View metadata, citation and similar papers at core.ac.uk

brought to you by CORE

provided by Elsevier - Publisher Connector

The Egyptian Journal of Medical Human Genetics (2014) **15**, 405–406

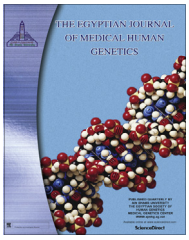
HOSTED BY

ELSEVIER

Ain Shams University

The Egyptian Journal of Medical Human Genetics

www.ejmhg.eg.net
www.sciencedirect.com



LETTER TO THE EDITOR

Hardy–Weinberg equilibrium and association study of insertion/deletion polymorphism of *ACE* gene and Alzheimer's disease in Egyptian patients

Mostafa Saadat

Department of Biology, College of Sciences, Shiraz University, Shiraz 71454, Iran

Received 14 July 2014; accepted 27 July 2014
Available online 22 August 2014

Dear Editor

I read with interest the recent article entitled "Association of insertion/deletion polymorphism of *ACE* gene and Alzheimer's disease in Egyptian patients" by Hassanin et al. [1]. The authors investigated whether insertion/deletion polymorphism (dbSNP rs1799752) of the angiotensin converting enzyme (EC 3.4.15.1; *ACE*; OMIM: 106180) was associated with the risk of Alzheimer's disease in Egyptian patients. The authors reported that their findings support the hypothesis of implication of the I (insertion) allele in the development of Alzheimer's disease [1]. However, I would like to make a few comments about the study.

The Hardy–Weinberg equilibrium (HWE) predicts that in a very large population with random mating, the allelic frequencies will remain stable from generation to generation provided there is no mutation, no migration and no natural selection. The "STrengthening the REporting of Genetic Association" study (STREGA) statement, strongly recommended that authors in genetic association studies, state whether HWE was considered [2].

I used the data present in Tables 1 and 2 of the article of Hassanin et al. [1]. Hassanin and his colleagues stated that the prevalence of the D (deletion) allele was equal to 0.95, whereas by using the counting method, I estimated it as 0.9012 $(= [2 \times 73 + 9] \div (2 \times 86) = 0.9012)$. Based on my analysis, there is a significant deviation between observed genotypic frequencies with the expected genotypic frequencies based on the HWE ($\chi^2 = 11.85$, df = 1, $P < 0.001$).

We know that the above-mentioned disequilibrium might not be explained by non-random mating (consanguineous marriages mainly first cousin marriages), mutation, natural selection and migration. Considering that it has been suggested that the deviation from the expected genotypic frequencies based on the HWE may be a sign of genotyping error [2], I think that during genotyping some kinds of errors occurred. My suggestion might be confirmed by comparison between the studies of Hassanin et al. [1] with other reports from Egypt [3–7] on the prevalence of the D allele. It should be noted that the study of Hassanin et al. [1] showed a higher prevalence of the D allele (and alternatively a lower prevalence of the I allele) compared with the other studies [3–7].

On the other hand, Hassanin et al., reported that they did not find significant difference in plasma ACE activities when compared with different studied genotypes [1]. Based on the data present in Table 3 of the above mentioned article, it seems that plasma ACE activity in patients increased as a function of the number of the D allele ($P < 0.05$) which is in accordance with the previous reports indicating that the D allele has been associated with a higher ACE activity in the serum and tissue than the I allele [8] and the D allele leading to a higher expression of the ACE mRNA [9].

Finally, it seems that the reliability of the results of Hassanin et al. [1] dramatically decreased and their findings must be interpreted with caution.

E-mail addresses: saadat@shirazu.ac.ir, msaadat41@yahoo.com
Peer review under responsibility of Ain Shams University.

http://dx.doi.org/10.1016/j.ejmhg.2014.07.004
1110-8630 © 2014 Production and hosting by Elsevier B.V. on behalf of Ain Shams University.

Conflicts of interest

The author declares no conflict of interest. There is no financial and personal relationship with other people or organizations that could inappropriately influence this work.

Acknowledgments

This study was supported by the Shiraz University.

References

[1] Hassanin OM, Moustafa M, El Masry TM. Association of insertion–deletion polymorphism of ACE gene and Alzheimer's disease in Egyptian patients. Egypt J Med Hum Genet 2014;15:355–60.

[2] Little J, Higgins JP, Ioannidis JP, Moher D, Gagnon F, von Elm E, et al. STrengthening the REporting of Genetic Association studies (STREGA) – An extension of the STROBE statement. Eur J Clin Invest 2009;39:247–66.

[3] Abdel-Aziz AF, Elsaid A, Elmongy R, Abd-Al-Samad A, Elwaseef AM. Angiotensin I-converting enzyme (*ACE*) insertion/deletion polymorphism in Egyptian patients with coronary artery disease. Int J Biochem Res 2012;2:106–19.

[4] Elshamaa MF, Sabry SM, Bazaraa HM, Koura HM, Elghoroury EA, Kantoush NA, et al. Genetic polymorphism of *ACE* and the angiotensin II type1 receptor genes in children with chronic kidney disease. J Inflamm (Lond) 2011;8:20.

[5] El-Shafei MS, Farres MN, Shahin RY. Evaluation of angiotensin converting enzyme gene polymorphism and susceptibility to bronchial asthma among Egyptians. Allergol Immunopathol (Madr) 2012;40:275–80.

[6] Morsy MM, Abdelaziz NA, Boghdady AM, Ahmed H, Abu Elfadl EM, Ismail MA. Angiotensin converting enzyme DD genotype is associated with development of rheumatic heart disease in Egyptian children. Rheumatol Int 2011;31:17–21.

[7] Raslan HM, Amr KS, Elhosary YA, Ezzat WM, Abdullah NA, El-Batae HE. Possible role of angiotensin-converting enzyme polymorphism on progression of hepatic fibrosis in chronic hepatitis C virus infection. Trans R Soc Trop Med Hyg 2011;105:396–400.

[8] Rigat B, Hubert C, Alhenc-Gelas F, Cambien F, Corvol P, Soubrier F. An insertion/deletion polymorphism in the angiotensin I-converting enzyme gene accounting for half the variance of serum enzyme levels. J Clin Invest 1990;86:1343–6.

[9] Suehiro T, Morita T, Inoue M, Kumon Y, Ikeda Y, Hashimoto K. Increased amount of the angiotensin-converting enzyme (ACE) mRNA originating from the ACE allele with deletion. Hum Genet 2004;115:91–6.