

RTP1. Our experience in kidney transplantation

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Aim: Prospective study of kidney transplantation

Materials and methods: Total of 38 Live related kidney transplantation cases were included. Variables like age, gender of donor, recipients, immunosuppressants details, time duration therapeutic CNI level attained and RFT normalization, graft biopsy details, post transplant complications including mortality were analyzed.

Results: Among 38 patients, 28 were female donors, triple immunosuppressants comprised of Tacrolimus, MNa, Prednisolone, 3 were HCV positive pretransplant, 1 became HCV positive post-transplant, CMV status was D+/R+, except one who had D-/R-, 2 received induction agents (basiliximab 20mg on D0,4), 5 required diltiazem and 1 required ketoconazole to enhance tacrolimus trough level, 1 needed conversion from tacrolimus to everolimus due to CAN, mean duration required to attain therapeutic CNI level was 4-5 days, mean duration required for RFT normalization was 7 days, 12 required graft biopsy among which ATN (11 cases) was most common finding, 5 patients had surgical complications like ureter necrosis, lymphocele, wound dehiscence, bleeding from native nephrectomy site done for ADPKD, 2 had CMV infection, 2 had NODAT, 1 had rifampicin induced optic atrophy, 9 patients expired due to aspiration, disseminated tuberculosis, dengue shock syndrome, CMV/GIT perforation, CAN after self cessation of immunosuppressants, Pericardial effusion and among them 4 died with functioning graft.

Conclusion: Mortality was 23%, graft biopsy was done in 31%, ATN was most common finding in 91%, followed by ACR, surgical complications were noted in 20%.

RTP2. Severe factor VII deficiency and venous thrombosis in renal transplant Rare case report

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Introduction:

Factor VII is the most common autosomal recessively inherited clotting factor deficiency (0.5–1%) which is phenotypically pleomorphic. Few patients are asymptomatic throughout their lives and while some can present with life threatening bleeding manifestation. We discuss a ESKD case with severe factor VII deficiency and venous thrombosis, who underwent live renal transplant.

Case report:

38 year old man on hemodialysis with hearing and speech difficulty from young age, hypertension and high myopia presented for live related transplant. Alports syndrome was phenotypically ruled out. He was on hemodialysis for last one and half years. He had prolonged PT (27.3 sec) and INR=2.5, with normal APTT (33.5 sec). He denied history of neither bleeding after trauma including surgery (AV fistula surgery) nor spontaneous bleeding. Surprisingly he had thrombosis of right IJV post HD catheter insertion one and half year ago. Mixing study showed correction of PT and INR with addition of normal human plasma. On factor assay was found to have severe deficiency of factor VII (<1%) and normal level of all the other factors. Platelet functional analysis was normal. Rotational thromboelastometry analysis was done and showed patient having a tendency of hypercoagulability in spite of severe factor VII deficiency. His family was screened for similar disorders. While his elder brother has history of deafness since childhood, sister has abnormal bleeding parameter (elevated PT/ INR) without bleeding history. None of the family members have kidney diseases. He underwent live related transplant without any intra or post operative bleeding complications and without any requirement of blood product. He was given post operative thromboprophylaxis with LMWH. He developed thrombosis of left IJV post CVP line insertion. We discharged him on oral anticoagulant and plan to continue oral anticoagulant for life long. At present he is doing well with normal graft function.

Discussion:

Coagulation factor deficiencies are generally associated with a bleeding tendency. The occurrence of thrombosis in these disorders is a matter of great interest and has never been studied in detail. Occurrence of thrombosis in patients with congenital FV II deficiency has been considered a paradoxical phenomenon. Individual cases with factor VII deficiency with thromboembolic events have been identified and reported. The majority of patients had no or only a mild bleeding tendency. Some patients were studied by means of molecular biology techniques. The *Arg304Gln* mutation was found in alleles. Considered possibility that the FVII gene mutations found in these subjects with thrombotic events impair interaction with tissue factor pathway inhibitor (TFPI), which is potentially thrombogenic feature.

Heparin and Coumadin together with adequate substitution therapy were carried out in patients with satisfactory results.

Conclusion:

FVII deficiency has varied presentations including pro-thrombogenic state and with extensive evaluation major surgeries can be performed safely.

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RTP3. Deceased Donor kidney transplantation in Government Medical College Kozhikode – our experience

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Aim To study the clinical profile of deceased donor kidney transplant recipients in Govt Medical College, Kozhikode from 2012- 2016

Materials and Methods : Study Design – Cross sectional observational study
Study Period - 2012 – 2016

Inclusion criteria – All patients who had undergone deceased donor kidney transplantation in our centre till November 2016.

Details regarding native kidney disease, cold ischemia time, intraoperative complications, post-transplant issues of rejection, infection and other non-immunologic complications were collected and analyzed.

Results and Conclusion : Till date a total of 35 patients have undergone cadaver transplantation. 25 were males and the rest females. Maximum number of recipients were in the age group of 30-39 years. The most common native kidney disease was chronic glomerulonephritis. One patient was HCV positive. Induction was given with ATG in 19 and the rest were given Basiliximab. 10 patients had DGF and 13 had excellent graft function.

Rejection was identified in 10 patients. AMR in 7 patients, TCMR in 3 and borderline rejection in 3 patients. Other causes of graft dysfunction were AIN in 2 patients, recurrence of IgA in 1 and cortical necrosis in 1 patient.

The most common infection was UTI in 6 patients. 1 case each of bacterial pneumonia, CMV pneumonia, pulmonary aspergillosis, pulmonary tuberculosis were present. 1 patient presented with pheohyphomycosis.

Other complications identified were PTDM in 3, foot drop in 2 and lymphocele in 1 patient. Transplant renal artery stenosis, renal vein thrombosis could be identified in each one of the patient. 7 patients expired. 3 patients have graft failure and is currently on maintenance hemodialysis.

