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THE RELATION BETWEEN HYPERTENSION AND ANGIOTENSIN CONVERTING ENZYME GENOTYPE IN IRAQI

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ABSTRACT

The source of most common chronic condition attributed to high blood pressure or hypertension, which affect about 20%–30% of the adult males and female's population. The present study is aimed to determine the association, of angiotensin converting enzyme genotype with Iraqis' hypertensive patients. The study was carried out on 30 Iraqi patients having hypertension and 30 healthy subjects as control. Blood samples were collected from both patients and the healthy subjects, DNA from the patients and control specimens were isolated, Detecting of ACE insertion deletion genotype was done by polymerase chain reaction. The results show association between ACE genotype with hypertension DD genotype was increase in patients than control. The present study reported the relation between angiotensin converting enzyme genotype among Iraqis' hypertensive patients.

Keywords: essential hypertension; (ACE I/D); Iraqis' hypertensive patients.

INTRODUCTION:

Hypertension represents a severe public health problem in Iraq. It is one of the main contributory factors for heart attacks and stroke that found the main causes of mortality in the country (Borlay, *et al.*, 2017; Rukavina Mikusic, *et al.*, 2018).

In Iraq, the prevalence of high blood pressure among the adult population (25 years and above) and the use of medication to control it, was found to be 40% in 2008 (WHO, 2008). Record (90–95 %) hypertension is idiopathic and actually all types (essential and secondary hypertension) are responsible for kidney and heart diseases (Carretero *et al.*, 2000). Genes are responsible about 30 % of hypertension; however, the role of gene-environment interactions and gene-gene interactions still indefinite (Zhu *et al.*, 2003, Ehret, 2010). The renin-angiotensin system controls sodium homeostasis and blood pressure (Konoshita, 2011). Angiotensin converting enzyme is responsible for forming of angiotensin II from angiotensin I and also deactivating bradykinin. There is a 187bp Alu repeat insertion/deletion (I/D) polymorphism in the Angiotensin converting enzyme gene predicts the half-life ACE in the serum (Rigat *et al.*, 1990). Expecting the effect of a certain antihypertensive mediator in persons is a problematic task. To overwhelm this problem, investigators are presently studying which genes impact the respond to different antihypertensive medication (Taverne *et al.*, 2010). Several studies have studied the effect of the insertion and deletion gene polymorphism of angiotensin converting enzyme gene on blood pressure response in patients suffering from heart disease treated with ACE inhibitors (ACEIs) (Hermida *et al.*, 2011, Arnett *et al.*, 2005). Some researchers found that the deletion allele have bigger effect in lowering blood pressure (Schelleman *et*

al., 2006, Chung *et al.*, 2010), while a few revisions failed to find the relationship between angiotensin converting enzyme genotype and dropping the high blood pressure (Yu *et al.*, 2003, Schelleman *et al.*, 2005). The present study was planned for detection the association between high blood pressure and angiotensin converting enzyme gene polymorphism in hypertensive Iraqi patients.

MATERIALS AND METHODS

Thirty Iraqi patients suffering from hypertension were choosing in this study, while in vice versa of healthy subjects as control. Both groups were taken blood samples, and the healthy subjects by vein puncture then 2.5 ml of blood were treated with in EDTA anticoagulant tubes and kept in -20°C. The DNA extraction from whole the blood using ReliaPrep Blood Genomic Miniprep System from (Promega, USA) according to manufacturer instruction, then it electrophoresis was performed under electrical power (100 volt) for 10 minutes and 50 volts for 1 hour by using Agaro Power™ instrument (Bioneer, Korea) and photo'd by gel documentation system.

Detecting of ACE insertion deletion polymorphism was carried out by polymerase chain reaction using the same specific primers used by Deepika *et al.* (2013).

PCR reactions for the healthy subjects as well as patients were done using GO Taq Green master mix (Promega, USA), using a final reaction volume 25 μl having: 1μl of both forward and reverse primers, 5 μl of the DNA. PCR amplification was performed in a Applied biosystem thermocycler with same condition of Deepika *et al.* (2013). PCR products were separated on 2% agarose gel with the use of 100bp DNA ladder H3 (Genedirex, Korea) as

a size marker and photo'd by gel documentation system.

