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.

Respiratory Medicine 181 (2021) 106387

Contents lists available at ScienceDirect

Respiratory Medicine

journal homepage: http://www.elsevier.com/locate/rmed

Correspondence

Alpha-1 antitrypsin deficiency severity and the risk of COVID-19: A Portuguese cohort

ARTICLE INFO

Keywords
COVID-19
AATD
Alpha-1 antitrypsin deficiency
SARS-CoV-2

Dear Editor,

Alpha-1 antitrypsin deficiency (AATD) is highly prevalent in Portugal. It is estimated that 1:5249 individuals have a ZZ genotype, and 1:281 have a SZ genotype [1]. Patients with AATD have recently been proposed as a susceptible population for COVID-19 and disease severity [2]. Data from an Italian registry of AATD revealed a geographical distribution of AATD similar to that of COVID-19 [3]. A significant positive correlation was reported between the combined frequencies of the PI*SZ genotype in 67 countries and their reported COVID-19 mortality [4]. In January 2021, Portugal presented one of the highest incidences of SARS-CoV-2 infection and mortality in the world [5].

Based on these assumptions and in an attempt to address the risk of COVID-19 infection in a Portuguese cohort, we gathered data from all AATD patients followed at Pulmonology consultation in our tertiary hospital in Porto. In Portugal there is a national COVID-19 status database where all SARS-CoV-2 swab results are registered. We checked all our AATD patients' SARS-CoV-2 positive results until the end of January 2021. AATD patients with a diagnosis of COVID-19 were compared with the remaining AATD cohort regarding pre-infection α1-antitrypsin (AAT) serum levels, clinical and functional status.

From a total of 77 AATD patients (68% male), COVID-19 was diagnosed in 9 (12%). Myalgia (88.9%), fever (77.8%) and anosmia/dysgeusia (55.6%) were the most commonly reported symptoms of COVID-19. Pi*ZZ was significantly associated with greater COVID-19 incidence (33.3%, $p = 0.012$), followed by Pi*MS (14.3%) and Pi*SZ (10.0%). Baseline AAT levels were significantly lower in COVID-19 patients (42.9 ± 12.1 vs 65.5 ± 2.8mg/dL, $p = 0.012$). This is in agreement with the suggestion that severe AATD patients may be at higher risk of infection [2].

Computed tomography evidence of emphysema ($p = 0.720$) or bronchiectasis ($p = 0.881$) was not associated with higher SARS-CoV-2 infection rate. Similarly, there was no association with symptoms (mMRC/CAT score) or smoking status. Body mass index≥25kg/m2 (overweight or obesity) was present in 77.8% of infected patients and represented the only significant comorbidity as a risk factor for COVID-19 infection ($p = 0.047$; OR = 4.7), in opposition to diabetes ($p = 0.954$), hypertension ($p = 0.856$) or chronic kidney disease ($p = 0.602$). This supports the idea that AATD itself, and not its comorbidities, may play a role as a risk factor for increased COVID-19 prevalence. However, the small sample size warrants cautious interpretation of the findings.

Three patients were hospitalized due to acute respiratory failure (ARF), none requiring NIV or HFNC. Patients with ARF were heavier smokers (30.0 ± 25.2 pack-year vs 5.2 ± 2.9, $p = 0.09$) and had a lower baseline DLCO (53.0 ± 18.8% vs 87.8 ± 4.6%, $p = 0.042$).

Our data support the hypothesis that severe AATD patients (Pi*ZZ and/or low AAT serum levels) may be a particularly susceptible population for COVID-19, in need of close follow-up. Further investigations with larger samples are required to determine the real risk of COVID-19 infection in AATD patients and to develop actions to prevent severe illness and mortality.

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https://doi.org/10.1016/j.rmed.2021.106387
Received 3 March 2021; Received in revised form 28 March 2021; Accepted 29 March 2021
Available online 2 April 2021