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Original Research Article

Post-COVID-19 manifestations-are they a matter of concern?

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ABSTRACT

Background: COVID-19 is an infectious disease caused by a new coronavirus (SARS CoV-2) which may seriously affect the respiratory system. Global data shows 80% of the patients suffer from mild symptoms such as fever, dry cough and fatigue. 87.4% of COVID-19 patients reported persistence of at least one symptom after recovery. The aim of the study was to estimate the prevalence of Post COVID-19 Manifestations (PCM) and its determinants among those declared positive for SARS-CoV-2 in Kannur district of Kerala.
Methods: A cross-sectional study was carried out among COVID-19 recovered individuals who were tested positive for SARS-CoV-2 during the period from March 2020 to September 2020 in Kannur district. Study participants were contacted over phone and details collected were entered into Microsoft excel and analysed using Stata 14.4. Descriptive analysis, chi-square test and binary logistic regression were used to interpret the data.
Results: The prevalence of PCMs among the study population was found to be 19.5%. The most common type of PCM reported was loss of taste. Major predictor variables of the outcome were symptom status during testing for COVID-19, hospital admission for COVID-19 treatment and excessive fatigue.
Conclusions: The study found that PCMs occurred in about one-fifth of the study population. Considering the burden of PCMs among the study population, this study provides rationale for strengthening and sensitization of primary health care providers and the general public for the identification and management of PCMs.

Keywords: COVID-19, Kerala, Post-COVID-19 manifestations, Prevalence

INTRODUCTION

Multiple outbreaks of infectious diseases in the recent past have significantly impacted the lives of millions of people across the globe. This not only adversely affected our medical and public health system but also had a huge impact on the economist and the society to address the financial hardship, countering the public anxieties, expectations and the discovery of vaccines.[1,2] One such infectious disease which China encountered at the end of 2019, was days before the Chinese new year.[3] At the end of December 2019, Wuhan city encountered pneumonia cases with unknown aetiology. Later the causative agent was identified as novel coronavirus and which is currently referred as SARS CoV-2 and the disease caused by it as COVID-19.[4] Then the world witnessed a rapid spread of the SARS CoV-2 crossing the international borders in no time. Considering the situation, the government of India swiftly initiated multi-sectoral steps for the mitigation of this public health issue. Surveillance was strengthened in all the international airports and capacity building activities were carried out for catering COVID-19 cases in designated hospitals. Kerala was the first state to report cases of COVID-19 in late January

2020. Later the second and third confirmed cases of COVID-19 were also reported from the same state. After nearly a gap of one-month, other states also began to report cases. As on 2021, September last week, total confirmed SARS CoV-2 cases were 46,41,587, and 24,661 SARS CoV-2 deaths were reported from the state.[5]

Irrespective of age and gender, acute respiratory tract infections (ARTIs) are the commonest among various communicable diseases.[6] Various microorganisms including a variety of bacteria and viruses typically cause these diseases. However, respiratory syncytial virus (RSV), influenza A and B and corona viruses are considered to be having the greatest contagious ability and has a history of causing multiple epidemics and pandemics.[7] COVID-19 is an infectious disease caused by a new coronavirus (SARS CoV-2) which may seriously affect the respiratory system.

The major mode of transmission is via respiratory droplets from an infected person generated during coughing or sneezing.[8] It primarily affects the lung parenchyma which may result in asymptomatic manifestations to severe symptoms leading to death of the COVID-19 infected person. 80% of the patients suffer from mild symptoms such as fever, dry cough and fatigue.[9] In comparison with the classical symptoms during the infectivity phase, the post recovery manifestations can be entirely different. Other than the general symptoms, specific organ damage can happen as a consequence of direct tissue invasion by the virus, cytokine storm, profound inflammation, damage to immune system or hypercoagulable state.[10] 87.4% of COVID-19 patients reported persistence of at least one symptom after recovery.[11] Post-COVID-19 manifestations (PCMs) can be post-acute COVID-19 or chronic COVID-19, depending upon the duration of persistence of symptom from the date of symptom onset. Post-acute COVID-19 Cases are those in which symptoms can extend beyond 3 weeks from the symptom onset, whereas Chronic COVID-19 cases are those in which the symptoms extend beyond 12 weeks. The most commonly reported symptoms include fatigue, dyspnoea, cough, arthralgia, and chest pain.[12]

As studies on PCMs are few in our settings, the present study aims to estimate the prevalence of PCMs and to find out the factors associated with its occurrence among COVID-19 recovered persons in Kannur district, Kerala.

