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Short Communication

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# Choosy Corona: Females are at an Advantage

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## Abstract

*Tiny Corona has no brain but still it is very choosy, it does not infect equally to all the human population. It infects more men than women more older population than younger one. There are reasons for that. Men are on the priority list because of certain reasons; if they are bald more venerable. However, the subjects who are carrying blood group 'O' they can be spared. Bald man with blood group 'A' is worst hit. It is not yet certain but data show that sex steroid hormones and X chromosome products are able to keep this virus away besides immunity, life style, environment and genetic reasons. Strong immunity can certainly fight with this virus as it does for all infections.*

## Introduction

Viruses can be compared with plant seeds; they remain dormant and germinate and become active only when they get favourable conditions. Viruses remain dormant until they invade the host cell where they divide by using cell components such as nutrition and enzymes. In the host body they also favour certain types of cells over the others. Probably, certain viral proteins act as "receptor protein" to recognise the cell which is most beneficial to the virus. One would wonder how a small (about 100 micrometer in size) non living particle and lowly evolved in the scale of organic evolution, has its choices.

The new corona virus (SARS-CoV2) latches its spiky surface proteins to receptors on healthy cells, especially those in the lungs. Specifically, the viral proteins bust into cells through the angiotensin-converting enzyme 2 (ACE2) receptors. ACE2 expression levels were the highest in the small intestine, testis, kidneys, heart, thyroid, and adipose tissue, and were the lowest in the blood, spleen, bone marrow, brain, blood vessels, and muscle. However, in the lungs they are positive in the older and negative in the younger groups but there is no difference in male and females [1]. Once inside, the corona virus hijacks healthy cells and takes command, eventually, kills some of the healthy cells [2].

Human-to-human transmission was of SARS-CoV-2 initially assumed to occur primarily via respiratory droplets from coughs and sneezes within a range of about 1.8 metres (6 ft). Many studies identified viral components (RNA, proteins) in multiple organs, including the pharynx, trachea, lungs, blood, heart, vessels, intestines, brain, male genitals and kidneys, in various body fluids such as mucus, saliva, urine, cerebrospinal fluid, semen and breast milk it also shows its presence [3].

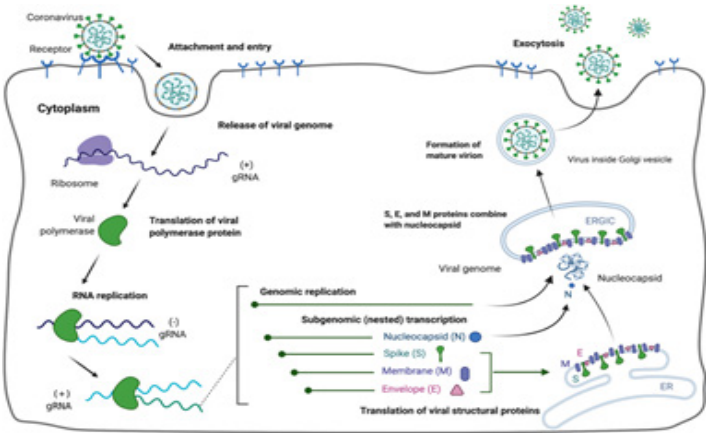


**Figure 1:** Mode of Infection and replication of the virus

The virus that causes COVID-19 disease infects people of all ages. However, evidence to date suggests that two groups of people are at a higher risk of getting severe disease. These are older people (that is people over 60 years old); and those with underlying medical conditions (such as cardiovascular disease, diabetes, chronic respiratory disease and cancer). The risk of severe disease gradually increases with age starting from around 40 years. It's important that adults in this age range protect themselves and in turn protect others that may be more vulnerable. WHO has issued advice for these two groups and for community support to ensure that they are protected from COVID-19 without being isolated, stigmatized, left in a position of increased vulnerability or unable to access ba-

sic provisions and social care [3].

## The Gender Gap

Researchers were busy in solving the problem of the gender gap in covid-19; are the reasons life-style or biological? True, women generally make healthier lifestyle choices as compared to men. Women do not smoke or drink as much as men, and they have a lower burden of those diseases (heart disease, diabetes or chronic lung conditions) that are known to be significant factors in the higher death rates among men with COVID-19 [4]. But there is compelling evidence for a role for biological (hormonal) factors [5]. Genes may also likely play an important role in gender gap [4,6].

Men overall are more vulnerable to corona virus than women. Females have a higher macrophage and neutrophil activity as well as antibody production and response. Furthermore, in-vivo studies of ACE2 and trans-membrane serine protease 2 (TMPRSS2) showed higher expression in the kidneys of male than female patients, which may explain the differences in susceptibility and progression of COVID-19 between male and female patients. However, it remains unknown whether the expression of ACE2 differs in the lungs of male and female patients [7, 8].

