UKPDS 15: Relationship of rennin-angiotensin system gene polymorphisms with microalbuminuria in NIDDM

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UK Prospective Diabetes Study XV: Relationship of rennin-angiotensin system gene polymorphisms with microalbuminuria in NIDDM. We performed a case-control study to determine whether molecular variants of genes of the rennin-angiotensin system were associated with the presence of albuminuria in non-insulin dependent diabetes mellitus (NIDDM). A total of 180 diabetic patients with persistent microalbuminuria [median urinary albumin (interquartile range) of 74 (54 to 126 mg/liter)] were matched with two control groups of diabetic patients without microalbuminuria [median urinary albumin 7 (5 to 10) mg/liter] for variables known to be associated with raised urinary albumin concentration including hemoglobin A1c and triglyceride. One control group was also matched for blood pressure and the other group was not, to allow assessment of interactions with hypertension. Association with the I/D polymorphism of the ACE gene and M235T variant of the angiotensinogen gene (AGT) with microalbuminuria and retinopathy was examined. There were no significant differences in genotype frequency between cases and controls for ACE or AGT irrespective of blood pressure matching. However, among subjects with microalbuminuria, those with the ACE DD genotype had a significantly greater urinary albumin excretion than individuals with a non-DD genotype [median 88 (68 to 170) mg/liter vs. 67 (53 to 113) mg/liter, $P < 0.001$]. More subjects with the DD than non-DD genotype had persistent albuminuria > 100 mg/liter, twice the upper normal range (60% vs. 38%, $P = 0.006$). When increased albumin excretion occurs, the presence of the ACE DD genotype appears to be associated with higher urinary albumin levels. No association with retinopathy was observed.