Original Research Paper

Volume - 13 | Issue - 02 | February - 2023 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Community Medicine

POST COVID COMPLICATIONS - A FOLLOW UP STUDY AMONG COVID-19 PATIENTS OF RURAL AHMEDABAD

Dr. Debanjana Saha* — 3rd Year Post Graduate Resident. *Corresponding Author

Dr. Aroor Bhagyalaxmi — Professor, Dept. of Community Medicine.

ABSTRACT Post Covid complication occurs in individuals with a history of confirmed covid-19 infection, that develop within 3months of onset of COVID-19 illness, last for at least 2months and cannot be explained by alternative diagnosis. We aim to estimate the magnitude of post covid complications and its association with risk factors. A follow up study was conducted among 250 COVID-19 positive patients from July 2021 to Jan2022. These patients were interviewed telephonically at 3rd month & 6th month after recovery. Majority of post COVID symptoms identified were fatigue (29.6%), anosmia (26.8%) & ageusia (15.2%). At least one of these symptoms was present in 67.6% and 28% patients at 3rd and 6th month post infection respectively. Other clinical features included insomnia (8%), skin rashes (7.6%) and mood disorders (4%). Systemic involvement was seen in 1.2% as new onset hypertension. No significant gender difference was identified in any of the symptoms ($\chi 2$=0.24, p=0.6). Risk factors associated in developing long COVID-19 were high BMI[RR=1.2], age >60yrs [RR=1.3], poor vaccination status [RR=1.45]and long duration of illness (>14 days) [RR=1.4]. 4 deaths (1.6%) were reported among 8.8% hospitalized patients having severe comorbidities (e.g. Coronary artery disease). Nearly 2/3rd patients were having one or the other symptoms at the end of the 3rd month and 1/4th at the end of 6th months. Also, death during the post COVID period, strongly suggests continuous follow up visits for high risk patients and spreading public awareness to seek health care facilities for follow up.

KEYWORDS : Long COVID-19, Fatigue, Anosmia, Ageusia

INTRODUCTION

The coronavirus disease 2019 (COVID-19) continues to be of critical medical concern. This is attributable not only to the rapid spread of the pandemic throughout the world but also to the complex pathophysiology that has intensively engaged medical science in finding appropriate solutions to this problem. (Jason et al., 2021) Significant mortality and morbidity are being experienced worldwide as a result of the SARS-CoV-2 infection (COVID-19). Within the affected population, 80% had mild to moderate disease, and 5% of those with severe disease went on to acquire critical illness.(Raveendran et al., 2021). The majority of patients recover without lung damage, although a sizable proportion will experience long-lasting effects. The long-term consequences of COVID19, which can impact numerous organ systems, are the subject of developing scientific research. (E JOURNAL AUG 2021-18-23, n.d.)

Several weeks after the acute phase of the infection, some individuals continue to develop COVID-19-related new, recurring, or persistent symptoms. Numerous terms, including "long COVID," "long-haul COVID," "chronic COVID," "post-COVID syndrome," and "post-acute COVID-19 syndrome," as well as the scientific term "post-acute sequelae of SARS-CoV-2 infection (PASC)," are used to describe these symptoms.

In 2021, the World Health Organization published a case definition of post-COVID conditions that was developed by Delphi consensus:- "Post COVID-19 condition occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis. Common symptoms include fatigue, shortness of breath, cognitive dysfunction but also others which generally have an impact on everyday functioning. Symptoms may be new onset, following initial recovery from an acute COVID-19 episode, or persist from the initial illness. Symptoms may also fluctuate or relapse over time. A separate definition may be applicable for children." (CDC, 2021). Post-acute COVID-19 is a syndrome characterized by the persistence of clinical symptoms beyond four weeks from the onset of acute symptoms. Post-acute COVID-19 syndrome is a multisystem disorder that commonly affects the respiratory, cardiovascular, and hematopoietic systems. In addition, neuropsychiatric, renal, and endocrine systems are also involved to a lesser extent.

Most common symptoms of post COVID-19 condition include fatigue, shortness of breath, anosmia, ageusia, irritability, depression, insomnia, etc.

Majority of the data available focuses on health-related incidents following serious infections and hospitalization during acute COVID-19. However, as only, around 5-10% of patients were hospitalized, these studies did not account for the great majority of patients with a milder course of infection (WHO score 13).

Hence, we provide a longitudinal, prospective investigation of health outcomes in individuals with severe acute respiratory syndrome coronavirus type 2 (SARSCoV-2) infection who initially presented with no or minimal symptoms. As a result, we concentrate mainly on majority of mild COVID-19 non-hospitalized (home isolated) patients in our study.

This study aims to identify the range of post-COVID complications, it's magnitude and associated risk factors among positive COVID-19 patients (both hospitalized and non- hospitalized).