METHODS

Study design and sampling

A cross-sectional study was carried out among COVID-19 recovered patients, who had been declared positive in Kannur district of Kerala from March 2020 to September 2020. Study duration was from October 2020 to December 2020. COVID-19 cases who were tested positive during the time period starting from 1/03/20 to 30/09/20 were only included in the study. Additionally, COVID-19 positive cases who were tested positive through antigen/Truenat/RTPCR/POC were only considered in this study. Any acute or chronic condition that would limit the ability of the patient to participate in the study were excluded. Respondents were also excluded if they express dissent towards giving responses. Sample size calculated was 200, using the formula:

$$N = \frac{Z \propto^2 pq}{d^2}$$

with 20% relative precision giving a non-response rate of 10%. The state technical guideline quoted PCM prevalence of 35%, of which 1% had post-chronic COVID-19 symptoms.[13] Study population was listed out and grouped into two categories based on the month of declaration, so that both post-acute and chronic COVID-19 manifestations that have occurred could be recorded. From March 2020 to June 2020, out of 866 total declared cases, 20 people were selected using simple random sampling. Of the 16454 cases declared from July 2020 to September 2020, 180 were selected using simple random sampling.

Data collection and analysis

List of COVID-19 cases available were taken and sampled. Study participants were contacted over phone and details were collected regarding demographic profile, medical history and clinical details including post-COVID-19 manifestations. Data were entered into Microsoft excel and analysed using Stata 14.4. Quantitative variables were summarized using measures of central tendencies and qualitative variables were expressed as proportions. Bivariable analysis using Pearson Chi-square test was performed for all the categorical variables. If any of the cells in the contingency table had expected value less than 5, Fischers exact test was used, instead of Chi-square test. The odds ratio and its 95%CI were used as a measure of strength of association.

Binary logistic regression was used to predict PCMs which is the outcome of the study. A significance level less than 0.05 was used for assigning covariates to the regression model. Backward conditional method of regression was employed for discarding non-significant exposure variables.

Ethical considerations

Confidentiality and privacy were maintained at every step of the investigation. The present study is the result of district COVID-19 surveillance done as instructed by district medical officer, Kannur. Hence it was exempted from obtaining clearance from the institutional ethics committee.

RESULTS

Demographic details

Among 200 respondents, 126 (63%) belonged to the age group of 16-45 years. The 53.5% (107 out of 200) had above high-school level education. Majority of the respondents (43.5%) were unemployed. Demographic variables are given in (Table 1).

COVID-19 details

Among the 200 study participants 122 were symptomatic. 39% (78 out of 200) of the respondents stated that they were asymptomatic at the time of testing. The most common reported symptom during the period of positivity was fever (53%). Other common symptoms included loss of taste or ageusia (41%), headache (40%), fatigue (38%), loss of smell or anosmia (31%), cough (25.5%) etc. Symptom profile of the study participants is as shown in (Figure 1).

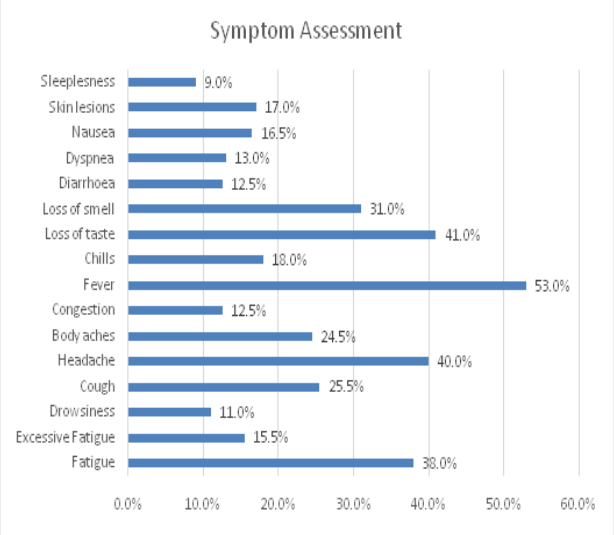

Figure 1: COVID-19 symptom profile of study participants, (n=200).

