

# SARS COV-2 (COVID-19) and Testosterone Level in Males, Is There a Relation?

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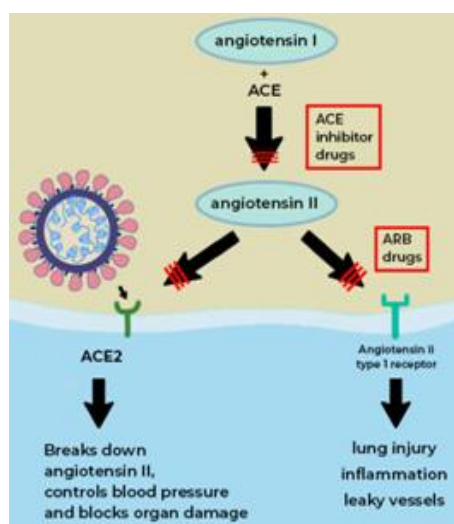
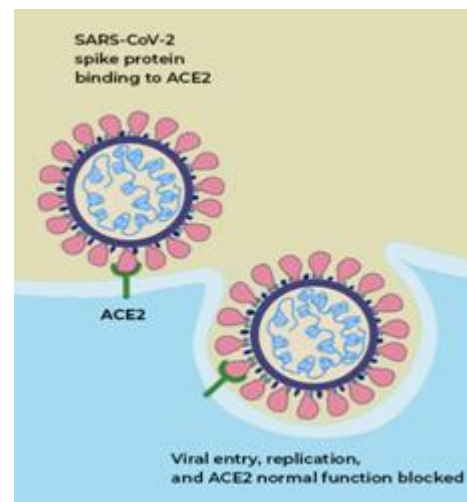
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**Abstract:** ***Introduction:** COVID-19 outbreak was declared global pandemic since March 2020 due to the increased number of infected people and fatalities which affected all the countries worldwide, it is known mainly at the beginning to target the respiratory system which can lead to death, but shortly after the outbreak appeared it was proven that COVID-19 can lead to multi organ failure, as it was proven that it affects respiratory system (pneumonia), cardiovascular system (causing inflamed heart) renal system (causing acute kidney injury), also affect neurological systems (causing loss of taste and smell). Recently a lot of studies were done trying to prove if the COVID-19 can affect the male and female genital system. In this article review we will review the relationship between SARS COV-2 and Testosterone trying to give a better idea about how SARS COV-2 affect testosterone level and we will put the light about all the studies which was done relating to this subject, also it was thought that low testosterone level can increase the severity of SARS cov-2 and increase the risk of need of helped assisted ventilation. **Objective:** The main aim of the article is reviewing our current knowledge of the effect of the (SARS COV2) on the Male genital system and the relation between SARS COV-2 and testosterone. **Methods:** All data of this review article were obtained from the publicly available websites which was published by different organizations worldwide. Also, the keywords used in search on PUB MED, Google scholar using the keywords: COVID-19, SARS COV2, coronavirus combined with testosterone, male genital system, androgens.*

**Keywords:** SARS COV-2, COVID-19, Testosterone in COVID-19patient, COVID-19 and male genital system, COVID-19 and genital system

## 1. How COVID-19 Work

Structure of SARS COV-2 was found to share 76% amino acid with the previously reported SARS COV in 2002, also was found to enter the targeted cells with the same route. AS It is started to be clear that COV SARS-2 as all the SARS-related coronavirus covered by spike protein contain variable receptor binding domain (RBD) [9]. Then binding of RBD with angiotensin converting enzyme receptor (ACE2) receptor facilitates viral entry into the cell with the help of TMPRSS2 (transmembrane protease serine 2). Consequently, cells which contain high presentation of ACE2 receptors and TMPRSS2 combined are more prone to infection with SARS COV-2and regarding site of ACE2 receptors, they are found mainly in the respiratory system and digestive system, cardiovascular and urinary system as well as the testicular tissue, seminiferous duct tissues, spermatogonia, Leydig cells and Sertolicells.



### Male genital tract:

It is almost clear now that males are more risk for infection with SARS COV-2 than females, also fatality rate is more in males than in females. It was found that the blood testicular barrier doesn't work in the proper way to prevent passage of the SARS COV2 during viremia, that's why various cases of COVID-19 patient reported having orchitis during the acute phase of infection [8], which could be an indicator that the testes have been affected during the COVID-19 infection which could means that testicular damage is happening during the acute phase of SARS COV2 infection.