RESULTS AND DISCUSSION

Presence of bands with size of 490 bp only shows the homozygous genotype of insertion (II genotype), bands with size 190bp only shows the homozygous genotype of deletion (DD genotype), while the presence of 490 and 190bp band together point to heterozygous genotype (ID genotype).

The PCR amplification results in different patterns of DD, ID, and II gene polymorphism for both patients besides the healthy subject these patterns represented in Figure 1 and table 1.

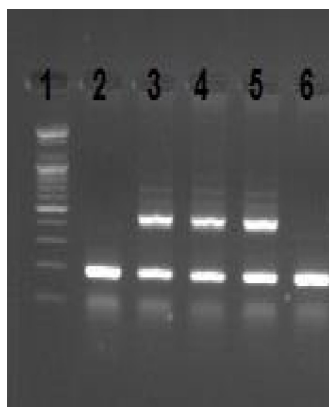


Figure 1: Profile gel electrophoresis of PCR product showed the different patterns of ACE gene Lane1 100 bp DNA Ladder, Lane2, 6 DD genotype of ACE gene, Lane 3, 4, 5 ID genotype of ACE gene

Table 1: Results of PCR amplification of ACE gene

DD genotype	ID genotype	II genotype
Healthy subject no. 6	Healthy subject no. 20	Healthy subject no. 4
Patient no. 16	Patient no. 8	Patient no. 6

ACE gene polymorphism of the genetically analyzed 30 patients compared with the healthy subjects shown in Table 1. ACE gene different genotype with hypertension showing increase in the DD genotype in the patients. Our finding agrees with similar studies done in other population including Iranian and Japanese showing increase in hypertension and DD polymorphism of ACE gene (Higashi *et al.*, 2000, Nakhjavani, *et al.*, 2007).

Renin-Angiotensin System (RAS) shows a significant part in regulating the pressure level of the blood through by regulating fluid homeostasis. Genes coding the constituents of renin-angiotensin system like angiotensinogen (AGT), Angiotensin converting enzyme (ACE), angiotensinogen II type -1 receptor (AGTR1) have been expansively considered in many populations as genetic determining factor of essential hypertension (Rigat *et al.*, 1990, Thiel *et al.*, 2000, He *et al.*, 2015). Subjects having the deletion genotype of angiotensin converting enzyme have been shown to have increase in the angiotensin converting enzyme activity in seum (Rigat *et al.*, 1990, Tsukada *et al.*, 1997), however the T235 AGT variant has been related to raising angiotensin levels (Miller and Scholey, 2004). Fayyad and Aziz (2015) reported an association between, a mutation changing of adinine to cytosine A-20C in the promoter of the AGT and hypertension in Iraqi patients.

Conclusion

This work provides the main related with either angiotensin converting enzyme gene insertion/deletion polymorphism and hypertension in Iraq. The genotype DD increase in patients with hyper-

tension while the genotype ID showed increase in the control groups which may refer that ID genotype may act as a protective agent against hypertension.

REFERENCES

- Arnett D.K., B.R. Davis, C.E. Ford, et al., Pharmacogenetic association of the angiotensin-converting enzyme insertion/deletion polymorphism on blood pressure and cardiovascular risk in relation to antihypertensive treatment: The Genetics of Hypertension-Associated Treatment (GenHAT) study. *Circulation* 111: 3374–3383 (2005).
- Borlay, A.J., Suharsono, et al., Development of single nucleotide polymorphisms (SNPS) marker for oleic acid content in oil palm (*Elaeis guineensis* Jacq.). *Pak. J. Biotechnol.* 14: 55-62 (2017).
- Carretero O.A. and S. Oparil, Essential hypertension. Part I: Definition and etiology. *Circulation*. 101: 329–335 (2000).
- Chung C.M., R.Y. Wang, J.W. Chen, et al., A genome-wide association study identifies new loci for ACE activity: Potential implications for response to ACE inhibitor. *Pharmacogenomics* 10: 537–544 (2010).
- Deepika, N.L.N., K.R. Reddy, V.U. Rani, M. Balakrishna, K.P. PrasannaLatha and J. Parveen, Do ACE I/D gene polymorphism serve as a predictive marker for age at onset in PCOS? *J. Assist. Reprod. Genet.* 30: 125–130 (2013).
- Ehret G.B., Genome-wide association studies: Contribution of genomics to understanding blood pressure and essential hypertension. *Curr. Hypertens. Rep.* 12: 17–25 (2010).

