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Early post-transplant urinary tract infection epidemiology and risk factor

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Abstract

Background and objectives: Renal Transplantation became the most successful management for end stage renal failure; postoperative urinary tract infection is the most common complication. The aim is to evaluate the outcome and risk factors of posttransplant urinary tract infection.

Methods: This is a prospective study for renal transplant patients between 2018-2019 in Hawler/ Rizgary and Paky hospital. Patients, who underwent renal transplant, with 1 year follow up. Variable risk factors assessment done including chronic renal failure etiology, preoperative dialysis duration, operation time, length of drain and Foley's catheter, type of immune suppressive therapy used, time and numbers of hospitalization associated with posttransplant urinary tract infection were examined, the relation between the risk factors and urinary tract infection was evaluated.

Results: Total of 63 patients was involved, 12 had a total of 24 urinary tract infection attacks; the most common isolated microorganisms were E-coli and Klepsiella. The infection frequently appeared during the first 120 days postoperatively. Among the analyzed variables, there was no significant difference. Assessing all the variables, number of hospitalization after discharge were significantly more frequent in the 12 patients with infection attacks, although 31 patients out of 63 had hospitalized, as compared to patients without infection, but this difference was statistically insignificant.

Conclusions: The most significant period for infection in renal transplanted patients after 1 year follow up is the first 4 months postoperatively. Patients who were admitted to hospital for different reasons and those who had preoperative history of urinary tract infection, have a higher risk.

Key words: Renal Transplant; Risk factors; Urinary tract infection.

Introduction

Chronic kidney disease has increased in prevalence and those patients will eventually inter to end stage renal failure and will be in need of renal replacement therapy. Lately in selected renal failure patients, renal transplant has become the most successful therapy reaching 75% success rate; in the first year post transplant urinary tract infection is a common complication. In this urinary tract infection; although viral infection is encountered but bacterial infection is the most common and frequent among them especially the first 4 months postoperatively, 1 out of 3 patients will have

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attacks of urinary tract infection. Post renal transplant urinary tract infection is common, despite immune suppressive drugs dose manipulation and prophylactic antibiotics use, still there is 35-80 % bacteruria. Infections seen in the post-transplant are examined and classified according to specific periods; 1 month, 1 to 6 months, after 6 months post-operative[1-6]. Recipient patients in the post-transplant first month period 95% will have the same risk as normal immune competent patients regarding urinary tract infection, catheter related infection, wound infection and pulmonary infections. Although the perioperative antibiotic therapy is important factor but still the surgical technique and close post-operative follow up is the most crucial factor in preventing any infection[1-3,6]. In the first month period despite high dose of immunosuppressive therapy;opportunistic infection is rare. In this period the most common infections are viral and opportunistic infections. Viral infection causes immune modulation resulting in higher risk for opportunistic infections. The most common inciting agents in this period are CMV, EBV, HHV-6, HBV, HCV and HIV, CMV has 2-3 times more febrile attacks. Pneumocystis carinii, Listeria monocytogenes and Aspergillus spp are the most common opportunistic infection. After 6 months of the renal transplant in 80 % of the patients who had serum creatinine below 1.7 mg/dl, the most common infections in this period are community acquired, such as influenza, parainfluenza, RSV like respiratory infections. Chronic hepatitis with HBV and HCV was found in 10% of patients, and the other 10% patients had high dose immunosuppressive drug administratio n caused by transplant failure and graft rejection resulting in multi viral infection. In these patients; opportunistic infection mostly caused by with Pneumocystis carini, Cryptococcus neoformans, Nocardia asteroids, Listeria monocytogenes, Aspergillus spp and other fungi infections. If this happened; the immunosuppressive medication doses should be lowered and in some circumstance cessation of the drugs should be offered and before sending the patients to dialysis,Trimethoprim/sulfameth oxazole TMP-SMX should be started with antifungal fluconazole for long period[1,3-4,6].The most important goal in post-renal transplant cases is to prevent graft rejection. Currently; available immunosuppressive agents can be classified into three categories: “induction agents”, “maintenance therapy” and “treatment for rejection. The standard immune suppressive drugs given in a renal transplant patient are; Calcineurin inhibitors (cyclosporine and tacrolimus), antiproliferative agents (azathioprine and Mycophenolate sodium, Mycophenolate mofetil), corticosteroids (Prednisone and Methylprednisolone) and Induction agents (basiliximab, anti-thymocyte globulin and alemtuzumab). The aim of our study is to determine the infection ingredients and risk factors of urinary tract infections after renal transplantation at the patients in our department.

