

# Gender Differences in Patients with COVID-19- Focus on Age Difference and Clinical Symptoms in Tertiary Health Care

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## ABSTRACT

Coronavirus disease (COVID-19) is an infectious viral disease caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2 virus). Reported first in Wuhan, Hubei Province, China, in late December 2019. In February 2020, the World Health Organization (WHO) named the disease 'coronavirus disease 2019' (COVID-19) and by March 11, 2020, WHO declare it as a global pandemic.

Human-to-human transmission of SARS-CoV-2 occurs mainly between family members, including relatives and friends who are close contacts with the patients or with the incubatory carriers. Till date the transmission of COVID-19 is still uncontrollable. This retrospective study is done keeping in view about the limited availability of sex and age disaggregated data regarding Covid 19 positive patients so as to better understand the impact of sex and gender on incidence and case fatality of the disease in relation to treatment. In our study out of 58,971 nasopharyngeal samples, 555 samples came out to be positive by RT-PCR and they were further distributed according to age, gender and symptoms to see the co relations of these factors in regard to covid 19 positivity. As early identification of risk factors not only will help to identify clinical and epidemiological characteristics but also to facilitate the appropriate supportive care and treatment and prompt access to the intensive care units.

**Keywords:** COVID-19, SARS-CoV-2 virus, WHO, Acute Respiratory Distress Syndrome (ARDS), Acute Lung Injury (ALI).

## INTRODUCTION

Coronavirus disease (COVID-19) is an infectious viral disease caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2 virus) (1). It was first reported in Wuhan, Hubei Province, China, in late December 2019 and on February 2020, named as 'Coronavirus disease 2019' (COVID-19) by World Health Organization (WHO) (2) and by March 11, 2020, WHO declare it as a global pandemic. Human-to-human transmission of SARS-CoV-2 occurs mainly between family members, including relatives and friends who are close contacts

with the patients or with the incubatory carriers, infection is mainly transmitted through large droplets generated during coughing and sneezing by symptomatic patients or by touching contaminated surfaces (3). Till date the transmission of COVID-19 is still uncontrollable with the fact that the numbers of confirmed, and death cases are still increasing (4).

Coronaviruses belong to the Coronaviridae family in the Nidovirales Order (5) named as such due to the presence of crown-like spikes on the outer surface of the virus, are 65–125 nm in diameter and contain a single-

stranded RNA (2). The subgroups of coronaviruses family are alpha ( $\alpha$ ), beta ( $\beta$ ), gamma ( $\gamma$ ) and delta ( $\delta$ ) coronavirus (6). The severe acute respiratory syndrome coronavirus (SARS-CoV), H5N1 influenza A, H1N1 2009 and Middle East respiratory syndrome coronavirus (MERS-CoV) cause acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) which leads to pulmonary failure and result in fatality (2). These viruses were thought to infect only animals (7), until the world witnessed a severe acute respiratory syndrome (SARS) outbreak caused by SARS-CoV, 2002 in Guangdong, China (WHO, 2004). Only a decade later, another pathogenic coronavirus, known as Middle East respiratory syndrome coronavirus (MERS-CoV) caused an endemic in Middle Eastern countries (7). And now recently a new public health crisis threatening the world with the emergence and spread of COVID-19 or SARS-CoV-2.

Various studies have demonstrated that COVID-19 produces more severe symptoms and higher mortality among men than among women thereby showing significant impact on the outcome of infections (8). Like prevalence of Hepatitis A and tuberculosis are significantly higher in men as compared to women. Viral loads are consistently higher in male patients with Hepatitis C virus (HCV), Hepatitis B virus (HBV) and human immunodeficiency virus (HIV). These findings collectively suggest a strong ability among women to control infectious agents. Similarly various studies have been done which shows male bias in COVID-19 infections and mortality and presence of one or more co-morbidities further accentuate the infection (3). The common COVID-19 symptoms include fever, cough, sore-throat, headache, fatigue, headache, myalgia and breathlessness and it may progress to pneumonia, acute respiratory distress syndrome (ARDS) and multi organ dysfunction (9).

