Serological tests confirm the low incidence of COVID-19 in chronic rheumatic inflammatory diseases treated with biological DMARD

We read the interesting epidemiological study on 600 patients with rheumatic diseases hospitalised for COVID-19 infection (COVID-19 Global Rheumatology Alliance Registry) published by Gianfrancesco *et al*.[1] Data analysis showed a slightly increased risk of hospitalisation for prednisone doses of ≥10 mg, while biological disease-modifying anti-rheumatic drug (b-DMARD)/targeted synthetic disease-modifying anti-rheumatic drug (ts-DMARD) monotherapy just prior to COVID-19 diagnosis appeared protective, in particular, the tumour necrosis factor targeting agents, as result of a subsequent subanalysis. The epidemiological impact of COVID-19 in patients with rheumatic diseases being treated with b-DMARD has been the subject of several reports by Italian groups. In the first report, only 4 cases were confirmed through rhinopharyngeal swabs out of 320 observed cases.[2] In another study assessed in the emergency period in Lombardy through visit or phone contact, only 3 cases through rhinopharyngeal swabs out of 520 cases were confirmed.[3] Another study of 859 patients in another rheumatology centre in Tuscany, which applied a phone contact methodology, identified only 2 patients suffering from COVID-19 pneumonia.[4] As part of the Tuscany population serological screening, the Incidence COVID-19-Rheumatic Disease–Biologics study has been planned. The anti-Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) IgM and IgG were quantitatively measured in consecutive rheumatic patients followed up at our centre in the period from 25 March to 25 May 2020. In one previous study coming from our centre and performed by iFlash1800 CLIA Analyzer for anti-SARS-CoV-2 antibodies IgM and IgG in patients who were positive for gold/nasopharyngeal swab reverse transcription PCR, a high sensitivity as well as a very good specificity performance was achieved, with a cut-off value of 10.0 absorbance unit (AU)/mL for both IgM and IgG antibodies.[5] Comparison between the study population and the general reference population was performed by Fisher exact test. A p value of <0.05 was considered significant. The OR was then calculated with 95% CI. The incidence of COVID-19 in the reference general population was checked in the Regional Health Agency website, considering all the positive cases among the inhabitants of the Unità Sanitaria Locale (USL) Toscana Centro. The study was approved by the local ethics committee of the ASL-Toscana Centro, within the COVID-TC Project. A total of 295 patients were studied (138 with rheumatoid arthritis (46.8%), 76 with psoriatic arthritis (25.8%), 55 with ankylosing spondylitis (18.6%) and 26 with other rheumatic diseases (8.8%) (8 with systemic lupus erythematosus, 12 with giant cell arthritis and 6 with polymyositis). Six out of 295 patients (2.03%) were positive for IgM or IgG anti SARS-CoV-2. Among them, in only 4 patients (66.7%), the presence of SARS-CoV-2 was confirmed by nasal pharyngeal swab. The four patients were women and all were hospitalised for SARS-CoV-2 pneumonia. Online supplementary table S1 summarises the clinical characteristics of the four patients and their outcome. Finally, the incidence of COVID-19 in our study was calculated, taking into account the number of patients with a positive nasal pharyngeal swab among the 295 initially tested for SARS-CoV2 serology. The incidence of COVID-19 in patients taking b-DMARDs resulted 4/295 (1.4% (95% CI 0.4% to 3.4%)), while the incidence in the 'USL Toscana Centro' population was 7393/1 620 952 (0.5% (95% CI 0.4% to 0.5%)), with a p value of 0.047 and an estimated OR of 3.01 (95% CI 1.13 to 8.09). The results of this study showed a tendency for an increase risk of COVID-19 infection in patients receiving b-DMARD. The data also confirm a prevalence study where, although not significant, patients on biological therapies showed a higher value of COVID-19 infection than the general population.[6] Quantitative serological tests can capture a greater number of positive patients, including those who were asymptomatic, and the integration of serology with nasopharyngeal swab test may provide the best picture of COVID-19 infection among rheumatic patients. In our case history, a patient with RA receiving baricitinib and a patient with ankylosing spondylitis receiving secukinumab, despite the positivity of IgM 41.1 AU/mL in the first case and IgM 61.9 AU/mL and IgG 25.9AU/mL in the second case, showed a negative nasopharyngeal swab, and they did not develop symptoms compatible with the COVID-19 infection. Our four confirmed patients were then included in the COVID-19 Italian Society of Rheumatology Registry sponsored registry and the European EULAR-COVID-19 Database. We recognise the great value of the study on patients hospitalised for COVID-19 infection,[1] but we believe that a general screening with serological tests integrated by swab-based COVID-19 testing may bring new data in asymptomatic patients with rheumatic diseases.

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Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, conduct, reporting or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval The study was approved by the local ethics committee of the ASL-Toscana Centro, within the COVID-TC Project prot 1253.

Provenance and peer review Not commissioned; internally peer reviewed.

► Additional material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/annrheumdis-2020-218214).

To cite Benucci M, Damiani A, Giannasi G, *et al*. *Ann Rheum Dis* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/annrheumdis-2020-218214

Received 5 June 2020
Revised 9 June 2020
Accepted 27 June 2020

Ann Rheum Dis 2020;**0**:1–2. doi:10.1136/annrheumdis-2020-218214

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