
Comparison of Early Symptoms of COVID-19 Patients with Different Variants Before and After Vaccination

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Abstract: Corona virus disease (COVID-19) first detected in Wuhan, China in December 2019, spread rapidly to many geographical areas within a few months. As a result, on March 11, 2020 the World Health Organization (WHO) declared COVID-19 as a global pandemic. This disease mainly affected the respiratory system. The review of literature showed a diverse array of clinical features within 2-14 days, that range from asymptomatic and mildly symptomatic to severe illness. However, there is a need to recognize the diversity of clinical features produced by COVID-19 and its variants in Pakistan. The objective of this study is to determine the frequency of various clinical features during the initial stages of COVID-19 infection. This descriptive cross-sectional study was conducted at Fazaia Medical College and PAF hospital Islamabad from April 2020 to March 2022 after approval from the institutional ethical committee. By using WHO sample size calculator, the calculated sample size was 385. The data was collected by using a self-administered questionnaire. Only those patients were included in the study who had a positive RT-PCR for SARS-COVID-19. Data was entered and analyzed by using SPSS version 22.0. Chi-square test was applied. We divided our study into two phases. Out of 385 patients, 218 were included in phase-1 while 167 were included in phase-2. Dominant symptoms of phase 1 were fever (92.7%), anosmia / parosmia (82.1%), taste disturbance (81.2%), sore throat (74.3%) and lethargy (74.3%) but the dominant symptoms of phase 2 were fever (91.6%), sore throat (80.8%), lethargy (78.4%), odynophagia (73.7%) and cough (70.7%). P-value was < 0.001 and was extremely significant for dyspnea, loss of taste and anosmia. This study concludes that the most reliable symptoms for clinical diagnosis and referral for PCR are Fever, Sore throat and Lethargy.

Keywords: COVID-19, Diarrhea, Smell Disorder, Clinical Symptom, Taste Disorder, Meta-analysis

1. Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) first caused the Corona virus disease (COVID-19) in Wuhan, China in December 2019 [1]. This disease mainly affected the respiratory system and spread rapidly to many geographical areas within a few months owing to its extremely infectious nature [2-4]. As a result, on March 11, 2020 the World Health Organization (WHO) declared COVID-19 as a global pandemic. This pandemic resulted in over 3.8 million deaths globally and became one of the most disastrous health related event in history [5].

The first case of COVID-19 in Pakistan was reported on 26th February, 2020. Since then, the number of people infected with COVID-19 has increased to 1.53 M and 30383 deaths have been reported over the last two years of the pandemic [6].

After the review of literature, it was observed that exposure to the COVID-19 virus may produce a diverse array of clinical features within 2-14 days [7-9]. The clinical features of COVID-19 range from asymptomatic [10-12] and mildly symptomatic to severe illness that may result in respiratory failure, septic shock and multiple organ failure requiring hospitalization and mechanical assistance for ventilation [13-15].

The National Institute of Health (NIH) published a criterion [5, 10, 14, 16, 17] that categorized the COVID-19 patients into the following five types based on clinical signs and symptoms, radiological evidence and laboratory findings:

1) Asymptomatic:

Patients not having any symptoms but having a positive SARS-COV-2 PCR test.

2) Mild Disease:

Patients having COVID-19 symptoms like fever, fatigue, cough, sore throat, nasal congestion, headache, vomiting, diarrhea, anosmia, dysgeusia, anorexia, malaise, muscle pain or sore throat but without dyspnea, need for oxygen or radiological abnormalities.

3) Moderate Disease:

Patients having oxygen saturation (SpO_2) \geq 94% on room air or clinical features or radiologic findings consistent with pneumonia.

4) Severe Disease:

Patients having oxygen saturation (SpO_2) \leq 94% on room air.

5) Critical Disease:

Patients having respiratory failure with need for mechanical ventilation, Acute respiratory distress syndrome, septic shock or multi-organ failure.

The constant spread of COVID-19 and the severity of disease has been controlled to an extent by more awareness of the virus gained through clinical researches [1, 18] conducted all over the world and also by widespread vaccination against the virus. However, there is an urgency to recognize the diversity of clinical features produced by COVID-19 and its variants in Pakistan.

The objective of this study is to determine the frequency of various clinical features during the initial stages of COVID-19 infection and change in the frequency of these features in different waves of the pandemic caused by numerous variants of the virus. The study will also compare the clinical features of COVID-19 patients before and after vaccination. In the future, this study will be beneficial for early clinical diagnosis as well as for carrying out timely PCR (polymerase chain reaction) testing, even when the pandemic is over.