A fundamental difference between women and men is their hormonal milieu, which is responsible for other differences such as, behavioural immune responses and differences in infections including SARS -CoV2 virus [9]. In addition to hormones, consequences of differential expression of X-chromosome-encoded genes on immune responses to pathogens also work differently [10].

Women have an inherent genetic advantage when it comes to fighting corona infection. Having two X chromosomes was not appreciated for many years but now at least as far as corona infection it definitely showed advantage. Many of the genes on the X chromosome have to do with making and maintaining the brain and making and maintaining the immune system. So having two populations of cells — where one is predominantly using one X chromosome over the other — that can interact and cooperate is an immense advantage when you're faced with unforeseen challenges in life, such as famine and pandemics. Many of those genes are actually immune response genes. Another advantage is that the presence of two X chromosomes in women emphasizes the immune system even if one is inactive. The immune regulatory genes encoded by X chromosome in female gender causes lower viral load levels and less inflammation than in man. This could put women in more advantageous position compared to men. Toll-like receptor 7 (TLR7), and its functionally related gene TLR8 located on the X chromosome, encode proteins that recognize endogenous RNA-containing auto antigens [11]. TLRs are expressed on macrophages and other innate immune cells, where they collaborate to read the molecular fingerprint of different microbes and initiate inflammatory signalling pathways. These proteins play critical roles in pathogen recognition, specially RNA viruses and activation of innate immunity against them. They are single-pass membrane-spanning receptors usually expressed on sentinel cells such as macrophages and dendritic cells, that recognize structurally conserved molecules derived from microbes.

Further, TLR7 is higher in women than in men and its biallelic expression leads to higher immune responses and increases the resistance to viral infections. TLR7 is expressed in innate immune cells which recognizes single strand RNA virus by promoting the production of antibodies against the virus and the generation of pro-inflammatory cytokines including IL-6 and IL-1 family members. Several possible factors such as higher expression of ACE 2; greater numbers of receptors for coronavirus in male than female [12].

The presence of genetic variation within population (polymorphisms) was more likely to be associated with cardiovascular and pulmonary conditions by altering the angiotensinogen-ACE2 interactions, such as p.Arg514Gly in the African/African-American population. Ethnic groups often have higher levels of medical comorbidities and lower socioeconomic status, which may increase their risk of contracting COVID-19 through weak cell-mediated immunity [13].

Generally, men and women who are exposed to other viral infections also show differences in prevalence and outcomes, with women being less susceptible than men, owing to a generally more efficient immune response. Indeed, women may be more protected than men during physiological conditions, including pregnancy or across the menstrual cycle when fluctuation of reproductive steroids warrants a stronger immune protection [14, 15].

## Pregnancy

Current evidence from the UK suggests that pregnant women are at no greater risk of becoming seriously unwell than other healthy adults if they get infected by coronavirus (16). The majority of pregnant women experience only mild or moderate symptoms. Out of 427 pregnant women admitted to hospital with corona virus, while most women in the study were discharged to go home after getting well around one in ten women required intensive care, and sadly five women with coronavirus died, although it is currently unclear if coronavirus was the cause of their death [16].

Pregnant women with COVID-19 who deliver by caesarean section may be at greater risk for complications that affect them and their babies, new research suggests. The study focused on 82 women with COVID-19 -- four of them with severe symptoms -- who gave birth in hospitals in Spain. Thirty-seven women delivered by caesarean section including eight as a direct result of COVID-19 issues. Nearly 30% of babies delivered by C-section had to go to the neonatal intensive care unit, compared with fewer than 20% of babies delivered vaginally, the researchers found [17-20].

Only a few studies evaluated COVID-19 symptom severity in late pregnancy (high hormone levels) and after delivery (low hormone levels). Observational studies have noted that some SARS-CoV-2-positive pregnant women with mild or absence of COVID-19 symptoms on admission to obstetrical service escalated symptoms severity immediately postpartum in coincidence with the drastic hormonal decrease following childbirth. Some women required unplanned intensive care unit admission [21-23].

Pregnant women can transfer antibodies against coronavirus through placenta to their babies [24-27]. In blood samples from

more than 1,470 pregnant women it was discovered that about 87% of their new-borns showed COVID antibodies (IgG) in their umbilical cords, however no IgM antibodies, which are the first antibody to appear in the response to initial exposure to an antigen, were found in cord blood of the mothers, nevertheless some reports are there to show even IgM antibodies in the foetal blood [25-26]. Among 6 mothers with confirmed COVID-19, SARS-CoV-19 was not detected in the serum or throat swab by RT-PCR in any of their new-borns. However, virus-specific antibodies were detected in neonatal blood sera samples. The IgG concentrations were elevated in 5 infants. IgG is passively transferred across the placenta from mother to foetus beginning at the end of the second trimester and reaches high levels at the time of birth.However, IgM, which was detected in 2 infants, is not usually transferred from mother to foetus because of its larger macromolecular structure. In another study of mothers, the placentas of 2 women who were convalescing from SARS-CoV infection in the third trimester of pregnancy had abnormal weights and pathology. Whether the placentas of women in this study were damaged and abnormal is unknown. Alternatively, IgM could have been produced by the infant if the virus crossed the placenta.

