



COVID-19 PANDEMIC & THE UNUSUAL GENDER SKEW IN INDIA : EXPLORING THE CAUSES

General Medicine

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ABSTRACT

While Covid-19 cases continue to increase everyday and we get used to the new 'normal', I have compiled a study looking at how a person's sex can influence the risk of infection, risk of disease and worse clinical outcomes including death with Covid-19. I have compared data from around the world where the infection ratio between men and women is near 50-50 in most countries, to India, where men are disproportionately testing positive for Covid-19 as compared to women (76% men vs 24% women). When it comes to death due to Covid-19, India shows similar trends as the rest of the world. In this paper, I have explored the possible and probable causes of the infection being predominant in the male sex, especially in India. Along with biological causes like differences in innate and adaptive immunity, estrogen hormone and ACE-2 enzyme and more comorbidities in men, socio-behavioral causes like smoking and higher likelihood of men being outside their homes and exposed to infection while the country is in lockdown, are also explored. This should encourage further studies and help triage patients infected with Covid-19 into higher risk and lower risk criteria.

KEYWORDS

INTRODUCTION

While Covid-19 wreaks havoc on the world, there has been a literal frenzy of research on every imaginable aspect of it, hence the body of research on it grows and metamorphosis's on a daily basis. An interesting and possibly useful detail while studying data has come to the fore. In a striking contrast with many countries, men in India more than women appear disproportionately likely to test positive for COVID-19, an analysis of global data shows. On April 6 2020, the Health Ministry said 76% of the confirmed cases in India were men. It also stated that 73% of Covid deaths were that of men.¹

GlobalHealth5050, an independent research initiative that tracks gender and health, compiling data from 40 countries, suggest that the gender-split in all countries is roughly 50-50, barring two exceptions: India and Pakistan. This is regarding Covid infection rates.²

The data from 13.05.2020, which has been compiled in Fig 1, shows that most countries from around the globe have generally an even distribution of infection, hovering around 50-50 for men and women. While males superseded females by a small margin in most countries. China had 51% of its infections in the male population, while percentage of men being Covid-19 infected (as compared to females) was 56% for Greece, 57% for Iran, and 54% for Dominican Republic.²

While, India had an overwhelming preponderance of men being infected (76%).¹

On the other hand, a strong female preponderance of infection was seen in South Korea (41% males and 59% females) and Denmark (42% males and 58% females). Some countries showed a small female lead in percentage of Covid infections (Germany with 58% females, Italy with 53% females).²

The case fatality ratio, according to GlobalHealth 5050 Sex disaggregated data from 40 countries, is higher in men than women. The proportion between males and females, though, varies across different countries.²

Fig 2 shows the percentage of deaths by gender due to Covid-19; where Greece (74%) and Dominican Republic (72%) have very high percentage of male deaths. China (64%) and Italy (61%) and Iran (59%) have high, but not so disproportionate percentage of male deaths, while Denmark (57%), Germany (56%) and South Korea (52%) while still showing a male preponderance of Covid-19 deaths, have much less gender gap in the deaths. This was the data compiled by GlobalHealth 5050 on 13/05/2020.

India in comparison, shows that the percentage of death in men is very high at 73% (data from Government of India on 06/04/2020)¹

The reasons behind this are likely to be multifactorial, and include biology, behavior and socio-cultural differences between men and

women. In this report, we explore the causes (globally) of worse outcomes in men infected with covid as compared to women. We will also explore the causes of much higher rates of infection in men (as compared to women) in India as compared globally that may be unique to India.

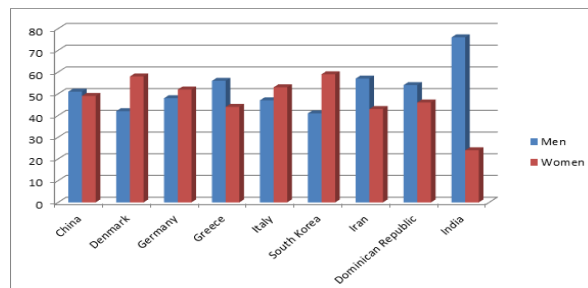


Fig 1- Percentage Of Covid-19 Infection Among Men And Women In Different Countries

Source: Global Health 50/50. Last updated: 13 May 2020
Source: India Today : 6 April 2020

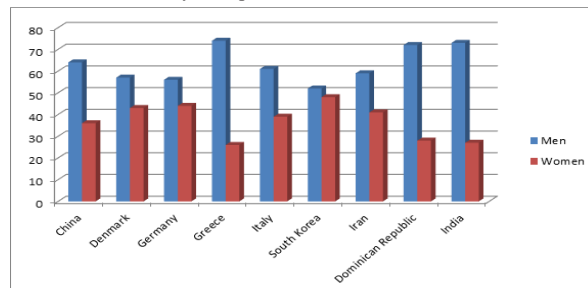


Fig 2- Percentage Of Deaths By Sex Due To Covid-19 Disease

Sources: Global Health 50/50 - 13/05/2020
India Today April 6 2020 (MOFHW)

Focusing On India, Why Are Men More Infected And More Severely Infected With Covid-19?