2. Methodology

Firs Approval from the institutional ethical review committee was sought before conducting this descriptive cross-sectional study. This study was conducted at Fazaia Medical College and PAF hospital Islamabad from April 2020 to March 2022.

The sample size was calculated by using WHO sample size calculator. At prevalence of 50% and confidence level of 95%, keeping the relative precision at 10%, calculated sample size was 385. We divided our study into two phases. Phase I was conducted from April 2020 to June 30, 2021. Phase II was from July 2021 to March 2022. The data was collected by using a self-administered questionnaire. Only those patients were included in the study who had a positive RT-PCR for SARS-COV-2. The patients who were critically ill and admitted in the ICU were excluded from the study.

Pretesting was done for the validity of questionnaire and Cronbach's Alpha was calculated to be 0.68. Various symptoms like fever, headache, lethargy, insomnia etc. were asked with a special focus on symptoms related to ENT. Data was entered and analyzed by using SPSS version 22.0. The clinical symptoms were compared on the basis of positive PCR results.

3. Results

Out of 385 patients, 218 were included in phase-1 while 167 were included in phase-2.

There were 115 males and 103 females in phase-1 while in phase-2 there were 79 males and 88 females. The age range was 18-75 years. The mean age in phase 1 was 39.2 ± 14.1 while in phase 2 it was 35.9 ± 9.8 . [table 1]

Table 1. Age and Gender Distribution.

		Phase -1 (n= 218)	Phase -2 (n=167)
Gender	Male	115(52.8%)	79 (47.3%)
	Female	103 (47.2%)	88 (52.7%)
Age	Mean (SD)	39.2 (14.1)	35.9 (9.8)

Table 2. Descriptive Statistics of COVID-19 Symptoms.

Symptom	Phase -1 (n= 218)%		Phase -2 (n=167)%		Chi. square test	Statist-ically Signifi-cant Difference
	Yes	No	Yes	No		
FEVER	92.7	7.3	91.6	8.4	0.705	No
BODYACHES	52.8	47.2	59.9	40.1	0.163	No
ANOREXIA	45.4	54.6	46.7	53.3	0.801	No
HEADACHE	27.1	72.9	24.6	75.4	0.577	No
LETHARGY	74.3	25.7	78.4	21.6	0.346	No
INSOMNIA	26.1	73.9	18	82	0.057	No
SORE THROAT	74.3	25.7	80.8	19.2	0.131	No
ODYNOP-HAGIA	67.9	32.1	73.7	26.3	0.220	No
RHINORR-HEA	17.9	82.1	14.4	85.6	0.355	No
NASAL CONGEST-ION	22	78	18	82	0.327	No
PND	28.1	71.9	28.1	71.9	0.994	No
ANOSMIA/PAROSMIA	82.1	17.9	64.7	35.3	0.000***	Yes
TASTE	81.2	18.8	50.3	49.7	0.000***	Yes
EARACHE	11.9	88.1	9.0	91	0.353	No
HEARING LOSS	0.9	99.1	0.6	99.4	0.599	No
TINNITIS	0.9	99.1	0.6	99.4	0.599	No

Symptom	Phase -1 (n= 218)%		Phase -2 (n=167)%		Chi. square test	Statist-ically Signifi-cant Difference
	Yes	No	Yes	No		
COUGH	65.9	34.1	70.7	29.3	0.322	No
SPUTUM	28	72	23.4	76.6	0.305	No
DYSYPNEA	42.2	57.8	25.7	74.3	0.000 ***	Yes
GIT	12.4	87.6	10.8	89.2	0.627	No

*** extremely significant (p-value<0.001).

Table 3. Dominant Symptoms in Phase 1 and 2.

Dominant symptoms (> 70% frequency)	
Phase 1	Fever 92.7%
	Anosmia / parosmia 82.1%
	Taste disturbance 81.2%
	Sore throat 74.3%
	Lethargy 74.3%
Phase 2	Fever 91.6%
	Sore throat 80.8%
	Lethargy 78.4%
	Odynophagia 73.7%
	Cough 70.7%

4. Discussion

The purpose of this research paper is to describe the early signs and symptoms of SARS-COV-2 variants among the patients and also to compare these symptoms in both vaccinated and unvaccinated individuals.

