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Angiotensin Converting Enzyme (ACE) and Angiotensinogen (AGT) Gene Variants in Pakistani Patients of Diabetes Mellitus and Diabetic Nephropathy

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Abstract : Introduction: Diabetes mellitus (DM) is a prevalent non-communicable disease worldwide. In most high-income countries as well as middle-income and low- income countries. DM is among the top causes of deaths. DM may lead to many vascular complications like hypertension, nephropathy, retinopathy, neuropathy, and foot. Diabetic nephropathy (DN) characterized by persistent albuminuria is a leading cause of end stage renal failure (ESRF). Pathogenesis of diabetic nephropathy is implicated by the polymorphisms in genes encoding the components of reninangiotensin- aldosteron system (RAAS) which include angiotensinogen (AGT), angiotensin-II receptor and particularly angiotensin converting enzyme (ACE) gene. Method: Study subjects include 110 control, 110 patients with DM without hypertension, 110 patients with DM with hypertension and 110 patients with DN. Blood samples were collected for Biochemical analysis and PCR and sequencing for the specific region of both genes. Results: The frequency of DD genotype and D allele of ACE (I/D) was significantly ($p<0.05$) high in DM normotensive, DM hypertensive and DN patients when compared to control. The ACE G2350A genotypes and allele frequencies were significantly different ($p<0.05$) in DM hypertensive patients as compared to control and DN, while no difference was observed between DM normotensive and DN when compared to control. The genotypes and alleles of AGT (M268T) polymorphism were significantly different ($p<0.05$) in DM normotensive, DM hypertensive and DN when compared to control. Conclusion: The DD genotype and D allele of ACE (I/D), GG genotype and G allele of ACE (G2350A) and the TT genotype and T allele of AGT (M268T) polymorphism have shown a significant difference in genotype and allele frequencies between controls and patients.

Keywords : genetic variations, ACE, AGT, diabetes mellitus, diabetic nephropathy, Pakistan
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