## **Brief Communication**

# Should Women with Polycystic Ovarian Syndrome be Prioritized to Receive the COVID Vaccine?

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**C**OVID-19 first manifested as a severe respiratory syndrome caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). However, it is now understood that it can affect vascular, cardiac, gastrointestinal, renal, and central nervous systems apart from respiratory system.<sup>[1]</sup> Current understanding of the pathophysiology of COVID-19 infection suggests that the expression of angiotensin-converting enzyme 2 (ACE2) receptors facilitates the entry of the virus into the cells.<sup>[2]</sup> It causes endothelial vascular damage, alters the immune response, creates an inflammatory state, and contributes to the involvement of multiple organs.<sup>[3]</sup>

Polycystic ovarian syndrome (PCOS) is a syndrome which presents with multiorgan symptoms. The polycystic morphology of ovaries is the result of hyperandrogenaemia, but not its cause. PCOS is today considered as a proinflammatory disorder.

Both men and women are equally affected by COVID-19, with a propensity for severe disease and a higher mortality in men compared to women.<sup>[4]</sup> These gender disparities made researchers study the influence of male hormones on the immune response to COVID-19 infection.<sup>[5,6]</sup> The findings can be summarized as:

- 1. Behavioral differences between men and women such as higher rates of smoking, noncompliance to using protective measures, a higher prevalence of noncommunicable diseases, and low Vitamin D levels could be contributory to the higher incidence of COVID-19 infection seen in men versus women<sup>[7-10]</sup>
- 2. SARS-CoV-2 uses ACE2 and transmembrane protease serine 2 receptors to enter the cells. These entry points are positively influenced by the presence of androgens<sup>[11]</sup>
- 3. There is a difference in the immune responses of men and women to COVID-19 infection. Women

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demonstrate a stronger T-cell response while a milder T-cell response is seen in men.<sup>[12]</sup>

More severe Covid-19 infection has been observed in bald men and in women with androgenic alopecia.<sup>[13,14]</sup> Deprivation of androgens as seen in patients with prostate cancer is found to make these men partially protected, compared to those who are not androgen deprived.<sup>[15,16]</sup> Reduction in viral load has also been observed in men and women who were on androgen receptor inhibitors.<sup>[17,18]</sup> Thus, androgenic status could be one of the important contributory factors for the increased severity of COVID-19 in men.

Women with PCOS may have clinical or biochemical hyperandrogenemia. Eighty percent of PCOS women are obese and a large percentage of them are insulin resistant, with a higher risk of developing gestational diabetes mellitus during pregnancy and Type 2 diabetes mellitus (T2DM) at a relatively young age. There are considerable data indicating that diabetes and obesity are the predictors of severe morbidity and mortality in COVID-19 infection.<sup>[4,19-22]</sup>

Obesity is often accompanied by comorbidities including T2DM, hypertension, cardiovascular disease, and renal disease, which affects the severity of any infection. Since adipose tissue has a higher expression of ACE2 receptors, there is a prolonged presence of the SARS-CoV-2, leading to a greater exposure and increased risk of severe disease.<sup>[23,24]</sup> Obesity is also associated with chronic inflammation, abnormal cytokine activation, and dysfunction of inherent immunity, leading to a worse prognosis in those infected. Hence,

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obese women with a proinflammatory disorder of PCOS have an increased risk of severe COVID-19 infection.

There is a high prevalence of PCOS in women of Indian ethnicity. Recently, the European Society for Endocrinology has published guidelines for the endocrine phenotype of the COVID-19 pandemic. The guidelines suggest that patients with endocrine disorders should be considered as high priority for vaccinations, especially those individuals with diabetes and obesity.<sup>[25]</sup>

Hence, I strongly recommend that PCOS women with their strong predisposition to both T2DM and obesity should be included as a high-risk group and prioritized for COVID vaccination in India.

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#### **Conflicts of interest**

There are no conflicts of interest.

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