The virus has mutated into numerous variants since the beginning of the COVID-19 pandemic [10]. During the last two years, the disease has spread in the form of 'waves'. Each wave showed an abrupt rise in the number of infected people at a certain point of time and was caused by a different variant. Initially the diagnosis of COVID-19 was challenging as the patients presented with a wide variety of clinical features [9, 10, 19]. Another issue was the change in these clinical features due to the appearance of newer variants of the virus.

Throughout the pandemic, many variants of SARS-COV-2 have been identified, however, the WHO has labelled the following five variants [9, 10, 20, 22, 23] as 'variants of concern' as of December 2021:

- 1) Alpha: Reported in United Kingdom in November 2020.
- 2) Beta: Reported in South Africa in December 2020.
- 3) Gamma: Reported in Brazil in January 2021.
- 4) Delta: Reported in India in December 2020.
- 5) Omicron: Reported in South Africa in November 2021. [24]

COVID-19 can be asymptomatic, present with mild symptoms or as a severe illness leading to acute respiratory failure, septic shock, and multi-organ failure [10, 12, 16]. However, the most common presenting symptoms include fever, cough, sore throat, myalgias and dyspnea. Fewer people present with insomnia, anosmia [10, 25, 26], loss of taste, dysgeusia, anorexia, nausea, malaise and diarrhea [10, 19, 20, 21].

In the presenting study, males predominate in phase I and females in phase II. In phase I, most of the patients were unvaccinated and were infected during the first 3 waves and most probably by Alpha, Beta and Gamma variants. In phase II of the study, patients presented with milder symptoms and

were infected during last two waves. Most of these patients were vaccinated; those who were unvaccinated had slightly different and more severe symptoms.

As observed in this study, the most common symptoms in phase I, (experienced by more than 70% of the patients) included Fever (92.7%), Anosmia/Parosmia (82.1%), Taste Disturbances (81.2%), Sore throat (74.3%) and Lethargy (74.3%). Other symptoms that were noteworthy although observed in less than 70% of the patients include Cough (65%), odynophagia (67%), Myalgia (52%), Anorexia (45%), Insomnia (26%), Headache (27%), and Diarrhea (12%). Least common symptoms observed were tinnitus, sputum, rhinorrhea, post nasal drip, earaches and hearing loss.

These observations are similar to studies conducted previously. A meta-analysis of 78 studies comprising of 12,797 patients was conducted by Tariq et al [8]. The review concluded that GI symptoms were present in up to 1 in 5 patients. These included diarrhea, nausea and/or vomiting, anorexia, and abdominal pain. The weighted pool prevalence of diarrhea was 12.4% (95% CI, 8.2% to 17.1%), nausea and/or vomiting was 9% (95% CI, 5.5% to 12.9%), loss of appetite was 22.3% (95% CI, 11.2% to 34.6%) and abdominal pain was 6.2% (95% CI, 2.6% to 10.3%).

In phase II of the presenting study the most prominent symptoms which were experienced by more than 70% of the patients included Fever (91.6%), Sore throat (80.8%), Lethargy (78.4%) Odynophagia (73.7%), Cough (70.7%). Other significant symptoms included anosmia (64%), myalgia (59%), loss of taste (50%), anorexia (46%), headache (24%), insomnia (18%) and diarrhea (10%).

A study conducted by Stokes et al. [5] supports the results of the 2nd phase of our study. In their study it was reported that among 373,883 confirmed symptomatic COVID-19 cases in the US, 70% experienced fever, cough, shortness of breath, 36% reported myalgia, and 34% suffered from headache [5].

As the most common symptoms seen in Phase II were fever, cough and sore throat, it is likely that these patients were infected by the Delta variant of SARS-COV-2. This variant is proven to cause the symptoms similar to the original corona virus and its strains [10, 27]. Predominant symptoms include fever, sore throat and a persistent cough.

5. Conclusion

As of now, this pandemic has continued for over 2 years and is still ongoing. The wide array of symptoms produced by this disease should be kept in mind to ensure timely diagnosis and avoid complications, as in phase I the dominant symptoms were anosmia and taste disturbance along with fever and lethargy but in phase II odynophagia

and sore throat predominated along with fever and lethargy. This study also concludes that the most reliable symptoms for clinical diagnosis and referral for PCR are fever, Sore throat and Lethargy. Although we only found out the early symptoms of the disease but in later research we can broaden our study by determining the late and serious symptoms along with morbidity. Moreover, we can also compare the difference of symptoms after having different types of vaccines in future studies.

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