World Academy of Science, Engineering and Technology
International Journal of Health and Medical Engineering
Vol:18, No:04, 2024

# The Contribution of Genetic Polymorphisms of Tumor Necrosis Factor Alpha and Vascular Endothelial Growth Factor into the Unfavorable Clinical Course of Ulcerative Colitis

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**Abstract :** The research aimed to assess the functional significance of tumor necrosis factor-alpha (TNF-α) gene polymorphism at the -308G/A (rs1800629) region and vascular endothelial growth factor A (VEGFA) gene polymorphism at the -634G/C (rs 2010963) region in the development of ulcerative colitis (UC), focusing on patients from the Perm region, Russia. We examined 70 UC patients and 50 healthy donors during the active phase of the disease. Our focus was on TNF-α and VEGF concentration in the blood serum, as well as TNF-α and VEGFA gene polymorphisms at the -308G/A and -634G/C regions, respectively. We found that TNF-α and VEGF levels were significantly higher in patients with severe UC and high endoscopic activity compared to those with milder forms of the disease and low endoscopic activity. These tests could serve as additional non-invasive markers for assessing mucosal damage in the large intestine of UC patients. The frequency of allele variations in the TNF-α gene -308G/A (rs1800629) revealed a significantly higher occurrence of the unfavorable homozygote AA in UC patients compared to donors. Additionally, the major allele G and the allele pair GG were more frequent in patients with mild to moderate disease and 1-2 degree of endoscopic activity than in those with severe UC and 3-4 degree of endoscopic activity ($\chi2=14.19$; $p=0.000$). We also observed a mutant allele A and the unfavorable homozygote AA associated with severe progressive UC. The occurrence of the mutant allele increased the risk of severe UC by 5 times (OR 5.03; CI 12.07-12.21). We did not find any significant differences in the frequency of the CC homozygote ($\chi2=1.02$; $p=0.6$; OR=1.32) and the mutant allele C of the VEGFA gene -634G/C (rs 2010963) ($\chi2=0.01$; $p=0.913$; OR=0.97) between groups of UC patients and healthy individuals. However, we detected that the mutant allele C and the unfavorable homozygote CC of the VEGFA gene were associated with more severe endoscopic changes in the colonic mucosa of UC patients ($\chi2=25,76$; $p=0,000$; OR=0,15). The presence of the mutant allele increased the risk of severe UC by 6 times (OR 6,78; CI 3,13–14,7). We found a direct correlation between TNF-α and VEGFA gene polymorphisms, increased production of the same factors, disease severity, and endoscopic activity ($p=0.000$). Therefore, the presence of the mutant allele A and homozygote AA of the TNF-α gene at the -308G/A region and the mutant allele C and homozygote CC of the VEGFA gene at the -634G/C region are associated with risks related to an unfavorable clinical course of UC, frequent recurrences, and rapid progression. These findings should be considered when making prognoses regarding the clinical course of the disease and selecting treatment strategies. The presence of the homozygote AA in the TNF-α gene (rs1800629) is considered a sign of genetic predisposition to UC.

**Keywords :** gene polymorphism, TNF-α, ulcerative colitis, VEGF
**Conference Title :** ICIMHS 2024 : International Conference on Internal Medicine and Health Sciences
**Conference Location :** Seoul, Korea, South
**Conference Dates :** April 25-26, 2024