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MOLECULAR-GENETIC DETERMINANTS OF IRON METABOLISM DISORDERS IN SCHOOLCHILDREN OF THE FERGANA VALLEY AND SYSTEMATIC ANALYSIS OF THEIR PREDICTIVE VALUE

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Introduction. Iron deficiency anemia (IDA) is a common diet-related disorder among school-aged children, leading to impaired physical growth, cognitive development, and immune system function. Scientific evidence indicates that 20–30% of the variability in serum iron levels is determined by genetic factors. Recent large-scale genomic studies have shown that polymorphisms in the TMPRSS6 gene, which regulates iron homeostasis, are associated with hemoglobin levels and erythrocyte indices.

Within the framework of the Law of the Republic of Uzbekistan No. 251 (2010) “On the Prevention of Micronutrient Deficiencies in the Population” and national healthy nutrition strategies, early detection and systematic prevention of iron deficiency have been prioritized.

Study Objective. To identify the molecular-genetic determinants of iron metabolism disorders in schoolchildren of the Fergana Valley and to systematically analyze their diagnostic value in predicting the severity of iron deficiency anemia.

Materials and Methods. The study was conducted using a case–control design and included a total of 201 schoolchildren aged 8–17 years. The main group consisted of 101 children diagnosed with IDA (mild – 26; moderate – 68; severe – 7), while the control group included 100 healthy children.

The severity of IDA was assessed based on hemoglobin (Hb) levels and erythrocyte count: mild – Hb 90–110 g/L; moderate – Hb 70–89 g/L; severe – Hb <70 g/L.

Molecular-genetic analysis was performed using the PCR method to examine the following **TMPRSS6** gene polymorphisms: rs855791 (c.2207T>C), rs4820268 (c.1536C>T), and rs11704654 (c.72G>A).

Statistical analysis was carried out using the χ^2 test, t-test, and logistic regression model. A p-value <0.05 was considered statistically significant.

Results. For the rs855791 polymorphism, the frequency of the C allele in the severe IDA group was 78.6%, which was significantly higher compared to mild (19.2%) and moderate (27.9%) cases ($p < 0.01$). The CC genotype was observed exclusively in severe anemia (57.1%), indicating its etiopathogenetic significance.

In the rs4820268 polymorphism, the CC homozygous variant of the C allele was associated with severe IDA; however, no statistically significant differences were observed in mild and moderate cases.

For the rs11704654 polymorphism, the frequency of the A allele increased to 71–78% in severe cases, and the AA genotype was detected only in the severe IDA group ($p < 0.05$). In mild and moderate cases, the GG genotype predominated.

Logistic regression analysis identified the rs855791 C allele and rs11704654 A allele as independent predictors of severe IDA development.

Discussion. The results confirm the critical regulatory role of the TMPRSS6 gene in iron homeostasis. The marked increase in the frequency of the C allele in the rs855791 polymorphism in severe cases reflects the genetic control of hepcidin expression and iron absorption mechanisms. These findings are consistent with international GWAS studies.

The association of the AA homozygous genotype in rs11704654 with severe IDA indicates that disruptions in iron metabolism in children have a molecular-genetic basis. In mild and moderate cases, dietary and socio-hygienic factors may play a more dominant role than genetic factors.

The small number of severe cases may also limit the statistical significance of some differences. Nevertheless, the observed trends support the need to integrate molecular-genetic screening into annual medical examinations.

A systematic approach that combines genetic, hematological, and hygienic factors allows for early detection of iron deficiency anemia and the development of individualized preventive measures.

Conclusion. In schoolchildren of the Fergana Valley, the rs855791 and rs11704654 polymorphisms of the TMPRSS6 gene are significantly associated with the severity of iron deficiency anemia. The rs855791 C allele and rs11704654 A allele can be considered independent genetic risk factors for the development of severe IDA. Integrating molecular-genetic markers with hematological parameters enables early prediction of severe IDA.