## MATERIALS & METHODS

An analytical retrospective study was conducted at Viral Research and Diagnostic Laboratory (VRDL), Department of Microbiology, Government Medical College, Jammu. Wherein 58,971 upper respiratory tract samples (nasopharyngeal swabs) of patients were tested during the period of three months (w.e.f July – September,2021) for SARS-CoV-2 by real-time reverse transcriptase polymerase chain reaction (RT-PCR).

### RNA extraction and real-time polymerase chain reaction

The RNA extraction was performed using Genetix Purifier HT 96 as per manufacture's guidelines using GeneMag Viral DNA/RNA Purification kit. SARS-CoV-2 RNA detection was performed using Meril COVID-19 One Step RT-PCR Kit, manufactured by Meril Diagnostics Pvt Ltd, India. It has the sensitivity and specificity of 100% and it detects the Open Reading Frame 1ab (ORF 1ab) and Nucleocapsid (N gene) of the SARS-CoV-2. A Ct value of <35 was used as the cut-off for determining positivity, according to ICMR guidelines.

We concluded the data based on

- gender differences,
- presence of symptoms,
- age groups (divided into 5 groups, < 20, 20-30, 31-40, 41-50, >50).

## RESULT

A retrospective study was done at VRDL, Department of Microbiology, Government Medical College, Jammu from month July to September,2021, wherein 58,971 samples were tested for COVID-19 RTPCR with a positivity of 0.009% (555/58,971) as shown in Figure 1. Among the positive samples, 65% (360/555) males and 35% (195/555) females (Figure 2) clearly depicting male preponderance.

Out of these positive samples for COVID-19, asymptomatic and symptomatic patients were separated and 70% (389/555) came out to be symptomatic (with symptoms like fever, cough, sore-throat, headache, fatigue,

myalgia, and breathlessness) and 166 were asymptomatic.

Among the COVID-19 positive patients reported, gender role in respect to symptoms were also observed and it came out that out of 389 symptomatic COVID-19 positive patients, 80% (290/360) males were having symptoms as compared to females which constituted only 50% (99/195) as shown in Figure 4, thereby depicting that percentage of males having COVID-19 symptoms were higher in comparison with the female

COVID-19 positive patients as males are more likely to exhibit enhanced disease severity and mortality than females.

And the most common symptoms encountered were fever, cough, sore-throat, headache, fatigue followed by breathlessness and diarrhoea. Out of 389 symptomatic patients, 80% were having fever followed by cough 67%, myalgias 58%, sorethroat 45%, headache 13.9% and breathlessness 13.9% (Figure 5).