RTP4. The spectrum of infections in renal transplant recipients in our centre– an overview

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Aim : To identify the pattern of infections in live kidney transplant recipients in our centre
2. To study the clinical profile and treatment response of infections in transplant recipients

Materials and Methods : Study design – cross sectional study

Study period – January 2012 – October 2016

Inclusion Criteria – All post renal transplant patients admitted with features of infection

The clinical details of all patients satisfying the inclusion criteria were noted and all relevant investigations were recorded. Clinical course and treatment response were noted. Post mortem lung biopsy was taken and analysed for those patients who died of respiratory infection.

Results and Conclusion: A total of 55 patients were admitted with features of infection during the study period and all of them were on triple drug immunosuppression and received cotrimoxazole prophylaxis. The most common focus identified was respiratory followed by urinary tract infection. 22 patients had respiratory tract infection. 3 patients had klebsiella pneumonia and responded to antibiotics. CMV pneumonia was identified in 4. There were 9 cases of pneumocystis carinii pneumonia. Invasive pulmonary aspergillosis and fungal sinusitis due to aspergillosis was present in each one of the patient. 3 patients had suspicious fungal pneumonia. 1 presented with sputum positive TB. A total of 18 patients had culture proven UTI which responded to antibiotics. 3 patients had CMV colitis, 1 had CMV esophagitis, 2 patients with persistent dyspeptic symptoms were detected to have CMV infection. 4 had skin fungal infection with chromoblastomycosis in 1 and pheohyphomycosis in 3. 1 patient developed varicella. One patient each had infected lymphocele and staphylococcal cellulitis. 3 patients expired due to neutropenic sepsis

RTP5. Post renal transplant urinary tract infection from a tertiary care centre in South India

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Aim: To find the incidence, microbiological profile and risk factors associated with urinary tract infection in renal transplant recipients.

Materials and methods : We conducted a retrospective, observational study of 103 renal transplant recipients who underwent surgery (both live related donor and deceased donor) from January 2012 to December 2015 in our hospital. Stent was used for all patients. Chi-square test or Fisher exact test was used to compare data between the groups. SPSS version 16.0 was used for the statistical analysis. P values <0.05 were considered to be statistically significant.

Results: Of 103 kidney transplant recipients 52 (50.5%) developed UTI (male 35; 67.3% and female 17; 32.7%). There was neither any association between the kidney received from deceased (n=25; 69.4%) or live donor (n=27; 40.2%) (OR=1.53; 95% CI=0.64-3.62) and the development of urinary infection. Among UTI patients 34 (65.3%) had lower tract infection and 18 (34.6%) had pyelonephritis. Most of the patients were asymptomatic (n=40; 76.9%) with remaining 12 being symptomatic (n=12; 23%). Patients on prolonged catheterization (>7 days) had significant lower UTI vs upper UTI (p=0.026) and early UTI occurrence (p=0.004). The most frequently isolated pathogens were Klebsiella pneumonia (n=20; 38.4%), Escherichia coli (n=18; 34.6%) Candida albicans noted in 2 patients (3.8%). Use of induction (OR=3.50; 95% CI=1.55-7.89) agents, anti rejection therapy (OR=9.45; 95% CI=3.45-26.0) and occurrence of pre transplant UTI (OR=2.76; 95% CI=0.96-7.89) were found to have significant post transplant UTI. In this study there was no significant association between diabetes mellitus and UTI. Graft dysfunction was observed in 25% of patients (n=13; P=0.271).

Conclusion: Our study showed that the incidence of urinary tract infection in renal transplant recipients was 50.5%. Klebsiella and E. coli was the main pathogens. Use of induction agents, anti rejection therapy and occurrence of pre transplant UTI were found to have significantly associated with post transplant UTI.

RTP6. Graft Function And Outcomes In Deceased Donor Kidney Transplant Patients In Tertiary Care Centre: Our Experience

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Background : Deceased Donor transplant has seen enormous increase in the numbers and could bridge the gap between demand and supply of organs.

Objectives: To assess outcomes in deceased donor renal transplantation in terms of patient/graft survival, graft function, rejection episodes, and post transplant complications.

Study methodology : We conducted a retrospective analysis of renal transplant patients (n=105) who underwent deceased donor renal transplantation in the period between January 1996 to March 2016 at Stanley Government Hospital, Chennai. All donors and recipients were ABO compatible and all recipients had a negative CDC cross-match.

Results :

Patient demographics: A total of 105 patients underwent cadaveric renal transplantation in the study period including 81 men (77.14%) and 24 women (22.85%). The mean duration of our follow up was 38.14 ± 46.41 months. Our recipient age ranged between 18-57 years with mean age of 34.04 ± 7.98 years. The age of donor ranged between 12-68 years with a mean of 33 yrs. Main cause of brain death was road traffic accident (RTA) in 77 (73.35 %). Our centre was the source of kidney in 41 deceased donor transplantation (39.04%). All but one patient underwent their 1st renal transplant. All recipients received ATG induction followed by standard triple immunosuppression.

Graft vascular anatomy: In our series, 21 of our grafts had double renal artery (20%). 8 of our patients had triple renal arteries (76.19%).

Cold ischemic times (C.I.T.) In our series the mean Cold Ischemic times was $8.01 (\pm 2.73)$ hour with minimum CIT of 3 hours when graft was harvested from our centre and maximum time of 15 hours when the graft was harvested from other centres.

Assessment of Renal Function The mean serum creatinine levels were 2.43 ± 2.07 mg/dL at week 1 after transplant, 1.49 ± 1.05 mg/dL at month 1 and 1.24 ± 0.48 mg/dL month 6. The incidence of DGF and SGF was 30.47 % (n=32) and 7.6 % (n=8).

Graft Function, Rejection and Loss : After adjusting for graft loss due to mortality, 59 patients (56.1%) had normal graft function and 17 (16.19%) patients had varying levels of graft dysfunction out of which 9 patients became dialysis dependent. Graft rejection episodes were observed in 18 patients.

