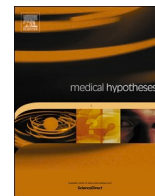




Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Letter to Editors

**Zinc supplementation for males during COVID-19: Is it beneficial?**

Kumar et al. discussed the role of zinc in prophylaxis and treatment of COVID-19 [1]. This is one of multiple manuscripts providing evidence of zinc benefits as intervention for COVID-19 patients. We greatly appreciate the suggested mechanisms and we want to propose an additional effect for zinc in COVID-19 infected males.

It is now well known that ACE2 is the key receptor for the viral entry into human cells. This process is also mediated by TMPRSS2. As both ACE2 and TMPRSS2 are expressed in the testes (spermatogonia, Sertoli and Leydig cells) and in the prostate, an interesting topic that emerged in COVID-19 era is the impact of the virus on the male reproductive system and its ability to induce infertility. Several studies have been conducted to determine if the virus is present in the semen of infected patients, however the results are limited and conflicting [2]. Recently, Bendayan et al. declared that even with the absence of the virus in the semen, COVID-19 can result in the dysregulation of spermatogenesis due to fever, a symptom observed in 80% of infected patients [3].

Zinc is one of the essential nutrients for proper spermatogenesis. It plays a key role in the production, storage and secretion of numerous enzymes involved in the function of spermatozoa and the protection against sperm damage. Zinc deficiency is associated with impaired spermatogenesis, and a daily intake of zinc is necessary for normal function of the male reproductive system [4].

Individuals with zinc deficiency are also at increased risk for severe SARS-COV-2 outcomes and multiple studies supported the potential benefits of zinc for COVID-19 patients [5,6]. Kumar et al. recommended the use of zinc in COVID-19 for its antiviral properties, represented by its ability to generate innate and acquired immune responses and inhibition of both viral entry and replication.

Our hypothesis is that zinc supplementation for males during COVID-19 will provide an additional benefit besides its antiviral effect by protecting the male reproductive system from the possible viral attack and ensuring adequate spermatogenesis. As male gender is an established risk factor for COVID-19 and the relationship between the virus and male infertility has not yet been understood, zinc supplementation

seems to be necessary for males, especially those with zinc deficiency while facing the second wave.

Funding acquisition

None.

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

References

- [1] Kumar A, et al. Potential role of zinc supplementation in prophylaxis and treatment of COVID-19. *Medical Hypotheses* 2020;144:109848.
- [2] Khalili MA, et al. Male fertility and the COVID-19 pandemic: systematic review of the literature. *World J Men's Health* 2020;38(4):506–20.
- [3] Bendayan M, et al. COVID-19 in men: With or without virus in semen, spermatogenesis may be impaired. *Andrologia* 2020. <https://doi.org/10.1111/and.13878>.
- [4] Harchegani AB, et al. Effects of zinc deficiency on impaired spermatogenesis and male infertility: the role of oxidative stress, inflammation and apoptosis. *Human Fertility* 2018. <https://doi.org/10.1080/14647273.2018.1494390>.
- [5] Jothimani D, et al. COVID-19: Poor outcomes in patients with Zinc deficiency. *Int J Infect Dis* 2020;100:343–9.
- [6] Wessels I, Rolles B, Rink L. The potential impact of zinc supplementation on COVID-19 pathogenesis. *Front Immunol* 2020;11:1712. <https://doi.org/10.3389/fimmu.2020.01712>.

Areej Mohamed Ateya^{*,1,2}, Nagwa A. Sabri^{1,3}

Department of Clinical Pharmacy, Faculty of Pharmacy, Ain Shams University, Cairo, Egypt

* Address: Building 10, Part 1, El Sefarat, Nasr City, Cairo, Egypt.
E-mail address: areeg.mohamed@pharma.asu.edu.eg (A.M. Ateya).

¹ Address: African Union Organization Street Beside Ain Shams University Specialized Hospital, Abbaseya, Cairo 11566, Egypt.

² ORCID ID: <https://orcid.org/0000-0001-8680-4971>.

³ ORCID ID: <https://orcid.org/0000-0002-2611-4853>.