Review 1: "Impact of Glucocorticoids and Immunosuppressive Therapies on Symptomatic SARS-CoV-2 Infection in a Large Cohort of Patients with Chronic Inflammatory Arthritis"

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RR:C19 Evidence Scale rating by reviewer:

- **Potentially informative.** The main claims made are not strongly justified by the methods and data, but may yield some insight. The results and conclusions of the study may resemble those from the hypothetical ideal study, but there is substantial room for doubt. Decision-makers should consider this evidence only with a thorough understanding of its weaknesses, alongside other evidence and theory. Decision-makers should not consider this actionable, unless the weaknesses are clearly understood and there is other theory and evidence to further support it.

Review:

This data has largely been confirmed already as part of the COVID-19 Global Rheumatology Alliance registry in a much larger cohort (Gianfrancesco et al, 2020), where prednisolone dose ≥ 10 mg daily is associated with an increased risk of hospitalization, unlike the use of JAK inhibitors/biologics.

The study included 205 adults with chronic inflammatory arthritis receiving a variety of different medications. Laboratory confirmed COVID-19 and highly suspicious infection occurred in 1.1 and 1.4% of cases respectively. The authors also stated that steroids were independently associated with an increased risk of COVID-19, with an adjusted alteration ranging from 1.23 to 3.20 depending on the different definitions used. Patients treated with targeted synthetic or biological DMARDs had a reduced risk of infection.

The study recruited patients with a variety of different inflammatory arthritides, not just rheumatoid arthritis. The study was conducted in 2 centers in northern Italy. Ethical approval was obtained to obtain data. The author has used a WHO definition of COVID-19 infection.

The study area was known to be an area of high risk for COVID-19 during the initial outbreak. The duration of disease was a median of 10 years pointing to an established prevalent cohort. It was noted that there was no difference between the two recruiting centers in terms of demographics, clinical or treatment characteristics.

Of the study population, only 23 had confirmed COVID-19, and a further 29 were highly suspicious for infection. The actual COVID-19 cohort is small, with n of only 52.

Any associations between treatments and risk of COVID based on this small cohort size should be regarded as speculative.

Gender, smoking was similar across the groups and also compared to non-COVID-19 patients. There was a preponderance of obesity, hypertension, and diabetes, although due to the low numbers no significant difference would have been detected here to suggest that these were independent risk factors – this should be emphasized as a weakness.

Patient participants have been "dichotomized" at the age variable of 58 years; it is unclear why age was not incorporated as a continuous variable within a logistic regression model.

It would be interesting to note what levels of disease activity the patients were in – should be stated as a further weakness of the study.

One-third of patients were on chronic treatment with glucocorticoids which seems rather a high proportion – is this normal for this region? – for example, was the higher disease activity a reflection of this?

The stated signal for the protective effect of targeted synthetic or biological DMARDs did not reach statistical significance and this should be stated in the abstract.

The data does not provide any information about the severity of infection or requirement for hospitalization, or mortality. The authors do acknowledge that there is a recruitment bias whereby patients with a more severe infection will not have been targeted by the phone survey.

The conclusion states that: "This study provides all specialists facing the COVID-19 emergency with a very reassuring message about the possibility of suggesting IMiD patients continue their current therapy with ts/bDMARDs without increased risk and probably with a milder infection course" – this statement is vague – the lack of statistical power does not provide a very reassuring message and the word "probably" should be removed – either the data does or does not reassure about a milder infection course.

In supplementary table 4, it states that patients have been on "home lockdown", "used masks and gloves", and "contact avoidance" – this will be very hard to verify and should be stated as a weakness of the study.