Progesterone, estradiol, and allopregnanolone concentrations increase up to 100 times, mainly from the first to the second trimester, and then remain elevated until delivery. This progression is consistent with a hormonal protective role during pregnancy and postpartum pathophysiology, which, in one in nine women, is associated with perinatal psychopathology and sustained inflammation. The CDC reports that on 22 October 2020, the mortality rate among SARC-CoV-2-positive pregnant women in the USA was 0.16% (44 total deaths for 27 566 cases) compared with 2.24% of the American female population, pointing to immunological and hormonal protective factors in lowering the risk of COVID-19-related deaths in pregnant women [28]. This protection may also be guaranteed during the administration of oral combinations of hormonal contraceptive or by treatment with hormone replacement therapy against hypoestrogenism in postmenopausal women. Nutrition may also play a role when diets are enriched with phytoestrogens (e.g., soy beans, lentils, oats) with the ability to bind directly to human estrogen receptors or that can be converted to estradiol by the microbiome.

None of the mothers who delivered vaginally developed severe medical problems, while nearly 14% who had a C-section had to go to the ICU. Five percent of women who delivered vaginally saw their COVID-19 worsen, compared with 22% who had a C-section, according to the report. Whether COVID-19 can be passed to a baby in the womb isn't known, but this study may shed some light on the possibility.

## Children & Teens

Children, on the other hand, may be less prone to disabling symptoms, in part, because their immune systems are better regulated and because they have fewer underlying conditions. The theory was simple and compelling: Children are less vulnerable to the new coronavirus because they carry antibodies to other common coronaviruses that cause the common cold. The idea might also explain why some people infected with the new virus have mild symptoms while others — presumably without antibodies to common cold coronaviruses — are much more severely affected.

While fewer children have been sick with COVID-19 compared to adults, children can be infected with the virus that causes COVID-19, can get sick from COVID-19, and can spread the virus that causes COVID-19 to others. Children, like adults, who have COVID-19 but have no symptoms ("asymptomatic") can still spread the virus to others. Most children with COVID-19 have mild symptoms or have no symptoms at all. However, some children can get severely ill from COVID-19. They might require hospitalization, intensive care, or a ventilator to help them breathe. In rare cases, they might die [29].

## Choice for Blood Group

People with blood group A are more susceptible to corona virus and likely to develop more severe symptoms. On the other hand, people with blood type O might be resistant to it. The study was conducted with 2000 coronavirus patients in Wuhan and Shenzhen. Wang Xinghuan from the Centre for Evidence-Based and Translational Medicine at the Zhongnan Hospital of Wuhan University wrote, "People of blood group A might need particularly strengthened personal protection to reduce the chance of infection. Sars-CoV-2- infected patients with blood group A might need to receive more vigilant surveillance and aggressive treatment." Out of the 206 patients who died from coronavirus in Wuhan, 85 had blood type A as compared to the 52 who had blood type O [30].

## It Infects Bald Men More Than Hairier Men

In China, researchers have noticed a higher incidence of death due to coronavirus in bald men, than their hairier counterparts. It is possible that androgens -- male sex hormones like testosterone -- may increase the ability of coronavirus to attack cells. That means treatments for baldness, which suppress these hormones, might fight off the coronavirus, "We really think that baldness is a perfect predictor of severity," Carlos Wambier, a Brown University professor who had done studies on the subject told The Telegraph. "We think androgens or male hormones are definitely the gateway for the virus to enter our cells." The findings suggest that androgens somehow make the virus more virulent and that this makes the disease more severe in men [31,32].

## Infects Older Men More Than Younger Men

But in some older people, or in those who have underlying immune deficits from chronic conditions, regulatory T cells do not function normally. When these people get corona, cytokine storms may cause excessive inflammation in the lungs and whip up new torrents of attacker cells, leading to life-threatening diseases. One Chinese study found that corona patients with severe illness had lower levels of regulatory T cells in their bloodstream.

SARS CoV2 virus in addition to respiratory diseases and affects the lungs also induces histopathological or functional changes in various organs like the testis and also the male genital tract. The renin-angiotensin system (RAS), also ACE 2 and TMPRSS2 play an important role in the cellular entry for SARS-CoV-2. [33]. Because the male genital system presents high ACE 2 expression, the importance of this pathway increases in COVID-19 cases. As the COVID-19 pandemic has affected the male genital system in direct or indirect ways and showed a negative impact on male reproduc-

tion, Nevertheless, it is too early to conclude either way without generating more data [34-36].

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