Post transplant complications: The two most common medical complications after excluding dgf/sgf was sepsis (24.7%) and atn (12.4%). the incidence of nodat was about 11.42% and post transplant erythrocytosis (4.8%). recurrent uti and graft pyelonephritis were seen in 2.8 and 1.9 % of patients. graft biopsy was done for 35 patients (33.33%). the findings revealed acr in 6, acr/amr in 4, amr in 2, ati in 14, chronic allograft nephropathy in 5, cni toxicity in 2, tma in 1 and cortical necrosis in 1 patient. mortality rate was 27.6 % with median survival time of 23 months. the leading cause of death was sepsis in 22 patients (75.86%), cardio vascular events in 5 patients (17.24%), graft artery thrombosis in 2 patients (6.8%).

Discussion: In our series, 96 recipients completed minimum of one year follow up. one year survival rates were 75% and 89.58% for patients and graft respectively. the incidence of graft rejection was 17.14 %.the mortality rate was 27.6%.the majority of the deaths occurred within the early transplant period of less than 6 months and sepsis was the major contributor for mortality.

Conclusion: The graft survival and function in our series was comparable with prior living related and deceased donor renal transplant series from India. The long duration of HD prior to transplant, triple immunosuppression, Induction with ATG, Tropical climate and Socioeconomic factors contribute to infections in early post transplant period with sepsis being the leading cause of death.

RTP7. Pre Transplant Dialysis Modality And Renal Transplant Outcome

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The effect of pre-transplant dialysis modality on renal transplant outcome is still controversial. Studies examining the same have produced conflicting results.

Aims: To evaluate the effect of pre transplant dialysis modality (HD vs CAPD) on the intra operative , immediate post operative status , rejection episodes , graft and patient survival at our hospital over the last four years.

Materials And Methods: The study analysed 50 renal transplants (22 CAPD vs 28 HD) performed at our center between Jan 2013 to Oct 2016.

Results And Discussion : Both the study groups were subjected to the same immunosuppressive protocol, (triple drug comprising steroid ,CNI and MMF), with the cadaver recipient receiving induction with ATG. Patients undergoing CAPD were relatively younger compared with their HD counterparts .A significant group of patients on PD belonged to places with hilly terrain where access to HD could have been a major problem. Contrary to expected there was no higher incidence of PTDM in the CAPD arm. The day of removal of drain was prolonged in CAPD patients in comparison with HD , which was statistically significant ($p < .001$). Hypoalbuminemia was more prevalent in the PD group . There was increased incidence of infections (wound and UTI) in the CAPD group. DGF , SGF and the global rejection rate was the same for all patients regardless of the pre transplant treatment. No cases of graft thrombosis was reported in the study in either arm. In the pd group 20 patients with functioning grafts are still being followed , one has returned to MHD and 1 patient expired.

Conclusions : As a pre transplant dialysis modality neither HD nor PD affects the outcome of renal transplant.

RTP8. Induction in deceased donor renal transplants – “ a bane or boon”

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Introduction : kidney transplantation is considered the treatment modality of choice for majority of patients with end stage renal disease (esrd) .In india , there are a large number of ESRD patients waiting for renal transplant.

The two sources of kidneys for clinical transplantation are deceased and live donor . Rejections are an important cause of poor graft outcomes. Acute rejection episodes are considered as a risk factor in the development of chronic rejection. Induction therapy is recommended for deceased donor transplants however the cost of induction therapy is high .

Aims And Objectives : To study and compare the complications and outcome of 40 cases of deceased donor renal transplantation in patients with and without induction therapy .

Methods : Prospective study of 40 cases of CKD patients who underwent cadaveric renal transplantation at tertiary care government hospital .

19 patients received basiliximab induction , while remaining 21 patients did not receive induction. Induction therapy was given to patients who consented for obtaining the drug .All patients received standard triple drug immunosuppression (prednisolone , MMF and Tacrolimus). All were 1st transplants . The baseline and donor characteristics were comparable among the two groups .HLA typing for donor and recipient was not done .

Primary endpoint was the incidence of acute rejection at 6 months .Secondary endpoints include the safety and tolerability of basiliximab , 1- year patient and graft survival ,and significant medical events upto 12 months .

Results : Mean age group was 35.08 years +/- 9.2 years ; M:F ratio was 3.2:1 .

Native kidney disease was CIN in 26 patients and CGN in 12 patients .

Mean cold ischaemic time was 6.14 hours +/-3.42 hours .

In induction therapy group 3 (15.8%) had rejection, 2 AMR and one cellular rejection.

While in non- induction group 7 cases (33.33%) had rejection, 4 cellular and 3 AMR (antibody mediated rejection) in the first 6 months , these rejections responded to anti rejection therapy.

Incidence of infections in induction group included 9 (47.4%) cases– bacterial in 6 cases i.e , UTI in 3 cases, pneumonia in 1 case , perineal and gluteal abscess in 1 case and leg ulcer in 1 ; fungal infections-mucormycosis in 1 case , fungal pneumonia in 1 ; CMV in 1 case.

Incidence of infections in non induction group included 11(52.4%) cases – bacterial in 4 cases (2 UTI , 2 pneumonia) ; viral - CMV colitis in 4 cases ; herpes zoster in 1 case ; fungal – oral candidiasis in 1 case , mucormycosis 1 case.

One year graft survival and patient survival in induction group was 94.74 % and 100 % respectively. One year graft survival and patient survival in non induction group was – 90.48 % and 95.2 % respectively.

Discussion :Basiliximab in combination with tacrolimus, steroids and MMF triple therapy was highly effective in reducing the incidence of acute allograft rejection , without increasing the incidence of infections.

The adverse effect profile of patients treated with basiliximab was indistinguishable from that of patients treated without induction.

RTP9. Recurrence of primary focal segmental glomerulosclerosis post renal transplant: risk factors, outcomes and response to therapy

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Aim: To study the risk factors and therapeutic efficacy of Plasmapheresis and anti CD-20 (Rituximab) therapy in recurrence of Focal Segmental Glomerulosclerosis (FSGS) in renal allograft.

