



## THE Y FACTOR: IS IT A RISK FOR INCREASED MORTALITY IN COVID-19?

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**ABSTRACT**

India is currently experiencing the second wave of the COVID-19 pandemic. It is widely known that there are sex-differences in the immune system and it is believed that these have affected clinical outcomes in men and women suffering from COVID-19.

We aimed to study the Case Fatality Rates in both genders in our institute and assess the gender difference, if any, and probable reasons for the same, in both waves of the COVID-19 pandemic.

We analysed data from our institute from April 2020 to June 2021. It included the total admissions and case fatality rates in men and women month wise, as well as their respective patterns during the first and second waves of the COVID-19 pandemic in our nation with a view to assess the gender difference in these groups.

Case Fatality Rate (CFR) is the percentage of the total number of deaths due to a particular disease and the total number of cases due to the same disease. It is the propensity of a disease to kill and is simply the ratio of deaths to cases.

Our study revealed a greater number of female admissions throughout the pandemic but a lower COVID positivity rate in women during the second wave. There were fewer Covid positive women in the second wave, but female CFR was greater than male. During the first wave, more women were Covid positive but male CFR was more than double that of women for that period.

**KEYWORDS** : COVID-19, Case Fatality Rate, Female, Male**INTRODUCTION**

Our country is currently witnessing the second wave of the COVID-19 pandemic. According to the data available, around 3.13 crore cases have been reported in India, with 4.19 lakh deaths.<sup>[1]</sup>

Sex differences have been widely documented in both, the innate and adaptive immune systems. With regards to the adaptive immune system, females have higher numbers of CD4+ T cells.<sup>[2]</sup> Therefore, the immunological advantage enjoyed by women against the SARS-CoV-2 virus, may be attributable to these facts.

Large-scale data have demonstrated that despite there being no sex difference in the proportion of people infected with SARS-CoV-2, male patients are at a significantly higher risk of severe disease and death as compared to females.<sup>[3]</sup>

We decided to look at the data from our institute, including the total admissions and case fatality rates in men and women, as well as their respective patterns during the first and second waves of the COVID-19 pandemic in our nation.

**AIMS AND OBJECTIVES**

- To assess Case Fatality Rate (CFR) in both the genders and compare the same.
- To assess the gender difference if any in first and second wave of COVID infection.

**METHODOLOGY**

Monthly data of COVID positive cases and deaths in our institute, was collected from the beginning of the pandemic and was sent to a centralised reporting system.

With institutional approval, we conducted a Retrospective Analytical study using data from April 2020 - June 2021, in a tertiary care institute in Mumbai, India.

We reviewed the data of the total indoor admissions month wise, from

the beginning of the pandemic when testing had started in our institute, from April 2020 till June 2021.

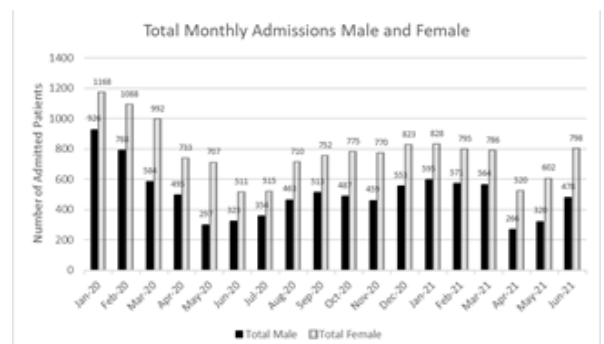
We also analysed the total COVID positive cases in men and women and the deaths in these groups respectively. Furthermore, the patterns of CFR in the 1st and 2<sup>nd</sup> waves COVID-19 were studied.

CFR is conventionally expressed as a percentage and represents a measure of disease severity.<sup>[4]</sup> We calculated the CFR month wise for each gender for the study period and plotted the data graphically.

Comparison of cumulative CFR for 2020 and 2021 was also evaluated in both the genders groups in our institute. The formula used for Case Fatality Rate is:<sup>[5]</sup>

**Case Fatality Rate (CFR) =**

$$\frac{\text{Total number of deaths due to a particular disease}}{\text{Total number of cases due to the same disease}} \times 100$$

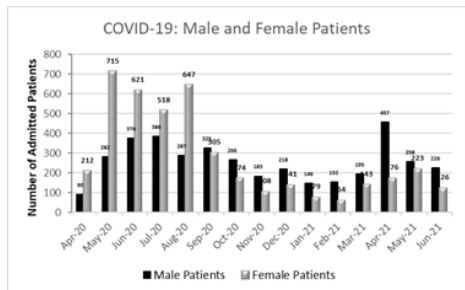
**RESULTS**

**Fig. 1. Total Indoor patients admitted in our institute:**

In 2020, our centre saw a total of 6242 male admissions and 9544 female admissions.