### ACE2 receptors presentation in males:

The ACE2 receptors are highly expressed in testes. As cells of seminiferous duct, spermatogonia, Leydig cells, Sertoli cells are the major main cells of testicular tissues. Those cells showed high expression of ACE2 receptors. It is worth to mention that the peak of presentation of ACE2 in testes in

males depends mainly on the age of the male and if he is fertile or infertile, it was found that the peak age of presentation of ACE2 receptors in males is 30 years and also infertile male showed higher rate of presentation of ACE2 receptors than fertile males which could increase the possibility that SARS COV2 can affect young males as well as infertile males more due to high presentation of ACE2 receptors.

### SARS COV-2 and testosterone:

Testosterone in men is mainly produced by Leydig cells in testes and is produced in small quantities by adrenal gland. There are two aspects regarding the relation between testosterone and SARS COV-2 firstly, it is thought that SARS COV-2 pneumonia can lead to low testosterone level, secondly that the patients with low testosterone level are at higher risk of developing severe manifestations which requires assisted ventilation [1]

Regarding the first aspect because of the fact that Leydig cells contain large amount of ACE2 receptors so it is thought that Leydig cells would be affected during SARS COV-2 which means that the level of testosterone will be reduced during the acute phase of SARS COV-2infection. We will review the research which could prove this relation.

First, Retrospective study which was done in Wuhan leishenshan Hospital in china and published on March 2020 [2] and involved (81 male patients) aged from 20-45 years (median 38 years) with SARS COV-2 infection and compared to 100 healthy men SHOWED significant increase in luteinizing hormones but decreasing testosterone/LH ration and decrease in follicular stimulating hormone level (FSH) /LH level which could be indicator of testicular damage during COV SARS-2, However it is difficult to confirm if the testicular damage happened due to SARS COV-2 OR it is related to increase the body temperature during the infection which can lead also to testicular damage.

Study was published November 2020 [4] which included 44 patients aged between 18-50 years old (median age 35.5 years) who presented to COVID-19 outpatient clinic and classified according to be polymerase chain reaction (PCR), and presence of pneumonia in thoracic computed tomography. It was found that 24 patients COVID-19 PCR positive and by evaluation of FSH, LH, Testosterone levels, it was found that there is no difference between FSH, Testosterone in the patients who is COVID-19 PCR positive, and the patient who had negative COVID-19 PCR but (LH) was significantly higher in the COVID-19 PCR positive test. Also 23 Patients who have proven to be COVID-19 pneumonia based on the thoracic Computed Tomography (CT) showed Total Testosterone was significantly low. FSH and LH showed NO significant change in levels.

Another cohort study was published in September 2020 [3] and included 221 patients who was confirmed SARS COV-2 And Patients was divided into 3 groups: asymptomatic patients (n: 46), symptomatic who didn't need intensive care unit (ICU) (n: 129) and patients who needed intensive care unit (n: 46) and the results was That patients with low or baseline testosterone had high probability of intensive care

admission also accompanied with higher mortalityrate. interestingly it was also found that patients who had pre COVID-19 serum Testosterone level showed significant decrease of testosterone level during the COVID-19 infection.

## 2. Conclusion

During the acute infection of the SARS COV-2 Testosterone level will decrease, also low testosterone level could be considered one of the comorbidities which can increase the severity of SARS COV-2 and increase the risk of need of assisted ventilation. But generally, Relation between SARS COV-2 and testosterone in males is still not clear and will need a lot of research to be done at the area before we will be able to get to the final answer about this relation.

