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Investigation of clinical characteristics of COVID-19 infection in rheumatoid patients on immunosuppressive drugs: a retrospective case–control study

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Abstract

Backgrounds Cytokine storm has been considered a major pathogenic in severe COVID-19 patients with severe disease. Inflammatory cytokines, such as interleukin-6 (IL-6), IL-1, and tumor necrosis factor alpha (TNF- α) released from the lung epithelium during COVID-19 infection resemble those involved in inflammatory rheumatic diseases. Immunosuppressive drugs are central in managing any rheumatologic diseases. Immunosuppressive drugs are central in managing any rheumatologic diseases, and prolonged use may alter clinical features of COVID-19 in these patients.

Objective To determine the clinical findings and disease severity of COVID-19 infection in patients with rheumatic diseases under immunosuppressive therapy.

Method A retrospective case–control study of 981 patients with rheumatic diseases attending university—affiliated clinics and hospital in Shiraz, Iran, including 539 patients with confirmed COVID-19 infection and 442 COVID-19—negative controls without documented infection.

Results Pre-exposure to prednisolone was associated with increased severity of COVID-19 (adjusted OR 2.52; 95% CI 1.19–4.26). Methotrexate (MTX) use was associated with milder disease (OR 0.35; 95% CI 0.21–0.58). Among biologic therapies, anti-TNF agents (etanercept, infliximab) users showed a significant association with lower severity (OR 0.33; 95% CI 0.16–0.69), whereas the smaller rituximab (anti-CD20) subgroup ($n = 54$) was insufficiently powered for separate analysis. Other conventional DMARDs showed no significant effect. Hydroxychloroquine did not show protective effects.

Conclusion In this cohort of Iranian patients with rheumatic diseases, prior corticosteroid use was associated with increased COVID-19 incidence and severity, whereas MTX and anti-TNF biologics were associated with milder disease outcomes. Due to sample size limitations and contrasting literature on rituximab (anti-CD20), we caution against generalizing protective effects across all biologics. Our findings suggest that immunosuppressive therapy influences COVID-19 outcomes, but prospective studies are needed to elucidate mechanisms and causality.

Keywords COVID-19, Immunosuppressants, Rheumatoid patients

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Introduction

The novel coronavirus, which had initially led to pneumonia of unknown etiology in a series of patients in Hubei province in China, in December 2019, has now precipitated a global health crisis caused by the Severe Acute

treatment duration was unavailable. Moreover, the sample sizes within the various drug subgroups were too small to allow meaningful comparisons across groups.

Conclusion

Among patients with rheumatic diseases, prior corticosteroid use was associated with higher risk of severe COVID-19, whereas methotrexate and anti-TNF biologics were associated with milder disease outcomes. Protective effects of anti-CD20 agents remain uncertain due to limited data. Our results should be interpreted as associations; prospective studies are warranted to clarify causal relationships.

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Authors' contributions

F.S: data gathering, analysis, drafted the manuscript and revised the manuscript. E.A: designing, data gathering the research and revised the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The information of the patients was collected through the treatment department of Shiraz University of Medical Sciences (SUMS), the hospitalization centers of COVID-19 patients in Shiraz, and the patients referred to rheumatology clinics. Informed consent was obtained from all subjects or their legal guardians. This study was conducted according to the ethical principles and recommendations outlined in the Declaration of Helsinki and approved by the ethics committee of SUMS with contract number of IR.SUMS.MED.REC.99-01-0122393.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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