Materials and Methods: Data of all patients who underwent renal transplantation between Jan 2010 and Oct 2016 were reviewed retrospectively. 28 patients who met strict diagnostic criteria of primary FSGS as native kidney disease were included in the study and analyzed in detail.

Results: Meanduration of follow up was 28 months (2-69). 21.42 % (n=6) had recurrence of FSGS in allograft. Median duration to recurrence was 4 days (1-299). No significant difference was observed between recurrent group and non-recurrent group (n=22) with respect to recipient age, sex, donor age, HLA match and immunosuppression protocol. Duration of progression to end stage renal disease (ESRD), and dialysis vintage had no bearing on the outcome.

Five out of six patients received therapeutic Plasmapheresis for recurrent disease while additional four patients received Rituximab. All patients were maintained on high Tacrolimus dosage. 80 % (n=4) achieved partial remission (PR) while one patient achieved complete remission (CR) and remained in CR at last follow up. At 1 year follow up, no significant difference was observed in graft survival and serum creatinine levels (1.4 ± 0.64 vs 1.1 ± 0.28), while proteinuria (3.61 ± 3.00 vs 0.30 ± 0.10) was significantly higher in the recurrent group.

One patient had graft loss due to FSGS recurrence (31 month) despite treatment. One patient who was managed conservatively failed to achieve remission and continued to have nephrotic range proteinuria at last follow up.

Discussion: Recurrence of FSGS is seen in ~30 % of patients with primary FSGS post renal transplant. Approach to management of this entity is not well defined. Plasmapheresis with Rituximab appears to be an attractive option in maintaining long term graft survival.

RTP10. Renal biopsy findings in renal allograft dysfunction- a single center experience

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Introduction: Renal transplantation is the treatment for patients with ESRD worldwide. In the last few decades the transplant scenario improved due to better surgical techniques, medical care, prevention & treatment of infections & advanced immunosuppressive treatment. Allograft dysfunction is common after transplantation & is due to acute rejection, chronic rejection, CNI toxicity, infections. Renal biopsy is the gold standard to establish the cause of allograft dysfunction as clinical diagnosis is unreliable.

Aim : To evaluate the causes of renal graft dysfunction as detected on renal allograft biopsies in renal transplant recipients.

Materials and methods: It is a retrospective review of 61 biopsies from 46 renal transplant patients, carried out over a period of 2 years . Renal allograft biopsies were performed when there was unexplained graft dysfunction (rise in serum creatinine of $\geq 20\%$ over baseline) and/ or proteinuria, fulfilling the established indications of graft biopsies .

Two cores of renal graft tissue are obtained with automated biopsy gun under real-time ultrasound guidance. The histological changes are interpreted and classified according to Banff working classification of renal allograft pathology .

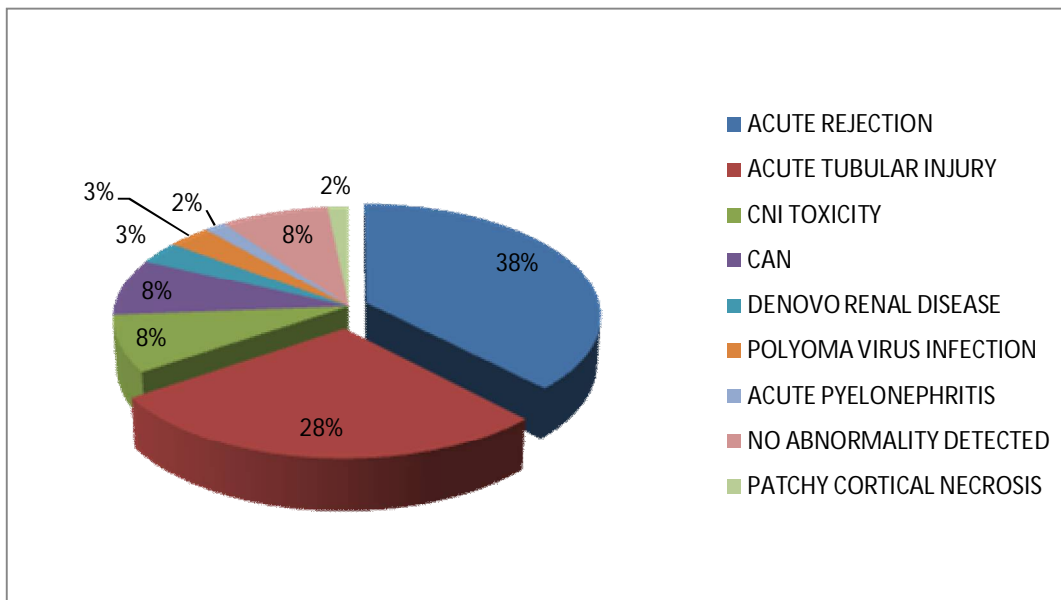
Results : A total of 61 biopsies were performed on 46 patients.

Males were predominant among the recipients.

Regarding pathological lesions acute rejection was seen in 23 (38%) cases followed by acute tubular injury and CNI toxicity (Tacrolimus) in 17 (28%) and 5 (8%) cases respectively.

Chronic allograft nephropathy (CAN) with variable degree of tubular atrophy was seen in 5 (8%) cases.

One case (2%) of acute pyelonephritis and 1(2%) case of patchy cortical necrosis was detected on graft biopsy. Rare lesions was also found including 2 (3%) cases of recurrent /denovo renal disease and 2 (3%) of Polyoma virus infection.No histopathological abnormality was detected in 5(8%)cases



Conclusions : The incidence of acute rejection and acute tubular injury was comparable to many western studies. Recurrent /Denovo renal disease is uncommon in our patients.

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RTP11. Plasma cell rich acute cellular rejection causing acute allograft dysfunction - our experience

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Aims: Plasma cell rich acute rejection causing acute allograft dysfunction - our experience

Materials & methods: Renal allograft biopsies performed between 2011 to 2016 (total 492) were looked for histopathological features of Plasma cell rich acute rejection (PCAR) and correlated with management & outcome.

