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# PCOVID02 - INCIDENCE OF COVID-19 IN IMMUNOMEDIATED DISEASES TREATED WITH BIOLOGICS AND TARGETED SYNTHETIC DISEASE MODIFYING ANTIRHEUMATIC DRUGS

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## Resumen

Objectives: To analyze the incidence of COVID-19 among patients with immunomediated inflammatory diseases (IMID) treated with biologic or targeted synthetic disease modified antirheumatic drugs (bDMARD and tsDMARD) and to evaluate the influence of IMID or the therapies on the incidence, evolution of the infection and the need of intensive therapy.

Methods: This is an observational, transversal and ambispective study done from 31 January to 15 May 2020. Data were obtained from the clinical medical records from the hospital setting, primary care and community pharmacy. Inclusion criteria were adults with IMID treated with bDMARD or tsDMARD who started the therapy three months before 31 January 2020. Patients with poor adherence to treatments were excluded. COVID-19 was classified as “definitive” (SARS-CcV2 PCR-positive), “possible” (characteristic symptoms and negative PCR) and “suspected” (characteristic symptoms but PCR not done).

Results: COVID-19 was diagnosed in 70 (11 definitive, 19 possible and 40 suspected) of 902 patients. The cumulative incidence of definitive COVID-19 was 1.2%. When considering all cases, the incidence would have been of 7.8%. A significant relationship was found between COVID-19 and patients on biosimilars TNF-blockers (OR = 2.308, p 0.001). Patients on anti-B cell therapies had a lower incidence of infection (p = 0.046). Patients recovered in 94.3%, with low hospitalization rates (14.3%), pneumonia (14.3%), death (2.9%), or thrombosis (2.9%).

Table 1. Frequency of cases in the two hospitals, type of IMID, type of treatment (bDMARD or tsDMARD) in the 902 patients with and without COVID-19

| Total (902) | No COVID-19 (n = 832, 92.2%) | COVID-19 (n = 70, 7.8%) | Difference |
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| | | | 30 (42.9%) | |
| | HUIS (n = 536, 59.4%) | 506 (60.8%) | 4 (5.7%) Definitive<br>12 (17.1%) Possible<br>14 (20%) Suspected | |
| Hospital | | | 40 (57.1%) | p = 0.003 |
| | HUIL (n = 366, 40.6%)) | 326 (39.2%) | 7 (10%) Definitive<br>7 (10%) Possible<br>26 (37.1%) Suspected | |
| AGE | | 52 yr (SD 19) | 50 (SD 19) | p = 0.85 |
| Sex (female) | | 59.4% | 61.4 | p = 0.737 |
| Diagnosis | | | | |
| Rheumatoid arthritis (n = 296, 32.8%) | | 273 (32.8%) | 23 (32.9%) | p = 0.994 |
| Spondyloarthritis (1) (n = 360, 39.9%) | | 324 (38.9%) | 36 (51.4%) | p = 0.04 (2) |
| CD or UC (n = 134, 14.9%) | | 126 (15.1%) | 8 (11.4%) | p = 0.401 |
| Other IMIDs (3) (n = 112, 12.4%) | | 109 (13.1%) | 3 (4.3%) | p = 0.032 |
| Year after diagnosis | | 8 (SD 8) | 6 (SD 9.3) | p = 0.473 |
| Treatment | | | | |
| Innovator TNF-blockers (4) (n = 314, 34.8%) | | 287 (34.5%) | 27 (38.57%) | p = 0.492 |

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| Biosimilar TNF-blockers (5) (n = 229, 25.4%) | 199 (23.9%) | 30 (42.9%) | P0.0001 |
| Anti-B cell (6) (n = 67, 7.4%) | 66 (7.9%) | 1 (1.4%) | p = 0.046 |
| Anti-il 17/23 (7) (n = 97, 10.8%) | 92 (11.1%) | 5 (7.1%) | p = 0.310 |
| Anti-il-6 (8) (n = 92, 10.2%) | 88 (10.6%) | 4 (5.7%) | p = 0.197 |
| Vedolizumab (n = 30, 3.3%) | 30 (3.6%) | 0 | p = 0.161 |
| Abatacept (n = 19, 2.3%) | 19 (2.3%) | 0 | p = 0.390 |
| Jak inhibitors (9) (n = 42, 4.76) | 40 (4.8%) | 2 (2.9%) | p = 0.765 |
| Anakinra (n = 4. 4.4%) | 4 (0.5%) | 0 | |
| Apremilast (n = 8, 8.9%) | 7 (0.8%) | 1 (1.4%) | |
| Months with bDMARD OR tsDMARD | 30 (SD 44) | 25 (SD 51.5) | p = 0.271 |
| csDMARs (n = 340, 37.7%) | 318 (38.2%) | 22 (31.4%) | p = 0.260 |
| Methotrexate (n = 187, 20.7%) | 173 (20.8%) | 14 (20%) | p = 0.875 |
| Leflunomide (n = 58, 6.4%) | 55 (6.6%) | 3 (4.3%) | p = 0.614 |
| Azathioprine (n = 38, 4.2%) | 36 (4.3%) | 2 (2.9%) | p = 0.762 |
| Sulfasalazine (n = 26, 2.9%) Hydroxychloroquine (n = 23, 2.6%) | 25 (3%) | 1 (1.4%) | p = 0.714 |
| Mycofelonate (n = 14,1.6%) | 20 (2.4%) | 3 (4.3%) | p = 0.414 |
| Others (n = 8, 0.9%) | 14 (1.7%) | 0 | p = 0.617 |
| | 8 (1%) | 0 | p = 1 |

