Angiotensin Converting Enzyme Gene Insertion/Deletion Polymorphism in Gaza Strip-Palestine and Type 2 Diabetic Nephropathy

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Abstract

Intron 16 of the Angiotensin Converting Enzyme (ACE) gene has an insertion/deletion (I/D) polymorphism of 287 bp Alu repeat sequence, resulting in three genotypes: I/D, D/D, and I/I. The expression of the ACE gene is linked to ACE levels in cells and plasma. It was discovered that the polymorphism could affect the ACE gene's expression. The D/D genotype is thought to have a negative impact on a variety of pathologies, and it may also be a cause-effect for type 2 diabetic nephropathy (T2DN). By comparing the genotype data of T2DN patients to healthy controls, Type 2 diabetes mellitus (T2DM), and nephropathy patients in this study, we were able to determine the frequency of different ACE gene genotypes and see if there is a link between ACE gene polymorphism and T2DN.

The Insertion Deletion (ID) polymorphism in intron 1 of the ACE gene is a functional polymorphism that has been shown to affect ACE levels in healthy people. The ACE ID polymorphism is linked to an increased risk of thrombosis and is maybe causally linked to Coronary Heart Disease (CHD).

Keywords: Angiotensin Converting Enzyme (ACE) gene • Insertion/deletion (I/D) • Polymerase Chain Reaction (PCR) • Type 2 diabetes

Introduction

Type 2 Diabetes Mellitus (T2DM) is a metabolic condition characterised by insulin resistance in peripheral tissues as well as decreased insulin production from pancreatic cells. It can be caused by a variety of factors. T2DM is expected to affect 438 million people globally by 2030, up from 285 million people in 2010 [1]. This is a 65 percent increase. T2DM complexity is influenced by a number of factors, including heterogeneity, gene interactions, and the effect of the environment. The metabolic syndrome, which includes T2DM, Hypertension (HTN), obesity, and dyslipidemia, is common in the populations of developed countries. Obesity status has been reported to influence the genetic vulnerability to T2DM. Insulin resistance-related genetic variants were only linked to T2DM in obese people, whereas insulin secretory variations were only linked to T2DM in non-obese people, implying that these variants may interact with obesity status in T2DM occurrence [2,3]. Type 2 Diabetic Nephropathy (T2DN) is a chronic kidney disease caused by capillary angiopathy in the glomeruli of the kidney. Chronic Kidney Disease (CKD) is a disorder in which anomalies in the structure or function of the kidneys, as well as a decrease in the Glomerular Filtration Rate (GFR), produce progressive and irreversible kidney damage lasting three months or longer. Kidney dysfunction is indicated by abnormal blood (serum creatinine) and urine tests (urine albumin), pathological indicators, or imaging tests for the kidneys. GFR is the best estimate of kidney function and identifies the stage of kidney disease; renal failure occurs when the GFR is less than 15% of that of normal kidneys and the kidneys are no longer capable of functioning normally. In the case of urine albumin, precise quantification of the amount of albumin lost in the urine has important clinical implications: healthy adults excrete less than 30 mg of albumin in 24 hours; excretion of amounts between 30 mg and 300 mg in 24 hours is referred to as microalbuminuria, and excretion of amounts greater than 300 mg in 24 hours is referred to as macroalbuminuria [4-7].

In the course of T2DN, microangiopathy is the first visible alteration. Glomerular hyperfiltration and an elevated albumin excretion rate characterise the progression of T2DN. The amount of albumin lost in the urine has substantial clinical implications, with macro-albuminuria defined as excretion of more than 300 mg in 24 hours and microalbuminuria defined as excretion of less than 30 mg in 24 hours. T2DN affects around one-third of diabetic people and is the major cause of End-Stage Renal Disease (ESRD), which necessitates dialysis or transplantation in both industrialised and developing Asian nations [8]. T2DN can occur in one-third of T2DM patients with excellent blood glucose control; although T2DN is not seen in the majority of patients, even with antihypertensive medication and subpar blood glucose control. As a result, it has been claimed that hereditary vulnerability to diabetic nephropathy exists.

The ACE gene has 26 exons and 25 introns and is located on chromosome 17q23. The insertion/deletion of an Alu repeat sequence in intron 16 of the ACE gene results in three genotypes: I/I, I/D, and D/D. These genotypes have varying plasma expression, with the D/D genotype having the highest plasma expression and the I/I genotype having the lowest. Furthermore, these genotypes are thought to play a role in either harmful or protective effects. The D/D genotype may have negative consequences on numerous disease path-genetic pathways [4-6]. The I/I genotype, on the other hand, is regarded to have protective properties. As a result, the ACE I/D gene polymorphism has been proposed as a tool for determining therapy regimens in antihypertensive patients.

