

Assessment of Coronavirus Disease 2019-Related Symptoms during and after the Disease – A Questionnaire Study on Affected Individuals

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Abstract

Background: The symptoms of coronavirus disease 2019 (COVID-19) are varying and include those pertaining to involvement of multiple body systems and organs. Since, cells in the oral cavity express viral entry receptor angiotensin-converting enzyme 2 that allows viral replication and may cause tissue inflammation and destruction. **Objective:** The objectives were to assess the symptoms of COVID-19-related symptoms in individuals during and after their phase of COVID-19 infection; to assess the attitude in terms of psychological impact, of COVID-19 on individuals during and after their phase of COVID-19 infection; and to assess the practices followed by individuals afflicted by COVID-19 during the period of their infection. **Methods:** A descriptive and cross-sectional questionnaire-based survey study was conducted among the general population in India, who had recovered from COVID-19 infection. **Results:** The questionnaire was answered by 419 individuals, of which 121 (28.9%) experienced loss of taste, 150 (35.8%) had dry mouth, 15 (3.6%) burning mouth, 26 (6.2%) had excessive salivation, and 28 (6.7%) had blisters or ulcers. Anxiety was reported by 101 (27%) depression by 22 patients, irritability and lack of focus were reported by 69 (18.4%) symptomatic participants which were statistically significant ($P \leq 0.05$). Residual symptoms, tiredness, muscle pain, and joint pains were reported by 36 (9.6%), 45 (12%), and 48 (12.8%) of the symptomatic participants, respectively, and were found to be statistically significant ($P \leq 0.05$). **Conclusion:** Individuals who have diagnosed with COVID-19 should undergo long-term monitoring for evaluation and management of symptoms during and after recovery.

Keywords: Anxiety, Coronavirus disease 2019, Depression, Fatigue, Fever, Ulcer.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) has developed into a full-scale global pandemic of epic proportions in a very short period of time. It has affected all age groups with alarming mortality, besides causing long-term effects in survivors.^[1] This infection is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that clinically affects multiple organs of the human body.^[2] Coronaviruses are positive-stranded RNA viruses with a crown-like appearance under electron microscope due to the presence of spike glycoproteins on the envelope. Like other RNA viruses, it is prone to various mutations, resulting in variants that are different in genomic characters and produce varying symptoms than their ancestral strains.^[3]

COVID-19 has had a massive fatal effect on the world's population resulting in more than 65.67 lakh deaths reported worldwide, as on October 31, 2022.^[4] It has emerged as the

most consequential global health crisis since the era of the influenza pandemic of 1918. Although the disease presents with milder symptoms in the general population, those people with underlying systemic conditions such as hypertension, cardiovascular diseases, uncontrolled diabetes mellitus, chronic respiratory diseases, immunosuppression, and aged over 60 years are more prone to get some serious complications from the infection which may even include death.^[5]

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The symptoms of COVID-19 are varying and include those pertaining to involvement of multiple body systems and organs, including the lungs, gastrointestinal tract, liver, blood vessels, heart, nervous system, and kidneys. There is evidence of possible post-COVID-19 symptoms in infected individuals. Since, cells in the oral cavity express viral entry receptor angiotensin-converting enzyme 2 that allows viral replication and may cause tissue inflammation and destruction,^[6] proper documentation of oral manifestations is as yet limited.^[7] This may be due either to the rarity of oral manifestations of COVID-19, or poor detection of such symptoms by attending physicians who may do only a cursory examination of the oral mucosa due to the overwhelming gravity of the other major systemic presentations. Therefore, this questionnaire-based survey was designed to find the various oral symptoms/changes during the period of infection. The objectives of this study were to assess the symptoms of COVID-19-related symptoms in individuals during and after their phase of COVID infection; to assess the attitude in terms of psychological impact, of COVID-19 on individuals during and after their phase of COVID infection; and to assess the practices followed by individuals afflicted by COVID-19 during the period of their infection.

MATERIALS AND METHODS

Study Design and Study Participants

This descriptive and cross-sectional questionnaire-based survey study was conducted from April 20, 2022, to June 25, 2022, among the general population in India, who had recovered from COVID-19 infection.

