Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Rapid Communication

Single-center experience of patients with interstitial lung diseases during the early days of the COVID-19 pandemic

J. Guiot a,*, M. Henket a, A.N. Frixa a, M. Delvaux a, A. Denis a, L. Giltay a, M. Thys b, F. Gester c, M. Moutschen c, J.L. Corhay a, R. Louis a, on behalf of the COVID-19 clinical investigators of the CHU de Liège

a Pneumology Department, CHU Liège, Domaine Universitaire Du Sart-Tilman, B35, B4000 Liège, Belgium
b Department of Medico-economic Information, University Hospital of Liège, Liège, Belgium
c Department of Infectious Diseases and General Internal Medicine, University Hospital of Liège, Liège, Belgium

ARTICLE INFO

Article history:
Received 28 May 2020
Received in revised form 6 August 2020
Accepted 19 August 2020
Available online 19 September 2020

Keywords:
COVID-19
Interstitial lung diseases
Lung fibrosis
Clinical epidemiology

ABSTRACT

Introduction: Patients with interstitial lung diseases (ILD) can be suspected to be at risk of experiencing a rapid flare-up due to COVID-19. However, no specific data are currently available for these patients.

Methods: We retrospectively analyzed a cohort of 401 patients with ILD and determined the proportion of patients hospitalized for proven severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and specific symptoms of COVID-19.

Results: We found that 1% of patients (n = 4) were hospitalized (1 in ICU) for COVID-19. In total, 310 of the 401 patients answered the phone call. Only 33 patients (0.08%) experienced specific symptoms of SARS-CoV-2 infection.

Conclusion: Our study did not demonstrate any increased occurrence of severe COVID-19 in ILD patients compared to the global population. Based on our findings, we could not make any conclusion on the incidence rate of SARS-CoV-2 infection in patients with ILDs, or on the overall outcome of immunocompromised patients affected by COVID-19.

© 2020 The Japanese Respiratory Society. Published by Elsevier B.V. All rights reserved.

1. Brief report

In December 2019, health authorities in Wuhan (China) reported clustered pneumonia cases of unknown etiology. A new coronavirus has been identified as the cause of the epidemic, which has since affected many countries globally. The ongoing outbreak of coronavirus disease (COVID-19) has rapidly spread worldwide, and infections in European countries are steadily increasing. The clinical presentation of patients with COVID-19...
Clinical characteristics of patients with COVID-19 and patients of our ILD cohort.

Followed-up in Liège University Hospital. We excluded patients who died before January 2020. We then investigated whether those patients who were closely followed-up in our ILD cohort was composed of patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD), IPF, sarcoidosis, CTD-PF, fibrosing non-specific interstitial pneumonia, and other ILDs (15.7%; 11.2%; 11.6%; 18.5%; 10.3%; and 32.7%, respectively). In our cohort, 37% of the patients were administered specific immunosuppressive therapy (prednisolone >5 mg/day, mycophenolate mofetil, azathioprine, or methotrexate). We compared the four hospitalized PCR-confirmed COVID-19 patients and those with specific symptoms (not hospitalized) to our hospital cohort of patients with a proven severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (PCR-positive) (n = 687) without any underlying ILD. Confirmed cases of COVID-19 were identified through rhinopharyngeal swabs.

Different viral agents are associated with an increased risk of a more severe disease course and respiratory complications in immunocompromised patients [2]. Surprisingly, we found that only 4 patients (2 men/2 women) were hospitalized for COVID-19 out of the 401 selected patients, which is in line with the global incidence of the disease [3,4]. Those 4 patients who suffering from SSc-ILD, hypersensitivity pneumonitis, sarcoidosis, and lipidic pneumopathy, respectively. The fourth patient was admitted to the ICU and is now discharged. She was not on any specific background therapy. All the four patients received at least an antibiotic course (amoxicillin + clavulanic acid), empirically associated with hydroxychloroquine. None of them benefited from plasma therapy or anti-viral therapy. As of now, there has been no significant relapse of their underlying ILD. After calling the other ILD outpatients, we found that 33 of them experienced specific symptoms of SARS-CoV-2 infection and met the COVID-19 screening criteria (Table 1) [5]. The symptoms are presented in Table 1 and were mainly cough (67%), dyspnea (58%), rhinorrhea (42%), hyperthermia (48%), and asthenia (51%). Only two of them where tested and recognized as positive for COVID-19.

