

Smoking and COVID 19: Analysing this controversy in a Brazilian COVID-19 Reference Centre

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Abstract

Introduction: Due to the COVID-19 pandemic, it is extremely important to determine the risk factors that define patients who are more susceptible to the severe form of the disease; however, the observation of supposedly protective factors is also of great relevance. Smoking has been the subject of controversy as to whether it is a protective factor or a risk factor for COVID-19. **Objective:** To assess how smokers behave within the context of the COVID-19 pandemic. **Patients and methods:** The participants in this study were a spontaneously recruited sample from the Rio de Janeiro State University COVID-19 Reference Centre, between March and May 2020. All patients underwent clinical, laboratory, and nasal swabs for the Sars-Cov-2 PCR investigation. Whenever it was the necessary case, patients were referred to hospitalization. **Results:** A total of 4,636 patients with suggestive symptoms of COVID were evaluated. There was 230 (4.9%) smokers in this group; there is a 10.3% smoking prevalence in the state of Rio de Janeiro as described in 2018. A number of 2,246 patients (48.6% of the total sample) were diagnosed with COVID-19, only 82 of these (3.7% of the total positive COVID) were smokers. Only 1 (0.01%) of the smokers with COVID-19 needed hospitalization. As far as the assessed symptoms, smokers showed fewer symptoms during the disease. **Conclusion:** The study suggests that smokers have fewer symptoms (mild or asymptomatic symptoms) and that there is a need to expand specific testing for that group.

Keywords: COVID-19; SARS-CoV-2; Smoking; Risk factor.

Introduction

The COVID-19 pandemic that started in December 2019, in China is caused by the new coronavirus known as Sars-Cov-2.¹ The viral transmission occurs through droplets dispersed in the air and the disease incubation varies from 2-14 days. The virus spectrum is wide, from asymptomatic forms to severe pulmonary conditions.² Due to its high degree of transmissibility, it is important to determine the risk factors for the susceptibility to acquiring the disease and its severe form, as well as those that possibly confer protection.

Several risk factors have been identified since the beginning of the pandemic, namely: age > 60, the presence of comorbidities such as systemic arterial hypertension, diabetes mellitus, chronic cardiovas-

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BJHBS, Rio de Janeiro, 2021;20(2):105-108

DOI: 10.12957/bjhbs.2021.63961

Received on 04/20/2021. Approved on 06/30/2021.

cular diseases and chronic respiratory diseases.^{3,4} In addition to these, chronic kidney diseases, history of transplantation, immunosuppression, including HIV despite CD4+ and the use of immunobiologicals are also described.⁵

As for smoking, this was initially understood as a risk factor, as it doubles the risk for infection by the influenza virus and it is a risk factor for bacterial pneumonia.⁶ Smoking has been considered a risk factor for mortality, but the frequency of smoking patients with active COVID infection has been controversial.⁷ Smoking is responsible for around 200 thousand deaths per year in the USA and it is a risk factor for various diseases, including cardiovascular, pulmonary, and neoplastic diseases which are risk factors for the COVID-19. Nevertheless, the assessment of smoking patients and its relationship with the COVID-19 has been the focus of interest.⁸

In a cross-sectional study, we evaluated the relationship between the COVID-19 and smoking in a sample obtained from spontaneous subjects for the assessment of symptoms and diagnosis of the COVID-19.

Methods

Study procedures

A cross-sectional study carried out between March 19th and May 18st 2020, at the Rio de Janeiro State University Reference Centre for screening patients and health professionals with symptoms of COVID-19. These 4,636 individuals who pursued assistance were recruited and all of them reported the COVID-19 symptoms within a time span of up to 10 days before the evaluation. All patients were invited to participate in the study and signed the CAAE Informed Consent Form numbered - 30135320.0.0000.5259.

The patients were clinically evaluated and their epidemiologic data was collected (Table 1), such as smoking history and smoking load and they were referred to nasal swab collection for Sars-Cov-2 Specific real-time reverse transcription polymerase chain reaction (rt-PCR) performed with the nasopharyngeal swab technique, at each nostril, up to the nasopharynx (NPhS-PCR). rt-PCR assays were performed using commercial kits or designed rt-PCR kits (Biomanguinhos Fiocruz, Rio de Janeiro, and Molecular Biology, Institute of Paraná, Paraná) approved by Brazilian Vigilance (ANVISA). Patients who presented relevant respiratory symptoms or oxygen saturation below 95% underwent

a chest ultrasound with the use of the GE Logico E PRO equipment and whenever they needed, they were hospitalized. The COVID-19 diagnosis was confirmed in the presence of the PCR positive nasal swabbing.

Statistical analysis

Statistical analysis was performed using the statistical program SPSS 2017. Age, gender, and smoking load are described as average and standard deviation. The differences between the groups were evaluated by T Student, ANOVA, and the Chi-Square model whenever it was suitable. Statistical significance was defined by p lower than 0.05.

Results

A total of 4,636 patients were assessed for the diagnosis of the COVID-19, 4,406 (94.3%) non-smokers, and 230 (5.6%) smokers. The COVID-19 diagnosis was confirmed by NPhS PCR in 2,246 patients (48.4% of total patients), of whom, 2,164 (96.3%) were non-smokers and 82 (3.7%) were smokers. Of the 4,406 non-smoking patients, 2,164 (49.1%) presented a positive NPhS-PCR, 456 (10.3%) were non-conclusive and 1,786 (40.5%) negative (Table 2).