Biological Causes:

1.Immunity and the X-Chromosome: Females have well-documented immunological advantage (mount stronger innate and adaptive immune response) over males. They being functional mosaics for X-linked genes, and the X-chromosome having a high density of immune-related genes, helps them fight off many viral, bacterial, fungal and parasitic infections better than men. Consequently, on the flip side, they are more susceptible to inflammatory and autoimmune diseases.³

Therefore, females may be mounting stronger immune response to Covid-19 infection and may comprise a smaller proportion in the serious and critical Covid-19 cases.

A study conducted in Mumbai, India demonstrated that females cleared the SARS-COV 2 infection significantly earlier than males, median difference was of 2 days to achieve a negative PCR result. This explains why the mild and moderate cases are also lesser in females.⁴

2.ACE-2 and Sars-Cov 2 : ACE-2 is an enzyme that is increased in heart failure. It is also a functional receptor on cell surfaces for Sars-Cov and Sars Cov-2, highly expressed in various tissues like heart, testis, kidney and lung; from where it is shed into the plasma.

In a study published in European Heart journal, in 2 large independent cohorts with heart failure, it was found that ACE2 concentrations in NPX units were higher in males as compared to females, which may result in higher tissue expression of this receptor for SARS Cov 2 infections.

The study also explores post transcriptional events in the testes regarding the Sars Cov 2 protein.⁴

This EXPLAINS why male gender is more susceptible to infection with, or the consequences of, SARS-CoV-2.

3.estrogen And Protection: A study in J Immunology states that testosterone suppresses innate immune response, while estrogen stimulates immune response at low concentrations.⁵

The research in this study was done in mice highlighted sex-based differences in susceptibility to SARS-CoV. Male mice were seen to have higher virus titers and more neutrophil infiltration in the lungs, which suggested that various factors contributed to disease severity in male mice. While the protective effects of estrogen was demonstrated by treating female mice with ovariectomy and estrogen receptor antagonist, which showed a worse outcome than normal female mice when exposed to Sars Cov.⁵

These results prove that the virus acts in a differential way on the basis of sex in mice, and paves way for the understanding of worse outcomes in human males infected with sars cov.

4.Co-morbidities In Men -

Many studies across the globe have demonstrated beyond doubt, that Covid-19 infection shows much worse outcomes and greater severity in patients with underlying chronic conditions like cardiovascular disease, respiratory diseases and diabetes. Also more number of co-morbidities correlates with higher covid-19 severity.

One of these studies analysed the composite end-points, which were: 1. admission to an intensive care unit, 2. invasive ventilation 3. death. This study took underlying conditions as co-morbidities: 1. COPD 2.Diabetes 3. Hypertension 4. Malignancy. The hazard ratio was 1.79 among patients with at least one comorbidity and 2.59 among patients with two or more comorbidities.⁶

I studied the data on the gender differences in prevalence of some common chronic diseases in India, which have been implicated in being notorious in causing worse outcomes in covid patients.

The Global burden of Diseases study reported that DALY lost by CHD in India is projected as 14.4 million for men and 7.7 million for women by 2020, reveals nearly a double burden of disease in men as compared to women.⁷

The Indian study of Asthma, Respiratory symptom and Chronic Bronchitis (INSEARCH) reported the prevalence of chronic bronchitis as 4.29% in males and 2.7% in females.⁸

These studies support the hypothesis that many serious chronic conditions, especially cardiovascular and respiratory, and those which have been linked to causing worse outcomes in Covid-19 patients worldwide, predominate in men, making them at higher risk for critical/worse outcomes with Covid 19 infection.

Social And Behavioral Causes:

1.Smoking–Statistically speaking, smoking is very much predominant in men in India. Data from 2015 reveals about 108 million men were smokers, while 11 million women smoked.⁹ The huge gender gap in this is directly responsible for men having more prevalence of chronic lung diseases like COPD, and therefore men are at greater risk of worse outcomes with Covid-19 infections, as the virus primary attacks the respiratory endothelium.

