management. Clin Infect Dis. 1998 Nov; 27(5):1266-77.

20. Kiuchi T, Inomata Y, Uemoto SA, et al. Hepatic graft tuberculosis transmitted from a living-related donor. Transplantation 1997; 63: 905-7.

21. Allen U, Green M. Prevention and treatment of infectious complications after solid organ transplant-tation in children. Pediatr Clin North Am. 2010 Apr; 57(2):459-79, table of contents. doi: 10. 1016/j. pcl. 2010.01.005.

22. Falkinham JO 3rd. Nontuberculous mycobacteria in the environment.Clin Chest Med.2002Sep;23(3):529-51

23. Bassem Hamandi, Shahid Husain, Paul Grootendorst, Emmanuel A. Papadimitropoulos. Clinical and microbiological epidemiology of early and late infectious complications among solid organ transplant recipients requiring hospitalization. Transplant International 2016;29(9):1029-1038

24. Isabel Trouillhet, Natividad Benito, Mari´a Angeles Marcos, Carlos Cervera, Federico Oppenheimer, Paula Rivas, Jorge Puig de la Bellacasa, FedericoCofa´n, Toma´s Pumarola and Asuncio´n Moreno-Camacho. Influence of Age in Renal Transplant Infections: Cases and ControlsStudy.Transplantation.2005;80(7):989-992

25. Khan A, El-Charabaty E, El-Sayegh S. Fungal infections in renal transplant patients. J Clin Med Res. 2015 Jun;7(6):371-8. doi: 10.14740/jocmr2104w. Epub 2015 Apr 8.

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