Majority of graft dysfunction occurred after 6months of post-transplant period. It showed highly uneven distribution.ACR occurred even after 2 years and the CR occurred even after few months. So the graft dysfunctions should not be classified either as acute or chronic rejection based on the duration.

In this study, most common indication for transplantation was Chronic Glomerulo-Nephritis (CGN)-65%, Diabetic Nephropathy -52%. Rest of other causes includes hypertensive nephropathy, focal segmental glomerulosclerosis, chronic interstitial nephritis and adult polycystic kidney disease. Also we observed that the level of serum creatinine was not correlating with the histological diagnosis of rejection. Some of the cases were shown high level of serum creatinine biochemically but their histological diagnosis did not show any evidence of rejection.

All the 50 cases were graded according to Banff 2003 and CCTT criteria[3,4,16] for both acute and chronic rejection. Among the 50 cases 38 cases (76%) were found to have rejection, in the form of Acute Cellular Rejection, Chronic Allograft Nephropathy and combined rejection. 12 cases (24%) were found to have no rejection in our study(figure 1& 2). The inter-observer reproducibility of the present Banff criteria is improved after the incorporation of the CCTT criteria[20,21]

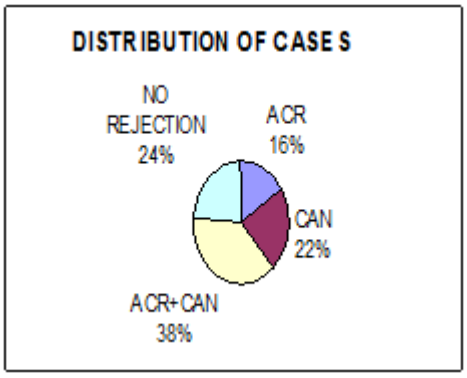

Figure 1: Distribution of cases

Table 1: Histological classification of cases

BANFF ACR Grade	No. of Cases (n=50) (%)	CCTT ACR Grade	No. of cases (n=50) (%)
0	23(46)	0	23(46)
Borderline	4(8)	I	6(12)
Ia	1(2)	II	21(42)
Ib	1(2)		
IIa	9(18)		
IIb	12(24)		

On applying Banff CAN criteria, it shows highly unequal distribution. 20 cases (40 percent) were found to have no rejection. 16 cases (32 percent) were found to have chronic allograft nephropathy of grade I.

In a Canadian series of 184 protocol biopsies, agreement rate for rejection was 74 percent but there was only 43 percent agreement on the suspicious cases[22,23]. A recent European series reached similar conclusions[22,23]. CCTT has a 91% agreement rate on acute rejection[20]. Even experienced pathologists do not reproducibly score certain Banff features. Among a group of 21 European pathologists, the agreement rate was poor for all of the acute Banff scores (t, i, v, g) in transplant biopsy slides[23].

CCTT criteria was superior to Banff in predicting graft survival and also simpler and easily reproducible. Threshold for diagnosing acute cellular rejection was comparatively less in CCTT criteria than the Banff 2003 criteria[20]. In our study 4 cases which were diagnosed as grade I acute cellular rejection, were actually placed in 'suspicious' or borderline category according to Banff 2003 criteria[5]. The rationale for the term 'suspicious' or borderline is that many but not all of these cases are indeed rejection; also it draws attention to the need for further studies to distinguish those cases of rejection from those that will resolve spontaneously[24,25].

Two large studies[24,25] have shown that 75 to 88 percent of patients with suspicious or borderline rejection improve renal function with increased immunosuppression, comparable to response rate in type I rejection (86 percent). In follow up biopsies 1 month later, the histology often progressed to florid rejection (33 percent to type I; 46 percent to type II or III). Others find that a minority (28 percent) untreated suspicious cases progress to frank acute rejection in 40 days[24,25].

Arterial lesions are considered to be one of the strong prognostic significance either individually or in combination and it alone doubled the rate of graft loss[26,27].In our study - 12 out of 50 cases (24 %) showed features of arteritis and dilatation of peri-tubular capillaries, neutrophillic margination. These cases also showed high creatinine value and the workup for humoral rejection should be followed up for those cases. Recognition of humoral rejection may be problematic in biopsies with dense mononuclear inflammatory infiltrates that fulfill criteria for acute rejection by the Banff schema[17]

5. Conclusion

CCTT criteria are simple and reproducible but the threshold for diagnosing acute cellular rejection was comparatively less than the Banff 2003 criteria.Further studies needed to distinguish those cases of borderline (suspicious) or subclinical rejection from those that will resolve spontaneously. Recognition of humoral rejection may be problematic in biopsies with densely cellular inflammatory infiltrate. All the transplant biopsies should be screened for humoral component irrespective of the rejection status.

6. Future Scope

All the transplant biopsies should be studied and classified according to the latest immuno-pathological criteria proposed by BANFF. C4d immuno-staining should be done in all the transplant biopsy workup as a routine for the detection of coexisting humoral component irrespective of the rejection grade.

