

Involvement of Angiotensin Converting Enzyme Gene Polymorphism with Hypertension in Babylon Province

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Abstract

The study intended to assess the prevalence and involvement of ACE I/D gene polymorphism with hypertension in Babylon province. A study includes two groups, the first group comprises 123 patients with essential hypertension and second group comprises 98 apparently healthy subjects. The analysis of results indicated that the II, ID, and DD genotypes distributions (frequencies) of ACE I/D gene polymorphisms as follow: 33 (26.8%), 55 (44.7%) and 35 (28.5%) in hypertensive patients group respectively and 41 (41.8%), 38 (38.8%) and 19 (19.4%) in control group respectively. The DD genotype was established to be significantly raise the hazard of hypertension with respect to those of the II genotype. The I and D alleles distributions (frequencies) of ACE I/D gene polymorphisms were established to be 121 (49.2%) and 125 (50.8%) in hypertensive patients group respectively and 120 (61.2%) and 76 (38.8%) in control group respectively. The minor allele (D) were established to be significantly greater in hypertensive patients group when compared with that of the control group. In conclusion, DD genotype of ACE I/D were allied with hypertension in Babylon province.

Keyword: Angiotensin Converting Enzyme Gene, Hypertension, polymorphism

INTRODUCTION

Hypertension is a continues raise of blood pressure that is produced by genetic and environmental factors (1, 2). The renin angiotensin system (RAS) acts an essential role in controlling of arterial blood pressure, fluids and electrolytes balance. This is done by its vascular smooth muscle constriction and through its effect on adrenal cortex to aldosterone secretion and by transporting of electrolyte in tubules of kidney (3, 4, 5).

Through RAS stimulation, the enzyme renin catalyze the formation of angiotensin I from angiotensinogen. Then, the angiotensin I converting enzyme (ACE) catalyze the formation of angiotensin-II (potent vasoconstrictor) from angiotensin I and also inactivates the bradykinin (potent vasodilator) (6, 7). The ACE is the main enzyme in RAS which has an essential role in regulation of blood pressure and electrolyte levels (8, 9). The genetic factors are responsible for about thirty to sixty per cent of the hypertension while the environmental factors being responsible for the remaining (10). Functional polymorphisms of RAS genes has been considered to explain the genetic vulnerability to hypertension (11). The gene of ACE is the main gene in RAS and attractive gene to study the development of hypertension (12).

In human, the gene of ACE is sited on chromosome 17q23, it consisted from twenty six exons and twenty five introns (8, 9). The insertion / deletion in intron sixteen is the greatest extensively studied ACE gene polymorphisms. In the insertion (I) variant, the fragment is present while in the deletion (D) variant, the fragment is absent, which marks a three genotypes [II, ID and DD] (13, 14). This study intended to assess the prevalence and involvement of ACE I/D gene polymorphism with hypertension in Babylon province.

MATERIALS AND METHODS

The study includes two groups, the first group comprises 123 patients with essential hypertension. They were diagnosed by specialist physicians and selected from several health centers in Babylon Province. Any subject suffered from any other health problems were excluded from the present study. The second group comprises 98 subjects, those are apparently healthy were used as control.

From all subjects, 2mL of blood were drawn by vein puncture and placed in EDTA containing tube. The DNA extracted from blood by genomic DNA mini kit (Geneaid) (15). Genotyping of ACE I/D gene polymorphism at intron 16 was done via polymerase chain reaction (PCR). The PCR was used for

amplification of DNA by using particular primers [the forward primer (5'CTGGAGACCACTCCCATCCTTCT3') and the reverse primer (5'GATGTGGCCATCACATTCGTCAGATT3')] (16).

The products of PCR were analyzed on agarose gel (2%) electrophoresis. The PCR product fragments are 190 bp and 490 bp, the fragment with 190 bp indicate to the existence of a D allele (deletion), while the fragment with 490 bp indicate to the existence of I allele (insertion). After electrophoresis, there are a three possible forms of genotype for each DNA sample, DD genotype have one band (190 bp), II genotype have one band (490 bp), and ID genotype have two bands (190 and 490 bp).

The mean \pm SD and t-test were utilized for the assessment of general characteristics data, while odds ratio (OR) and confidence interval (CI) 95% were utilized for the assessment of genotype data. A statistically significant level was deliberated once the P-value lower than 0.05.

RESULTS

The characteristics of hypertensive patients and control groups as revealed in table (1-1). Genotyping frequencies of ACE gene were consistent with Hardy Weinbergs equilibrium ($\chi^2 = 1.368$, $P = 0.24$ and $\chi^2 = 3.294$, $P = 0.07$) in hypertensive patients and control groups respectively.