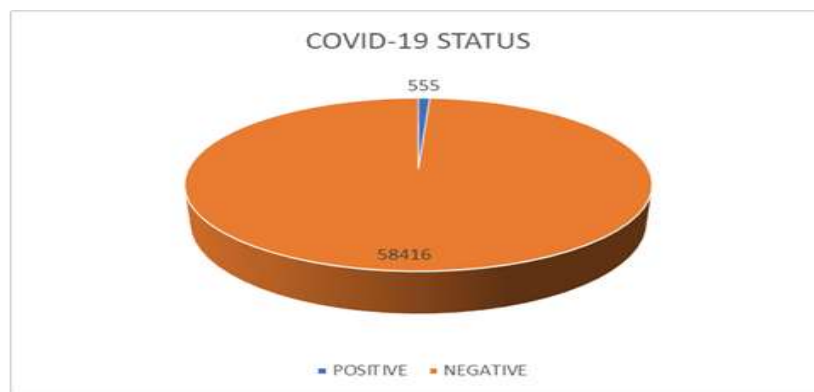


Figure 1: COVID-19 status

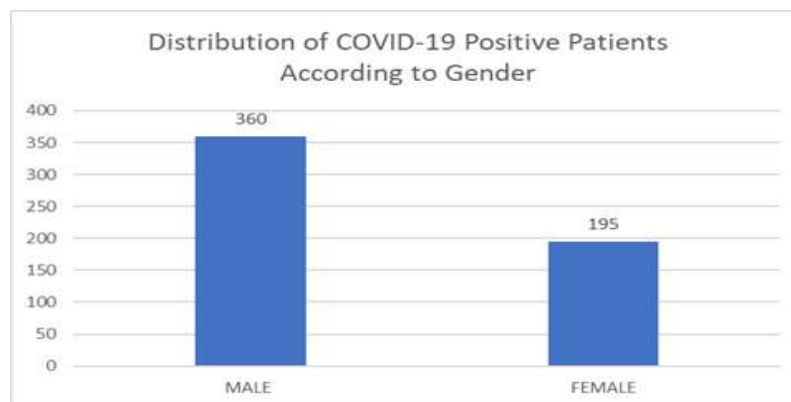


Figure 2: Distribution of COVID-19 positive patients according to gender

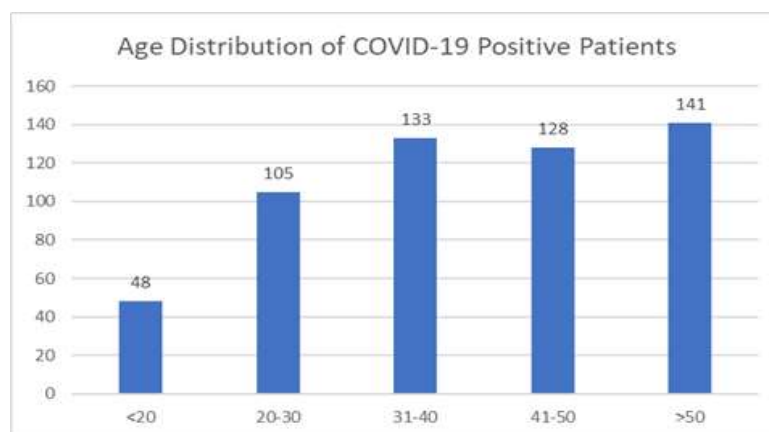


Figure 3: Distribution of COVID-19 positive patients according to age

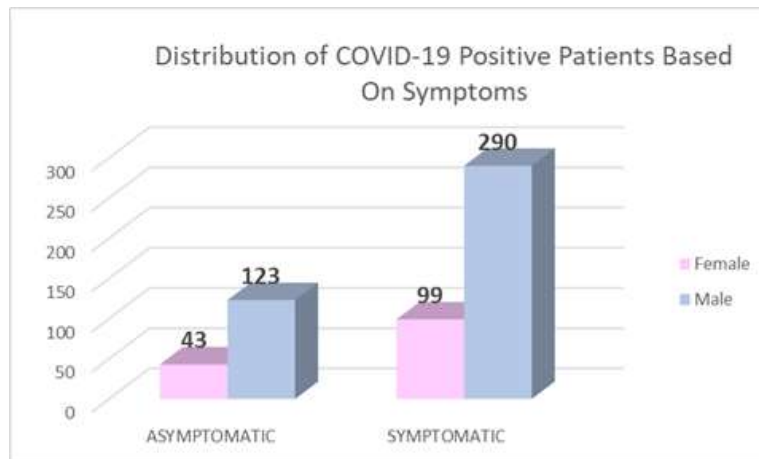


Figure 4: Distribution of COVID-19 positive patients according to symptoms

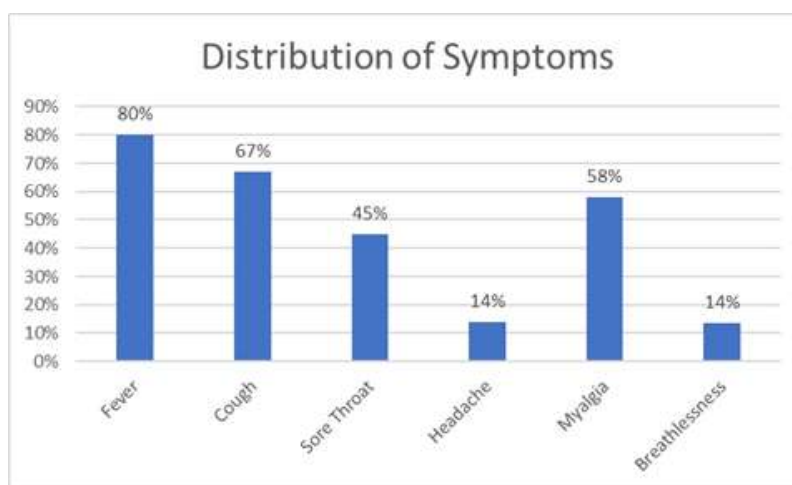


Figure 5: Distribution of symptoms among COVID-19 positive patients

## DISCUSSION

In our study, male patients constituted the majority as compared to female patients affected with COVID-19. This finding was in coherent with the study done by (8). They stated that more severe symptoms and higher mortality were associated among men than women. It might be because male patients have higher plasma levels of innate immune cytokines such as IL-8 and IL-18 along with increased monocytes as compared to female patients who have more T cell activation than male patients during SARS-CoV-2 infection. A similar study was done by (4) which also stated male predominance.

