Late sequelae of COVID-19 and its effect on the quality of life

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ABSTRACT

Background: COVID pneumonitis presents with symptoms of fever, cough, fatigue, myalgia, inability to smell and shortness of breath. However, certain symptoms have been reported to be persistent in some people or novel post recovery symptoms have developed. Due to the day today rise in the number of covid-19 cases in Pakistan, it is the need of the hour to determine the long-term consequences associated with this disease, to educate the general population and to establish the long-term management of the patients.

Patients and methods: This cross-sectional study was conducted using non-probability purposive sampling, in which a total of 75 patients who had recovered from Covid-19 infection in the past 2-10 months visiting tertiary care hospitals in Lahore for follow up were recruited and filled survey forms bearing different questions regarding their disease, post recovery symptoms and quality of life. Data collected was then analyzed by SPSS-26.

Results: The most common symptoms were fatigue (66.7%), dry cough (46.7%), headache (44%) and joint pains (41.3%), followed by other general, neurological, pulmonary and psychological symptoms. The quality of life was analyzed in different domains exhibiting an average range of 60-68% which shows that covid-19 has significantly affected the quality of life of its victims.

Conclusion: Various post disease recovery symptoms have been seen in the covid-19 victims and their quality of life has been deteriorated in physical, psychological, environmental and social domains; therefore, we need a multi-disciplinary team comprising of physicians, nurses, psychologists, social and occupational health workers who should work in liaison to tackle with these issues.

Keywords: Covid-19, late sequelae, SARS-CoV-2, quality of life

INTRODUCTION

Currently we are facing one of the deadliest pandemics in the history of the world: COVID-19 caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2, the first case been identified in December 2019 in Wuhan, China to be declared as a pandemic¹ by WHO in March 2020. As of 7 April, 2021, 131,837,512 cases have been confirmed worldwide² with 2,862,664 deaths attributed to this disease. In Pakistan², there have been 696,184 confirmed cases of COVID-19 with 14942 deaths, reported to WHO till 7th April, 2021. In addition to the health-related consequences, this pandemic has posed a serious threat to world's social and economic stability.

Coronavirus is an enveloped RNA virus initially known to have caused some cases of Severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS) and the common cold, has now emerged as a new deadly strain; mainly spreading through exposure to respiratory droplets containing the

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virus and contact transmission. There is a variability in the presentation of this disease ranging from asymptomatic/mildly symptomatic to severe morbidity and mortality³ and also depending upon age, immune status of the individual, co-morbid conditions⁴ and availability of healthcare facilities. The classical symptoms include fever (41%), cough (51%), fatigue (26%), myalgia (38%) inability to smell (16%) and shortness of breath; however, these may vary in different demographic populations.

The mild cases of COVID-19 usually take 1-2 weeks to recover; the severe ones may take up to 6 weeks or more. However, persistence of a few existing symptoms has been reported insome patients even after the virus can no longer be detected in the body⁵. These symptoms may include fatigue⁶, weight loss, hair loss⁷, joint pains, muscle weakness, persistent headache⁸, blurring of vision⁹, anosmia¹⁰, ageusia¹⁰, vocational problems, insomnia¹¹, decreased cognition and memory¹², dry cough¹³, shortness of breath^{13,14}, repeated infections¹⁵ and various psychological manifestations especially depression¹⁶ and anxiety¹⁶. Thromboembolic events¹⁷ and the worsening of previously existing diseases has also been demonstrated in a subset of patients¹⁸. In a nutshell, covid-19 is seen to have affected the quality of

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life to various degrees¹⁹.

Due to the day today rise in the number of covid-19 cases in Pakistan, due to the heterogeneity of presenting spectrum of symptoms and persistence of post infectious manifestations, it is the need of the hour to determine the long-term consequences associated with this disease, to educate the general population and to establish the long-term management of these patients. We need a multi- disciplinary team comprising of physicians, nurses, psychologists and occupational health workers who should work in liaison to tackle with the issues related to the physical and mental health of the patients who are suffering from post covid-19 recovery symptoms.

