Objectives: To identify risk factors for severe COVID-19, requiring hospitalization, in patients with IRDs.

Methods: Multicenter, unmatched nested case control study in four rheumatology centers in the Netherlands. Cases are IRD patients requiring hospitalization for COVID-19 between March 1st 2020 and May 31st 2020. Control patients are IRD patients not hospitalized for COVID-19 within this period and were included in a 1:4 ratio. Patient-, disease- and treatment characteristics were extracted (still ongoing) from electronic patient files, and a questionnaire was used to collect additional data (e.g. on behavioral aspects). Potential risk factors for severe COVID-19 were analyzed using unconditional logistic regression, corrected for confounders.

Results: 77 cases and 198 controls were included. 26 case patients died as a result of COVID-19, 14 were admitted to the ICU. Crude ORs for female sex, age, BMI and presence of one or more comorbidities were 0.46 (95% CI 0.27-0.79), 1.1 (95%CI 1.0-1.1), 1.0 (95%CI 0.98-1.1) and 3.0 (95%CI 1.7-5.2) respectively. Table 1 displays corrected OR, highlighted when OR <0.5/>2.0. Corrected ORs were not significantly increased for any IRD, but a trend for gout was present. Use of hydroxychloroquine (HCQ) shows a protective effect, while use of other csDMARDs than methotrexate or HCQ leads to a higher risk of severe COVID-19. Trends were present for increased risk for rituximab (RTX), glucocorticoids and ACE inhibitors, and protective effect for IL-6R blockers.

Conclusion: The outcomes of this study are in agreement with other research regarding risk of severe COVID-19 related to IRDs and use of IA¹. The suggested increased risk of severe COVID-19 in RTX use is of concern and should be monitored closely. Strengths of this study include low bias due to behavioral effects as only cases early in the pandemic were included, completeness of the determinants of interest and ultimately, it provides answers to a relevant and urgent question.

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Table 1. Corrected ORs for several potential risk factors

Potential risk factor	Corrected OR (95% CI)
IRD	
RA*	1.38 (0.68 – 2.8)
Spondylarthritis	0.60 (0.25-1.5)
Gout	2.8 (0.80-9.8)
Polymyalgia	0.54 (0.18-1.6)
Systemic diseases	1.6 (0.49-5.0)
DMARDs	
csDMARDs (any)	0.39 (0.17-0.88)
Methotrexate	0.90 (0.46-1.7)
HCQ	0.40 (0.16-0.98)
Other	2.0 (0.99-4.1)
bDMARDs (any)	0.96 (0.43-2.2)
TNF-inhibitors	1.0 (0.43-2.6)
IL6R-blockers	0.43 (0.044 – 4.2)
RTX	4.5 (0.25-79)
tsDMARDs	0.89 (0.08-9.8)
Other	
Glucocorticoids > 10 mg/day	2.5 (0.70-9.0)
NSAIDs	0.82 (0.37-1.8)
ACE-inhibitors	3.4 (1.6-7.1)
Vitamin D sufficient	0.77 (0.40-1.5)

*incl. unspecified arthritis

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POS1198

THE ROLE OF SOCS3 IN COLCHICINE ANTI-INFLAMMATORY EFFECT ON COVID-19 INFECTION

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Background: In the fight against COVID-19, the use of an old anti-gout agent which is inexpensive and easily administered (1). A meta-analysis suggests a definite benefit with the addition of colchicine in patients with COVID-19(2). It was suggested that colchicine can have efficacy for hospitalized patients with a severe course of COVID-19 and concurrent inflammatory rheumatic diseases who have a higher risk of venous thromboembolism (3). On the other hand, some reports suggested that colchicine is associated with an increased risk of infections (4). Currently, there are nine clinical trials using colchicine for COVID-19(5), nevertheless, the exact mechanism of action is not well understood.

Objectives: Using publicly available transcriptomic data profiling human cells' response to colchicine to identify core differentially expressed genes (DEGs) then examine the dynamics of the identified DEGs in different datasets of COVID-19 transcriptomics databases to suggest the possible mechanisms of action on the molecular level.

Methods: Gene Expression Omnibus was searched for human samples treated with colchicine compared to controls. GSE4090 dataset was identified where global gene expression of HUVEC (human umbilical vein endothelial cell line) cells exposed to various concentrations of colchicine (n=9) compared to controls (n=7). We reanalyzed this dataset using GEO2R online tool to identify DEGs. The identified DEGs were searched in SARS-CoV-2 transcriptome datasets using metascape online tool to identify gene sets where the DEGs identified showed significant similarity.

Results: Fifty DEGs were identified in response to colchicine no matter what the concentration is used, (Figure 1A). Two gene sets (COVID323, RNA_Wilk_CD4+T-cells_patient-C2_Up [peripheral immune cells] and COVID008, RNA_Blanco-Melo_A549_Up[lung epithelial cells]) showed significant enrichment of the identified DEGs, (Figure 1B). SOCS3, ZC3H12C, CD55, GLIPR1, BACH1, PHLD1, JUNB, NFKB1Z, and MYLIP were the shared genes between the identified DEGs, and the two gene sets with top enriched terms related to important immune-related pathways like IL-6, chemotaxis, leukocytes migration, cytokine release, and response to glucocorticoid, (Figure 1C). Only Suppressor of cytokine signaling 3 (SOCS3) was shared in the three datasets. SOCS3 expression was significantly downregulated in the HUVEC cells exposed to colchicine, (Figure 1D). Next, the normalized gene expression of SOCS3 from whole blood of 62 COVID-19 patients was compared to that of 24 healthy controls using (GSE15264) showed significant upregulation of SOCS3 in the blood of COVID-19 patients indicating its role in COVID-19, (Figure 1E).

Figure 1-4: Volcano plot showing DEGs between GSE4090 dataset and GSE15264 dataset. Panel 1-A: Volcano plot showing DEGs between GSE4090 dataset and GSE15264 dataset. Panel 1-B: Venn diagram showing the overlap between gene lists. Panel 1-C: Heatmap of enriched terms across input gene lists. Panel 1-D: Bar chart showing the normalized gene expression of SOCS3 in HUVEC cells. Panel 1-E: Scatter plot showing the normalized gene expression of SOCS3 in COVID-19 patients compared to healthy controls.

Conclusion: Our reanalysis showed that the possible beneficial effect of colchicine in COVID-19 patients might be through its direct effect on SOCS3 which is specifically upregulated in COVID-19 by IL6 and interferon (IFN)-gamma.

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