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Letter to Editors

SMOKING AND COVID-19, THE PARADOX TO DISCOVER:An Italian retrospective, observational study in hospitalized and non-hospitalized patients

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Keywords

Smoking; SARS-CoV2; COVID-19 disease

We have read with great interest the article published on Medical Hypotheses by de Bernardis & Busà about the putative role for the tobacco mosaic virus in smokers' resistance to COVID-19 [1]. We agree with the Authors and we also believe that smoking has a complex and not yet clear link with COVID-19. We considered 2 cohorts of 601 patients from 2 Northern Italian cities (Brescia and Bergamo) most affected by the SARS-CoV-2 infection : one concerning patients admitted to our hospital in Brescia, and another one concerning non-hospitalized patients evaluated at the territorial medicine level in Bergamo. The aim of the study was to assess whether or not there was a correlation between current active smoking and severity of COVID-19 disease. 299 consecutive hospitalized COVID-19 patients (M/F = 208 (70%)/ 91(30%) were included and among these 46 (15%) were current active smokers. The mean age was 68.8 years (±11.7). The patients who

died as a consequence of COVID-19 disease were 87 (29%). Table I shows that active smoking and COVID-19 are independent variables (p-value = 0.99) in our hospitalized patients. Garufi et al. claim that the current available data on the relationship between COVID-19 and smoking only concern hospitalized patients [2]**.** In our study 302 consecutive non-hospitalized COVID-19 patients (M/F = 176 (58.3%) /126 (41.7%;) were also included and among these 92 (30%) were current active smokers. The non-hospitalized patients who died as a result of COVID-19 disease were 28 (9.3%). The table I shows that current active smoking and COVID-19 were independent variables (p-value = 0.66) also for non-hospitalized patients. These data are in line with the results of the study performed by Meini et al. and Lippi et al. that reported an unexpectedly low prevalence of current smokers among COVID-19 hospitalized patients [3], [4]. We agree with the Authors and we also found no significant correlation between active smoking and severity of COVID-19 disease. We believe that our study can add important information about the link between smoking and COVID-19 in Italian hospitalized and non-hospitalized patients too.

Probably the link between smoking and COVID-19 is not simple and does not concern a single factor.

If it is true that smoking increases the expression of ACE2 receptors to which the SARS-Cov-2 attaches, it is equally true that up regulation of this enzyme can decrease the risk of developing serious systemic complications of coronavirus infection [5], [6]**.** This is due to the fact that ACE2 converts angiotensin II (ANG II) to Angiotensin 1-7 (ANG 1-7) thus decreasing the powerful pro inflammatory effect of ANG II [7], [8]. Other Authors have confirmed that ACE2 mitigates pro inflammatory effects by decreasing the circulating amount of ANG II [9]. Moreover, studies in mice have shown that in smokers there is an upregulation of ACE2 which protects from the development of the Acute Respiratory Distress Syndrome (ARDS) [10], [11]. Consequently, studies have hypothesized that the up-regulation of this enzyme may protect patients from severe lung damage and that this also occurs in patients with COVID-19 [11].Table 1.

Table 1. see text.

PATIENTS	VARIABLE	DEATHS	OR	95% CI OR	P-VALUE
Hospitalized	Smoking	No 0.280Yes 0.283	1.01	(0.45;2.18)	0.99
Not-hospitalized	Smoking	No 0.310Yes 0.250	0.74	(0.26;1.89)	0.66

Although it seems like a paradox, the latest scientific evidences are in favour of the hypothesis that smoking is not associated with the severity of COVID-19 patients. Our case series is interesting because it reports the data of hospitalized and non-hospitalized patients, confirming

the non-association between smoking and COVID-19 disease. Future studies will be need to confirm this hypothesis and to discover the underlying pathophysiological mechanisms.

Declaration of Competing Interest : None

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