Treatment adherence of patients with systemic rheumatic diseases in COVID-19 pandemic

We read with great interest the preliminary German Society of Rheumatology recommendations for the management of patients with autoimmune inflammatory rheumatic diseases (AIRD) during the COVID-19 pandemic.\(^1\) As other regulatory bodies suggest,\(^2,3\) patients should not discontinue their anti-rheumatic treatment because of fear.\(^1\)

Herein, we investigated to which extent patients with AIRD altered their treatment during COVID-19 pandemic and whether there are any factors that affected their decision. We telephone-interviewed (14 April 2020–22 April 2020), 500 consecutive AIRD-patients followed-up in our centre and recorded the following parameters: age, sex, cohabitation, region of residence (urban, semiurban, rural), level of education (first, second, third), employment status, disease duration, current treatment and presence of co-morbidities (hypertension, hyperlipidemia, coronary heart disease, diabetes mellitus, chronic obstructive pulmonary disease (COPD), depression, anxiety).

Specific questions referred to the COVID-19 pandemic period in Greece, starting on 26 February 2020, with predefined answer-options, were asked: discontinuation of any medication received for AIRDs, possible reasons that led to drug discontinuation (including fear of immunosuppression and lack of resources/drug shortage), whether advise was received from a clinician or other sources, symptomatology compatible with COVID-19 infection, subjective assessment (on a five-point Likert scale) of disease activity and a questionnaire to detect nocebo behaviour (cut-off score: 15).\(^3\) Univariate and binary logistic regression analyses were performed using ‘discontinuation of medication due to fear of infections’, ‘discontinuation of medication due to lack of resources/drug shortage’ and ‘consultation by a clinician’ as dependent variables, in three different models.

We interviewed 500 patients (73.2% female, mean (±SD) age: 53.7±15.3 years, disease duration: 10.0±9.4 years) with various AIRDs: inflammatory arthritis: 52.4%, connective tissue diseases: 33% (systemic lupus erythematosus: 16%, systemic sclerosis: 11%, anti-phospholipid syndrome: 3.6%, Sjögren’s syndrome: 1.2%, polymyalgia rheumatica: 1.2%), vasculitis: 9.4%, auto-inflammatory diseases: 5.2%. Of them, 65.8% were cohabiting with another person, 83.6% were living in urban area, 47.6% and 38.2% had a second and third level of education, respectively and 6% were unemployed. Half (46.6%) of our patients were on steroids, 73.4% on biologics (bDMARDs), 6.8% on targeted DMARDs and 43.8% on non-biologic (cDMARDs).

Collectively, 11/500 (2.2%) discontinued AIRD treatment due to fear of immunosuppression; all but two were on bDMARDs. Nineteen (3.8%) patients stopped their treatment because of lack of resources/shortage of drug; 7/19 (36.7%) were on treatment with hydroxychloroquine. noteworthy, 53.8% (7/13) of patients who discontinued treatment with hydroxychloroquine did so because of drug shortage. Additionally, 13/500 (2.6%) and 30/500 (6.0%) discontinued their medication due to a respiratory infection or for other reasons (eg, side-effects), respectively. In total, 124 (24.8%) patients received advice about possible modification of their treatment. All but three, were guided by a clinician.

Therapy withdrawal due to fear of immunosuppression was associated with underlying COPD in univariate analysis ($p=0.022$), and with unemployment (OR, 95% CI: 9.19, 1.30 to 64.7, $p=0.03$) and COPD (OR, 95% CI: 27.53, 3.17 to 239.1, $p=0.003$) in regression analysis. Treatment discontinuation due to lack of resources/drug shortage was not associated with any parameter tested. Decision about consulting a clinician was associated with unemployment status, COPD and male gender ($p=0.001$, $p=0.03$ and $p=0.03$, respectively) in univariate analysis. Regression analysis confirmed these findings: unemployment (OR, 95% CI: 3.55, 1.58 to 7.93, $p=0.002$); COPD (OR, 95% CI: 3.93, 1.11 to 13.95, $p=0.03$); male gender (OR, 95% CI: 1.82, 1.13 to 2.93, $p=0.01$).

COVID-19 infection symptomatology was reported in 39 patients, two of whom were tested and found negative. For most patients (66%) the disease remained stable during the pandemic. Ninety-three (18.6%) patients reported improvement and 77 (15.4%) deterioration from their last visit. Treatment discontinuation due to fear of infections or lack of resources/shortage of drugs was not associated with a disease exacerbation ($p=0.472$). Nocebo behaviour was detected in 10.2% of the patients.

In conclusion, discontinuation rate due to fear of immunosuppression in our cohort was low, mostly observed in patients on bDMARDs. Hydroxychloroquine shortage was a considerable problem for our patients. Special consideration should be given to patients with certain social or clinical characteristics, such as unemployment status and COPD.

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**Contribution of funding agencies**

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**Competing interests**

GEF: has received speaker honoraria from Janssen, travelling grants from AbbVie and MSD. MGT: has received consultant fees and unrestricted grants from AbbVie, MSD, Novartis, Pfizer, GSK and UCB deposited to the Special Account for Research Funding (ELKE) of the National and Kapodistrian University of Athens Medical School. PPS: has received consultant fees and unrestricted grants from AbbVie, Pfizer, MSD, Roche, UCB, GSK and Novartis deposited to the Special Account for Research Funding (ELKE) of the National and Kapodistrian University of Athens Medical School.

**Patient and public involvement**

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication**

Not required.

**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.

**Ethics approval**

This study was conducted according to the Declaration of Helsinki and was approved by the Scientific Council of the ‘Laiko’ hospital (No: 2020/14/4).

**Provenance and peer review**

Not commissioned; internally peer reviewed.

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Received 10 May 2020
Accepted 12 May 2020
Published Online First 31 May 2020

http://dx.doi.org/10.1136/annrheumdis-2020-217987

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