MATERIAL AND METHODS

This follow-up study was conducted from July 2021 to Jan 2022 among COVID-19 confirmed cases of Rural Ahmedabad districts. 250 patients were recruited from the list of contact tracing that is being done by our Dept. of Community Medicine, B. J Medical College. These patients were telephonically interviewed by a preformed questionnaire to inquire about their health status post recovery of COVID-19 at the end of 3rd month & 6th month. Verbal consent was taken from respondents during telephonic interview. Prior to any formal interview, they were asked open-ended questions about their general self-reported health state and how they felt about any symptoms. The following post-viral symptoms were questioned about and noted, depending on whether they persisted: cough, persistent nausea/vomiting, headache, sleep issues (including insomnia and restless sleep), decreased appetite, chest discomfort, depressed mood, dizziness, palpitations, myalgias, and fatigability. After thoroughly analyzing prior research on symptoms linked to or attributed to post-viral syndrome, this list of symptoms was created.

96 patients were drop outs at the end of 6 months. Hence,154 patients had completed follow up till 6 months. Patients from all age groups were included except children of less than 10 years.

Demographic data and comorbidities were recorded as frequency and percentages. Chi-square test was used for comparison between nominal variables. Z-test was used to compare differences between ages. The data was analyzed using SPSSv25.Clinical data and patients' characteristics were systematically recorded via Google forms. Analysis done using Microsoft Excel 2019 and SPSS.

RESULTS

Out of 500 patients from Rural Ahmedabad who were traced during COVID-19 illness,250 were respondents at the end of 3rd month post recovery. In total 96 were lost to follow up by the end of 6 months and 4 died during follow up period. Hence, 154 patients completed the study. 91% of all SARS-CoV-2 infected patients presented with a mild disease in our study.

Most of the patients studied in post COVID period belong to the age group of 30-39 years (23.6%) followed by 20-29 years (22%).18.4% were in 40-49 years and only 15.2% above 60years (Table 1).

Most of the patients were males (62%) and only 38% were females. Male: Female ratio was 1.6:1. This variation mirrors the variation in COVID positive cases, which are more frequently recoded in men.

20.4% of them had at least one co-morbid conditions among hypertension (12%), diabetes mellitus (10.8%), coronary artery disease (1.2%), hypothyroidism (1.2%) & asthma (0.4%). 4 deaths (1.6%) were reported among 9% hospitalized patients having severe comorbidities (e.g. Coronary artery disease, HTN, DM).

Most of the patients presented with fever (57.6%) and cough (35.6%) in their acute phase of COVID-19 illness. Other clinical features reported were anosmia (14.4%), body ache (5.2%) and headache (4%). Average duration of illness calculated was 11.6 days with majority (80%) suffering for about 7-14 days.

Incidence of post COVID complications was 68% at the end of 3rd month of acute illness. Post viral fatigue was the most prevalent symptom (31.2%) in all age groups. Other common complications were anosmia (27%), ageusia (15.2%), skin rash (8%), myalgia (6%), exertional dyspnea (5%), chest pain (4.4%), headache (4%), vertigo (3.2%) and palpitation (2%). Psychological complications include insomnia/sleep disturbances (8%), irritability/low mood (8%) and anxiety (4%). Anxiety issues were most commonly reported by females as one of the post COVID-19 symptoms.

More serious complications include new onset hypertension (1.2%) and death (1.6%) in patients who were mostly hospitalized (9%). 11 out of 47 asymptomatic patients during the acute phase of illness has also reported to develop at least one of the post COVID complications. Only 15.2% patients were vaccinated with at least one dose of vaccine by the end of 6 months of follow-up.

There is significant association between age and duration of illness [t=29.32, p <0.0001]; also, between gender and duration of illness [x2 =6.38, p <0.05]. Males are having longer duration of illness than women. Patients below 50 years have comparatively higher duration of illness.

High BMI [RR=1.2,95% CI:1.05-1.48, p=0.01], Vaccination status [RR=1.45,95% CI: 1.26-1.67, p<0.0001], age > 60 years [RR=1.46,95% CI:1.26-1.69, p <0.0001] and longer duration of illness (>14days) [RR= 5.9,95% CI:3.58-9.75, p <0.0001] are few associated risk factors with development of post COVID complications. Approx. 2 % variation in duration of illness can be predicted from the BMI of the patient (as per regression analysis).

4deaths (1.6%) were reported among 9% hospitalized patients having severe comorbidities (e.g. Coronary artery disease, HTN, DM)
23% of the asymptomatic people has reported with at least one of the post COVID-19 symptoms at 3rd month of follow-up.

Table No. 1- Demographic profile of COVID-19 patients in the study

Age group (years)	Males		Females		Total	
	N	%	N	%	N	%
10-19 years-can be deleted	14	5.6	5	2	19	7.6
20-29 years	33	13.2	22	8.8	55	22
30-39 years	39	15.6	20	8	59	23.6
40-49 years	27	10.8	19	7.6	46	18.4
50-59 years	22	8.8	11	4.4	33	13.2
>60 years	20	8	18	7.2	38	15.2
Total	155	62	95	38	250	100
Mean ± S. D	40±16 years					

Table No. 2 – Post COVID symptoms at the end follow-up period

Post COVID-19 Symptoms	At the end of 3rd month (%)	At the end of 6th month (%)
FATIGUE	31.2	12.90
ANOSMIA	26.80	0
AGEUSIA	15.20	1.90
INSOMNIA	8	6.40
IRRITABILITY/LOW MOOD	8	0.40
RASH	7.60	3.80
DYSPNOEA	4.80	1.29
CHEST PAIN	4.40	0
NASAL BLOCKADE	4.40	0
ANXIETY	4	3.89