PATIENTS AND METHODS

This cross-sectional study was conducted at tertiary care hospitals of Lahore from March till May 2021 using non-probability purposive sampling. approval from Institutional Board of Studies, a total of 75 patients (including healthcare professionals) who had recovered from Covid-19 infection in the past and visiting two tertiary care hospitals in Lahore for follow up were recruited on the basis of inclusion and exclusion criteria. The recovery time was taken from 2 to 10 months and only those patients were included who had got a positive PCR-Covid-19 report. Those with active illness, pregnant females and mentally retarded patients were excluded from the study. Procedure of the research was explained to participants and informed consent was taken. Our survey forms with questions divided in five major sections: biodata, co morbidities and risk factors, covid-19 status, post recovery symptoms and quality of life, were filled by our research team in the month of April, 2021. Data collected was then analyzed by SPSS-26 where quantitative variables like age and post covid-19 recovery time were presented as mean± SD and qualitative variables like gender, post covid-19 symptoms etc. were presented as frequency and percentages. For the quality of life analysis, we used the WHOQOL BREF²⁰ questionnaire; an abbreviated form of 100 item questionnaire designed by WHO in 1998 to assess the quality of life of the respondent. The BREF type consists of four domains, physical health, psychological, social relationships and environment, each comprising of multiple questions that add up to be 26 in number rated in a five-point scale. Each domain was separately analyzed by generating the raw score first and coverting it to transformed score (0-100); 0 being the lowest score and 100 being the highest. The higher

the score, the higher the quality of life. We calculated the mean and standard deviation for each domain.

RESULTS

The mean age of the study population was 34.24 ± 11.93 SD with minimum age 17 year s and maximum age 62 years (Table-1). Out of 75 patients, 38 were females (50.7%) and 37 were males (49.3%). 59 (78.7%) had greater than 30,000 income and 65 (86.6%) had university and postgraduate qualification. Smokers constituted 5 (6.7%) of the total sample size with 68 (90.7%) being non-smokers. Among 75 patients, 7 (9.3%) were diabetics and 12 (16%) had hypertension. Regarding other co-morbidities, 2 (2.7%) had heart disease, 3 (4%) had lung disease, 2 (2.7%) had kidney disease and 3 (4%) had thyroid disease. Psychiatric illness was present in 1 (1.3%) of the patients while 4 (5.3%) of the patients mentioned having some other medical problems.

In our study, 64 (85.3%) of the patients had mild disease (managed at home), 10 (13.3%) had moderate (requiring supplemental disease oxygen hospitalization) and 1 (1.3%) had severe disease (managed in ICU setting). These patients had an average recovery duration of 2-10 months (mean ± SD = 6.13 ± 2.95). Among these, many patients reported certain symptoms to be present or persisting even after their Covid-19 PCR reports came negative. Dry cough persisted in 35 (46.7%) of the patients. Fatigue was present in 50 (66.7%) of the patients with 19 (25.3%) complaining of it at certain times of the day, 20 (26.7%) throughout the day and 1 (14.7%) only after exertion. 17 (22.7%) of the patients reported having hair loss, 16 (21.3%) had loss of smell, 12 (16%) had loss of taste, 5 (6.7%) had some problem in speaking while 16 (21.3%) had sleeping problem. Blurred vision was found to be present in 9 (12%) and memory loss in 18 (24%) of the subjects. Joint pain was found to be prevalent in 30 (41.3%) of the patients with 6 (8%) having pain in only 1 joint, 1 5(20%) in 2-4 joints and 9(13.3%) in 5 or more than 5 joints. Similarly, headache was persistent in 33 (44%) of the subjects with 9 (12%) experiencing it throughout the day. Some patients reported having repeated infections after recovery from Covid-19 involving throat 7 (9.3%), urinary tract 1 (1.3%), respiratory tract 1 (1.3%) and gastrointestinal tract 3 (4%). 29 (38.7%) of the patients were having shortness of breath; among these 14 (18.7%) had it after strenuous activities, 8 (10.7%) after ordinary activities, 4 (5.3%) after less than ordinary activities and 3 (4%) had it at rest. Anxiety and depression were the two