Results: Among the total biopsies, 3 were identified with the features of acute cellular rejection (ACR) with plasma cell rich acute rejection (PCAR) & C4d (Immunohistochemistry) was negative. Case 1 underwent renal transplantation in 2011, NKD-unknown, developed graft dysfunction after 10 months with creatinine 6.6 mg/dl requiring biopsy, after 1 year creatinine was 4.3 mg/dl, later had graft loss and underwent second transplant. Case 2 underwent renal transplantation in 2013, NKD-?CGN, had graft dysfunction at 12 months, creatinine of 4.4 requiring biopsy, after 1 year creatinine was 3.8 mg/dl. Case 3 underwent renal transplantation in 2014, NKD-unknown, developed graft dysfunction at 24 months, creatinine of 3.1, requiring biopsy, after 6 months creatinine was 2.6 mg/dl.

All 3 cases were pulsed with methylprednisolone and immunosuppression was optimized. In our study partial response was observed in 2 out of 3 cases & there was no component of AMR (Antibody mediated rejection), which has been a common observation in some studies.

Conclusion: Plasma cell rich acute rejection (PCAR) is a unique entity due to its peculiar morphology and poor prognostic behavior. Plasma cells in the allograft biopsies have created lot of importance regarding the treatment and long term graft survival. This study highlights the presence of PCAR in the allograft biopsies & its poor response to standard anti rejection therapy.

RTP12. Post transplant glomerulonephritis

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Aim: To analyse the prevalence and outcome of post-transplant glomerulonephritis in a tertiary care hospital.

Materials and methods: 780 post transplant patients from January 2003 to November 2016 were retro-prospectively studied. Renal biopsy was done when patient presented with proteinuria or graft dysfunction after ruling out reversible causes.

Results

Prevalence of Post transplant GN	4.87%
Male to Female ratio	4.6:1
Mean age	31.4 yrs
Mean period at diagnosis	21.6 months
Mean period of follow up	49.2 months
Deceased donor transplant-PTGN	5

AT PRESENTATION	
Graft dysfunction	84.21%
Nephrotic proteinuria	57.4%
Subnephrotic proteinuria	47.36%
Recurrence within first month	8
Recurrence within first year	26(68.4%)
Recurrence between 1 and 3 yrs	8
Recurrence after 3 yrs	4

Discussion

Categories	Histological types
Recurrent GN-6(15.78%)	FSGS-12(31.57%)
De nova GN -3(7.89%)	TMA-12(31.57%)
PTGN with unknown primary-29(76.31%)	IgA Nephropathy-5(13.15%)
	Mesangioproliferative GN-2(5.26%)
	IRGN-1(2.6%)
	Collapsing GN-3(7.89%)
	Diabetic nephropathy-2(5.26%)
	Membranous nephropathy-1(2.61%)

OUTCOME	FSGS	TMA	IgAN	CG	IRGN	DN	MN
Normal graft function	2	3	0	1			
CKD-ND	8	4	4			2	1
MHD	1	4	1		1		
DEATH	1	1	0	2			

FSGS was the cause of PTGN in 12 patients, of which majority of them were PTGN with unknown primary. Most of the TMA patients presented with sub nephrotic proteinuria with graft dysfunction. Ig A Nephropathy was seen in 5 patients, 2 with recurrent GN and three with unknown primary. All recurrent IgA nephropathy patients developed chronic allograft failure.

Conclusion : PTGN with unknown primary was the most common type of PTGN. FSGS (31.57%) and TMA (31.57%) were the most common histology observed followed by Ig A nephropathy (13.15%).

Most of the PTGN (68.4%) patients presented within the first year of transplantation. Post transplant recurrent glomerulonephritis has high incidence (84.21%) graft failure.

RTP13. Efficacy of Interleukin 2 receptor antagonist induction therapy in renal transplant recipients

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Introduction: Interleukin 2 receptor antagonist (IL 2 RA) has the best safety profile in renal transplant recipients without an increased risk of infection or malignancy. An observational study performed in intermediate immunological risk live-donor renal transplant recipients by S. Gundlapalli et al reported that Basiliximab induction did not confer an additional advantage in patients on Tacrolimus and Mycophenolate based triple drug immunosuppression

Aim: To analyze the outcome of renal transplantation in patients who had received induction with IL 2 RA in our hospital, a tertiary care Nephrology and Urology centre

Materials and Methods: Medical records of chronic kidney disease stage 5D patients who had undergone renal transplantation from January 2007 till June 2016 were analyzed for immunosuppression protocol, biopsy proven acute rejection (BPAR) episodes, patient and graft survival and episodes of infection

Data collection until December 2016

We do only living related donor and deceased donor renal transplantation

Transplant protocol – triple drug immunosuppression; use of Mycophenolate Mofetil or Azathioprine based on HLA matching, pre-existing viral hepatitis, abnormal liver function in the post transplant period and affordability for MMF; IL 2 RA used if match on HLA typing is less than 50% and there is affordability for the same; second transplants and cadaver transplants

Statistical analysis by Fisher Exact test for categorical variables

Results:

IL2 RA use in 49; Daclizumab in 17 and Basiliximab in 32

	Overall	Induction	No induction	p value
Total	142	49	93	
Males	109	40	69	0.40
Mean age (in years)	35.5	41.08	32.6	
Cyclosporin	70	22	48	0.48
MMF	64	37	27	0.0001
Patient loss	22	10	12	0.32
Graft loss	36	14	22	0.54
CMV infection	20	7	13	1.00
BPAR	33	13	20	0.53
Spouse donation	59	36	23	0.0001

Conclusion: Though there does not seem to be benefit in IL2 RA induction as far as prevention of BPAR, this has to be interpreted in the context of its use in a subset of patients who did not have good match on HLA typing. Incidence of CMV infection is more or less same in comparison to those patients who had not used IL2 RA

RTP14. Study of early graft nephrectomy

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Aim: To evaluate the indications, etiology and complications following early (< 3months post transplant) graft nephrectomy

Materials and methods: All cases of early graft nephrectomy (< 3months) post renal transplant from live related donors were analysed retrospectively for a period of 3 years from January 2014 to Decemner 2016. Cadaveric transplants were excluded. Late graft nephrectomy > 3months were excluded.