It was also found that 81.5% of the infections were locally acquired whereas 18.5% (37 out of 200) were imported cases. The main psychological impact respondents experienced was sleeplessness (20.5%) during their positivity period.

As far as psychological support services are concerned, 98.5% reported that they had received some sort of psychological support. Majority (90%) of the patients had received calls from the nearby peripheral health institutions. The 76% of the respondents stated that they received calls from the district mental health program (DMHP) counselling team. On an average a rating of 4.5 out of 5 were given by the respondents upon asking regarding the overall care giving of the public health system towards them.

The probable source of infection, mental health status and psychological support services during the positivity phase are given in (Table 2).

Post-COVID-19 Manifestations

Of the total 200 respondents, 39 (19.5%) had developed post-COVID-19 manifestations. The most common symptoms in persons who reported acute post-COVID-19 manifestations were loss of taste (25%) and loss of smell (21.8%). Mental confusion (42%) was the most common chronic post-COVID-19 manifestation. The frequency of post-acute and chronic COVID-19 manifestations are enlisted in (Table 3).

Bi variable analysis

Persons who were symptomatic at the time of COVID-19 testing were found to have higher chance for development ($p<0.001$) of PCMs. Among the symptoms fatigue, excessive fatigue, fever, loss of taste and loss of smell were associated with PCMs. But severity of COVID-19 was not found to have any statistical significance with PCMs ($p=0.12$) whereas hospital admission due to COVID-19 showed statistical significance p value of 0.03). Bivariable analysis done is as shown in the Table 4).

Table 1: Demographic variables of the study participants.

Variables	Categories	Frequency of respondents, (n=200)	Percentage (%)
Age (in years)	0-15	19	9.5
	16-30	64	32
	31-45	62	31
	46-60	44	22
	61-75	9	4.5
	>75	2	1
Education	Nil	2	1
	Primary school	24	12
	Middle school	11	5.5
	High school	56	28
	Higher secondary	42	21
	Diploma	12	6

Continued.

Variables	Categories	Frequency of respondents, (n=200)	Percentage (%)
	Graduation	41	20.5
	Post-graduation	12	6
Occupation	Legislators/ senior officials and the managers	1	0.5
	Professionals	16	8
	Technicians or the associate professionals	22	11
	Clerks	4	2
	Service workers/ sales	29	14.5
	Agricultural/ fishery workers	4	2
	Craft/ related trade workers	6	3
	Plant/ machine operators	9	4.5
	Elementary occupation	15	7.5
	Workers not classified by occupation	7	3.5
	Unemployed	87	43.5

Table 2: The frequency of probable source of infection, mental health status and psychological support services during positivity phase.

Variables	Categories	Frequency of respondents, (n=200)	Percentage (%)
Probable source of infection	Interstate or international traveller	37	18.5
	Contact of a confirmed case	163	81.5
Mental health status	Little interest or pleasure in doing things	8	4
	Feeling down/ depressed/ hopeless	16	8
	Feeling nervous/ anxious/ on edge	13	6.5
	Not being able to stop or control worrying	11	5.5
	Sleeplessness	41	20.5
Psychological support services	Received psychological support from any source	197	98.5
	Received counselling support from DMHP*	152	76
	Received support from PHIs*	180	90
	Received support from local self-government	135	67.5
	Received support from community volunteers	92	46
	Received support from family	127	63.5
	Received support from friends	134	67

*DMHP-District mental health programme; PHIs-Peripheral health institutions.