Table 1. Sociodemographic data, commorbidities and COVID-19 severity status

Characteristics	Frequency n (%)		
Age(years), mean ± SD	34.24 ± 11.935		
Gender			
Male	37 (49.3)		
Female	38 (50.7)		
Education	` '		
Middle school	1 (1.3)		
High school	9 (12)		
University	55 (73.3)		
Post graduate	10 (13.3)		
Income	` '		
<10000	11 (14.7)		
10000-20000	3 (4)		
20000-30000	2 (2.7)		
>30000	59(78.7)		
Smoking	07(70.7)		
Current smoker	5 (6.7)		
Former smoker	2 (2.7)		
Non-smoker	68 (90.7)		
Diabetes	00 (70.7)		
No diabetes	68 (90.7)		
Uncontrolled diabetes	1 (1.3)		
Controlled diabetes	6 (8.0)		
Hypertension	0 (8.0)		
No hypertension	63 (84)		
Uncontrolled hypertension	1 (1.3)		
Controlled hypertension	11 (14.7)		
Heart disease	11 (14.7)		
Yes	2 (2.7)		
No	73(97.3)		
Lung disease	73(97.3)		
Yes	3(4)		
No	72 (96)		
Kidney disease	72 (90)		
Yes	2 (2.7)		
No.	73 (97.3)		
Thyroid Problem	73 (97.3)		
Yes	2 (4)		
No	3 (4)		
	72 (96)		
Cancer	0 (0)		
Yes	0 (0)		
No Povehistria Illassa	75(100)		
Psychiatric Illness	1 (1 2)		
Yes	1 (1.3)		
No.	74 (98.7)		
Any other disease	4 (5.0)		
Yes	4 (5.3)		
No	71 (94.7)		
Covid-19 severity			
Mild	64 (85.3)		
Moderate	10 (13.3)		
Severe	1 (1.3)		

main psychological manifestations of post covid-19 recovery period with anxiety being present in 6 (8%) and depression in 11 (14.7%) of the patients. 6 (8%) of the patients complained of requiring increased doses of their previous medications which they had been taking for their other medical illnesses. Only 3 (4%) out of 75 patients required blood thinners in their post covid-19 recovery period.

Our research questionnaire also included the

Table 2. Post COVID-19 symptoms

Post Covid-19 symptoms	Frequency
Fatique	<i>n</i> (%) 50 (66.7)
Certain time of day	. ,
,	19 (25.3)
Throughout the day Only after exertion	20 (26.7) 11 (14.7)
Hair loss	17 (22.7)
Joint pain	30 (41.3)
	6 (8)
1 joint 2-4 joints	15 (20)
5 or more joints	9 (13.3)
Headache	, ,
	33 (44) 9 (12)
Throughout the day Sometimes	24 (32)
Loss of smell	16 (21.3)
Loss of taste	, ,
	12 (16)
Difficulty in speaking	5 (6.7)
Difficulty in sleeping	16 (21.3)
Blurring of vision	9 (12)
Memory loss	18 (24)
Dry cough	35 (46.7)
Sometimes	27 (36)
Throughout the day	7 (9.3)
Only after exertion	1 (1.3)
Shortness of breath	29 (38.7)
After strenuous activity	14 (18.7)
After less than ordinary activity	8 (10.7)
At rest	4 (5.3)
Repeated infections	3 (4)
Throat	7 (9.3)
UTI	1 (1.3)
Respiratory tract	1 (1.3)
Gastrointestinal	3 (4)
Others	1 (1.3)
Depression	11 (14.7)
Anxiety	6 (8)
Status of previous disease	6 (8)
Requirement of blood thinners	3 (4)

Table 3. QOL-Bref domain scores

Table 6: QGE Brid derriam seer es						
Domain	Ν	Minimum	Maximum	Mean	Std.	
					Deviation	
Physical health	75	13.00	94.00	64.3200	18.71562	
Psychological	75	19.00	94.00	60.4133	18.20684	
Social relationships	75	6.00	100.00	63.0800	22.43173	
Environment	75	38.00	100.00	68.9333	12.98162	

WHOQOL- BREF; an abbreviated form of 100 item questionnaire designed by WHO in 1998 to assess the quality of life of the respondent. The BREF type consists of four domains, physical health, psychological, social relationships andenvironment, each comprising of multiple questions that add up to be 26 in number rated in a five-point scale. After our analysis of each domain separately, the physical health was found to have a score of 64.32±18.71562 (mean ± SD), psychological health 60.4133±18.20684, social relationships 63.08±22.43173 and environmental domain 68.9333±12.98162, out of a total score of hundred for each domain.

DISCUSSION

Currently, the world has been hit by the deadly

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pandemic of Covid-19 and our country, Pakistan is under the spell of its third wave resulting in large number of deaths on a daily basis. Many researches have been conducted in the past one year related to the transmission, pathogenesis, symptoms, treatment and prognosis of covid-19. The main focus of the researchers these days has been the treatment modalities and preventive therapies including vaccinations but very few literature manuscripts throw light on the post covid-19 recovery symptoms. Our study aims at exploring the various symptoms persisting in Covid-19 patients even after recovery and their impact on the quality of their life. This will aid the health care workers to better manage their patients and adopt a multidisciplinary approach to achieve their physical, psychological and social rehabilitation.