Results: Out of total 242 live related transplant 6 (2.4%) had early graft nephrectomy. 5 were males and 1 female. All were live related transplants. NKD was CGN in 2 patients, IgA nephropathy in 2 patients and diabetic nephropathy in 2 patients. 3 had brothers as donors, 2 mother and 1 was spousal donor. 5 were ABO compatible transplants and 1 was ABO incompatible transplant. 3 received ATG induction, 2 Basiliximab induction and 1 patient did not receive any induction. The indication for graft nephrectomy was mycotic aneurysm leading to vascular complication and renal dysfunction in 3 patients, acute antibody mediated reaction in 2 patients and patchy cortical necrosis with TMA in 1 patient with ABO incompatible transplant. 2 patients had to undergo femoro-femoral bypass surgery and 1 patient had ischemic neuropraxia of right lower limb. All the patients who had acute antibody mediated rejection were treated appropriately with plasmapheresis and Rituximab. There was no mortality. All patients were back on hemodialysis.

Discussion: It is estimated that 7 to 10% of all renal allografts fail during first year of transplantation. We had early graft nephrectomy in 2.3% of all the transplants. Most common indication was mycotic aneurysm leading to vascular complication. There was no mortality.

RTP15. Isolated foot drop following renal transplantation: two case reports

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Introduction:Neurologic complications can occur in renal transplant recipients, the causes being mechanical causes during the procedure, drug toxicity, infections or symptoms due to worsening of the renal allograft function. Isolated foot drop is a rarely described complication. Here we report 2 cases of foot drop after renal transplantation.

Materials and Methods: First case is that of a 25 year old female with IgA Nephropathy with no evidence of neuropathy in preoperative period who underwent renal transplant from a live related donor. The surgery was done with patient in supine position and duration of surgery was 2.5 hours. Immunosuppressant drugs included Tacrolimus and Mycophenolate mofetil given 2 days prior to transplant and Methyl prednisolone on the day of surgery followed by oral Prednisolone. Immediate post operative period was uneventful. Foot drop of right limb was noticed on 5 th post operative day when patient became ambulant. Serum Tacrolimus level was within therapeutic range during this period. There was no associated sensory loss or any other neurological deficit. Nerve conduction study was suggestive of axonopathy. Pressure induced CPN palsy was suspected and given conservative management.

Second case is that of a 50 year old male with IgA Nephropathy who underwent live related donor renal transplantation with triple immunosuppressants, with uneventful immediate post operative period. He developed foot drop, right followed by left 1 month after renal transplantation. Patient was thoroughly investigated to rule out infectious causes and electrolyte disturbances which were all negative. His tacrolimus blood levels were within normal therapeutic range. Nerve conduction studies showed motor axonal neuropathy.

Results: First case improved with conservative management, suggestive of possible mechanical cause as the reason for foot drop. In the second case conservative management failed to produce any improvement. Thinking of possible drug induced neurotoxicity CNI changed from Tacrolimus to Cyclosporine and after the conversion his weakness improved.

Conclusion:About 10-25% patients treated with calcineurin inhibitors develop some form of neurotoxicity and it is more common with tacrolimus. Idiosyncrasy may be a possible mechanism

RTP16. Fabry's diseases with end stage renal diseases – Post transplant BK virus nephropathy and late acute antibody mediated rejection.

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Abstract Fabry's disease is an X-linked lysosomal storage disorder caused by a deficiency of alpha-galactosidase A enzyme with the progressive accumulation of globotriaosylceramide in vascular endothelial cells leading to cardiovascular, renal, gastrointestinal, neuropathic, lenticular, and dermatological manifestations. It is rare cause of end-stage renal disease. It classically affects males whereas 10–15% of female heterozygote carriers are affected depending on localization. Both the FD and its association with ESRD is very rare. We hereby writing case report of patient with FD having ESRD, underwent renal transplant, father being donor and post renal transplant of two years found to have graft dysfunction secondary to late acute antibody mediated rejection with BK virus nephropathy. This case report describes an adult male patient who had history of decreased sweating and needle prick sensation on his extremities during hot water bath since in his childhood. Patient has been evaluated for his glomerular proteinuria and on renal biopsy light microscopy shows glomerular visceral epithelial cells are enlarged and vacuolated, tubules are showing more than 50% atrophy and blood vessels are abnormal. Because of his progressive renal failure which requires hemodialysis, after two month of regular intermittent hemodialysis patient underwent renal transplant, father being donor. Patient has received induction immunosuppressant with ATG (Anti Thymocyte Globulin) with steroid. Discharge with triple immunosuppressant with renal allograft function of 1.2 mg/dl of creatinine. After two years of post-renal transplant, patient developed graft dysfunction and on allograft renal biopsy showing features suggestive acute antibody mediated rejection with C4d positive and intranuclear basophilic and gelatinous-appearing viral inclusions in epithelial cells. His BK viral load in serum was very high. Treated with Iv Ig (immunoglobulin) of five doses even though he requires intermittent hemodialysis. In this paper, we describe a rare case report of Fabry's disease with post renal transplant late acute antibody mediated rejection with BK virus nephropathy.

