Dear Editor,

We read the publication entitled “Klotho Gene Polymorphism and Markers of Bone Metabolism in Patients Receiving Maintenance Hemodialysis” in the November 2017 issue of the **Iranian Journal of Kidney Diseases** with great interest. Nazarian and colleagues found that “Homozygote and heterozygote individuals for the A allele at G395A SNP (A allele carriers) were more likely to be on hemodialysis (odds ratio, 1.43; 95% confidence interval, 0.60 to 3.30), but this association was not true for T allele carriers of C1818T SNP.” In fact, the Klotho gene is a specific gene that plays important roles in regulation of S-formylglutathione hydrolase; hence, it is related to several biochemical parameters in the patients. Similar to other genes in medical disorders, the polymorphism of Klotho gene can result in phenotypic difference. Basically, the polymorphism will result in molecular mass change, and this can further result in different amounts of product of biological reaction regulated by that genetic component. The difference in phenotypic appearance is confirmed for the relationship to molecular mass change in several disorders. For the case of Klotho gene polymorphism, if we use a simple quantum chemical calculation for the molecular mass change according to the change according to genetic polymorphism, change from G to A in G395A SNP and C to T in C1818T SNP will result in molecular mass change equal to -16 g/Mol and +15.02 g/Mol, respectively. It can imply that the G395A SNP will result in decreased final mass of biological product per reaction comparing to naive type while this is not observed in C1818T SNP. Hence, the deficit phenotypic manifestation might be expected in G395A SNP and this can further result in inadequate regulation of S-formylglutathione hydrolase and might further result in increased requirement for hemodialysis.

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