Materials and methods

This study was conducted as a prospective study for renal transplant patients between 2018 -2019 in hawler/ rizgary and paky hospital. Total of 63 patients, who underwent renal transplant, with 1 year follow up were included. During clinical and outpatient follow-up of patients, fever, malaise, uremia, dysuria, infection symptoms such as elevated white blood cell, clinical findings, and laboratory findings including urine, blood, and when necessary sputum, abscess and drain cultures were

studied. Patients, who were examined and had positive culture results, were considered to have had an infection attack.Serum biochemical parameters, blood drug level, hematological tests were routinely done in these patients. In all these patients' chronic renal failure etiology, type and duration of dialysis were evaluated. Donor's kidney cold ischemic time duration, drain, catheter, double J stent duration and postoperative hospital stay duration were also evaluated. All patients have been followed up for 1 year, during this period blood transfusion, hospital re-admission number and durations and graft rejection, with immunosuppressive drugs were recorded. All patients received intravenous Ceftriaxone 500 mg, postoperatively for 5 days. All preoperative and 1st month postoperative investigations, fasting blood sugar, serum blood urea nitrogen, serum creatinine, sodium, potassium, calcium, phosphate, alanine transaminase ALT, aspartate transaminase AST, hematological investigations were done and documented. Blood samples taken from patients were sent for culture in MacConcey agar and chocolate agar; urine samples cultured in McConcey agar and EMB (eosin methylene blue) medium; abscess samples were cultured by planting in thioglycolate medium. For statistical analysis of the data SPSS 25.0 package program was used. In Categorical measurements numbers and percentages are used, and in continuous measurements average and standard deviation are used, and if required (median and minimum - maximum) are used in some places. Chi-square statistics test were used for comparison between categorical measurements groups. Between continuous measurements groups in comparison T test were used, if the assumptions criteria are not met, Mann Whitney U test was used. In dependent groups in comparing the measurements before and after the operation T test or alternative Wilcoxon Signed Rank test was used. In all tests, the statistical significance level was 0.05.

Results

In this study 63 transplant patients were selected, 40 forty (63.5 %) were male patients with median age 36 years old (19-67). Patients other demographic data explained below in Table (1).

Table (1): Patients demographic data .

Data	Patients Number 63 (100%)
Gender	
Male	40 (63.5%)
Female	23 (36.5%)
Preoperative dialysis	
Hemodialysis	53 (84.1%)
Peritoneal dialysis	10 (15.9%)
CRF etiology	
Unknown	36 (57.1%)
Hypertension	14 (22.2)

Polycystic kidney disease	2 (3.2%)
Renal stone	4 (6.3%)
Sickle cell anemia	1 (1.6%)
Amyloidosis	1 (1.6)
Gout	2 (3.2%)
Membranoproliferative glumeriolonephrits	3 (4.8%)
Concomitant disease	
Diabetes mellitus	5 (7.9%)
Hypertension	32 (50.8%)
Gout	2 (3.2%)
Asthma	2 (3.2%)
Anemia	3 (4.8%)

Data	**Patients Number 63 (100%)**
Immunosuppressive Drugs	
Prednisolone (solumedrol®)	63 (100%)
Mycophenolic acid (myfortic®)	48 (76.2%)
Cyclosporine (sandimmune®)	2 (3.2%)
Tacrolimus (prograf®)	52 (82.5%)
Mycophenolate mofetil (cellcept®)	4 (6.3%)
Basiliximab (simulect®)	51 (81%)
Antithymocyte globulin-rabbit (thymoglobulin®)	20 (31.7%)
Azathioprine (Imuran®)	2 (3.2%)
Everolimus	2 (3.2%)
Sirolimus, Rapamycine	1 (1.6%)
Transfusion	
Blood Transfusion	36 (57.1%)
Plasma Transfusion	2 (3.2 %)
Hospitalization*	**31 (49.2 %)**
Rejection	
Acute	7 (11.1 %)
Chronic	3 (4.8%)

*Total number of patient's hospitalization after transplantation and discharge number.

Postoperatively; 12 (19%) of transplant patients during follow up in the first year developed urinary tract infection. A total of 24 urinary infection attacks developed in 12 patients with culture positive, seven patients had one attack of urinary tract infection, while the other five patients had at least two attacks. The most frequently isolated microorganisms are found to be E. coli and K. pneumonia. The most common time interval for infections in post-transplantation patients was determined as the first 120 days. Microbiological data of the patients are presented in Table (2).

Table (2): Evaluation of infection attacks

data	Number (n=63)	Percentage (100 %)
Culture positive	12	19 %
Infection attacks	24	
Single attack	7	11.1 %
Multiple attacks	5	7.9 %
2 attacks	1	1.6 %
3 attacks	1	1.6 %
4 attacks	3	4.7 %
Cultured Microorganism		
E. coli	7	29.1 %
K. pneumonia	6	25 %
Citrobacter freundii	4	16.6 %
Actinobacter baumanni	4	16.6 %
E. faecalis	2	8.3 %
S. epidermidis	1	4.1 %
Culture sites		
Urine	17	70.8 %
Urine and Blood*	5	20.8 %
Abscess	1	4.1 %
Drain	1	4.1 %
Culture Day (time)		
Day 0-15	1	4.1 %
Day 16-30	6	25 %
Day 31-60	3	12.5 %
Day 61-90	4	16.6 %
Day 91-120	7	29.1 %
Day 121-180	1	4.1 %
Day 181-240	1	4.1 %
Day 241-360	1	4.1 %

*No patients with only blood culture growth ,When comparing the number of hospitalizations developed in the first year after transplantation in both patients with and without infection, although statistically it was not significant, but still higher in patients with infection.