This observation corroborates with the global incidence of COVID-19. Unsurprisingly, since the severe respiratory

| Table 1 – Clinical characteristics of patients with COVID-19 and patients of our ILD cohort. |
|---------------------------------|-----------------|----------------|-----------------|-----------------|-----------------|-----------------|
| All hospitalized with COVID-19 in CHU Liège n = 687 | I LD (n = 400) |                         |                         |                         |                         | Suggestive n = 33 |
| Gender, M (%) | 315 (53%) | F | M | M | F | 20 (61%) |
| Age, Year | 58 ± 20 | 45 | 37 | 39 | 74 | 60 ± 14 |
| Cough, N (%) | 268 (84%) | Yes | Yes | Yes | Yes | 22 (67%) |
| Dyspnea | 162 (51%) | – | Yes | Yes | Yes | 19 (58%) |
| Chest pain | 105 (33%) | – | – | – | – | – |
| Rhinorrhea | 167 (52%) | Yes | – | – | Yes | 14 (42%) |
| Diarrhea | 99 (31%) | – | – | – | – | 5 (15%) |
| Hyperthermia | 216 (68%) | Yes | Yes | Yes | Yes | 16 (48%) |
| Asthenia | 201 (63%) | – | Yes | Yes | Yes | 17 (51%) |
| Cephalalgia | 202 (64%) | – | Yes | Yes | – | 9 (27%) |
| Hospitalization | 406 (59%) | 8 days | 5 days | >7 days | >7 days | 5 (15%) |
| ICU | 55 (8%) | – | – | – | 6 days | – |
| Treatment | ECI, Azathioprine | CS 10 mg/d | – | CS 5 mg/d | ICS high dose | CS 14 (42%) |
|                         |                          |                          |                          |                          | IS 10 (30%) |

The data for symptoms are available for only 318 COVID-19 patients.

ECI: enzyme conversion inhibitor; CS: corticosteroids (Prednisolone); ICS: inhaled corticosteroids; IS: immunosuppressors (Azathioprine, Mycophenolate Mofetil, Ledertrexate); ICU: intensive care unit; ILD: interstitial lung disease; SSc-ILD: systemic sclerosis-associated interstitial lung disease.

All the ILD patients were contacted by phone (at least 2 attempts). In total, 77% of them responded. Patients were suspected to have COVID-19 when they experienced at least one of the COVID-19-specific symptoms of acute onset.
complications caused by the SARS-CoV-2 infection are thought to be driven by the aberrant inflammatory and cytokine responses perpetuated by the host's immune system [6], patients benefiting from immunosuppressive therapy could hypothetically be at a low risk of ARDS. Contrary to this, however, immunosuppressive therapies may lead the patients to an immunocompromised state, which could result in severe infectious diseases with lethal respiratory failure such as pneumocystis pneumonia or cytomegalovirus infection that can increase the risk of non-COVID-19-related severe respiratory failure. We cannot conclude from such a small cohort thatILD patients could be at increased risk of SARS-CoV-2 infection. Nevertheless, the main limitation of this study is the highly preventive intervention of the Belgian government and the awareness of ILD patients that they may be at risk of experiencing a severe form of pulmonary involvement and their consequent containment. Through these observations, it seems essential to maintain active observation of our patients to identify a resurgence of this infection in this specific group of fragile patients. Notably, one study focusing on patients with rheumatoid arthritis [7] implemented these observations. They identified 4 out of 320 patients positive for SARS-CoV-2 infection and 4 with suggestive symptoms but without positive PCR results. Another study on 530 patients identified that 2% of the patients were suspected to be positive [8].