Regarding the 230 smoking patients, 82 of them (35.6%) had the diagnosis confirmed, 24 of them (10.4%) had a non-conclusive diagnosis and 124 of them (53.9%) negative. When comparing non-smokers with smokers

Table 1. Epidemiological data for smoking and non-smoking patients from the total sample

Profile	Non-smokers (n=4,406)	Smokers (n=230)
Male (n%)	1265 (28.7%)	84 (36.5%)
Age (n +/- DP)	40.4 +/- 10.6	42.8 +/- 11.8
Caucasians (n%)	2007 (45.5%)	98 (42.6%)
Education > 12 years (n%)	3010 (68.3%)	131 (56.9%)

Source: The authors (2021).

Table 2. SARS-COV-2 nasopharynx swab PCR result for smoking and non-smoking patients

	Non-smokers	Smokers	Total
Positive	2,164	82	2,246 (48,6%)
Non-conclusive	456	24	480 (10,3%)
Negative	1,786	124	1,910 (41,2%)
Total	4,406 (95,0%)	230 (5,0%)	4,636 (100%)

Obs.: The total number of smokers who sought the percent of diagnosis to perform the diagnostic investigation was lower in relation to the prevalence of smokers and also the frequency of diagnosis with $p < 0.001$.

Source: The authors (2021).

regarding the positive PCR, we noticed a significant higher frequency among non-smokers ($p=0.0001$). Only one COVID-19 smoker needed hospitalization. The symptoms evaluated are described in Table 3, where the presence of smoking and non-smoking patients with positive PCR for Sars-Cov-2 is compared.

Discussion

The prevalence of smoking in the Rio de Janeiro state population is 10.3%. Our study pointed to a lower frequency of symptomatic patients with COVID who seek the diagnosis centres of COVID and these, which is already being presented also in the world literature. The percentage of positive COVID-19 smokers is lower than the percentage of smokers concerning the total sample (1,8% vs 46,7%). In addition, the frequency of symptoms in COVID smokers with positive RT-PCR was much lower than in non-smokers.

Vardavas et al, in a meta-analysis, concluded that smoking is possibly associated with a negative outcome in patients with the COVID-19.¹⁰ Smoking seems to be a risk factor as it is associated with the increase of the expression of the gene of the angiotensin 2 converting enzyme (ACE2), which is fundamental for the entry of the virus into the cell.¹¹ The overabundance of ACE2 in the lungs of smokers may partially explain a higher vulnerability of smokers.¹²

In a recent document, the World Health Organization emphasized a possible relationship between smoking and a greater likelihood of developing the disease and death.¹³ Some meta-analyses have published a prevalence with a wide range of smokers among patients from 1.4 to 12.6%, with the prevalence pooled between 6.5 and 7.6%.^{14,15} In our study 3.7% of the cases of COVID were smokers. However, when assessing the risk of smoking for death it becomes an independent

and important variable. Some studies have shown that smoking is a well-established risk factor, with OR: 2.0 (95% CI 1.3-3.2) or OR 2.2 (95% CI 1.3-3.7).^{16,17}

SARS-Cov-2 uses the angiotensin converting enzyme 2 receptor to enter the cell and there is evidence related to nicotine modulation in the expression of angiotensin converting enzyme 2 and its subsequent modulation of nicotinic acetylcholine receptors. The virus would alter the acetylcholine control in these receptors.⁷ Cigarette smoking up regulates the SARS-Cov-2 receptor ACE2 in humans and could increase the likelihood of being infected. On the other hand, increase expression of this enzyme could attenuate the risk of a devastating lung injury.¹⁸

The inflammatory process of smoking should be a risk condition for COVID. It is associated with the risk of mortality. Perhaps the lower frequency of smoking patients looking for the places of diagnosis of COVID are related to previous infectious processes, particularly by Influenzae, inferring a defense against coronavirus infection (crossed immunity) or the devaluation or lack of its symptoms that indicate the need for go to the doctor.¹⁹ This can be identified in our article, bringing the need for comprehensive testing of the entire population due to the risk of asymptomatic carriers or with mild symptoms.

The main limitation of the study is the non-follow-up of patients who are positive in the COVID test and who were smokers and their clinical evolution. Another limitation is that the smoking status is self-reported.

Our study corroborates the findings of this group demonstrating that there was a lower demand for the screening service by smokers when compared to the prevalence of smokers in the state of Rio de Janeiro. This reinforces that it is important to explore the interaction between smoking and COVID.

Table 3. Symptoms presented by smoking and non-smoking patients with positive rt-PCR for Sars-Cov-2

Symptom (n/%)	Non-smokers (n=2,164)	Smokers (n=82)	P
Fever	1458 (64.5%)	51 (45.5%)	0.059
Dyspnoea	618 (52.7%)	29 (34.1%)	0.006
Cough	345 (37.2%)	8 (13.1%)	0.018
Sneeze	1096 (56.0%)	45 (38.4%)	0.017
Sore throat	930 (49.6%)	33 (34.7%)	0.001
Myalgia	1541 (60.7%)	59 (43.3%)	0.001
Headache	1591 (56.2%)	61 (40.9%)	0.002
Anosmia	1070 (74.7%)	46 (61.3%)	0.008

Source: The authors (2021).

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