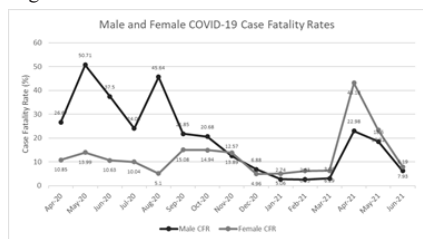
There were 2794 male and 4329 female admissions in the first six months of 2021.

The total admissions of women month wise, is consistently more in our institute possibly due to the obstetric workload.



**Fig. 2. Total COVID -19 diagnosed patients admitted in our institute:**

In the first wave, the number of COVID positive women was higher than men during the peak, it then declined and remained less than that of men during the second wave.



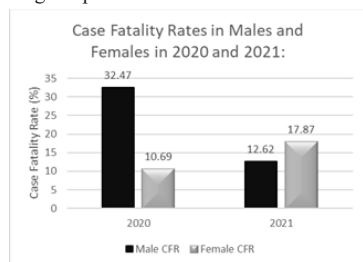
**Fig. 3. Case Fatality rate (CFR) of Male and Female month wise:**

**Table 1. Month wise Case Fatality Rates in men and women, April 2020 – June 2021**

Months	Male CFR (%)	Female CFR (%)
Apr-20	26.67	10.85
May-20	50.71	13.99
Jun-20	37.5	10.63
Jul-20	24.09	10.04
Aug-20	45.64	5.1
Sep-20	21.85	15.08
Oct-20	20.68	14.94
Nov-20	12.57	13.89
Dec-20	6.88	4.96
Jan-21	2.74	5.06
Feb-21	2.63	6.25
Mar-21	3.08	6.29
Apr-21	22.98	43.18
May-21	18.6	23.32
Jun-21	6.19	7.93

There is a marked difference in the CFRs of both genders in the first and second waves of the COVID-19 pandemic in our centre. The trend shows a significantly higher CFR in men in the first wave with a decline and reversal in the second wave.

CFR in women peaked during the second wave and was nearly double that of men during this period.



**Fig. 4. Cumulative CFR of COVID-19 for the years 2020 and 2021:**

As seen above, CFR in males was nearly triple that of females in 2020. However, in 2021, the cumulative CFR in women overtook that of men.

**Table 2. Overall mortality rate in our institute, year wise:**

Year	Overall mortality rate of our institute
2018	3.37%
2019	3.31%
2020 (During 1 <sup>st</sup> wave)	10.0%
2021 (During 2 <sup>nd</sup> wave)	10.3%

In the pandemic, overall mortality rates were around 10% in both years. However, it had tripled from previous years due to the addition of COVID mortality.

**DISCUSSION**

Our institute is a major referral centre, and despite not being a dedicated Covid Care hospital, we faced an increased workload throughout the pandemic, as seen in Fig. 1.

The higher numbers of COVID positive women notwithstanding, the female CFR was lower in the first wave as evidenced in Fig. 2.

As displayed in both Fig. 1 and 2, the number of female admissions was consistently greater throughout the pandemic. However, the covid positivity rate was lower in women in the second wave. Interestingly, despite the higher number of women being COVID positive in the first wave, the CFR was less than half of that in males during this period. On the other hand, although there were fewer COVID positive women than men in the second wave, the female CFR overtook that of men.

We experienced an increased obstetric during the pandemic due to referrals. In our institute, we had compared maternal mortality ratios in COVID & non-COVID cases in the pandemic, for both waves. Interestingly, we found no change in the Maternal Mortality Ratio (MMR) in both waves. Our study showed a lower CFR in pregnant women as compared to non-pregnant with COVID-19. A fascinating finding is a sudden rise in CFR during the second wave of COVID in 2021. This could be due to virus variants, but we do not have genotyping data available currently.<sup>[6]</sup>

Overall mortality data from our institute (which are yet unpublished), show an increased overall mortality during the 1<sup>st</sup> and 2<sup>nd</sup> waves of COVID 19 period (2020) as compared to the data from previous years.

India, despite the national curbs imposed at the start of 2020, we celebrated festivals like Diwali and Holi in the months of November 2020 and March 2021 respectively. Despite the imposition of strict restrictions and lockdowns, small social gatherings could have contributed to the increased cases seen in the second wave of COVID-19. Another possible reason is the “pandemic fatigue” that crept into the population, leading to laxity in covid appropriate behaviour.

