

Clinical and genetic risk factors for newonset diabetes mellitus after transplantation (NODAT) in major transplant centres in Malaysia

ABSTRACT

Background: New-onset diabetes after transplantation (NODAT) is associated with reduced patient and graft survival. This study examined the clinical and selected genetic factors associated with NODAT among renal-transplanted Malaysian patients. Methods: This study included 168 non-diabetic patients (58% males, 69% of Chinese ethnicity) who received renal transplantation between 1st January 1994 to 31st December 2014, and were followed up in two major renal transplant centres in Malaysia. Fasting blood glucose levels were used to diagnose NODAT in patients who received renal transplantation within 1 year. Two single nucleotide polymorphisms (SNPs), namely; rs1494558 (interleukin-7 receptor, IL-7R) and rs2232365 (mannosebinding leptin-2, MBL2) were selected and genotyped using Sequenom MassArray platform. Cox proportional hazard regression analyses were used to examine the risk of developing NODAT according to the different demographics and clinical covariates, utilizing four time-points (one-month, three-months, six-months, one-year) post-transplant. Results: Seventeen per cent of patients (n = 29, 55% males, 69% Chinese) were found to have developed NODAT within oneyear of renal transplantation based on their fasting blood glucose levels. NODAT patients had renal transplantation at an older age compared to non-NODAT (39.3 ± 13.4 vs 33.9 ± 11.8 years, $p = 0.03$). In multivariate analysis, renal-transplanted patients who received a higher daily dose of cyclosporine (mg) were associated with increased risk of NODAT (Hazard ratio (HR) =1.01 per mg increase in dose, 95% confidence interval (CI) 1.00–1.01, $p = 0.002$). Other demographic (gender, ethnicities, age at transplant) and clinical factors (primary kidney disease, type of donor, place of transplant, type of calcineurin inhibitors, duration of dialysis pre-transplant, BMI, creatinine levels, and daily doses of tacrolimus and prednisolone) were not found to be significantly associated with risk of NODAT. GA genotype of rs1494558 (HR = 3.15 95% CI 1.26, 7.86) and AG genotype of rs2232365 (HR = 2.57 95% CI 1.07, 6.18) were associated with increased risk of NODAT as compared to AA genotypes. Conclusion: The daily dose of cyclosporine and SNPs of IL-7R (rs1494558) and MBL2 (rs2232365) genes are significantly associated with the development of NODAT in the Malaysian renal transplant population.