In comparison to other studies conducted on the post covid-19 sequelae, the mean age of our study population was 34.24 ± 11.93 SD covering younger as well as older groups of patients with almost equal ratio of males and females. We questioned the people about the relevant co morbid conditions whose presence may have an impact on the severity of Covid-19 and also give a similar spectrum of symptoms in the affected subgroups. Among these 52 % percent of the people had previously existing co morbidities including hypertension (16%) as the most common risk factor, followed by Diabetes (9.3 %) and smoking (6.7 %). We included the Covid-19 PCR positive patients who have recovery time from covid-19 ranging from 2 to 10 months and then also classified them in mild (81.3 %), moderate (13.3%) and severe (1.3%) categories, according to whether they were managed at home, required oxygen and admitted in the ICU, respectively.

Among various symptoms thought to be a part of post Covid-19 syndrome, fatigue was found to be the most common and persistent symptom with 66.7% of our patients complaining of it even after 10 months of contracting Covid-19. Previous researches show fatigue to be common after certain viral infections like EBV, herpes simplex and cytomegalovirus. A significant association was found between T allele of Interferon- γ +874 T/A SNP and enhanced fatigue after infection. Single nucleotide polymorphism of cytokine genes for IL6 and IL10 was also found to play a role in this⁶. Hair loss was another symptom experienced by almost 22.7% of our study population which was also seen in 27% of individuals in a survey held by Indiana University school of medicine⁷. Telogen effluvium is the temporary hair loss due to excessive shedding of Telogen (resting hair) after some shock to the system

like acute or chronic illness, psychological stress etc. 41.3% of our subjects reported having joint pains; some having in only one joint and others involving multiple joints. Kamal et al. and Carfi A et al. in their separate studies showed joint pain to be present in 31.4% and 27.3% of their patients respectively^{21,22}. Various case reports show persistence of headache weeks after recovery and was fulfilling the criteria of new daily persistent headache NDPH8 and this was valid in our study in which 44% of participants reported headache at various times of day. Persistent glial activation and cytokines are thought to play some role in this development⁸ although, exact mechanisms are not known. In our study, 21.3% of subjects reported some difficulty in sleeping. Its incidence was found to be high in research conducted by Islam MF et al. (Post-viral fatigue and COVID-19: lessons from past epidemics) which showed poor sleep quality in about 56.3% of the subjects⁶. One proposal about the underlying mechanism responsible for this disturbance in post Covid-19 patients was the fact that injurious effects on neurological system might have impaired respiratory regulation which in turn has proved to be interfering with normal sleep patterns²³. Less than one third (21.3%) of our subjects showed concerns regarding loss of smell even after getting recovered from covid-19 and very few (16%) reported loss of taste. This correlates with post-viral anosmia which is caused by infection and inflammation of olfactory bulb induced, in this case, by SARS-CoV-2. Another study in Pakistan showed almost half (47.5%) of the patients with the same complaint of loss of smell and taste¹⁸.12.1% of our subjects complained of blurred vision. This was supported by another study in which blurred vision was present in almost 17.1% of the patients²¹.

In our study, 24% of the patients reported memory loss. Comparing our results with a cross sectional evaluation of post covid-19 recovery symptoms conducted at Dow university of Health sciences, Karachi in September 2020, 19% of the patient had a brain fog after recovery from covid-19¹⁸, while 34 percent in a clinical follow up of non-critical patients 2 months after recovery suffered from memory loss (descriptive clinical follow up by Carvalho-Schneider in October 2020)14. The pathophysiology of memory loss can be linked to the destruction of some neurons or reducing the formation of synapses between them. Dry cough was the second most common symptom in the analysis of our patients with 46.7 % of the people reporting it, in consistence with results of another research showing it to be 44.3 %¹⁸. Covid-19

can leave long term sequalae in the form of interstitial lung disease, manifested by fibrosis, interstitial thickening or ground glass opacities. A study conducted on 114 patients in their 6 months follow up, 62 % of the participants had residual abnormalities on the CT scan¹³. For the same reason, patients also have exertional shortness of breath as one of the post covid-19 recovery symptom with 38.7% of the patients reporting it in our analysis compared with 50 %¹⁸ and 43 %¹⁴ of two other studies done on post covid-19 symptoms respectively.

