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Symptoms and Associations of COVID-19 in Pakistan: A Single Centre, Descriptive Study

[1]Shehrbano Ali, [1]Muhammad Murad Murtaza, [1]Marriam Nasir, [2]Muhammad Ashraf Chaudhry
[1]*CMH Lahore Medical College, Lahore*
[2]*Department of Community Medicine, CMH Lahore Medical College, Lahore*

ABSTRACT

Introduction: Since SARS-CoV2 is a novel virus, not much was previously known about the disease, however recent studies have shown that it is transmitted via droplet infection and mainly affects the respiratory tract, causing symptoms of fever, fatigue and shortness of breath. Comorbidities increase risk of severe disease.
Aims & Objectives: Our study aims to determine the predominant manifestations and correlations of COVID-19 in Pakistan.
Place and duration of study: The study was carried out at CMH Lahore over ten-day duration from 1st June 2020 to 10th June 2020.
Material & Methods: Samples of 107 confirmed cases of COVID-19 was taken. Participants were administered a questionnaire by attending doctor which enquired regarding their symptoms, presence of complications, and comorbidities. Data was analyzed using SPSS 25.0. A p-value of <0.05 was considered significant.
Results: 77.6% of participants were male whereas 22.4% were female, with mean age 40.68 years. Symptoms commonly experienced were fever (71%), cough (32.7%), sore throat (36.4%), and myalgia (57%). Progression to complications was seen in 36 participants, most common being pneumonia (22.4%). Age of participants was significantly associated with symptoms of fever (p= 0.017), shortness of breath (p= 0.048) and fatigue (p= 0.021), and complication of pneumonia (p= 0.001). Comorbidities were associated with many symptoms and complications, most prominently cardiovascular disease was associated with development of complications like acute kidney injury (p= 0.002), cardiac failure (p= 0.005), and stroke (p= 0.005).
Conclusion: Symptoms of COVID-19 are respiratory in nature primarily, however, the virus also affects other organs like gastrointestinal tract, neurons, heart. Age and presence of comorbidities increase risk of getting more severe disease, with highest risk of complications occurring in patients with history of cardiovascular disease.

Key words: COVID-19, pandemic, symptoms, comorbidities, SARS-CoV2

INTRODUCTION

COVID-19 has taken the world by a storm. What initially started as a cluster of cases in Wuhan, China of pneumonia of unknown origin[1] has now progressed to a worldwide pandemic, officially declared so by the World Health Organization,[2] with over 97 million confirmed cases and 2 million deaths as of January 24,2021.[3] Covid-19 is caused by the virus now named as severe acute respiratory syndrome corona virus 2 (SARS-CoV2) by the International Committee on Taxonomy of Viruses.[4] This virus is a beta-coronavirus.[5] Other known beta-corona viruses include severe acute respiratory syndrome-corona virus (SARS-CoV) and Middle East respiratory syndrome- corona virus (MERS-CoV), both of which have previously been responsible for outbreaks in China and the Saudia Arabia respectively.[6,7]

SARS-CoV and MERS-CoV are associated with animal-to-human transmission, and human-to-human transmission is mostly nosocomial in nature.[8] These viruses primarily target the respiratory tract and present with a range of clinical presentations, varying from mild flu-like symptoms to severe acute respiratory distress syndrome (ARDS).[9,10]

Being a novel virus, not much was previously known about SARS-CoV2. However, studies during the pandemic have shown that the virus shares many similar features with the previously known beta coronaviridae mentioned above in terms of clinical manifestations, however its mode of transmission is more so via human-to-human contact through droplet infection and indirect contact via contaminated objects, instead of animal-to-human transmission.[11,12] The rapid transmission and spread of the virus via human-to-human contact, which is aided by the high reproductive number estimated to be between 2 to 2.5 and even as high as 5.7 in

Wuhan,[13] has been a major cause for concern in the current pandemic.

