Clinical course, severity and mortality in a cohort of patients with COVID-19 with rheumatic diseases

The recent outbreak caused by a novel severe acute respiratory syndrome coronavirus 2 disease 2019 (COVID-19) has spread rapidly worldwide, and it has been declared a pandemic by the WHO.1 Elderly people, male sex and some underlying comorbidities seem to be risk factors for morbidity and mortality, although an immunosuppressive status could favour the infection and the development of complications.2 However, as progress is made in the knowledge of the physiopathology of COVID-19, it has been observed that severe respiratory forms occur as a result of an hyperinflammatory status and an excessive production of cytokines.3

In this descriptive retrospective study, we aimed to characterise features related to severity and mortality in these patients and the influence of immune modulating drugs on the course of the infection. Patients were included from 25 February 2020 to 8 June 2020 with COVID-19 infection and rheumatic inflammatory diseases from Rheumatology Department of La Paz University Hospital.

One hundred and twenty-two patients were included. One hundred (82.0%) were confirmed through nasopharyngeal swabs. Twenty-two patients (18.0%) exhibited compatible symptoms with compatible lung imaging and/or positive serology. Patients characteristics are shown in table 1.

Variables associated with hospital admission in univariate analysis (table 2) were age (5-year intervals; OR 1.34, 95% CI 1.17-1.55), prednisone dose >5 mg/day (OR 2.55, 95% CI 1.07–5.59), chronic pulmonary disease (OR 5.34, 95% CI 1.47-19.35) and hypertension (OR 4.06, 95% CI 1.79-9.19). Independent risk factors for hospital admission were methotrexate (OR 2.06, 95% CI 1.01-5.29) and age (5-year intervals; OR 1.31, 95% CI 1.11-1.48). No association was found with hydroxychloroquine, other conventional disease-modifying antirheumatic drugs (cDMARDs), targeted synthetic disease-modifying antirheumatic drugs or biological disease-modifying antirheumatic drugs (bDMARDs) or laboratory parameters. Methotrexate treatment was not associated with age, sex, glucocorticoids or subtype of rheumatic disease.

Fourteen patients died (11.5%) due to respiratory failure. Nine patients were on cDMARDs (either in monotherapy or in combination), one was on bDMARD (rituximab) and four were taking only oral glucocorticoids. Hydroxychloroquine did not show differences in mortality. On univariate analysis, factors associated with mortality were age (OR 1.60, 95% CI 1.20-2.01), arterial hypertension (OR 12.17, 95% CI 1.79-9.19),...
pulmonary disease (OR 5.36, 95% CI 1.60-17.94) and prednisone dose >5 mg/day (OR 5.70, 95% CI 1.63-19.92).

The recent outbreak of COVID-19 represents a source of concern for the management of patients with inflammatory rheumatic diseases. However, there are some reports that suggest that treatments typically used for rheumatic diseases might be effective against COVID-19.4 In our series, there was a high proportion of patients that needed hospital admission due to severity of infection (56.6%) compared with other cohorts, which may be explained by the higher prevalence of comorbidity, particularly hypertension, the higher use of glucocorticoids or a potential selection bias towards more severe cases.5 6

Interestingly, methotrexate was a risk factor for hospital admission, but not for mortality, while other cDMARDs did not show differences. Notably, only one of our patients on tocilizumab was infected while all of our infected patients on rituximab needed hospital admission and one died. Additionally, patients on glucocorticoids had worse survival (78.5% vs 34.2%, p<0.01; see online supplementary material). However, mortality rate in hospitalised patients (17.4%) was lower compared with general population in our hospital (20.7%).7

Our preliminary results suggest that COVID-19 does not have a major impact on mortality in patients with rheumatic disease. However, glucocorticoids seem to increase the risk of mortality, while methotrexate and rituximab may have an increased risk of hospital admission. These findings suggest differences in drug mechanism, which may influence COVID-19 course and emphasise the importance of further investigating the impact of immunosuppressive treatment.

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REFERENCES