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ABCC2-24C>T Gene Polymorphism and Its Effects on Graft Survival Among Kidney Transplant Recipients

Chiau Ling Choong¹, Farida Islahudin¹, Mohd Makmor-Bakry¹, Nor Asyikin Mohd Tahir¹, Hin-Seng Wong², Rosnawati Yahya³

¹Department of Department of Pharmacy, Center of Quality Medicine Management, Faculty of Pharmacy, Universiti Kebangsaan Malaysia, Malaysia

²Department of Department of Nephrology, Department of Nephrology, Selayang Hospital, Ministry of Health Malaysia, 68100 Batu Caves, Selangor, Malaysia, Malaysia

³Department of Department of Nephrology, Department of Nephrology, Kuala Lumpur Hospital, Ministry of Health Malaysia, 50586 Kuala Lumpur, Malaysia, Malaysia

Objectives : Although tacrolimus is the gold standard drug for kidney transplant recipients (KTR), the acute graft rejection and/or ATN during the use of immunosuppressants continues to be a major clinical problem. So far, the impact of genetic polymorphism in CYP3A5 gene and ABCC2 gene on clinical outcome among the Malaysian KTR has not been studied. This study aims to investigate the influence of single nucleotide polymorphisms (SNP) in genes encoding metabolizing enzyme (CYP3A5) and transporters (ABCC2) on clinical outcomes (acute graft failure and/or ATN) in KTR.

Methods : This was a multi-center, prospective observational cohort study that included patients on tacrolimus-mycophenolate-prednisolone treatment. Ethnically diverse adult KTR who had undergone kidney transplantation between 2019-2020 that consented were enrolled into the study. DNA was extracted from the collected blood samples using a commercially available kit. CYP3A5*3, ABCC2 -24C>T and ABCC2 3972C>T SNP were determined by polymerase chain reaction (PCR).

Results : A total of 39 patients were included, of which 9 (23.1%) KTR had an incidence of acute graft failure and/or ATN. A multiple logistic regression showed that wildtype ABCC2 -24C>T C allele showed higher risk of developing acute graft rejection and/or ATN compared to the variant allele carriers (adjusted Odd Ratios [aOR]: 27.675, p=0.038). Recipients who had delayed graft function (DGF) (aOR: 49.214, p=0.012) and history of CMV infection (aOR: 18.097, p=0.009) were 49.2 and 18.1 times increased risk for acute graft failure and/or ATN, respectively.

Conclusions : This is the first study to determine the effect of ABCC2 -24C>T genetic polymorphism on clinical outcome in Malaysian KTR. Further work on ABCC2-24C>T should be performed to determine the effects of the gene on long-term KTR.