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SCIENTIFIC LETTER

Genotypic Effect of IVS4+44C>A and c.2044T>C *DMT1* Gene Mutations on Pathophysiology of Iron-Deficiency Anemia

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To the Editor: Genetic forms of iron-deficiency anemia (IDA) are caused by mutations in the gene encoding divalent metal transport protein (DMT1). Mutation in *DMT1* primarily affects iron utilization [1]. Rodent models exhibit hypochromic/microcytic anemia and iron deficiency caused by Arg substitution for Gly at position 185 (G185R) of the *DMT1* gene [2, 3]. We have collected 140 IDA patient samples. There were 75 males (mean age = 11.2 ± 5.3 y) and 65 females (mean age = 12.1 ± 4.6 y). Additionally, 140 control samples (75 males and 65 females, aged 10.3 ± 4.7 and 11.2 ± 5.1, respectively) were included. Two *DMT1* gene mutations, namely IVS4+44C>A and T c.2044T>C were examined as per previous reported literature [4]. There were 14 patients heterozygous for the IVS4+44C>A mutation. Twenty-eight patients were heterozygous for c.2044T>C mutation, while 8 patients were homozygous for IVS4+44C>A genotype and 9 patients were homozygous for c.2044T>C genotype. Control subjects included 12 heterozygous for IVS4+44C>A mutation, 11 heterozygous for c.2044T>C mutation, while 4 homozygous for IVS4+44C>A mutation. Clinical severity, including weakness, fatigue, breathlessness, tachycardia, angular stomatitis, atrophic glossitis, and pica, were worsening in nonmutants. In the mutant and nonmutant cases of IVS4+44C>A polymorphisms, mean hemoglobin values were 7.4 ± 1.5 g/dL and 6.5 ± 1.3 g/dL, respectively, while in mutant and nonmutant cases of c.2044T>C polymorphisms, mean hemoglobin values were 8.2 ± 1.7 g/dL and 7.2 ± 1.2 g/dL, respectively ($p = 0.0042$ and 0.0002). In mutant and nonmutant cases of IVS4+44C>A polymorphisms, serum ferritin levels were 11.7 ± 2.5 µg/L and 10.8 ± 1.3 µg/L, respectively, while 12.4 ± 3.1 µg/L and 11.6 ± 1.5 µg/L in c.2044T>C polymorphisms, respectively ($p = 0.0132$, 0.0220). We reported significant elevation of ferritin and hemoglobin in IVS4 + 44C>A and c.2044T>C mutations, while decreasing level of ESR and CRP. Clinical frequency of iron-deficiency anemia is less severe in IVS4+44C>A and c.2044T>C mutations. We concluded that IVS4+44C>A and c.2044T>C mutations may be predictor of IDA; these DMT1 variant genotypes need to be diagnosed.

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Declarations

Conflict of Interest None.

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