The convenience sampling method was used for recruitment of participants. Individuals who had been diagnosed as having COVID-19 through RT-PCR test, had internet access, could provide informed consent, and comprehend English, were invited to participate in this survey. Individuals who had never been diagnosed with COVID-19, who disagreed to participate in the study, with no internet access and had an inability to understand English, were excluded from this study. Those who had incompletely answered the web-based questionnaire were also excluded from this study.

Ethical Consideration

The ethical approval was obtained from the Institutional Ethics Committee (Uttaranchal Dental and Medical Research Institute, Mazri Grant, Dehradun, India, Ref. No. IEC/PA-01/2022, 27-January-2022). The ethics committee reviewed and approved this study protocol, participant information sheet, informed consent form, and the survey questionnaire.

Each of the study participants were requested to sign the informed consent to confirm their willingness to participate by answering an agree/disagree question. Informed consent included detailed information that was related to the aim and significance of the study so that the participants could make an informed choice about whether to participate or withdraw at any time if she/he so wished. The participants who selected the

“agree” option were directed to complete the self-administered questionnaire. The participants’ anonymity was ensured and no personal identifiers, including names, Email IDs, and details of COVID-19 exposure, were shared with any agency. Only one response per Internet Protocol (IP) address was allowed.

Survey Instruments and Data Collection

This survey questionnaire was developed through the Google Forms application (Google LLC, California, USA). For the survey, the participants submitted the data by either of the following methods, that is, through a personal interview by one of the investigators, by telephonic interview with one of the investigators including simultaneous entry selection of the options online, or by online dissemination of the survey link through emails and WhatsApp groups among the target populations. The participant information sheet and informed consent form in an electronic format were also attached.

Whenever personal interviews were conducted, all the preventive measures were followed to control disease transmissions such as the use of personal protective equipment, mouth masks, maintenance of hand hygiene, and social distancing. The participants were interviewed in well-ventilated rooms or open spaces. All survey forms were stored in an ultraviolet chamber (Halonix UV Shield Chamber, Halonix Technologies Ltd, Noida, India) for half a day. Oral examination on patients was not performed by the investigators due to risk of disease transmission.

The questionnaire comprising a total of eleven sections covering various aspects, which were not only related to symptoms and care but also about overall impact on the person physically as well as psychologically. Besides a basic information of the participant which included her/his name, age, sex, and qualifications, a detailed COVID-19 history, including duration of infection, month and year of infection, and vaccination history, was included in the study. The questions were designed to gain comprehension about the practices related to oral health during COVID-19, along with its major effects. Questions were also designed so that information was obtained about the medications consumed, infection-recovery period, and its consequences on oral health of the affected individual. The eleven sections were as follows:

- Section 1 – Informed consent
- Section 2 – Basis of study
- Section 3 – Information about the participant
- Section 4 – Information about symptoms during COVID-19
- Section 5 – Information about symptoms in oral cavity
- Section 6 – Information about hospital care during COVID-19
- Section 7 – Information on home care during COVID-19
- Section 8 – Information about medications and monitoring during COVID-19
- Section 9 – Effect of COVID-19 on mental health
- Section 10 – Practices during COVID-19
- Section 11 – Information about symptoms after recovering from COVID-19.

Statistical Analysis

The data collected from the participants were tabulated on Microsoft Excel® ver. 2019. The statistical analysis was carried out in IBM® SPSS® Statistics for Windows, version 26.0 (SPSS Inc., Chicago, Ill., USA). The quantitative data were expressed as frequency distribution. Test of association was done using Pearson's chi-square test with a confidence interval on 95% ($P \leq 0.05$).

RESULTS

The questionnaire was answered by 128 male and 291 female individuals who were affected by COVID-19. The age distribution of the participants is shown in Table 1. Majority (81.1%) of the participants belonged to 20–30 years of age. A total of 170 (40.6%) of participants had the infection for a duration of 1–7 days, 185 (42.2%) had the disease for 8–14 days, 50 (11%) of the participants had the disease for 15–21 days, 10 (2.4%) had for 22–45 days, and 4 (1%) had the disease for more than 45 days.

Forty-seven (11.2%) of the participants had comorbidities that included anemia, hypertension, diabetes mellitus, thyroid disorders, and psoriasis.