The clinical manifestations for SARS-CoV2 may include certain common symptoms including but not limited to fever, shortness of breath, cough, expectoration, hemoptysis, myalgia and fatigue,[14,15] and radiology reveals ground glass opacities and bilateral patchy shadowing.[16] Some findings unique to this viral strain include the involvement of lower airways leading to upper respiratory tract symptoms like rhinorrhea, sneezing and sore throat, as well as gastrointestinal tract involvement in the form of diarrhea, abdominal pain and vomiting.[17,18] Apart from these predominant symptoms, certain peculiar findings were also noticed in certain cases. Some of these findings include neurological involvement like headaches, olfactory and gustatory dysfunction.[19]

The intensity of the symptoms caused by SARS-CoV2 has also been seen to vary based on pre-existing comorbidities of the affected individuals. Individuals previously diagnosed with conditions like diabetes, hypertension, respiratory disorders and heart diseases made up a significant population of those affected by the virus and became critically ill as a result of it, due to increased expression of ACE-2 receptors in these comorbidities that aids viral entry and the morbidity due to it.[20,21]

Most of the above conclusions are based on the clinical findings seen in cases in different countries of the world especially China. This study however aims to shed light on how COVID-19 manifested in Pakistan and to analyze whether these manifestations are similar to those observed in the researches conducted worldwide or whether the virus presents differently in Pakistan.

MATERIAL AND METHODS

A cross-sectional single centre study was carried out at Combined Military Hospital (CMH) Lahore, Pakistan with the ethical approval from the CMH Ethical Review Committee (Institutional Review Board Approval Letter No: 4403/ERC/CMH/LMC). The inclusion criteria for this study were patients admitted to the hospital as confirmed cases of COVID-19, having been tested positive for the infection via reverse transcriptase-Polymerase Chain Reaction (RT-PCR).

The study was conducted over ten-day duration from 1st June 2020 to 10th June 2020. During this duration, there was a population of 276 COVID-19 patients admitted to the hospital. Among these, 22 patients passed away, and a questionnaire was administered to the remaining 254 patients. 107 patients from the total population consented to participating in the study, making the response rate 42.1%.

The questionnaire used for this study was constructed after a comprehensive literature review, and comprised of four sections. The first section pertained to demographic data that included information regarding the age, gender, and date of positive RT-PCR test of the participant. The second section pertained to questions regarding commonly experienced COVID-19 symptoms based on pre-existing studies, while the third enquired about development of complications during the course of the illness and the fourth section concerned the presence of comorbidities. The questionnaire was self-administered by the attending doctors in the ward designated for COVID-19 patients in the hospital, in Urdu language so that the questions could be easily comprehended by the patients.

Statistical analysis:

The data collected from the participants was then analyzed via the Statistical Package for Social Sciences (SPSS) version 25. The quantitative variables like age were presented as mean ± standard deviation, while nominal variables were presented as frequencies and percentages. Chi-square test of significance was used to examine the significance of association between age and various symptoms and complications, as well as association of co-morbidities with complications. P-value < 0.05 was considered statistically significant.

RESULTS

From the 107 participants in this research, 83 (77.6%) were male whereas 24 (22.4%) were female. The mean age of the patients was 40.68± 15.3 years, with the maximum age in the sample being 72 years and the minimum age being 18. 38 (35.52%) participants belonged to the age group of individuals between 18 to 30 years of age, 30 (28.04%) were between 31 to 49 years of age, 26 (24.3%) were between 50 to 60 years of age, and the remaining 13 (12.15%) were between 61 to 72 years of age (Fig-1).

Among these, 89 (83.2%) of the patients were symptomatic while 18 (16.8%) were asymptomatic. The symptoms commonly experienced by the patients were fever (71%), cough (32.7%), sore throat (36.4%), myalgia (57%), diarrhea (16.8%), shortness of breath (17.8%), headache (15%), and fatigue (16.8%) (Table-1). The progression to complications was seen in 36 (33.64%) of these participants, most common of these being pneumonia (22.4%) (Table-1).

The age of the participants was seen to be significantly associated with the symptoms of fever (p= 0.017), shortness of breath (p= 0.048) and fatigue (p= 0.021), as well as the complication of pneumonia (p= 0.001), with all of these appearing mostly in the age group 50-60 years (Table-2). Gender, however, was not significantly associated with presence of symptoms or complications.

