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## Comment on “Pre-hospital antiplatelet medication use on COVID-19 disease severity”



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To the Editor,

We avidly read the article “Pre-hospital antiplatelet medication use on COVID-19 disease severity” by Pan D et al. and we sincerely commend the authors for their bodacious efforts.<sup>1</sup>

As denoted by multifarious research on the effects of antiplatelet medication use on COVID-19 disease,<sup>2</sup> we are in accord with the conclusion of the study that minimal to no association has been established between pre-hospital antiplatelet agents and severity of COVID-19 disease in hospitalized patients.<sup>1</sup> However, we deem it essential to state additional noteworthy points that would enhance the quality of this article and add to existing knowledge of this life-threatening morbidity.

First, the authors did not assess and evaluate key patient characteristics including the history of alcohol intake, paralysis, dementia, peptic ulcer disease, hypertension, hyperlipidemia, administration of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs), the incidence of metastatic tumors, leukemias, lymphomas, collagen disease, and immunosuppression.<sup>3</sup> Assessment of these characteristics, as done in other studies, would have further increased the validity of the findings and eliminated confounders.

Second, the authors did not include a record of the vital signs of the patients. A recent retrospective study in Iran assessed the vital signs of the experimental and control groups to check for differences.<sup>4</sup> Additionally, they reported baseline laboratory data such as a complete blood count and levels of important biomarkers including lactate dehydrogenase, c-reactive protein, ferritin, creatine phosphokinase, serum creatinine, serum urea, procalcitonin, aspartate aminotransferase, and alanine aminotransferase. They also reported the medication used by the patients to treat COVID-19.<sup>4</sup> The inclusion of such data by the authors would increase the validity of the findings.

Third, the authors failed to specify the antiplatelet agents included in the study. A 2020 observational study in Japan included the agents as part of the definitions of the study.<sup>3</sup> Additionally, the study investigated the effect of antiplatelet agents on D-dimer level elevations in patients on admission into the hospital.<sup>3</sup> The inclusion of D-dimer levels would have strengthened the findings of the study and provided further insight into the underpinning pathophysiology.

Fourth, the small sample size may increase the risk of bias and have an impact on the validity of the findings. For example, a 2021 study that evaluated 28,076 patients increased the strength of their study, and the findings seemed legitimate.<sup>5</sup> The association of antiplatelets with disease severity could be assessed using specific outcomes such as emergency department visits, inpatient hospitalization, intensive care unit stay, venous thromboembolism, mechanical ventilation, and mortality.<sup>5</sup>

Fifth, socioeconomic data and the ethnicity of the patients should have been reported. A significantly higher risk of severe outcomes has been observed in those with African, Asian, or Hispanic ethnicity.<sup>5</sup> Sixth, the authors should have commented on the association of severity with gender differences as male patients also have an increased risk of severe outcomes.<sup>5</sup> Finally, multifaceted approaches should be adopted to improve investigations and treatments.

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#### Declarations of Competing Interest

None.

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.

#### CRediT authorship contribution statement

**Arsalan Nadeem:** Conceptualization, Data curation, Methodology, Software, Writing – original draft. **Zoya Ejaz:** Supervision, Software, Writing – review & editing.

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