



Long COVID: Further Advances in Our Understanding of the Role of Specific Chemokines (CCR5, CCR6, CCR9, and CCL3) in Pediatrics

Hamidreza Farhadirad¹, Nasir Arefinia^{2*}, Zohreh-Al-Sadat Ghoreschi³, Fateme Sadeghzade¹

¹Student Research Committee Jiroft University of Medical Sciences Jiroft Iran

²Bio Environmental Health Hazard Research Center, Jiroft University of Medical Sciences, Jiroft, Iran

³School of Medicine, Jiroft University of Medical Sciences, Jiroft, Iran

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*Corresponding Author:

Bio Environmental Health
Hazard Research Center, Jiroft
University of Medical Sciences,
Jiroft, Iran

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ABSTRACT

Introduction: ARS-CoV-2 infection (COVID-19) is a major pandemic that has caused significant mortality and morbidity worldwide. About 80% of patients had mild or moderate disease, and 5% of patients with severe disease developed severe disease. Long COVID-19, also known as post-COVID-19 syndrome, is a condition in which individuals continue to experience symptoms for weeks or months after recovering from COVID-19. There is a lack of sufficient data on the risk factors for post-COVID-19 sequelae in children. This study aimed to evaluate the long-term effects of severe COVID-19 on promotor methylation and expression genes, including *CCR5*, *CCR6*, *CCR9*, and *CCL3* in children.

Methods and Materials: Clinical data and blood samples from 94 long COVID patients and 25 healthy subjects were collected. Promotor methylation and mRNA expression of *CCR5*, *CCR6*, *CCR9*, and *CCL3* genes in these patients and control group were assessed through methylation-specific PCR and real-time PCR assay.

Results: Our result indicated that promoters of *CCR5* ($p = 0.01$) and *CCL3* ($p = 0.006$) in convalescence COVID-19 children were hyper-methylated compared to the healthy control group. Subsequently, *CCR5* and *CCL3* transcripts decreased compared to the control group ($p = 0.01$). In addition, *CCL3* transcript in children with convalescent COVID-19 decreased compared to the control group ($p = 0.008$). However, we did not observe any significant modification in the transcript levels of *CCR6* ($p = 0.7$) and *CCR9* ($p = 0.46$) in children with convalescent COVID-19 compared to all the control groups.

Conclusion and Discussion: The *CCR5* and *CCL3* promoter region DNA methylation and the subsequent decrease in the expression of these genes were possibly correlated with long-term COVID-19 occurrence in children. Our study revealed additional data on the SARS-CoV-2-mediated inflammatory response.

Keywords: CCR5 receptor antagonists, Chemokine CCL3, Methylation