A total of 121 (28.9%) of the participants had experienced loss of taste out of which, 15 (12.4%) had loss of bitter taste, 65 (53.7%) had loss of salty taste, 43 (35.5%) has loss of sour taste, and 11 (9.1%) had loss of umami taste, as shown in Table 2. Other oral manifestations that were reported were dry mouth by 150 (35.8%), burning mouth by 15 (3.6%), bad breath by 57 (13.6%), excessive salivation by 26 (6.2%), blisters or ulcers by 28 (6.7%), and changes in the gingiva by 39 (8.3%) of the participants (Table 3). Among the participants, 74 (17.6%) reported changes in the tongue during the course of the disease. Among those individuals, 41 (82.3%) had coating on the tongue, 14 (9.8%) has redness, 11 (2.6%) had baldness of tongue, and 8 (1.9%) had blisters or ulcers.

An association of oral symptoms with general systemic symptoms was tested using Pearson's chi-square test. The association of oral symptoms, namely, loss of taste, xerostomia, burning sensation, halitosis, and excessive salivation with systemic symptoms was statistically not significant, as shown in Table 4.

Association of presence of systemic symptoms and psychological impact was tested. Anxiety was reported by 101 (27%) symptomatic participants which were statistically significant ($P \leq 0.001$). Depression was reported by 22 of symptomatic participant and this was found to be statistically not significant. Irritability and lack of focus were reported by 69 (18.4%) and 71 (19%) of the symptomatic participants, respectively, and were found to be statistically significant ($P \leq 0.05$) (Table 4). Among the post-recovery residual symptoms, tiredness, muscle pain, and joint pains were reported by 36 (9.6%), 45 (12%), and 48 (12.8%) of the symptomatic participants, respectively, and were found to be statistically significant ($P \leq 0.05$) (Table 4).

Table 1: Demographic data of the participants (n=419)

Gender	n
Male	128
Female	291
Age (in years)	n
10–20	8
20–30	340
30–40	41
40–50	10
50–60	11
60–70	4
70–80	5
80–90	0
90–100	0
Educational qualifications	n
Postgraduated/PhD	44
Graduated	116
Undergraduated	215
Secondary school	40
Primary school	4

Table 2: Occurrence of symptom of loss of taste (n=419)

	n	%	Type of taste	n	%
Yes	121	28.9	Bitter	15	12.4
			Salty	65	53.7
			Sour	43	35.5
			Umami	11	9.1
			Sweet	0	0
No	258	61.6			
Do not remember	40	9.5			

Table 3: Occurrence of oral symptoms (n=419)

n →	Yes	%	No	%	Don't remember	%
Symptom ↓						
Dry mouth	150	35.8	198	47.3	71	16.9
Burning mouth	15	3.6	380	90.7	24	5.7
Bad breath	57	13.6	318	75.9	44	10.5
Excess salivation	26	6.2	327	78	66	15.8
Blisters/ulcers	28	6.7	362	86.4	29	6.9
Changes in gum	39	8.3	333	79.5	47	11.2
Bleeding gums	12	2.8				
Painful gums	7	1.6				
Swollen gums	14	2.2				
Ulcers/blisters	7	1.6				
Changes on tongue	74	17.6	345	82.3	-	-

DISCUSSION

In the present questionnaire-based survey, 222 out of 419 (52.9%) participants reported oral symptoms during the course of their COVID-19 infection. The symptoms reported were new loss of taste, dryness of mouth, burning sensation, halitosis, excessive salivation, and blisters/ulcers.

Table 4: Association of oral symptoms with systemic COVID-19 symptoms (n=419)

Symptom ↓	No	Yes	Don't remember	Pearson Chi-square value	P value
Loss of taste	228	110	36	0.58	0.75
Xerostomia	175	134	65	0.55	0.76
Burning sensation	341	12	21	1.51	0.47
Halitosis	283	50	41	0.87	0.65
Excess salivation	293	22	59	0.63	0.73
Ulcers/blisters	325	24	25	0.75	0.69

Association of psychological impact with systemic COVID-19 symptoms (n=419)					
Anxiety	273	101	-	16.01	<0.001
Depression	352	22	-	2.79	0.09
Irritability	305	69	-	9.94	0.002
Lack of focus	303	71	-	10.29	0.001

Association of post-recovery symptoms with systemic COVID-19 symptoms (n=419)					
Abdominal cramps	360	14		1.74	0.19
Tiredness	338	36		3.74	0.03
Muscle pain	329	45		6.06	0.01
Joint pain	326	48		6.52	0.01

