

Does Smoking Decrease the Susceptibility for SARS-CoV-2?

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Binding to angiotensin-converting enzyme-2 receptor (ACE2) is the key entry mechanism for SARS-CoV-2 to enter the lung tissue. Consequently, blocking ACE2 receptor in the lung could prevent SARS-CoV-2 entry. Nicotine has been found to downregulate ACE2 receptors in smokers [1]. Hence smokers may be less susceptible for COVID-2 infection.

To investigate this hypothesis, I reviewed the rates of smokers and/or patients with COPD as concomitant disease in SARS-CoV-2 hospitalized patients and put them into perspective with the prevalence of smoking in the general population.

Authors	Setting	Sample size	Smoker/COPD	Non-smoker
Guan., <i>et al.</i> [2]	China	1099	12.6%	85.4%
Guan., <i>et al.</i> [3]	China	1590	1.5%	
Zhou., <i>et al.</i> [4]	China	191	3%	
Zhang., <i>et al.</i> [5]	China	140	1.4%	
Shi., <i>et al.</i> [9]	China	487	8.2%	89.1%

Table 1: Characteristics of the cohorts included.

Low rates of smokers within these hospitalized cohorts are surprising, since China has one of the highest prevalence of smoking worldwide [6]. In 2010, China had the highest male smoking prevalence only after Russia [10]. Other Asian countries have comparatively high rates: South Korea 50%, Taiwan 34%, Japan ~40%, whereas the prevalence for smoking in Europe and the U.S is much lower [10].

The new SARS-CoV-2 virus has a higher affinity for ACE2 compared with the prior SARS-CoV. ACE2 receptors are predominantly expressed by bronchial and alveolar epithelial cells in the lung. Nicotine has been shown to increase the expression and/or activity of renin, ACE and AT1R, whereas in the compensatory ACE2/ANG-(1-7)/MasR arm, nicotine downregulates the expression and/or activity of ACE2 and AT2R [1]. Chronic downregulation may have contributed to a relatively lower infection rate of active smokers, despite their general higher risk for lung infections, respiratory distress and concomitant cardiovascular disease. A recent manuscript warns over ACE inhibitors and angiotensin receptors blockers increasing the severity of COVID-19 by upregulation of ACE2 receptors in the respiratory tract [7]. Based on preliminary meta-analysis on Chinese patients, smokers appear not to have a significantly increased risk of progressing towards severe COVID-19 infection [8].

In conclusion, smokers may have a potential lower susceptibility for COVID-19 infection via the ACE2 downregulation. Further epidemiological studies need to confirm this hypothesis.

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