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## Letter to the Editor

**Commentary on the paper: Association of smoking and severity of COVID-19 infection among 5,889 patients in Malaysia: a multi-center observational study, by Ismail N, Hassan N, Hamid MHNA, Yusoff UN, Khamal NR, Omar MA, et al. Published in Int J Infect Dis 2022;116:189–96**



Dear Editor,

We read with interest the paper by Ismail et al. (2022) reporting data on the severity of COVID-19 in smokers concerning never smokers in a large group of hospitalized patients with COVID-19.

All studies published so far have reported a very low prevalence of active smokers among hospitalized patients with COVID-19 (Farsalinos et al., 2020; Lee et al., 2021; Miyara et al., 2020; Rossato et al., 2020). These observations hypothesize a “protective” effect of some component of cigarette smoking, possibly nicotine, mainly on severe respiratory complications of COVID-19 leading to acute respiratory distress syndrome. In this respect, the authors also reported in their study a low prevalence of current smokers among hospitalized patients for COVID-19 (9% of current smokers and 91% of nonactive smokers, i.e., former or never smokers) (Ismail et al., 2022) although they did not fully exploit this result in their paper.

One major problem in their paper is that the authors considered active smokers and former smokers as a whole, which could have modified their results. In a subanalysis, the authors reported a higher prevalence of kidney and liver injuries in former smokers than in current smokers, explaining this with a supposed longer smoking history in former than in current smokers, an explanation not supported by the demographic data reported in the paper.

Furthermore, to support the negative effects of cigarette smoking on COVID-19 outcomes, the authors have cited a reference dealing with the role of nicotine in inflammation; however, that referenced paper reported that nicotine exerts anti-inflammatory effects, and evidence has been reported that active smokers and nicotine users have a lower incidence of different inflammatory diseases (Kalra et al., 2004; Piao et al., 2009; Sopori et al., 1998).

Finally, the report that ever smokers have a higher proportion of severe outcomes is somehow misleading because these observations were not statistically significant, as stated by the authors.

The supposed “protective” effects of cigarette smoking (nicotine?) on SARS-CoV-2-related complications leading to hospitalization should definitely not push smoking addiction. On the contrary, cigarette smoking has to be blamed for its well-known unhealthy effects.

These observations should encourage researchers to investigate the reason for such putative “protective” effects. Thus, the conclusions shared by the authors seem to point in the opposite direction, despite their observations that the number of current smokers is quite low among hospitalized patients with COVID-19.

**Conflict of interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

**References**

- Farsalinos K, Barbouni A, Niaura R. Systematic review of the prevalence of current smoking among hospitalized COVID-19 patients in China: could nicotine be a therapeutic option? *Intern Emerg Med* 2020;15:845–52.
- Ismail N, Hassan N, Abd Hamid MHN, Yusoff UN, Khamal NR, Omar MA, et al. Association of smoking and severity of COVID-19 infection among 5,889 patients in Malaysia: a multi-center observational study. *Int J Infect Dis* 2022;116:189–96.
- Kalra R, Singh SP, Pena-Philippides JC, Langley RJ, Razani-Boroujerdi S, Sopori ML. Immunosuppressive and anti-inflammatory effects of nicotine administered by patch in an animal model. *Clin Diagn Lab Immunol* 2004;11:563–8.
- Lee SC, Son KJ, Kim DW, Han CH, Choi YJ, Kim SW, et al. Smoking and the risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. *Nicotine Tob Res* 2021;23:1787–92.
- Miyara M, Tubach F, Pourcher V, Morélot-Panzini C, Pernet J, Haroche J, et al. Lower Rate of daily smokers with symptomatic COVID-19: a monocentric self-report of smoking habit study. *Front Med (Lausanne)* 2022;8:668995.
- Piao WH, Campagnolo D, Dayao C, Luka RJ, Wu J, Shi FD. Nicotine and inflammatory neurological disorders. *Acta Pharmacol Sin* 2009;30:715–22.
- Rossato M, Russo L, Mazzocut S, Di Vincenzo A, Fioretto P, Vettor R. Current smoking is not associated with COVID-19. *Eur Respir J* 2020;55.
- Sopori ML, Kozak W, Savage SM, Geng Y, Soszynski D, Kluger MJ, et al. Effect of nicotine on the immune system: possible regulation of immune responses by central and peripheral mechanisms. *Psychoneuroendocrinology* 1998;23:189–204.

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