Iran Red Crescent Med J. 2016 December; 18(12):e42335. doi: 10.5812/ircmj.42335.

Published online 2016 December 4. **Letter**

The High Frequency of the C282Y-Mutant *HFE* Gene in Northeast Iran; New Finding or Genotyping Error?

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Received 2016 September 16; **Accepted** 2016 November 26.

Keywords: Hereditary Hemochromatosis, C282Y

Dear Editor,

We read with great interest the article by Gerayli et al. (1) in your esteemed journal recently. The authors assessed the H63D and C282Y polymorphisms of the *HFE* gene in Iranian patients from north east Iran with hepatitis C as well as healthy individuals. They found the distribution of C282Y CC, CY and YY genotypes in hepatitis C patients as follow: 84.61%, 10.76% and 4.61%, respectively. Moreover, the frequency of C282Y CC, CY and YY genotypes in healthy individuals was found to be 64.61%, 0% and 35.38%, respectively.

The C282Y polymorphism of the *HFE* gene is the main genetic factor in hereditary hemochromatosis (HH), which is used as the routine marker for molecular diagnosis of HH (2). In a study, 91% of the population in United Kingdom with HH was found to be homozygous for C282Y while only 1% of the control group were homozygous for C282Y (3). We are writing this letter to express our concern regarding the results of the study done by Gerayli et al. (1). They found a high prevalence (> 15%) of C282Y-mutant genotypes (CY and YY) in both groups of Iranian patients with hepatitis C as well as healthy individuals. In previous studies from Iran, the mutant genotypes of this polymorphism was rarely observed in healthy Iranian individuals (4, 5) and even in Iranian patients with liver diseases and HH (5-7). While the data presented by Gerayli et al. (1) regarding the high prevalence of C282Y-mutant genotypes in northeast Iran can be of great interest it should however be noted that this high prevalence of mutant-C282Y genotypes can be a result of genotyping error. It is important to note that distribution of the C282Y genotypes in the study done by Gerayli et al. (1), on healthy individuals was deviated ($P < 0.05$) from Hardy-Weinberg Equilibrium, which is in favor of genotyping error.

In conclusion, the frequency of the C282Y genotypes in individuals from northeast Iran should be investigated by another study using a valid method for confirmation of the results given by Gerayli et al. (1). Moreover, it is very important to validate the results of the methods in molecular studies with another gold-standard method even if it was developed, used and described by others (8).

Footnote

Authors' Contribution: Both authors equally contributed in the manuscript preparation.

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