In one single centre study carried out in a reputed Municipal Corporation of Greater Mumbai (MCGM) hospital with ICMR, the results showed an overall increase in the rates of severe COVID-19 infection, case fatality rate, maternal mortality ratio was higher in second wave as compared to the first wave. They did not report any gender difference.<sup>[7]</sup>

Previous reports describe fundamental differences between the sexes in the immune response to infection, which include a more robust antiviral innate interferon response and increased adaptive immunity towards viral antigens in females. In women infected with SARS-CoV-2, these differences are likely to lead to more effective viral control, which may contribute to the relatively lower risk of developing severe disease.<sup>[8]</sup>

Our study shows that in the first wave, we recorded higher male case fatality rates as compared to that of females in the year 2020, however this trend was reversed in the second wave in 2021, as seen in Fig No. 4. Many factors could have been responsible for the observed gender difference, other than the dissimilar innate immunities.

One possible factor that drove the second wave was the emergence of hotspots in major cities, in response to which various restrictions were implemented that led to an exodus of migrant workers back to the interiors, leading to spread of the virus from cities to villages.

When the year 2020 ended and people started moving out, the national COVID vaccination drive began on 16th January 2021, which changed things.<sup>[8]</sup>

A probable factor could be the large number of partially vaccinated individuals and an even larger number of unvaccinated individuals aged 18-60, who eventually bore the brunt of the second wave.

The above-mentioned factors, along with the emergence of new strains and possible clinically significant genotypes might have contributed to the increased mortality observed in women in the second wave of the COVID-19 pandemic. Further studies into the SARS-CoV-2 genotypes that drove the second wave are warranted, and will allow a deeper understanding of the multitude of factors that have led to the increased case fatality rates seen in women.

Determining the magnitude of the decrease in the CFR and the association between the rates of COVID-19 testing and CFR changes could also provide implications for future public health interventions.<sup>[9]</sup>

## CONCLUSIONS

Although further studies are still needed, these data have implications for the clinical management of COVID-19 and highlight the importance of considering sex as a variable in fundamental and clinical research.

## ACKNOWLEDGMENTS

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## REFERENCES:

1. Government of India, Ministry of Health and Family Welfare-COVID19, Accessed May 2021.
2. Abdullah, M. et al. Gender effect on in vitro lymphocyte subset levels of healthy individuals. *Cell. Immunol.* 272, 214–219 (2012)
3. Peckham, H., de Grijter, N.M., Raine, C. et al. Male sex identified by global COVID-19 meta-analysis as a risk factor for death and ITU admission. *Nat Commun* 11, 6317 (2020). <https://doi.org/10.1038/s41467-020-19741-6>
4. Rebecca A. Harrington, Case fatality rate at the Encyclopædia Britannica
5. Park K. Textbook of Preventive and Social Medicine 26<sup>th</sup> Edition, Page 428. M/s Banarasidas Bhanot Publishers, 2021
6. Dr. Reena Wani, Dr Shradha Ashok Mevada, Dr Mahin Bhatt, Dr Varun Wani, Zachary Di Biase, "Maternal Mortality Ratio and COVID Pandemic Impact: A Retrospective Analytic study in a tertiary care institute", IJMSIR- July -2021, Vol – 6, Issue - 4, P. No. 321 – 326.
7. Mahajan, N. N., Pophalkar, M., Patil, S., Yewale, B., Chaiithanya, I. K., Mahale, S. D., & Gajbhiye, R. K. (2021). Pregnancy Outcomes and Maternal Complications During the Second Wave of Coronavirus Disease 2019 (COVID-19) in India. *Obstetrics and gynecology*, 10.1097/AOG.0000000000004529. Advance online publication. <https://doi.org/10.1097/AOG.0000000000004529>
8. Challenges and Concerns in Setup of COVID Vaccination Centre: Experience from 2 Centres in Mumbai Panchal, Sanjay, Wani, Reena J.; Chauhan, Kinjal, Wani, Varun, Manihar, Priya. *Indian Practitioner*; 74(4):18-23, 2021.
9. Sylvia H. Hsu MD, PhD, Su-Hsin Chang PhD, Cary Gross MD, Shi-Yi Wang MD, PhD, Relative risks of Covid-19 fatality between the first and second waves of the pandemic in Ontario, Canada, *International Journal of Infectious Diseases* 2021