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Impact of genetic polymorphism in MMPs and TIMPs on allograft outcome in Renal Transplant recipients

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Objectives: To investigate the association of MMP-1, 3, 9, TIMP1and TIMP3 gene polymorphisms with risk of allograft rejection in renal transplant recipients. To evaluate role of circulating MMP-9 in recipients & donors. Correlation of gene variants of MMPs and TIMPs with circulating levels of MMP-9. Classification on the basis of cross match techniques like flow cytometry, Single antigen bead test and HLA- DSA by LUMINEX.

Methods: A total of 200 live related renal transplant donors and recipients sample was genotyped for MMP and TIMP gene polymorphisms by polymerase chain reaction–restriction fragment length polymorphism. Quantitative analysis of serum MMP-9 has been done by ELISA.

Results: The genotype frequencies of MMP1 [2G/2G; odds ratio (OR) = 2.97, 95% confidence intervals (95% CI) = 1.69-5.20, $P \leq 0.05$]; MMP9 [RQ; OR = 0.47, 95% CI = 0.25-0.99, P = 0.02 & QQ; OR = 0.49, 95% CI = 1.77-4.13, $P \leq 0.05$ & RR; OR = 2.70, 95% CI = 1.09-6.71, P = 0.03]; TIMP1[CT; OR = 15.41, 95% CI= 9.12-26.05, $P \leq 0.05$ & TT; OR = 7.01, 95% CI = 3.39-14.49, $P \leq 0.05$] and TIMP3 [CT; OR = 0.31, 95% CI = 0.19-0.50, $P \leq 0.05$] was significantly associated with allograft rejection. On comparing non-rejecters with donors a significant association was observed in MMP1 (-1607 1G/2G) [$P \leq 0.05$]; MMP9 (Q279R) [P = 0.02]; MMP9 (P574R) [$P \leq 0.05$]; TIMP1 [$P \leq 0.05$] and TIMP 3 [$P \leq 0.05$]. The MMP-9, ELISA results showed high serum level in Recipients 62.30±59.84 ng/ml as compared to Donors 48.92±31.99 ng/ml, (p-value= 0.02).

Conclusions: Mutant genotypes for MMP1 (-1607 1G/2G); MMP9 (Q279R); MMP9 (P574R); TIMP1 and TIMP3 are associated with reduced risk for allograft rejection and improved allograft survival in North Indian transplant recipients and could serve as an ideal marker to predict pre-transplant allograft outcome.