Discussion

Most of the studies which were based on monitoring the recipient's postoperative period showed that urinary tract infection attacks are observed more frequently in the

first six months. In our study; 1 year follow up for the recipients showed that postoperative urinary tract infection was observed in 25% of cases between days 15 and 30, and 29% of cases between days 90 and 120.When evaluating the gender as a risk factor for infection in recipient's, our study on post-transplant infection showed that in the first six 6 months post- transplant period; male and female recipients had the same risk, but when the follow up period extended to 3 years, the female patients had 60% risk rate compared to male's 47% risk rate for urinary tract infection[7]. In our study male had 20% and female had 17.4% rate of infection in the first postoperative year of follow up which was of no statistical significance.A retrospective study done by Jevnikar showed preoperative hemodialysis, female gender and use of JJ stent to be a risk factor for urinary tract infection[8]. In our study there was no significant statistical difference between the recipients with or without urinary tract infection in regard to catheter duration, transfusion, rejection and chronic renal failure etiology.Although immunosuppressive drugs are very important and crucial for graft compatibility, they are frequently evaluated in terms of their relationship with infections seen in transplant recipients. A study by Halloran on azathioprine, mycophenolate mofetil, tacrolimus, cyclosporine and induction therapy in renal transplant patients, had no risk for postoperative urinary tract infection, Halloran found that the the isolated microorganisms were Escherichia coli (59.1%), Klebsiella spp (16.9%), Enterococcus spp (6.5%), Enterobacter spp (6.5%), Pseudomonas aeruginosa (4.0%), Proteus spp (4.0%), Citrobacter spp (0.8%), Acinetobacter baumonnii (0.8%), Staphylococcus spp (1.6%) and Serratia marcescens (0.8%) in urine culture[9]. In our study, gram positive bacteria were seen in only three of 24 attacks, our results were similar to other studies; as we found E. coli was the most frequently detected microorganism with a rate of 29.1%, followed by Klebsiella pneumonia (25%), Citrobacter freundii (16.6%) and Acinetobacter baumannii (16.6%). In our study Citrobacter freundii was higher when compared to other studies, while staphylococci were less frequently isolated. In our study; when infection attacks were evaluated, 12 patients had urinary tract infection with total of 24 attacks, seven of these patients had a single attack and three of them had four attacks. In a retrospective study over 136 recipients, 55 patients had urinary tract infection, 22 patients had single attach, 14 patients had 2 attacks, 7 patients had 3 attacks, 7 patients had 4 and 5 patients had 5 attacks[9]. These findings are compatible with the finding in our study. When looking at the active inciting microorganisms, in almost all the studies reviewed; the most common was Escherichia coli. In another study with three-year follow-up of post-transplant patients with and without urinary tract infection, there was no significant difference in graft and patient survival rate. Also in this study, patients who developed graft failure within the first six months and a year were individually compared, no difference was observed in terms of urinary tract infection in patients who developed graft failure within the first six months and within the first 12 months[9]. In our study, urinary tract infection was not detected in any patients with acute rejection (11%), and in the three patients with chronic graft rejection (4.7%) only one patient had urinary tract infection.In our study, we found that the frequency of re-hospitalization after being discharged was higher, though statistically not significant (p =0,052), in patients who developed urinary tract infections during follow-up when compared with those who did not have infection.Ureteric stent in renal

transplant recipient was used to decrease the early postoperative complications, but it is thought to increase the risk of urinary tract infection. Ranganathan et al in their study by examining 100 post-transplant patients, ureteric stent was used in 79 patients and compared with 18 patients where ureteric catheter was not used, during follow up the rate of infection was 71% in stent used group while the rate was 39% in stentless group (p value =0.02), also when the stent was removed and follow up was continued; it was showed that the risk of infection was still higher than the other group, even when the stent was removed for 46 patients who had infection attacks, 25 patients of them (54%) had other attacks of urinary tract infection. Also patients with stent who had no infection and after stent removal; 30% had urinary tract infection after removal[10]. In our transplant center JJ stent are used routinely, and when comparing recipients with JJ stent who had infection attacks and those who had no urinary tract infection, no significant difference has been found. In all patients the ureteric stent followed up and removed after 1 month. In our study; in renal transplant recipients who developed urinary tract infections had no effect on patient and on graft survivors.The use of immunosuppressive therapy in the early postoperative period; most of the urinary tract infection needed hospitalization and parenteral treatment. Hospitalization for whatever reason results in psychological problems in the transplant patients and increases the risk of hospital acquired infections and significantly affects the cost of treatment. Especially in risky patients, prophylactic antibiotic therapy and immunosuppressant in the early postoperative period care must be taken for carefully drug regulation.

Conclusion

Post-renal transplant recipients have most of urinary tract infection in the first four months in the postoperative period. The most common isolated microorganisms in the recipients with urinary tract infection in the first year of post-transplant period were Escherichia coli. Urinary tract infection has no effect on transplant patients and graft survival.

Conflict of interests

There were no conflicts of interest.

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