References

[1] Cecka JM. The OPTN/UNOS Renal Transplant Registry 2003. Clin Transplant 2003;17:1
[2] Anderson CB, Ladefoged SD, Larsen S. Acute Kidney graft rejection. A morphological and immunohistological study on zero-hour and follow up biopsies with special emphasis on cellular infiltrates and adhesion molecules. APMIS. 1994;102(1):23-37
[3] Mauiyyedi S, Crespo M, Collins AB et al. Acute humoral rejection in kidney transplantation. II. Morphology, immunopathology and pathologic classification. J Am SocNephrol 2002;13:779
[4] Solez K, Axelsen RA, Benldiktsson H, et al. International standardization of criteria for the histological diagnosis of an renal allograft rejection: The Banff working classification of kidney transplant pathology. Kidney Int 1993;44:411-422
[5] Racusen LC, Colvin RB, Solez et al. Antibody-Mediated Rejection- an addition to the Banff 97 classification of renal allograft rejection. Am J Transplant 2003;3:703-714
[6] Sorof JM, Vartanian RK, Olson et al. Histopathological concordance of paired renal allograft biopsy cores. Transplantation 1995;60(11):1215-1219
[7] Pascual M, Vallhonrat H, Cosimi AB, et al. The clinical usefulness of the renal allograft biopsy in the cyclosporine era : A prospective study. Transplantation 1999;67:737
[8] Al-Awwa IA, Hariharan S, First MR. Importance of allograft biopsy in renal transplant recipients: Correlation between clinical and histological diagnosis. Am J Kidney Dis 1998;31:s15
[9] Evans RW, Kitzmann DJ. An economic analysis of kidney transplantation. SurgClin North Am 1998;78:149
[10] Hariharan S, Johnson C, Bresnahan BA et al. Improved graft survival after renal transplantation in the United States, 1988 to 1996. New Engl J Med 2000;342:605-612
[11] Paul LC. Chronic allograft nephropathy: An update. Kidney Int 1999;56:783-793
[12] Williamson CS. Further studies on the transplantation of the kidney. J of Urology 1926;16:231
[13] Cecka JM. The OPTN/UNOS Renal transplant Registry. In:Clinical Transplants 2003,Los angles: UCLA Immunogenetics Center, 2004:1
[14] Ahmed I, Abul-Ezz SR, Walker PD, et al. Acute rejection presenting as nephritic syndrome. Transplantation 2000;69:2663
[15] Nankivell BJ, Borrows RJ, Fung CL, et al. Calcineurin inhibitor nephrotoxicity: Longitudinal assessment by protocol histology. Transplantation 2004;78:557
[16] Poduval RD, Kadambi PV, Josephon MA, et al. Implications of immunohistochemical detection of C4d along peritubular capillaries in late acute renal allograft rejection. Transplantation 2005;79:228-235
[17] Racusen LR, Solez K, Colvin RB, et al. The Banff 97 working classification of renal allograft pathology. Kidney International. 1999;55:713-723
[18] Racusen LC, Colvin RB, Solez K, et al. Antibody mediated rejection criteria an addition to the Banff 97 classification of renal allograft rejection. Am J Transplant 2003;3:708
[19] Crespo M, Pascual M, Tolkoff-Rubin N, et al. Acute Humoral rejection in renal allograft recipients. I. incidence, serology and clinical characteristics. Transplantation 2001;71:652
[20] Colvin RB, Cohen AH, Saiontz C, et al. Evaluation of pathologic criteria for acute renal allograft rejection: Reproducibility, sensitivity and clinical correlation. J Am SocNephrol 1997;8:1930
[21] Maracussen N, Olsen TS, Benediktsson H, et al. Reproducibility of the Banff classification of renal allograft pathology. Inter or Intra observers variation. Transplantation 1995;60:1083
[22] Gough J, Rush D, Jeffery J, et al. Reproducibility of Banff schema in reporting protocol biopsies of stable renal allografts. Nephron Dial Transplantation 2002;17:1081
[23] Veronese FV, Manfro RC, Roman FR et al. Reproducibility of the Banff classification in subclinical kidney trasnsplant rejection Clin Transplant 2005;19:518
[24] Saad R, Gritsch HA, Shapiro R, et al. Clinical significance of renal allograft biopsies with 'borderline changes' as defined in the Banff schema. Transplantation 1997;64:992
[25] Schweitzer EJ, Drachenberg CB, Anderson L. Significance of the Banff borderline biopsy. Am J Kid Dis 1996;28:585
[26] Mueller A, Schnuelle P, Waldherr R, et al. Impact of the Banff 97 schema for histological diagnosis of rejection on clinical outcome and renal function parameters after kidney transplantation. Transplantation 2000;69:1123
[27] Macdonald FI, Ashraf S, Picton M, et al. Banff criteria as predictor of outcome following acute renal allograft rejection . Nephron Dial Transplant 1999;14:1692