



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

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Citation:

Farhadirad H, Arefinia N, Ghoreishi ZAS, Sadeghzade F. The Long COVID: Further Advances in Our Understanding of the Role of Specific Chemokines (*CCR5*, *CCR6*, *CCR9* and *CCL3*) in Pediatrics. *Iranian biomedical journal* 2024; 28(7): 332.

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