Table 3: Frequency of post COVID-19 manifestations.

Symptoms	PCMs, (n=39) (%)	
	Acute PCM, (n=32)	Chronic PCM, (n=7)
Fatigue	5 (15.6)	1 (14)
Excessive fatigue	2 (6.2)	2 (28)
Drowsiness	2 (6.2)	0
Cough	5 (15.6)	2 (28)
Headache	5 (15.6)	2 (28)
Body aches	2 (6.2)	2 (28)
Fever	1 (3.1)	0
Loss of taste	8 (25)	1 (14)
Loss of smell	7 (21.8)	1 (14)
Congestion	1 (3.1)	0
Skin lesions	1 (3.1)	0
Mental confusion	0	3 (42)

Table 4: Bivariable analysis.

Variables		Post COVID symptom present, (n=39) (%)	No post COVID symptom, (n=161)	OR (95% CI)	P value
Education	Up to high school	16 (41)	77 (47.8)	0.75 (0.37-1.5)	0.47
	Above high school	23 (59)	84 (52.2)		
Occupation	Sedentary	26 (66.7)	104 (64.6)	1.09 (0.52-2.2)	0.854
	Non-sedentary	13 (33.3)	57 (35.4)		
COVID-19 symptom status	Symptomatic	38 (97.4)	84 (52.2)	34.8 (4.6-259.8)	<0.001*
	Asymptomatic	1 (2.6)	77 (47.8)		
Fatigue	Yes	23 (58.9)	53 (32.9)	2.9 (1.42-6.0)	0.003*
	No	16 (41.03)	108 (67)		
Excessive fatigue	Yes	14 (35.9)	17 (10.5)	4.7 (2.07-10.8)	<0.001*
	No	25 (64.1)	144 (89.4)		
Cough	Yes	14 (35.9)	37 (23)	1.8 (0.88-3.9)	0.075
	No	25 (64.1)	124 (77)		
Headache	Yes	20 (51.2)	60 (37.2)	1.77 (0.87-3.5)	0.109
	No	19 (48.7)	101 (62.7)		
Body ache	Yes	9 (23.8)	40 (24.8)	0.90 (0.39-2.07)	0.818
	No	30 (76.9)	121 (75.1)		
Fever	Yes	30 (76.9)	76 (47.2)	3.7 (1.6-8.3)	0.001*
	No	9 (23)	85 (52.8)		
Loss of taste	Yes	26 (66.6)	59 (36.6)	3.4 (1.6-7.2)	0.001*
	No	13 (33.3)	102 (62.3)		
Anosmia	Yes	22 (56.4)	40 (24.8)	3.9 (1.8-8.0)	<0.001*
	No	17 (43.6)	121 (75.2)		
Abdominal pain	Yes	3 (7.6)	2 (1.2)	6.6 (1.0-41.1)	0.052
	No	36 (92.3)	159 (98.7)		
Severity of COVID-19	Severe	6 (15.4)	12 (7.5)	2.25 (0.79-6.4)	0.12
	Less severe	33 (84.6)	149 (92.5)		
Hospital admission	Yes	16 (41)	30 (18.6)	3 (1.4-6.4)	0.03*
	No	23 (59)	131 (81.4)		
Addictions	Yes	4 (10.3)	35 (21.7)	0.41 (0.13-1.2)	0.076
	No	35 (89.7)	126 (78.3)		
Co-morbidity	Yes	10 (25.6)	30 (18.6)	1.5 (0.66-3.4)	0.326
	No	10 (25.6)	131 (81.4)		
Diabetes mellitus	Yes	3 (7.7)	14 (8.7)	0.87 (0.23-3.2)	1.0
	No	36 (92)	147 (91.3)		
Hypertension	Yes	5 (12.8)	15 (9.3)	1.4 (0.48-4.2)	0.513
	No	34 (87.2)	146 (90.7)		
Travel history	Yes	7 (17.9)	30 (18.6)	0.95 (0.38-2.3)	1.0
	No	32 (82.1)	131 (81.4)		

Table 5: Multivariable analysis of significant exposure variables.

