## Could BCG Vaccination Indeed Have a Key Role for Reducing the Spread and Mortality of COVID-19 Worldwide?

BCG Aşısının Dünya Çapında COVID-19'un Yayılmasını ve Ölümcüllüğünü Azaltmada Gerçekten Kilit Bir Rolü Olabilir mi?

Mustafa Törehan Aslan<sup>1</sup>, İlke Özer Aslan<sup>2</sup>, Öner Özdemir<sup>3</sup>

 <sup>1</sup> Istanbul University Istanbul Faculty of Medicine, Department of Pediatrics, Division of Neonatology, Istanbul, Turkey
<sup>2</sup> University of Health Sciences, Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Department of Obstetrics and Gynecology, Istanbul, Turkey
<sup>3</sup> Sakarya University Faculty of Medicine, Training and Research Hospital, Department of Pediatrics, Division of Allergy and Immunology, Sakarya, Turkey

> Yazışma Adresi / Correspondence: Öner Özdemir

Sakarya University, Training and Research Hospital, Department of Pediatrics, Division of Allergy and Immunology, Sakarya/Turkey T: **+90 533 137 12 74** E-mail: **ozdemir\_oner@hotmail.com** 

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Orcid:

Mustafa Törehan Aslan https://orcid.org/0000-0002-3966-4635 İlke Özer Aslan https://orcid.org/0000-0002-3175-8354 Öner Özdemir https://orcid.org/0000-0002-5338-9561

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### Dear Editor,

COVID-19 is a new type of respiratory infection and might lead to serious pneumonia causing acute respiratory distress syndrome (ARDS). Most people infected with SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) manifest as having asymptomatic or mild to moderate upper respiratory tract disease. However, a minority of all can have severe course and even death, especially elderly patients.<sup>1</sup> Here, one of the possible reasons, BCG vaccination and its impact, causing this difference in a population is delineated more.

# Can BCG vaccine reprogram natural (innate) immunity and decrease spread of COVID-19?

Since the first use of BCG vaccine in Europe in the 1920s, a serious decrease in infant mortality has been reported. It is not likely to explain this decline only with the decrease in tuberculosis frequency. The reason for this decrease in infant mortality was reported to be associated with decline in neonatal sepsis and respiratory infections. In another study, this hypothesis was supported by showing that the frequency of respiratory syncytial virus (RSV) infection reduced in population after BCG vaccine.<sup>2</sup> In a South African study, 70 percent of BCG vaccinated adolescents had a decrease in respiratory infections as well. BCG application also reduced influenza A viral load in mice through affecting macrophages. Similarly, BCG vaccine increased the cytokines and peritoneal macrophages against many unrelated pathogens in mice. In the healthy population, BCG vaccination increased the release of proinflammatory cytokines (eg. IL-1β, TNF-α and IL-6).<sup>3</sup>

# Could BCG vaccine be a weapon in reducing the morbidity and mortality of COVID-19?

The countries such as Italy, Holland and USA applying non-universal BCG vaccination policies, it is noteworthy that COVID-19 progresses more severely, compared to the countries following the universal policy. In epidemiological studies, the rate and death of COVID-19 in countries where BCG vaccination applied was also quite lower than non-vaccinated countries. Statistical evaluation of the current data of both European countries and countries in the Northern and Southern Hemisphere, the incidence and mortality of COVID-19 per population was also found lower in BCG-vaccinated countries. If same countries were separately assessed, BCG vaccination has not been performed in Italy, England and France where mortality of COVID-19 was higher. Nevertheless the mortality rates were relatively lower in the countries (Qatar, Saudi Arabia and China); whose BCG vaccination rates in 2018 were very high at 99%, 98%, 99%; respectively.<sup>4,5</sup>

Although there are differences in genetic, demographic, non-pharmacological measures, diagnosis and reporting between nations, possible inverse direct relation between BCG vaccination and COVID-19 looks interesting. Severity of SARS-CoV-2 infection in elderly might be due to long time past after the BCG's positive effect on innate immunity.

Consistently, COVID-19 often manifests as asymptomatic/mildly symptomatic since shorter time passed in younger than in the elderly after BCG vaccination.

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### Contributors

ÖÖ: conceived the study and critical revision; MTA: manuscript writing and literatures review, İÖA: literatures review. All authors approved the final manuscript.

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