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| Corticosteroids | | | |
| 7.5 mg/d of prednisone (n = 147, 16.3%) | 138 (16.6%) | 9 (12.9%) | p = 0.206 |
| >7.5 mg/d of prednisone (n = 14, 1.6%) | 11 (1.3%) | 3 (4.3%) | |

1. Spondyloarthritis 2. In the group of patients with spondyloarthritis the difference was not found significant when the patients with biosimilars TNF blockers were excluded (p = 0.486). 3. Includes diverse systemic autoimmune diseases: systemic lupus erythematosus (n = 15), uveítis (n = 14), polymialgia without arteritis (n = 13), chronic juvenile arthritis (n = 12), giant cell arteritis (n = 11), Sjögren syndrome (n = 10), myositis or dermatomyositis (n = 10), other vasculitis (n = 8), Behçet´s disease (n = 6), scleroderma and related diseases (n = 5), Still´s disease (n = 4), overlap síndromes (n = 3) and sarcoidosis (n = 1). The signifficance disappeared when patients on rituximab and belimumab were excluded. 4. The group with innovator TNF-blockers includes 24 with infliximab, 131 with adalimumab, 66 with etanercept, 54 with certolizumab and 39 with golimumab. 5. Group with biosimilar TNF-blockers includes 52 with infliximab, 95 with adalimumab and 82 with Etanercept. 6. Anti-B cell group includes 58 patients with rituximab and 9 with belimumab. 7. Anti il 17/23 includes 53 patients with secukinumab, 9 with ixekizumab and 35 with ustekinumab. All COVID-19 cases observed in this group were treated with secukinumab. 8. Anti-il 6 includes 62 patients with tocilizumab and 30 with sarilumab. All COVID-19 cases observed in this group were treated with tocilizumab. 9. Jak inhibitors includes 24 patients with tofacitinib and 18 with baricitinib.Jak inhibitors includes 24 patients with tofacitinib and 18 with baricitinib.

Table 2. Frequency of symptoms and treatments in 70 patients with COVID-19 and IMID treated with bDMARD or tsDMARD.

| Symptoms | N (%) |
|---|---|
| General symptoms* | 67 (95.7) |
| Pneumonia | 10 (14.3) |
| Thrombosis | 2 (2.9) |
| Others** | 42 (60) |
| Therapies used to treat COVID-19 | |
| Antibiotics | 17 (24.3) |
| Hydroxychloroquine | 15 (21.4) |

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| Corticosteroids | 7 (10) |
| Heparin | 6 (8.6)*** |
| Tocilizumab | 4 (5.7) |
| Colchicine | 1 (1.4) |
| Antivirals | 1 (1.4) |
| Mechanic ventilation | 1 (1.4) |

Table 3. Frequency of comorbidities in 902 patients with IMIDs treated with bDMARD or tsDMARD

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|---|---|---|---|
| Comorbidities (n = 546, 60.5%) | No COVID-19 (n = 505, 60.7%) | COVID-19 (n = 41, 58.6%) | p = 0.727 |
| Hypertension (n = 206, 22.8%) | 190 (22.8) | 16 (22.9) | p = 0.997 |
| Dyslipemia (n = 156, 17.3%) | 144 (17.3) | 12 (17.1) | p = 0.972 |
| Smoking (n = 140, 15.5%) | 133 (16) | 7 (10) | p = 0.1840 |
| Obesity/overweight (n = 112, 12.4%) | 105 (12.6) | 7 (10) | p = 0.523 |
| Thyroid disease (n = 79. 8.8%) | 76 (9.1) | 3 (4.3) | p = 0.168 |
| Diabetes (n = 77, 8.5%) | 73 (8.8) | 4 (5.7) | p = 0.379 |
| Chronic obstructive lung disease (n = 29, 3.2%) | 24 (2.9) | 5 (17.1) | p = 0.067 |
| Asthma (n = 25, 2.8%) | 22 (2.6) | 3 (4.3) | p = 0.435 |
| Sleep apnea-hypopnea syndrome (n = 35, 3.9%) | 27 (3.2) | 8 (11.4) | p = 0.004 |

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| Heart diseases (n = 55,6.1%) | 51 (6.1) | 4 (5.7) | p = 1 |
| Psychiatric diseases (n = 37, 4.1%) | 32 (3.8) | 5 (7.1) | p = 0.199 |
| Cancer (n = 26, 2.9%) | 25 (3) | 1 (1.4) | p = 0.714 |
| Others (n = 115, 12.8%) | 107 (12.9) | 8 (11.4) | |

Conclusions: The cumulative incidence of definitive COVID-19 was similar to the general population, with low hospitalization, intensive care management and death rates and it was less frequent in the most immunosuppressed patients.