Furthermore, in our study, older age and a high number of comorbidities were associated with higher severity and mortality in patients with COVID-19 (10). The percentage of COVID-19 positive

patients was higher in males 65% (360/555) as compared to females 35% (195/555) which is in concordance with the study done by (4 & 11) in which they stated that males are more likely to get affected by COVID-19 because of potential causes which include differences in the regulation of hormone-regulated expression of genes encoding angiotensin-converting enzyme (ACE) 2 and the host type 2 transmembrane serine protease (TMPRSS2), which are necessary for SARS-CoV-2 to enter target cells. There are many other factors which influence our findings in terms of the immune responses that females exhibit higher inflammatory immune responses as well as adaptive immune responses as compared to male during viral infections (12). Females generally exhibit greater humoral and cell-mediated immune responses to antigenic stimulation. The

number and activity of innate immune cells such as monocytes, macrophages, dendritic cells and cytotoxic T cells are also higher in females than in males (4). Studies also reported that estrogen has a protective anti-inflammatory effect against coronaviruses by inhibiting most proinflammatory cytokines, such as IL-1 and IL-6 (13) thereby their results are also in concordance with our study as females with COVID-19 are lesser in number as compared to male COVID-19 positive patients. Differences in behaviours and activities such as higher smoking and drinking, low rates of hand washing and delayed healthcare seeking in males may also contribute to the sex differences in the incidence of COVID-19 (14 & 19).

Moreover, in our study, COVID-19 positive male percentage in age group > 50 years were having more symptoms along with other co morbidities and more so over their number was also higher as compared to other age groups, a similar study was done by (12) which also stated the same results. In our study, patients having age >50 years were high as compared to other age groups and were associated with longer stay in hospital. Same findings were observed in a study done by (15). A similar study was done by (10) which also stated that COVID-19-associated mortality was higher among geriatric population which correlated with our findings. It results because of weakened physiological functioning of vital organs, including the respiratory system, leading to impaired mucociliary clearance of foreign particles or micro-organisms in aged individuals. Moreover, with advancing age, both innate and adaptive immune systems get weakened, thereby increasing the possibility of underlying chronic diseases upsurge, ultimately leading to higher incidence of infections in old age (10).

In our study, the percentage of symptomatic COVID-19 positive patients were high in males as compared to females, same findings were observed in a study done by (16) which also stated that men being more susceptible than women to the infection and

having a worse outcome. In our study, fever, cough and sorethroat were the most common symptoms followed by headache and breathlessness. These findings were in concordance with this study (17-18) in which they stated that out of 1099 laboratory confirmed COVID-19 patients, 88.7% were having fever followed by cough (67.8%). However, in our study the third most common symptom was sorethroat followed by headache and breathlessness which were in concordance with the findings done by (18) and more so over the male constituted the majority of symptomatic COVID-19 positive patients which comes out to be 80% (290/360), similar findings were observed in this study (19).

## CONCLUSION

So, our study illustrates that the percentage of males being positive were higher and that too with more symptoms in elderly age group (>50) which may be due to higher incidence of comorbidities (diabetes, cardiovascular diseases, hypertension, etc) and poor immune responses to COVID-19. The study also highlighted the potential protective effect of estrogen in females against Covid-19 infection.

The sex and gender disparities observed in COVID-19 vulnerability emphasize the need to better understand the impact of sex and gender on incidence and case fatality of the disease in relation to treatment according to sex and gender. The ongoing prophylactic and therapeutic treatment studies must also include prospective sex and gender-sensitive analysis also. As early identification of risk factors, not only to identify clinical and epidemiological characteristics but also to facilitate the appropriate supportive care and prompt access to the intensive care unit (ICU) if necessary.

### *Declaration by Authors*

**Ethical Approval:** Approved

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