- Fayyad, H.A.D. and I.H. Aziz, Genetic polymorphism of angiotensinogen gene in high blood pressure. *World Journal of Pharmacy and Pharmaceutical Sciences* 4: 1910-1917 (2015).
- WHO, Iraq celebrates World Health Day under the theme of hypertension (<http://www.emro.who.int/irq/iraq-events/world-health-day.html>).
- William J. He, Changwei Li, Dabeeru C. Rao, James E. Hixson, Jianfeng Huang, Jie Cao, Treva K. Rice, Lawrence C. Shimmin, Dong-feng Gu and Tanika N. Kelly, Associations of Renin Angiotensin Aldosterone System Genes with Blood Pressure Changes and Hypertension Incidence. *American Journal of Hypertension* 28: 1310-1315 (2015).
- Hermida R.C., D.E. Ayala, R. Fernández, et al., Circadian rhythms in blood pressure regulation and optimization of hypertension treatment with ACE inhibitor and ARB medications. *Am J Hypertens* 24: 383-391 (2011).
- Higaki J., S. Baba, T. Katsuya, N. Sato, K. Ishikawa, T. Mannami, J. Ogata and T. Ogihara, Deletion allele of angiotensin-converting enzyme gene increases risk of essential hypertension in Japanese men: the Suita Study. *Circulation* 101: 2060-2065 (2000).
- Miller J.A. and J.W. Scholey, The impact of renin-angiotensin system polymorphisms on physiological and pathophysiological processes in humans. *Curr. Opin. Nephrol. Hypertens.* 13: 101-106 (2004).
- Konoshita T., Do genetic variants of the renin-angiotensin system predict blood pressure response to renin-angiotensin system-blocking drugs? A systematic review of pharmacogenomics in the renin-angiotensin system. *Curr. Hypertens Rep.* 13: 356-361 (2011).
- Rigat B., C. Hubert, F. Alhenc-Gelas, F. Cambien, P. Corvol and F. Soubrier, An insertion/deletion polymorphism in the angiotensin I-converting enzyme gene accounting for half the variance of serum enzyme levels. *J. Clin. Invest.* 86: 1343-1346 (1990).
- Rukavina Mikusic, N.L., N.M. Kouyoumdzian, et al., Effects of chronic fructose overload on renal dopaminergic system: alteration of urinary L-dopa/dopamine index correlates to hypertension and precedes kidney structural damage. *Journal of Nutritional Biochemistry* 51: 47-55 (2018).
- Schelleman H., O.H. Klungel, C.M. Van Duijn et al. (2006): Drug-gene interaction between the insertion/deletion polymorphism of the angiotensin-converting enzyme gene and antihypertensive therapy. *Ann. Pharmacother.* 40: 212-218 (2006).
- Schelleman H., O.H. Klungel, C.M. van Duijn et al., Insertion/deletion polymorphism of the ACE gene and adherence to ACE inhibitors. *Br. J. Clin Pharmacol.* 59: 483-485 (2005).
- Taverne K., M. de Groot, A. de Boer et al., Genetic polymorphisms related to the renin-angiotensin-aldosterone system and response to antihypertensive drugs. *Expert Opin. Drug Metab. Toxicol.* 6: 439-460 (2010).
- Thiel B. and A.B. Weder, Genes for Essential Hypertension: Hype, Help, or Hope? *J. Clin. Hypertens.* 2: 187-193 (2000).
- Tsukada K., T. Ishimitsu, N. Tsuchiya, S. Hori-naka and H. Matsuoka, Angiotensin-converting enzyme gene polymorphism and cardiovascular endocrine system in coronary angiography patients. *Jpn Heart J.* 38: 799-810 (1997).
- Yu H., Y. Zhang and G. Liu, Relationship between polymorphism of the angiotensin-converting enzyme gene and the response to angiotensin-converting enzyme inhibition in hypertensive patients. *Hypertens. Res.* 26: 881-886 (2003).
- Zhu X., Y.P. Chang, D. Yan et al., Associations between hypertension and genes in the renin-angiotensin system. *Hypertension.* 41: 1027-1034 (2003).