Pre-existing comorbidities like hypertension, diabetes, cardiovascular diseases, chronic liver disease (CLD), chronic obstructive pulmonary disease (COPD), and history of smoking were also seen to be associated with many symptoms and complications (Table 3). From the 107 participants, 28 (26.2%) were suffering from diabetes mellitus, 26 (24.3%) from hypertension, 3 (2.8%) from CLD, 12 (11.2%) from cardiovascular disorders, 11 (10.3%) from COPD, and 25 (23.4%) have a history of smoking. Commonly associated symptoms with these comorbidities included fever and shortness of breath. Most of the comorbidities were also significantly associated with pneumonia and acute respiratory distress syndrome (ARDS) as complications of COVID-19. Those suffering from cardiovascular diseases previously also showed significant association with the development of other complications as well, like that of acute kidney injury (AKI) (p= 0.002), cardiac failure(p= 0.005), and stroke (p= 0.005) (Table-3).

Clinical Presentation	Present
Asymptomatic	18 (16.8%)
Fever	76 (71%)
Cough	35 (32.7%)
Sore throat	39 (36.4%)
Sneezing	13 (12.1%)
Myalgia	61 (57%)
Anosmia	4 (3.7%)
Ageusia	16 (15%)
Nausea/Vomiting	7 (6.5%)
Diarrhea	18 (16.8%)
Shortness of Breath	19 (17.8%)
Rhinorrhea	6 (5.6%)
Headache	16 (15%)
Fatigue	18 (16.8%)
Loss of hearing	1 (0.9%)
Expectoration	1 (0.9%)
Complications	
Pneumonia	24 (22.4%)
Acute Respiratory Distress Syndrome	7 (6.5%)
Acute Kidney Injury	3 (2.8%)
Cardiac Failure	1 (0.9%)
Stroke	1 (0.9%)

Table-1: Frequency of clinical presentations and complications among COVID-19 patients (n=107)

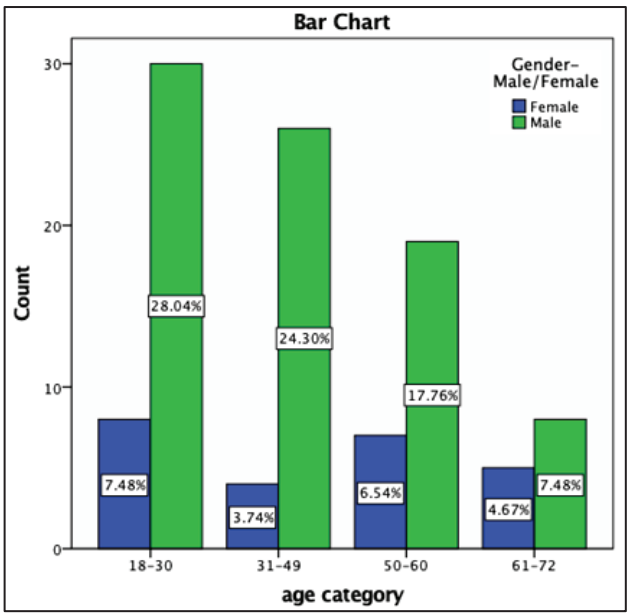

Fig-1: Distribution of male and female COVID-19 patients of different age groups in years (n=107)

Age Group (Years)	Fever+	Shortness of Breath+	Fatigue+	Pneumonia+
18-30	25 (23.36%)	4 (3.74%)	5 (4.67%)	37 (34.58%)
31-49	19 (17.76%)	3 (2.8%)	1 (0.09%)	26 (24.30%)
50-60	22 (20.56%)	7 (6.54%)	8 (7.48%)	14 (13.08%)
61-72	10 (9.35%)	5 (4.67%)	4 (3.74%)	6 (5.61%)
P-Value	0.017	0.048	0.021	0.001

Table-2: Association of age with symptoms and complications in COVID-19 patients (n=107)