RTP17. Post transplant atypical HUS in MPGN – A manifestation of abnormal alternative complement pathway: a case report

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Abstract: 36 year old female with a strong family h/o CKD presented with uncontrolled hypertension during the postpartum period of her third pregnancy. On evaluation she was found to have severe renal failure. Renal biopsy was s/o MPGN (membranoproliferative GN). In view of progressively worsening renal function, she was initiated on MHD. She underwent renal transplantation with mother as the donor. By the 3rd post operative day, there was decrease in urine output. There was also progressive fall in Hb and platelet count. C3 was low. LDH was raised. Peripheral smear was s/o microangiopathic hemolytic anemia. A provisional diagnosis of post transplant hemolytic uremic syndrome was made and plasmapheresis was started. She underwent a total of 10 plasmapheresis sessions. Post plasmapheresis, there was gradual improvement in urine output and her Hb and platelet count was also stabilized. She was relatively stable and was discharged on 22nd pod. Graft biopsy on electron microscopy showed endothelial detachment from the GBM, subendothelial widening with fluffy deposits and endothelial injury with thrombi causing partial obstruction of vessel lumen ie TMA thrombotic microangiopathy, which was s/o HUS. She was readmitted on the 30th pod with relapse of HUS precipitated by lower limb cellulitis. Again she was put on plasmapheresis and improved dramatically. Genetic analysis revealed a pathogenic deletion in the CFHR 1 and CFHR 3 gene. At present she is on twice weekly plasmapheresis

RTP18. Renal Transplantation in a patient with combined Factor V and Factor VIII deficiency (F5F8D)

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Abstract:

Combined deficiency of factor V and factor VIII (F5F8D) is an autosomal recessive, congenital bleeding disorder which represents about 3% of rare congenital bleeding disorders, with a prevalence of 1:1,000,000 in unselected population. There is only one case reports of such patients undergoing renal transplantation. Here, we discuss a 44 year old gentleman, with F5F8D who successfully underwent renal transplantation.

RTP19. Changing Trends of Cytomegalovirus Disease in Renal Transplant Recipients

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Aim :To study the clinical spectrum of CMV infection in renal transplant recipients and changing trends over ten year period

Materials and methods: Retrospective analysis of data of patients who underwent renal transplantation at Madras Medical College, Chennai between January 2006 to July 2016. Pre transplant serology for CMV was not known for any of these recipients and donors. Universal prophylaxis for 100 days was given for patients who received induction therapy. Diagnosis of CMV disease was established by DNA PCR or pp65 antigenemia assay or by tissue diagnosis. Treatment was with intravenous Ganciclovir followed by oral Valganciclovir. Factors analyzed were type of donor, use of induction agent, type of immunosuppression, presence of coexisting infection, NODAT, time line of CMV infection and treatment response.

Results: 759 case records were retrospectively evaluated for CMV infection based on clinical suspicion of CMV syndrome. Seventy six patients (10.01%) had CMV disease. Average age was 30, of which 10 were females. Fifty four received live related renal transplant. The incidence in patients without induction therapy was 9.8% (60/610) and with induction therapy was 10.7% (16/149)(p=0.54; Z score -0.6075).The incidence with ATG was 6.7% (7/104) and with basiliximab was 19.5% (9/45) (p=0.01; Z score=-2.402. Diarrhea (55%) was the most common presentation followed by neutropenia (51%). Thirty one (40.7%) out of the seventy six patients had acute rejection episodes.

	2006-2010	2011-2016
Incidence of CMV disease	(10.4%)30/384	9.6%(36/375)
Mean Time (after transplant)	9 weeks	17 weeks
Late onset CMV disease	27%	38%
Invasive CMV disease	25%	12%
Antiviral therapy		
IV Ganciclovir	72%	35%
Oral Valganciclovir	18%	65%
Recurrence rate	42%	35%
Mortality	12%	4%
NODAT	33%	35%
HCV co infection	12%	7%

Conclusion :The incidence of CMV disease is more common in those receiving basiliximab as induction therapy. Prior acute rejection was a contributing factor for CMV disease. In the later five years when CMV prophylaxis was used there is increase in late onset CMV and decrease in incidence of invasive disease and mortality. 1/3rd of the patients had NODAT. The most common coexisting infection was bacterial of which urinary tract infection was common.

RTP20. Utility of pre-implantation histological scoring by microwave assisted rapid kidney biopsy specimen processing in deceased donor organ transplant in single vs double kidney organ allocation.

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Introduction: In centers that lack frozen section rapid processing of marginal kidneys pre-implantation biopsy by microwave assisted rapid kidney biopsy specimen processing has only seldom used for organ allocation in deceased donor transplantation.

Aim: To study the feasibility and outcome of single versus double kidney transplantation in the setting of marginal kidney transplantation using histological scoring.

Patients and methods: This is a prospective study done between January 2015 and July 2016 (18 months) in a tertiary hospital in Coimbatore, Tamil Nadu. All marginal kidneys from beating heart deceased donors were included. The definition of marginal kidneys is as per the age, diabetes, hypertension, serum creatinine criteria as defined by the United Organs Organ Sharing Network. The marginal organs are subjected to two cores of kidney biopsy by trucut biopsy needle (18G) and subjected to rapid processing and staining assisted by microwave treatment of the specimen. The biopsy is generally ready in 150 to 180 minutes by this technique. Histological scoring was done by Remuzzi scoring system. Organs with score ≤ 3 were allocated for single organ transplantation and organs with score 4-6 were allocated for double kidney transplantation, organs with score >6 were discarded. Induction is given with 2mg/kg rabbit anti-thymocyte globulin in two doses, one on the day of surgery and the second on the next day. Calcineurin inhibitors were started once the kidney function improves or in 7 days post transplantation, whichever was earlier.

Results: A total of 34 recipients received marginal kidney for transplantation. The mean age of donor and recipient were 60 ± 11 years and 51.5 ± 10 years respectively. The mean terminal donor creatinine was 2.28 mg/dl. Six received double kidney transplant and had Remuzzi score between 3 and 6 in all cases. One pair of kidney with score >6 was discarded and was not included in the analysis. In the remaining 28 single kidney transplants pre transplant histological scoring was done in 11 kidneys and Remuzzi score was between 1 and 3. The mean serum creatinine after 12 months and 18 months were 1.6 and 1.5 mg/dl respectively. The patient and graft survival after one year in double kidney transplant were 100% and 100% respectively, while the same for single kidney transplant were 85.5% and 85.5% respectively. The one year patient and graft survival with Remuzzi score of 3, 2, 1 were 80%, 82% and 100% respectively. Due to double kidney transplantation the one year patient and graft survival was 100% with Remuzzi score of 4-6.