Regarding the psychological manifestations of covid-19, we questioned the people for anxiety and depression with 8% and 14.7% of the patients reported being anxious and depressed, respectively. In an online survey conducted from March to April 2020 on Italian population, 69% and 31% of the participants reported anxiety and depressive symptoms respectively¹⁶. In our study, 4% of the patients acknowledged the use of blood thinners during post recovery period. In a UK wide surveillance study for assessment of neurological complications of covid-19, 62% of the patients presented with a cerebrovascular accident in whom 74% had an ischemic stroke¹². In another retrospective cohort study of outpatients recently hospitalized for covid-19, 2 percent suffered from a thromboembolic event within 30 days of discharge¹⁷. 17.3 % of the recovered patients we questioned said they had suffered from repeated infections post covid-19 with the maximum (9.3%) reporting throat infections. There is a paucity of available literature on this aspect but the secretion of inflammatory cytokines as seen in cytokine release storm during acute covid-19 infection shows that the immune system is severely damaged by covid-19 becoming ineffective by lymphopenia¹⁵. This can be the possible explanation of the weakened or exhausted immune system post covid-19 infection susceptibility to other infections. 8% of the patients also reported the worsening of their previously existing co morbid conditions requiring increased doses of medication for them. In the cross-sectional evaluation of post covid-19 recovery symptoms done at Karachi, 36.7% of the covid-19 patients claimed that they needed extra investigations for the post covid-19 manifestations and 52.5% received medication; 6% developed diabetes, 1.3 % renal failure and 6 % stroke¹⁸. Vocational problems were identified in 6.7% of the patients interviewed in our study. This can be explained by the hoarseness and sore throat as a consequence of laryngitis, damage to the vocal cords and a continuous dry cough.

Our research questionnaire also included the analysis of quality of life of the patients interviewed; a questionnaire taken from WHOQOL BREF. 26 questions with a score of one to five were asked, each belonging to one of the four major domains related to the quality of life: physical, psychological, social relationships and environment. A normal individual with the best quality of life and answering 5 out of 5 in every question would have a cumulative score of 100/100 in each domain. In our study, the abovementioned domains had scores of 64.32±18.71562 (mean ± SD), 60.4133±18.20684, 63.08±22.43173 and 68.9333±12.98162 respectively. In comparison, the EuroQol 5 Dimension 5 Level was utilized in a follow up study of post discharge patients in UK; it showed a significant drop in EQ-5D-5L in 68.8 % of ICU and 45.6 % of ward patients. The parameters assessed were mobility, self-care, usual activities, pain/discomfort and anxiety/depression¹⁹. In another cross-sectional study done on the local residents of Liaoning Province in China, participants were assessed about the Impact of Event Scale (IES), indicators of negative mental health impacts, social and family support, and mental health related lifestyle changes. The mean IES score of the participants was 13.6±7.7, indicating a mild stressful impact²⁴.

After analysis of all the symptoms that were either novel or persistent in the post covid- 19 subgroup of patients, it is really necessary to properly identify and make the public as well as t he health workers aware about them to avoid the need of doing redundant clinical investigations and prescribing unnecessary medications. Another use of this study is that a good follow up of these patients can be done, for example, interstitial lung disease can be an irreversible complication which can be the cause of dry cough and exertional dyspnea for many years. If some symptoms are reported at even 10 months after recovery from covid-19, it is still not known that for how long they will prevail, will they ever disappear completely or not. Hence, this can open a pathway for many research scholars to follow these patients and have an eye on the recovery from post covid-19 manifestations. These patients can be managed properly and given rehabilitation by involving a multidisciplinary team.

CONCLUSIONS

In our study, the majority of the patients complained of fatigue, dry cough, joints pains and headache. Exertional dyspnea, hair loss, anosmia, insomnia and memory loss were also found in a subset of patients

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while a few of the people questioned reported depression, anxiety, ageusia, blurred vision, speaking problems, repeated infections, requiring increased dose of medication for their previous comorbidities and having used anticoagulants after recovery. The overall qualityof life has been found affected to various degrees following covid-19 infection. To get rid of the lingering effects of this pandemic on people's life, we need a platform for identification and management of these health problems and advise strategies to help them deal with these consequences using a multidisciplinary approach.

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