The analysis of results indicated that the II, ID, and DD genotypes distributions (frequencies) of ACE I/D gene polymorphisms as follow: 33 (26.8%), 55 (44.7%) and 35 (28.5%) in hypertensive patients group respectively and 41 (41.8%), 38 (38.8%) and 19 (19.4%) in control group respectively. The ID genotype was established to be non-significantly raise the hazard of hypertension with respect to those of the II genotype, while the DD genotype was established to be significantly raise the hazard of hypertension with respect to those of the II genotype as revealed in table (1-2) and figure (1-1).

The I and D alleles distributions (frequencies) of ACE I/D gene polymorphisms were established to be 121 (49.2%) and 125 (50.8%) in hypertensive patients group respectively and 120 (61.2%) and 76 (38.8%) in control group respectively. The minor allele (D) were found to be significantly greater in hypertensive patients group in comparison with that of the control group as revealed in table (1-3) and figure (1-2).

Table (1-1): Characteristics of Study Groups

Characteristic	Group	Mean ± SD
Number	Control	98
	Patient	123
Sex M/F	Control	56/42
	Patient	64/59
Sex M% / F%	Control	57.1% / 42.9%
	Patient	52% / 48%
Age (year)	Control	44.52 ± 9.34
	Patient	46.49 ± 8.59
Systolic blood pressure (mmHg)	Control	121.21 ± 9.37
	Patient	152.44 ± 12.83 (*)
Diastolic blood pressure (mmHg)	Control	80.4 ± 6.11
	Patient	97.42 ± 8.53 (*)
Duration of disease (year)	Patient	6.05 ± 4.43

(*) This means P < 0.05

Table (1-2): Genotypes Distributions of ACE I/D Gene Polymorphism in Study Groups

Genotype	Control	Patients	OR	95% CI	P-value
II	41	33	Reference	Reference	Reference
ID	38	55	1.79	0.97-3.333	0.062
DD	19	35	2.288	1.111-4.713	0.024
Total	98	123	-	-	-

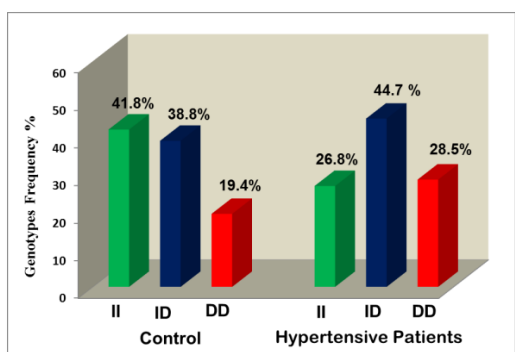


Figure (1-1): Genotypes Frequency of ACE I/D Gene Polymorphism in Study Groups

Table (1-3): Alleles Distribution of ACE I/D Gene Polymorphism in Study Groups

Allele	Control	Patients	OR	95% CI	P-value
I Allele	120	121	Reference	Reference	Reference
D Allele	76	125	1.630	1.114-2.387	0.011
Total	196	246	-	-	-

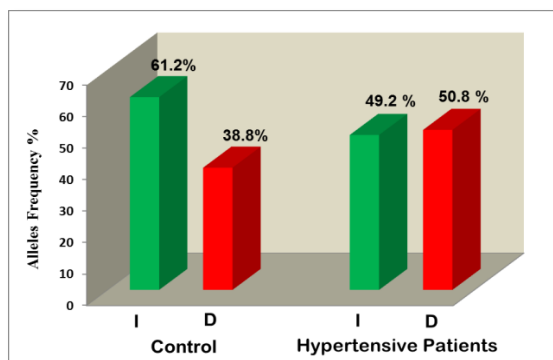


Figure (1-2): Alleles Frequency of ACE I/D Gene Polymorphism in Study Groups

DISCUSSION

It is identified that the RAS act an essential role in blood pressure regulation and every constituent of this system it has been revealed to be contribute in the hypertension pathogenesis (17, 18). The ACE is a main rate limiting enzyme in RAS, they catalyze the formation angiotensin II from angiotensin I, the plasma concentration of angiotensin II, is depending chiefly on ACE genotypes (19, 20). The II genotype subjects display the lesser ACE activity can also be disposed to the lesser angiotensin II concentration, while in contrast, DD genotype subjects observing the greater ACE activity can be disposed to the greater angiotensin II concentration (21).

The effect of polymorphism of ACE gene in hypertension endured debatable. Various studies have revealed an involvement of polymorphism of ACE gene with hypertension (22, 23, 24), while other study stated that the ACE gene polymorphism was not linked with hypertension (25). Nevertheless, in additional studies, the D allele was established to be allied with hypertension (26, 27).

The outcomes of this study illustrates that the DD genotype of ACE I/D gene was found to be allied with hypertension and the minor allele (D) were established to be significantly greater in hypertensive patients group in comparison with that of the control group. This agreement with the outcomes of Ramalingam K., *et al.* (28) and Yun-Fei Z., *et al.* (29) studies. Also, this outcomes disagree with the outcomes of Chiang F., *et al.* (30) and Vassilikioti S., *et al.* (31) studies. In conclusion, DD genotype of ACE I/D was allied with hypertension in Babylon province.

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