## References

- [1] Hussain AN, Hussain F, Hashmi SK. Role of testosterone in COVID-19 patients-A double-edged sword?. *Med Hypotheses*.2020; 144: 110287. doi: 10.1016/j.mehy.2020.110287.
- [2] Ma L, Xie W, Li D, Shi L, Mao Y, Xiong Y, et al. Effect of SARSCoV-2 infection upon male gonadal function: a single centerbased study. *Med Rxiv* 2020. <https://doi.org/10.1101/2020.03.21.20037267>.
- [3] Çayan S, Uğuz M, Saylam B, Akbay E. Effect of serum total testosterone and its relationship with other laboratory parameters on the prognosis of coronavirus disease 2019 (COVID-19) in SARS-CoV-2 infected male patients: a cohort study. *Aging Male*.2020 Sep 3: 1-11. doi: 10.1080/13685538.2020.1807930. Epub ahead of print. PMID: 32883151.
- [4] Okçelik, S. COVID-19 pneumonia causes lower testosterone levels. *Andrologia*.2021; 53: e13909. <https://doi.org/10.1111/and.13909>
- [5] Hallak J, Teixeira TA, Bernardes FS, Carneiro F, Duarte SAS, Pariz JR, Esteves SC, Kallas E, Saldiva PHN. SARS-CoV-2 and its relationship with the genitourinary tract: Implications for male reproductive health in the context of COVID-19 pandemic. *Andrology*.2021 Jan; 9 (1): 73-79. doi: 10.1111/andr.12896. Epub 2020 Sep 30. PMID: 32869939.
- [6] Morelli, F., Meirelles, L. E. d. F., de Souza, M. V. F., Mari, N. L., Mesquita, C. S. S., Dartibale, C. B., Damke, G. M. Z. F., Damke, E., da Silva, V. R. S., Souza, R. P., & Consolaro, M. E. L. (2021). COVID-19 Infection in the Human Reproductive Tract of Men and Nonpregnant Women, *The American Journal of Tropical Medicine and Hygiene*, tpm201098. Retrieved Mar 2, 2021, from <https://www.ajtmh.org/view/journals/tpmd/aop/article-10.4269-ajtmh.20-1098/article-10.4269-ajtmh.20-1098.xml>
- [7] Youssef Kharbach, Abdelhak Khallouk, <https://doi.org/10.1016/j.ajur.2020.06.005>.
- [8] Sheikhzadeh Hesari, F, Hosseinzadeh, SS, Asl MonadiSardroud, MA. Review of COVID-19 and male genital tract. *Andrologia*.2021; 53: e13914. <https://doi.org/10.1111/and.13914>
- [9] Sharma I, Kumari P, Sharma A, Saha SC. SARS-CoV-2 and the reproductive system: known and the

- unknown. . !!. *Middle East Fertil Soc J*.2021; 26 (1): 1.  
doi: 10.1186/s43043-020-00046-z
- [10] Stanley CP, Maghzal GJ, Ayer A, et al. Singlet molecular oxygen regulates vascular tone and blood pressure in inflammation. *Nature*.2019; 566 (7745): 548-552.
- [11] Yang M, Chen S, Huang B, et al. Pathological Findings in the Testes of COVID-19 Patients: Clinical Implications. *European Urology Focus*.
- [12] Ye M, Wysocki J, William J, Soler MJ, Cokic I, Batlle D. Glomerular localization and expression of Angiotensin-converting enzyme 2 and Angiotensin-converting enzyme: implications for albuminuria in diabetes. *J Am SocNephrol*.2006; 17 (11): 3067-3075.
- [13] Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med*.2020; 382: 1708-1732.
- [14] Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med*.2020; 382: 1708-1732.
- [15] Pan F, Xiao X, Guo J, et al. No evidence of SARS-CoV-2 in semen of males recovering from COVID-19. *Fertility and Sterility*.
- [16] Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA*.2020; 323: 1061-1069.
- [17] Wang Z, Xu X. scRNA-seq Profiling of Human Testes Reveals the Presence of the ACE2 Receptor, A Target for SARS-CoV-2 Infection in Spermatogonia, Leydig and Sertoli Cells. *Cells*.2020; 9: 4.
- [18] Wu ZS, Zhang ZQ, Wu S. Focus on the "Crosstalk" Between COVID19 and Urogenital Systems. *J Urol*.2020; 208: 7-8.
- [19] Gallagher TM, Buchmeier MJ. Coronavirus spike proteins in viral entry and pathogenesis. *Virology*.2001; 279 (2): 371-374.
- [20] Ye M, Wysocki J, William J, Soler MJ, Cokic I, Batlle D. Glomerular localization and expression of Angiotensin-converting enzyme 2 and Angiotensin-converting enzyme: implications for albuminuria in diabetes. *J Am SocNephrol*.2006; 17 (11): 3067-3075.
- [21] <https://theconversation.com/what-is-the-ace2-receptor-how-is-it-connected-to-coronavirus-and-why-might-it-be-key-to-treating-COVID-19-the-experts-explain-136928>