Comorbidity	Symptom/Complication	P-value
Diabetes Mellitus	Fever	0.012
	Myalgia	0.007
	Shortness of breath	0.004
	Fatigue	0.002
	Pneumonia	0.001
Hypertension	Fever	0.02
	Myalgia	0.05
	Nausea/Vomiting	0.036
	Diarrhea	0.005
	Shortness of breath	0.01
	Fatigue	0.001
	Pneumonia	0.001
	ARDS	0.001
Chronic Liver Disease	Ageusia	0.011
	Shortness of breath	0.025
	Rhinorrhea	0.034
	Headache	0.001
	Loss of hearing	0.001

Cardiovascular disorders	Nausea/Vomiting	0.006
	Shortness of breath	0.001
	Loss of hearing	0.005
	Pneumonia	0.001
	ARDS	0.006
	Acute Kidney Injury	0.002
	Cardiac Failure	0.005
	Stroke	0.005
COPD	Sneezing	0.009
	Ageusia	0.003
	Shortness of breath	0.001
	Loss of hearing	0.003
	ARDS	0.003
Smoking history	Fever	0.020
	Sneezing	0.038
	Ageusia	0.001
	Diarrhea	0.001
	Shortness of breath	0.001
	Headache	0.037
	Pneumonia	0.001
	ARDS	0.001

Table-3: Association of comorbidities with symptoms and complications of COVID-19 patients (n=107)

DISCUSSION

SARS-CoV2, much like its counterparts SARS-CoV and MERS-CoV, has a variety of clinical manifestations.[22] While some individuals may remain asymptomatic or have very mild symptoms, others might progress to much more severe complications or even death. The causes and patterns of these variations give much reason for research. This study aims to shed light on some of the patterns of these variations observed among the population.

The male gender appears to be more susceptible to the infection, with a majority of the COVID-19 patients being men, a finding previously discovered in other studies as well.[21,22] Similar to this, Gondal et al's study also found that most women acquire the virus from a male counterpart in their household.[23] The reason for this, however, remains unknown. Once the infection is acquired, our study shows that men and women are at equal risk of developing symptoms and complication. This finding differs from other studies which show that the mortality rate is higher among men with the infection.[21,23]

Age seems to be a significant factor that effects the severity of symptoms. A majority of the patients in our study belonged to the younger age groups less than 50 years, similar to Lian's study where majority of the participants fell in the 15-49 age group.[24] Nonetheless severe symptoms and complications were more common in older adults. This finding can be explained by the weakened defenses and immunity of the older individuals. Previous studies have also shed light on a similar correlation, however in these the ages most susceptible to COVID-19 are those above 65 years of age.[21,23] Our study, however, shows that although this age group does show many of the more severe symptoms and complications, however the most significantly affected age group is that of individuals between 50 and 60 years of age. According to our results, the complication of pneumonia, as well as the more severe symptoms of fever, shortness of breath and fatigue are most common among this age group, even more so than individuals older than 60 years of age. This appears to be a peculiar finding which was also observed in Shahid et al's study,[21] however the reason for this too remains to be uncovered as to why middle aged individuals between 50 to 60 years age are more affected as compared to individuals both above and below this age group.

The commonly experienced symptoms by the participants in our study were similar to those observed in patients suffering from the virus in China as well.[14.15] These symptoms included fever, fatigue, myalgia, headache, cough and sore throat. The most common of these was seen to be fever which is a usual finding in most infectious diseases, as the body's response to the pathogen. Other commonly experienced symptoms include those pertaining to the respiratory tract, like that of cough, sore throat, shortness of breath, and sneezing. These too can be explained on the basis that SARS-CoV2 is a droplet infection and primarily enters via and targets the respiratory tract, similar to SARS-CoV and MERS-CoV. This also explains why the most common complications of the disease are also those primarily involving the respiratory system, like pneumonia and ARDS.