Our findings do not allow us to draw any conclusion regarding the incidence rate of SARS-CoV-2 infection in patients with ILDs, or on the overall outcome of immunocompromised patients affected by COVID-19. By following-up these patients, we could possibly highlight a hypothetical unexpected benefit of certain therapies. For example, immunosuppressive treatments pursued by necessity or anti-fibrotic treatments maintained to reduce the evolution of IPF should be specifically reported within cohorts of patients suffering from COVID-19.

Although continuous surveillance of patients with ILDs receiving immunosuppressive drugs is warranted [9,10], these data can support clinicians in the management and counselling of their patients and in avoiding the unjustifiable preventive withdrawal of immunosuppressive therapy, which could lead to an increased risk of relapses and morbidity linked to uncontrolled chronic ILDs.

**Author agreement**

We certify that all authors have seen and approved the final version of the manuscript being submitted. They warrant that the article is the authors' original work, hasn't received prior publication and isn't under consideration for publication elsewhere.

**Funding source declaration**

There was no specific funding for this specific study.

**Permission note**

Not applicable.

**Conflict of Interest**

None.

**References**

[1] COVID-19-Bulletin Epidemiologique Du 3 MAI 2020. [cited 2020 May 3]. Available from: https://epistat.wiv-isp.be/covid.
[2] Memoli MJ, Athota R, Reed S, Czajkowski I, Bristol T, Proudfoot K, et al. The natural history of influenza infection in the severely immunocompromised vs nonimmunocompromised hosts. Clin Infect Dis 2014 Jan 15;58(2):214–24. Available from: https://academic.oup.com/cid/article-lookup/doi/10.1093/cid/cit725. [Accessed 27 April 2020].
[3] Duchemann B, Annesi-Maesano I, Jacobe de Naurois C, Sanyal S, Brillet P-Y, Brauner M, et al. Prevalence and incidence of interstitial lung diseases in a multi-ethnic county of Greater Paris. Eur Respir J 2017;50(2). Available from: https://erj.ersjournals.com/content/50/2/1602419. [Accessed 28 April 2020].
[4] Coultas DB, Zumwalt RE, Black WC, Sobonya RE. The epidemiology of interstitial lung diseases. Internet Am J Respir Crit Care Med 1994 Oct;150(4):967–72. Available from: http://www.atsjournals.org/doi/abs/10.1164/ajrccm.150.4.7921471. [Accessed 28 April 2020].
[5] Interim Guidance: Healthcare Professionals 2019-nCoV | CDC. [cited 2020 May 3]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-criteria.html.
[6] Shi Y, Wang Y, Shao C, Huang J, Gan Jianhe, Huang X, et al. COVID-19 infection: the perspectives on immune responses. Cell Death Differ 2020;27:1451–4. https://doi.org/10.1038/s41418-020-05530-3. Available from: . [Accessed 27 April 2020].
[7] Monti S, Balduzzi S, Delvino P, Bellis E, Quadrelli VS, Montecucco C. Clinical course of COVID-19 in a series of patients with chronic arthritis treated with immunosuppressive targeted therapies. Ann Rheum Dis 2020 May;79(5):667–8. https://doi.org/10.1136/annrheumdis-2020-217424. Epub 2020 Apr 2.
[8] Michaud K, Wipfler K, Shaw Y, Simon TA, Cornish A, England BR, et al. Experiences of patients with rheumatic diseases in the US during early days of the COVID-19 pandemic. ACR Open Rheumatol 2020 Apr 20;2(6):335–43. acr2.11148. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1002/acr2.11148. [Accessed 3 May 2020].
[9] Wong AW, Fidler I, Marcoux V, Johannson KA, Assayag D, Fisher JH, et al. Journal Pre-proof Practical considerations for the diagnosis and treatment of fibrotic interstitial lung disease during the COVID-19 pandemic. Available from: https://doi.org/10.1016/j.chest.2020.04.019. [Accessed 28 April 2020].
[10] Mihai C, Dobrota R, Schröder M, Garaiman A, Jordan S, Becker MO, et al. COVID-19 in a patient with systemic sclerosis treated with tocilizumab for SSC-ILD. Ann Rheum Dis 2020 May;79(5):668–9. Available from: http://ard.bmj.comlookup/doi/10.1136/annrheumdis-2020-217442. [Accessed 28 April 2020].