

World Journal of *Clinical Cases*

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Effect of gender on the reliability of COVID-19 rapid antigen test among elderly

Wassan Nori, Wisam Akram

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Abstract

Defining con-founders that affect the reliability of diagnostic tests for coronavirus disease 2019 is vital to breaking the chain of infection. The elderly population is a higher risk group for the emerging virus. However, gender seems to exert a critical role in modifying the infection risk among women owing to hormonal changes. The menopause transition is an exceptional period for older women where the protective and immunomodulatory effects of the estrogen hormone are lost. Accordingly, attention should be given to postmenopausal women since they will have an increased risk compared to their pre-menopausal peers.

Key Words: COVID-19; Rapid antigen test; Real-time reverse transcription-polymerase chain reaction; Age; Gender; Postmenopausal women

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Core Tip: One of the main strengths of coronavirus disease 2019 (COVID-19) is the limitation of tests confirming the infection. The rapid spread of the virus was accredited to false negative tests and asymptomatic carriers. The elderly are described as a high-risk group with increased morbidity and mortality rates. However, some discuss that COVID-19 is gender specific; as males suffer from a worse course of infection in comparison to age-matched females. COVID-19 diagnostic tests rely on patients' immunological responses, we aimed to verify whether gender has an effect on the test reliability and if the test performance will be different among women in their menopausal years.

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TO THE EDITOR

With interest, we read Tabain *et al*[1] study that was published in *World J Clin Cases* 2022 and how the elderly population experienced a meaningfully lower cycle threshold (Ct) value than younger groups; thus, increasing false negative rapid antigen test (RTA) tests results[1].

Aging is a risk factor for coronavirus disease 2019 (COVID-19) severe infection, attributed to a weakened immune system exacerbated by medical co-morbidities such as diabetes and high blood pressure. Establishing confounding factors that affect the test reliability is vital to diagnosing high-risk groups[2].

However, we think an essential confounder was missed in the study; the authors in Table 1 (<https://www.wjgnet.com/2307-8960/full/v10/i19/6456.htm>). Perceptions of false-ve RAT detection tests and reverse transcription polymerase chain reaction (RT-PCR) cycle values based on age groups are described. In addition, they showed the number and percent of female patients tested alongside the overall numbers and percent without addressing the male patients' numbers and percentages, *i.e.*, the effect of gender on the results presented was not addressed. A calculation was made of the total female to male ratio, and a simple Chi-square test was conducted. The analysis highlighted a significant difference ($P = 0.021$) between female numbers and percentages *vs* males, particularly among the 19–65 year age group [698 (58.46%) *vs* 496 (41.54%)]. As for the results of other subgroups, the numbers were comparable.

In most regions of the globe, males have a higher confirmed and fatality ratio than females[3]. This gender disparity in COVID-19 infections can be linked to a variety of reasons. Women's immune systems detect infections a bit earlier than those of men; females display higher innate and adaptive immunological responses than males due to the greater number of immune-related genes on the X chromosome. Additionally, the COVID-19 virus relies on angiotensin-converting enzyme 2 (ACE2) to enter the host cell; unfortunately, males have a higher ACE2 than females[4]. As a result, men may be more susceptible to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) than women. Compared to men the same age, pre-menopausal women are less likely to get COVID-19, which points to the role of sex hormones[5].

The immunomodulatory effects of estrogen on cardiovascular, metabolic, and viral infections have already been discussed[6,7], and COVID-19 viruses are no exception. Estrogens influence pro-inflammatory signaling pathways and have significant anti-inflammatory and immunomodulatory effects in SARS-CoV-2 infection. While young women have lower risks of severe COVID-19, this protection is lost throughout the menopausal transition and women become comparable to men in infection risk[2].

In good agreement with the aforementioned work[2,5], estradiol therapy was used in symptomatic postmenopausal women with confirmed SARS-CoV-2 infection and proved valuable in non-severe cases. D-dimer, IL-6, and C-reactive protein levels were found to be lower. The authors declared a meaningful difference in the rate of-ve RT-PCR in the estradiol group *vs* the controls ($P = 0.007$; $P = 0.026$) on days five and seven of the admission[8].

For that, we think that adding an age-reference sub-group from 19-50 and 50–65 years will better explore the effect of aging on the female gender. Moreover, adding the patients' gender and examining its effect on the false negative RTA and RT-PCR might reveal a new prospect of estrogen deficiency in postmenopausal women.

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FOOTNOTES

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