Of interest are the extra pulmonary symptoms caused by SARS-CoV2, including gastrointestinal manifestations like diarrhea, and olfactory and gustatory manifestations like anosmia and ageusia. Gastrointestinal manifestation are thought to be caused by a rather indolent strain, causing longer duration of infection and so the virus can be found in the gastrointestinal tract even after it has been cleared from the respiratory tract.[18,25] Anosmia and ageusia are also certain interesting manifestations of COVID-19, which point towards a possible neurological effect caused by the virus, similar to one found in SARS-CoV as well.[26] Preliminary findings show that these symptoms may be due to entry of the virus into the neuronal tissue via ACE-2 receptors present in the tissue, similar to its entry into the respiratory tract.[27]

Furthermore, as has already been observed in other studies, comorbidities were seen to have a significant impact on the severity of the disease as well.[20,21] The most common comorbidities present in the patients were those of diabetes and hypertension, as observed in Shahid et al's study as well.[21] Other comorbidities found in a lesser number of patients include COPD, CLD cardiovascular disorders, and a history of smoking. These comorbidities are seen to be associated with the presence of more severe symptoms. It was found in Ejaz et al's study that this association could be because of a weakened immune system and increased ACE-2 receptor expression due to the comorbidities, which promotes the viral entry and replication in the body causing a more severe presentation of COVID-19.[20] COPD and smoking also cause chronic damage to the lungs and COVID-19 being a respiratory infection primarily can aggravate this damage leading to severe respiratory complications like shortness of breath, pneumonia and ARDS.

The most prominent finding of our study, however, is the correlation observed between pre-existing cardiovascular disorders (CVD) and the development of complications in COVID-19 patients. A similar association has also been observed earlier between CVD and other beta-coronaviridae like SARS-CoV and MERS-CoV,[28,29] which is another indication towards the similarities between SARS-CoV2, SARS-CoV and MERS-CoV. It has been suggested in Ejaz et al's and Bonow etal's studies that patients suffering from CVD also appear to have a weakened immune system as in case of the other comorbidities, thus causing more severe disease.[20,30] Alongside this, the myocardial tissue also expresses ACE-2 receptors, which is a route of entry of the SARS-CoV2 virus,[20] thus allowing the virus to enter into the heart and cause damage to myocardial tissue leading to death of the tissue and in severe cases, cardiac failure. Bonow also hypothesized that the cytokine storm and intense inflammatory response caused by the virus can also lead to atherosclerotic plaque instability and procoagulant effect in CVD patients.[30] From this, it can be deduced that the CVD patients with chronic atherosclerotic changes underway in different vessels of the body can undergo plaque rupture due to the inflammatory stress in the body during a COVID-19 infection, and ultimately experience thrombosis and ischemia as the plaque occludes the different vessels. Depending on the vessel undergoing these changes, damage and complications can be observed in different organs of the body as suggested by our findings. Thrombosis and occlusion in the coronary arteries can lead to cardiac failure, occlusion in arteries of the brain can lead to stroke, while occlusion of vessels leading to hypoperfusion of the kidneys can lead to acute kidney injury.

CONCLUSION

Some of the clinical features of COVID-19 commonly observed in our study include fever, fatigue, headache, diarrhea, myalgia, shortness of breath, and cough. Other peculiar symptoms include those of anosmia, ageusia and loss of hearing. Our study also found that in some cases, these symptoms also progressed to severe complications like pneumonia and ARDS. The severity of the symptoms and risk of developing the complications was seen to be significantly associated with the age group of individuals as well as pre-existing comorbidities, specifically cardiovascular disorders. As a result, it should be recommended for old age as well as middle aged individuals, especially those with comorbidities to observe the preventative measures in order to avoid being infected by the virus as this population is found to be the most at risk of severe disease.

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The Authors:

Shehrbano Ali
Final Year MBBS Student,
CMH Lahore Medical College, Lahore.

Muhammad Murad Murtaza
Final Year MBBS Student,
CMH Lahore Medical College, Lahore.

Marriam Nasir
Final Year MBBS Student,
CMH Lahore Medical College, Lahore.

Dr. Muhammad Ashraf Chaudhry
Professor and Head of Department,
Department of Community Medicine,
CMH Lahore Medical College, Lahore.

Corresponding Author:

Shehrbano Ali
Final Year MBBS Student,
CMH Lahore Medical College, Lahore.
E-mail: shehrbanoali@gmail.com