Nuno-Gonzalez *et al.*,^[8] in their cross-sectional observational study, evaluated 666 COVID-19 patients and reported that 78 (25.65%) had oral manifestations including transient lingual papillitis (11.5%), glossitis with lateral indentations (6.6%), aphthous stomatitis (6.9%), patchy depapillation (3.9%), mucositis (3.9%), and burning sensation (5.3%). Farid *et al.*^[9] reviewed various case studies that reported oral manifestations and concluded that along with gustatory changes, COVID-19 patients may present with ulcerative, erosive, vesiculobullous, and plaque-like oral lesions. Halboub *et al.*^[10] also reviewed different case reports about the oral manifestations involving 25 patients. The most common orofacial manifestations were ulcerative lesions, vesiculobullous/macular lesions, and acute sialadenitis of the parotid gland (parotitis). In four cases, oral manifestations were the first signs of COVID-19 suggesting that these oral signs may be the “inaugural” signs of the disease.^[10] It has been reported that angiotensin-converting enzyme 2 (ACE2) cell receptors are expressed on respiratory epithelium and oral epithelium, especially on the tongue.^[11,12] Direct damage to nasal and oral epithelium and the neuroinvasive nature of this virus can result in olfactory and gustatory disorders. Some studies have considered olfactory and gustatory disturbances as a single entity rather than two separate entities.^[13,14] Some of the manifestations like vesicles caused by Herpes, aphthous ulcers may be attributed to the stress related to the COVID-19 disease and not the virus directly. In the present study, the association of the oral symptoms and presence of general symptoms was not significant.

Individuals affected by COVID-19 had the difficulty of coping with the fear of spreading coronavirus, loss of loved ones,

economic and occupational burden, and other psychosocial issues. In the present study, the participants reported that they experienced anxiety, depression irritability, and lack of focus during the course of the disease. Passavanti *et al.*^[15] carried out a cross-sectional survey that involved 1612 COVID-19-positive individuals spread over seven different countries and reported significant levels of anxiety, depression, and post-traumatic stress disorder among those individuals. Some of the factors linked to the increased psychological effects could be related to the socioeconomic status, educational level, and worsening of the systemic symptoms. Brooks *et al.*^[16] reviewed 24 studies reporting the psychological effects during COVID-19 and most common were post-traumatic stress symptoms, confusion, and anger. They concluded that the stressors for these psychological effects were longer quarantine duration, infection fears, frustration, boredom, inadequate supplies, inadequate information, financial loss, and stigma.^[16] Luo *et al.*^[17] systematically analyzed eight studies and found that the main psychological problems of patients with COVID-19 were anxiety, depression, and loneliness. In the present study, the psychological impact such as anxiety, depression, irritability, and lack of focus was found to be significantly associated with COVID-19.

The long-term consequences of COVID-19 still remain to be fully understood. Many individuals either hospitalized or not have reported physical and psychological symptoms persisting even after the viral clearance. In this study, a significant number of participants have reported persistence of psychological symptoms such as anxiety, depression, irritability, and loss of focus and physical symptoms such as abdominal cramps, tiredness, muscle pain, and joint pain. Liyange-Don *et al.* have conducted questionnaire-based survey in 153 patients 3-months after their discharge from the hospital and reported persistence of body ache, headache, shortness of breath, and psychological symptoms such as depression and post-traumatic stress syndrome.^[18] Iqbal *et al.*, in their questionnaire-based survey on 158 COVID-19-recovered patients, have reported that a large number of patients had at least one post-recovery symptom that significantly affected their quality of life.^[19] In an ambidirectional cohort study, Huang *et al.* surveyed 1733 post-recovery patients wherein 63% reported fatigue and weakness, 26% had sleep difficulties, and 23% had anxiety and depression.^[20] These suggest the need for the post-recovery management of psychological and physical conditions to improve the quality of life of these patients.

CONCLUSION

The care and management of COVID-19 patients require addressing the oral symptoms during the disease period, as there is growing evidence of the presence of oral manifestations. The prevalence of post-COVID-19 symptoms, both physical and psychological, has also been increasingly reported with possible more serious consequences in some individuals. Individuals who have recovered from COVID-19

should undergo long-term monitoring for evaluation and management of these symptoms.

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