2.More Mobility During The Pandemic – This is a hypothesis that I want to postulate in this paper. India is a country where, especially in rural areas, gender disparities exist in a way that men are generally the financially and socially independent gender. Therefore, it is men who step out of the house much more often, to buy groceries and items of daily need for a family, as well as for services of bank, ATMs etc. They are overwhelmingly likely (compared to women) to be the vendors (vegetables/fruits/general stores) that are one of the essential services in this pandemic. They are also disproportionately more in the police force and military/paramilitary forces that are being deployed widely during the pandemic to ensure a successful lockdown. There are more men in government and public services right from administrative officers and politicians to clerks. Men are much more in number when we look at cleaners and sanitation workers as well.

All in all, men are much more likely to be 'not be locked down' in the lock down and are more exposed to the infection by virtue of being exposed to infected people.

CONCLUSION:

The human race is going through a critical and crucial juncture. How we deal with this pandemic will define how we go down in history as well as how we will shape our future.

In order to deal effectively with THE ENEMY 'Covid-19', we must have as much information about it as possible. Sex disaggregated data will help us understand the differences in risk, infection, disease and disease outcomes on the basis of sex. This will ultimately help the health care workers while they face difficult questions on triage of patients suspected or infected with Covid-19.

While reviewing data regarding Covid and gender, many reasons for men being more severely afflicted and having worse outcomes came to the fore. But this was a general trend worldwide including India, and I delved into causes – Biological – immunity, estrogen, ACE-2 enzyme and behavioral – smoking.

I also have presented the possible reasons for the interesting statistic unique to India- much more men being infected with Covid-19 overall in India, while worldwide the statistics show a nearly equal prevalence of infection between men and women. Besides biological causes as mentioned above, I think soci-behavioral factors like much greater mobility of men during the pandemic in India (this is quite different from more developed countries) may have played a role in this.

Should older men with co-morbidities be top priority while identifying cases most vulnerable to Covid-19? Should they be considered for early intensive intervention (eg. ICU admission, intubation) than younger people/women or patients with no co-morbidities?

These are some of the difficult triage questions that don't have definite answers, and I want to contribute to the evidence for these answers through this paper.

There is always a caveat, and it is postulated by some that the infection gap between men and women in India may not be so stark, it is only because more men are being tested. And the gap will narrow as more people are tested during the course of this pandemic. As the pandemic unfolds, we will have more answers. For now, we have to go forward with the body of evidence we have. We have to also be careful that as doctors and health care workers of this country, we don't become biased on basis of incomplete evidence and deny women, who are already at a disadvantage when it comes to availing health care, their right to the highest standards of care. It is a fine balance and we have to trudge carefully.

REFERENCES:

1. MoHFW, India
2. Global Health 5050.org
3. Walter LA, McGregor AJ, West J. Sex and Gender specific Observations and Implications for COVID-19. *Emerg Med* 2020 May; 21(3): 507–509.
4. Shastri A, Wheat J, Agrawal S, Chatterjee N, Pradhan K, Goldfinger M et al. Delayed clearance of SARS-CoV2 in male compared to female patients: High ACE2 expression in testes suggests possible existence of gender-specific viral reservoirs. doi: <https://doi.org/10.1101/2020.04.16.20060566>
5. Channappanavar R, Fett C, Mack M, Patrick P, Meyerholz DK and Perlman S. Sex-Based Differences in Susceptibility to Severe Acute Respiratory Syndrome Coronavirus Infection. *J Immunol* May 15, 2017, 198 (10) 4046–4053
6. Guan W, Liang W, Zhao Y, Liang H, Chen Z, Li Y et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis *Eur Respir J*. 2020 May; 55(5): 2000547
7. Krishnan MN. Coronary heart disease and risk factors in India – On the brink of an epidemic? *Indian Heart J*. 2012 Jul; 64(4): 364–367.
8. Rajkumar P, Pattabi K, Vadivoo S, Bhome A, Brashier B, Bhattacharya P et al. A cross-sectional study on prevalence of chronic obstructive pulmonary disease (COPD) in India: rationale and methods. *BMJ Glob Health*. 2016; 1(1)
9. Mishra S, Joseph RA, Gupta PC, Pezzack B, Ram F, Sinha DN et al. Trends in bidi and cigarette smoking in India from 1998 to 2015, by age, gender and education. *BMJ Glob Health*. 2016; 1(1)