Conclusion: Histological scoring can be done in less than 3 hours even in centers lacking frozen section by adopting microwave assisted processing technique and by staining with hematoxylin-eosin. Thereby marginal kidneys can be safely allocated for either single or double kidney transplantation with good patient and graft function outcomes.

RTP21. Role of elastography in evaluation of renal allograft - a preliminary study

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Evaluation of Renal allograft has been always an vexing problem for the Nephrologist. The available modalities including USG, Doppler, Isotope renogram, urinary and blood markers are at the best only suggestive and not conclusive, making us rely more on renal biopsy. Hence the quest for any non invasive reliable test which can be repeated frequently without any harm to to the graft is always on.

Elastography, is a non-invasive technique for evaluating the elastic properties of soft tissue either quantitatively or qualitatively. Transient elastography using mechanical impulse has been found very useful in studying breast, liver, thyroid which are superficial and amenable to mechanical stress by the probe. Native kidney being deeply placed was never considered for elastography. With renal allograft being placed superficially in the iliac fossa, we have an exciting opportunity to study by elastography. The stiffness of the kidney at various levels, namely cortex, subcortex and renal sinuses vary. It is hypothesized that we can utilize the changes in the variability of the stiffness caused by different pathological processes like tubular necrosis, rejection, calcineurin toxicity, chronic allograft nephropathy and fibrosis can be utilized in diagnosis of graft dysfunction.

In this preliminary study, we have studied 50 renal transplants by elastography and attempted to correlate the measurement with clinical diagnosis, allograft functional status, USG, Doppler, and renal biopsy. As the measurement of stiffness/elasticity will be limited by the body habitus of the subjects and depth of tissue, we have excluded very obese patients and those grafts which were deeper than 1.5 cm from the surface. To minimize subject to subject variation, we have taken the stiffness of the renal sinus which is not only the softest but also pathologically inert as the reference measurement. Results show some patterns evolving in different pathological states. The findings, its limitations and scope for future are discussed.

RTP22. Sensorineural deafness following tacrolimus use

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A 45-year-old gentleman underwent deceased donor renal transplantation about 2 years back. His primary renal disease was presumed chronic glomerulonephritis. He was also a hypertensive and non-diabetic. He received injection basiliximab 20 mg on day 0 and day 3 after renal transplantation. He also received injection methylprednisolone 15 mg/kg/d for the first three days followed by prednisolone 20 mg/kg/d, tacrolimus (0.05 mg/kg/d) and mycophenolatemofetil, 1.0 g bds. The serum creatinine reached the nadir by day 6. It remained around 1.3 mg/dL. There were no significant events like acute rejection, cytomegalovirus infection, and new onset diabetes mellitus after transplantation or tuberculosis. He remained at regular follow up – thrice a week for the first two months, twice a week for the next two months and once a week during the fifth and sixth month. Later he consulted us once in a month. At the end of six months the medications were prednisolone 10 mg/kg, tacrolimus (0.05 mg/kg/d) and mycophenolatemofetil, 750 mg bds. After 14 months of transplantation he complained hardness of hearing and tinnitus of one month duration. The examination of ears was normal. An audiogram revealed moderately to severe sensorineural hearing loss in both the ears. There was no sign of middle ear disease. An MRI brain was normal. The serum tacrolimus levels and serum creatinine levels were tabulated in table 1.

Table: Serial values of serum tacrolimus levels

Duration after renal transplantation	Serum creatinine (mg/dL)	Serum tacrolimus (ng/mL)
13 days	1.1	3.2
31 days	1.2	4.6
58 days	1.1	4.8
68 days	0.9	5.0
95 days	0.9	6.1
99 days	0.9	7.3
9 months	1.4	11.0
10 months	1.4	9.7
11 months	1.2	3.2
	6.4 ± 2.5	

Subsequent to this patient, thirty renal transplantation patients who completed six months after transplantation and receiving tacrolimus were subjected to ear examination and audiometry. Two more patients had moderately to severe hearing loss in both the ears. The serum tacrolimus levels in them were 8.9 ± 1.2 and 7.65 ± 1.2 ng/mL. These two patients underwent live related renal transplantations about 12 and 60 months before. None of the patients with hearing loss received drugs which can cause deafness like aminoglycosides, frusemide or quinine. Neither they received any induction therapy

These results were tabulated in table 2.

Table 2:

Parameter	Patients with hearing loss (n = 3)	Patients without hearing loss (n = 30)
Age (mean) (years)	39.3 ± 4.1	32.0 ± 9.0
Males (%)	3	29
Serum tacrolimus levels (ng/mL)(mean±SD)	7.65 ± 1.25	7.90 ± 4.90
Duration after renal transplantation (months)(mean±SD)	28.1 ± 12.1	22.1 ± 13.1

The first report of hearing after the use of tacrolimus was in kidney pancreas transplant recipient. This patient on day 17 of tacrolimus therapy developed sudden hearing loss with tinnitus. The patient's tacrolimus level was between 28.3 ng/mL and 34.9 ng/mL.(1) Hearing loss had been reported in two paediatric renal transplant recipients. Both of them – a girl and a boy developed hearing loss in fourth year after renal transplantation. The serum tacrolimus levels reported to be 22.01 and 29.97 ng/mL. (2) Majority of other reports are from liver transplantation patients. Tacrolimus has been identified to be a risk factor for hearing loss in 27% of patients after orthotopic liver transplantation (OLT) both in univariate and multivariate analysis. The mean time since liver transplantation at onset of hearing impairment was 4 ± 4 yr. In 43% of the patients, onset of hearing impairment was within 2 year of OLT. (3) In another report, a liver transplant recipient complained deafness after 10 weeks of transplantation. The serum tacrolimus level was 10.9 ng/mL. (4) None of the early trials (5-8) of tacrolimus in renal transplant recipients revealed hearing loss as an adverse effect. The results in table 2 demonstrated that there was no significant difference in serum tacrolimus between patients with hearing loss and without. The reason for hearing loss could be the cumulative toxic effect of tacrolimus.

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