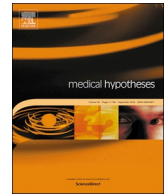




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Letter to Editors

Antibiotic consumption may be linked to exaggeration of COVID-19

When we observe the history of the deadliest pandemics on earth from Antonine Plague to current COVID-19 [1], no bacterial pandemic has occurred since the discovery of Penicillin [2]. The misuse of antibiotics in respiratory viral infections is well established [3]. We hypothesize that use of antibiotics is linked with the exacerbation of viral infections like COVID-19 on the basis of epidemiological and immunological evidence.

Eili Y. Klein et al. [4] shows that United States, France, and Italy consumed the highest quantity of antibiotics among high income countries in 2015, while India, China, and Pakistan did it among lower middle income countries. Surprisingly, these countries are also burdened with high COVID-19 cases [5]. Turkey, Tunisia, Spain, Greece, Algeria, Romania, Belgium, France, New Zealand and Ireland were the leading 10 countries for antibiotic use in total [4] and they are the countries with high disease prevalence [5]. Brazil is the leading country for antibiotic consumption [4] and same for COVID-19 cases [5] in Latin America. In 2018 WHO data [6], the total antibiotic consumption (in metric tons) was higher in Brazil, Turkey, Iran, Russia, France, Tanzania, Sudan, Italy, UK and South Korea chronologically. We all are aware of the deadliest attack of current pandemic in these countries. In the current ECDC report on antibiotic consumption [7], the most COVID prevalent Spain, France, Italy, Ireland, Belgium, Portugal, Poland, UK are also listed as high antibiotic users in Europe [5,7].

Thackray et al. [8] have identified impaired T cell response and enhanced viral burden in response to flaviviruses (Dengue, Zika and West Nile virus) in mice after giving oral antibiotics including the ability of oral antibiotics (e.g. Ampicillin) to increase disease severity just with 3 days' dose.

Morbid COVID-19 patients develop a hyper inflammatory state called the "Cytokine storm syndrome" with the increased production of proinflammatory cytokines like IL1 β , IFN γ , TNF- α [9]. We consider this type of immune response can be associated with antibiotic therapy. Antibiotics like Linezolid and Vancomycin can augment cytokine production (TNF α , IL-1 β , IL-6, IL-10) through activating Toll-like receptors [10]. Again, gut microbiota can halt the respiratory RNA virus replication in the lung epithelia through increased type 1 interferon signaling which can be delayed or severely hindered by antibiotics through reducing interferon-stimulated genes (ISGs) in lung stroma [11]. Our hypothesis is further supported by a recently published article [12] where the authors have described the possible pathophysiology of antibiotic induced septic shock in COVID-19 patients. In the absence of bacterial infection if antibiotics are administered, the cytokine storm may initiate with unregulated release of Toll-like receptors (TLRs), IL-

1 β , IL-6, and TNF- α and gut endotoxins [12].

Despite having several other factors, the fatality in COVID-19 infection is higher in European and high income countries where antibiotic consumption is higher. We recommend the containment of irrational use of antibiotics especially for respiratory symptoms in this pandemic era.

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Prior presentation

No data from this manuscript were presented in a scientific meeting before.

Declaration of Competing 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.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.mehy.2020.109913>.

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