Variable	Adj OR	95% CI	P
COVID-19 symptom status	24.7	3.2-187.4	0.002
Hospital admission	2.3	1.03-5.4	0.042
Excessive fatigue	3.0	1.2-7.3	0.015

Multivariable analysis

Backward conditional binary logistic regression was done after disregarding non-significant exposure variables. Maximum value of Nagelkerke R square with minimum number of variables and significance of the model in the Chi-square table were the criteria used for finalising the model. The model significance was <0.001 and could explain 32% (Nagelkerke R square=0.321) of the variability seen in occurrence of PCMs. Multivariable analysis done is as shown in the Table 5.

DISCUSSION

In this study majority (58.5%) of the individuals were from the age-group 30 years and above. 81.5% of the participants have attained high-school education or more. Most of them (43.5%) were unemployed. The study revealed a 19.5% prevalence of PCM among the COVID-19 recovered individuals. In a multi-state health care system study conducted in United States, it was found that 35% of the respondents had experienced some kind of PCMs.[14]

The knowledge of mechanism underlying 'post-covid manifestations' are essential in order to design early preventive treatment modalities for the same. In one review it was found that the pathogenesis of cough may be induced by SARS-CoV-2 itself via neuroinflammatory and neuroimmune mechanisms.[15] Direct infection or viral recognition by vagal sensory neurons or sensory neuron-associated glial cells could promote a neuroinflammatory state. So other than breathing exercises, anti-inflammatory drugs like steroids can alleviate symptoms like cough.

Unprecedented COVID-19 pandemic has triggered the stress levels of public in the community initiating fear and panic regarding their future. Many were anxious and had experienced loss of job which added the dilemma during the phases of lockdown. Not only these factors but also the infection caused by SARS-CoV-2 would impair cognitive functions.[16] Our study revealed that, 20.5% had sleeplessness and 6.5% had anxiety during the time of positivity phase, thereby proving that mental health issues surrounding COVID-19 infections are pertaining in the society. Mental confusion which is one of the commonest PCM, may be precipitated by the isolated environments. Prevention of mental fogging can be done by maintaining adequate hydration, ensuring effective communication and orientation, ensuring adequate lighting, averts immobilization, treating pain, maintaining oxygenation, and prevention of sleep deprivation. Medical management using low-dose lorazepam and haloperidol is advisable in severely affected individuals.[17]

After multivariable adjustment, patients showed an odds ratio (OR) 2.3 (95%CI=1.03-5.4) for patients who required hospitalization against the non-hospitalised patients for having PCM. This is similar to a study done in China which also found that hospitalised patients who had severe kind of disease experienced post-COVID symptoms.[18] So, proper communication should be conveyed to patients who required hospitalisation, regarding the chance of developing post-COVID-19 manifestations. Other variables found to be significant are symptom status and presence of excessive fatigue during the initial phase. In one study conducted among doctors, the significant variables predicting the outcome were female gender and presence of co-morbidities.[19]

Limitations

Our study had two main limitations. Those with more severe illness might have been less likely to respond to telephone calls and might have differed from survey respondents due to hospitalisation or severity of illness. Since data collection was carried out using telephone, this study relied on patient self-report and might have been subject to recall bias also.

CONCLUSION

In conclusion patient care has to be continued even after recovery from SARS-CoV-2 infection. Hence sensitisation of health staff and general public are needed for the proper identification and management of PCMs. Along with that, strengthening of post-COVID-19 clinics should be done at each institution level. Preventive measures, including social distancing and frequent hand washing. Also, the correct use of face mask in public should be strongly encouraged to slow the spread of SARS-CoV-2 and thereby the incidence of PCMs.

Recommendations

As the pandemic progresses, the burden of PCMs is equally rising. Sensitization and strengthening of primary care providers are essential to tackle PCMs. The pathophysiology and duration of how long PCMs may last, is still completely not clear. Hence more studies are needed focussing post covid manifestations and its management.

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