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 from Renal 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, Haematopoietic stem cell, Transplant, Infections, Resistance

Introduction

Organ transplantation was made an effective option for the management of organ failure with advances in transplantation 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].

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 know the 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 Vitek 2 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 compared using 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 positives | BMT positives | liver | heart |
|--------------------------|-----------------|---------------|-------|-------|
| Blood culture            | 250             | 25            | 3     | 1     |
| exudates                 | 296             | 7             | 0     | 0     |
| urine                    | 456             | 3             | 0     | 3     |
| BW- fungal culture       | 27              | 2             | 0     | 1     |
| BW & serumGAL           | 27              | 1             | 0     | 0     |
| BW,sputum-TB culture    | 51              | 0             | 0     | 1     |
| total                    | 1107            | 38            | 4     | 9     |

**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 Klebsiella (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 Klebsiella 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.

**Discussion**

The factors which influence 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 microorganisms. 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 from 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 Snyderman, in the first month after transplantation they are related to surgical complications, and include wound infections, UTI, pneumonia, IV catheter sepsis, Clostridium difficile, 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 widely from 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 in immunosuppressed 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]. Trouilliet 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.

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Permission from IRB: Yes

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