Many researchers have attempted to explain the link between the ACE I/D polymorphism and T2DM risk and its associated renal and cardiovascular problems in various ethnic groups, but their findings have been very inconsistent. In Tunisia, India, and Iran, the D allele was found to be more common in T2DM and related problems, while other studies in Malaysia and Indonesia revealed no link between either allele and T2DM or related cardiovascular disease (CVD) and renal disease. As indicated by the different disease outcomes controlled by gene-gene or gene-environment interactions, these discrepancies are mainly related to multifactorial or polygenic disorders. Other studies looked at treatment response in T2DM patients and compared it to different ACE genotypes, finding that patients with the D/D genotype had a lower pharmacological response than those with the I/I allele of the ACE gene [9]. It appears that inheriting risk alleles at numerous susceptibility loci increases the risk of diabetes-related kidney damage.

ACE Gene PCR Amplification

The sequence of the ACE gene primers utilised in this work was described before. The genomic DNA fragments on the intron 16 of the ACE gene were amplified using a PCR reaction. About 150ng of extracted DNA (3 litres) was mixed with 7 litres of master mix and 0.5 litres of each primer in a 0.2 ml thin-walled micro-centrifuge PCR tube [10]. After centrifugation, the tubes were placed in a heat cycler. The following PCR heat cycles were carried out

- 1 minute of denaturation at 95°C
- 36 cycles of 15 seconds melting at 95°C, 15 seconds annealing at 59°C, and 10 seconds extension at 72°C
- Final elongation at 72°C for 10 minutes.

To evaluate the polymorphism of the gene, the PCR product was electrophoretically separated on a 2% ethidium bromide-stained agarose gel. With I/I genotype, the amplicon produced from the ACE gene should be 490 bp and 190 bp with D/D genotype. As a negative control, nuclease-free water was utilised instead of the DNA template. The size of the amplicon

(PCR result) was determined by comparing it to a DNA marker (50-bp DNA ladder) performed on the same gel.

Discussion and Conclusion

Renal destruction with or without renal function loss distinguishes chronic kidney disease, which is associated with significant morbidity and mortality across the continuum from early to advanced stages, necessitating renal replacement treatment. Although the exact cause of CKD is not usually known, kidney disease can be caused by any ailment or disease that destroys blood vessels or other structures in the kidneys. Diabetes and high blood pressure are the most prevalent causes of chronic kidney disease (CKD) that leads to kidney failure, and they can also hasten the advancement of chronic kidney disease in people who already have it. CKD is considered a public health condition that requires attention and monitoring, despite the multiple ways employed to prevent, diagnose, and treat it.

In comparison to healthy, T2DM, and nephropathy individuals, the current study focused on the association of ACE gene (I/D) polymorphism in the Gaza Strip and the relationship between those genotypes and T2DN. In all groups, the D/D genotype was the most prevalent. Finally, we found no statistical link between T2DN, T2DM, and nephropathy and the ACE I/D polymorphism in our findings.

References

1. Saqer, L., et al. "Association between angiotensin converting enzyme gene insertion\deletion polymorphism and coronary heart disease in Gaza Strip." *Int J Biomed Mat Res*. 4 (2016):18-26.
2. Abuaisha, A., et al. "Insertion / Deletion Polymorphism of Angiotensin Converting Enzyme Gene Does Not Contribute to Chronic Kidney Disease in Palestine." *Biomed Res Ther*. 5 (2018):2160-2170.
3. Shaikh, R., et al. "Genetic variants of ACE (Insertion/Deletion) and AGT (M268T) genes in patients with diabetes and nephropathy." *J Ren Angio Aldoster Sys*. 15 (2014):124-130.
4. Zhou, D., et al. "Angiotensin-converting enzyme I/D polymorphism is not associated with type 2 diabetes in a Chinese population." *J Ren Angio Aldoster Sys*. 13 (2012):372-378.
5. Sinorita, H., et al. "ACE gene insertion/deletion polymorphism among patients with type 2 diabetes, and its relationship with metabolic syndrome at Sardjito Hospital, Yogyakarta, Indonesia." *Acta Medica Indonesiana*. 1 (2010):12-16.
6. Cauchi, S., et al. "The genetic susceptibility to type 2 diabetes may be modulated by obesity status: implications for association studies." *BMC Med Genet*. 9 (2008):45.
7. Shin, Y., et al. "Relations between eNOS Glu298Asp polymorphism and progression of diabetic nephropathy." *Diabetes Res Clin Prac*. 65 (2004):257-265.
8. Hubert, C., et al. "Structure of the angiotensin I-converting enzyme gene. Two alternate promoters correspond to evolutionary steps of a duplicated gene." *J Biol Chem*. 266 (1991):15377-15383.
9. So W.Y., et al. "Angiotensin-converting enzyme (ACE) inhibition in type 2, diabetic patients-- interaction with ACE insertion/deletion polymorphism." Kidney Int. 69 (2006):1438-1443.
10. Naresh, V.V., et al. "Angiotensin converting enzyme gene polymorphism in type II diabetics with nephropathy." Ind *J Nephrol*. 19 (2009):145-148.

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