Table no.3 – Risk factors associated with Long COVID syndrome

Risk Factors	RR	95% CI	P value
Age	1.46	1.26-1.69	<0.05
Duration of illness	5.9	3.58-9.75	<0.05
Vaccination status	1.45	1.26-1.67	<0.05
BMI	1.2	1.05-1.48	0.01

DISCUSSION

In the present study, we assessed the prevalence amplitude and characteristics of the Long COVID—in majority of patients suffering from mild to moderate symptoms during acute phase of COVID-19. The incidence of post-COVID-19 syndrome was 68% in this research out of 250 individuals by the end of 3 months. Most COVID-19 patients survived the acute phase, but a significant proportion of these patients developed variety of health problems.

The presentations varied greatly. Most of the patients in present study belonged to < 40 years (53.2%) and the Male: Female ratio was found to be 1.6 :1.

Previous studies had reported PCS in a wide range varying from 27.8% to 46%. The differences in the study designs (e.g., active questioning, analysis of outpatient clinic and readmission records, or self-reporting apps), study population characteristics (e.g., inpatients/outpatients, differences in disease severity of patients enrolled in the study), or time since acute infection can all be used to explain the variation in study results.

Similar results were obtained by Mahmud R et al. where approx. 46% developed PCS with a ratio of 1.4:1 between male and female patients and a majority of patients were (60%) under the age of 40.(Mahmud et al., 2021) .

In another study by M. Augustin et al. among 442 non-hospitalized, mild to moderate symptom patients the median age group was 43 years (IQR-31-54 years). The study also reported the incidence of post COVID-19 syndrome to be 27.8% (123/442) and 34.8% (123/353) at the end of 4th and 7th month respectively. (Augustin et al., 2021). Another related research showed 58% of PCS in patients evaluated in tertiary care hospital among which about 37.5% belonged to <40 years of age.(Shah et al., 2022)

The majority of studies focusing at protracted symptoms comprised hospitalized COVID-19 patients who had symptoms for 6-12 months after the onset of the disease. Hospitalized patients are more vulnerable

to long-term symptoms than patients with moderate COVID-19, which are a result of mechanical ventilation or prolonged immobility but are not COVID-19-specific. Therefore, a prolonged convalescence period is anticipated for these patients. Our study has a key benefit that most of the COVID-19 cases in our dataset are mild, and they have been prospectively tracked for a duration of 6 months. COVID infection, even if mild, can trigger an immune response that last longer than the initial infection and recovery.

The findings published in the Journal of Translational Medicine revealed that people with a prior infection of SARS-CoV-2, have a wide variety of autoantibodies up to six months after they have fully recovered. Some of these autoantibodies can attack the body's own organs and tissues over time. The study also showed that the percentage of asymptomatic infections was higher among group younger than 39 years of age than in any age groups, possibly because young adults were more likely to show only mild or moderate clinical symptoms. This indicates that those who are young adults who often present with mild symptoms were important and potential source of transmission in the community (Liu et al., 2021).

Recently, it has been apparent that certain patients, regardless of the severity of the disease, continue to have symptoms weeks and months after the onset of COVID-19(Goërtz et al., 2020 ;Mandal et al., 2021; Sudre et al., 2021). Neither specific terminology nor new illness entity itself have been defined as of yet. The terms used so far have included "long COVID"(Mandal et al., 2021), "chronic COVID syndrome"(Kayaaslan et al., 2021), "post-COVID syndrome" (Goërtz et al., 2020), and "post-acute COVID-19 syndrome"(Nalbandian et al., 2021).

Numerous studies have documented various post-COVID-19 symptoms. Most common post COVID-19 symptom evident in our study was fatigue (29.6%). Similar researches have documented fatigue in up to 70% of COVID patients. A study by Kayaaslan B et al. reported 24.3% of patients suffering from easy fatigability. Several other studies also emphasized fatigue as the most common symptom. (Kayaaslan et al., 2021; Kumar, 2021; Liu et al., 2021; Mahmud et al., 2021). The reason for the dominance of fatigue could be explained by viral infection related immune dysregulation within the hypothalamus. (Mahmud et al., 2021; Nigro et al., 2020). We noticed that even individuals with initially mild symptoms may acquire fatigue as a primary symptom of PCS (Townsend et al., 2020), which is consistent with data published by Townsend et al. However, it should be understood that levels of fatigue can differ from person to person and that no one test can definitively validate a diagnosis of fatigue.

In addition, anosmia & ageusia were well described symptoms in COVID-19 patients which continued to persists in the post recovery period but it is very much evident that these symptoms gradually lessen over time. In our study anosmia was only noted for the first 3months of recovery in 26% patients. Loss of smell / taste could be due to neurotropic infection to the gustatory or olfactory systems. In a study from western Rajasthan persistent loss of taste or smell was noted in only 2.4% of post COVID-19 patients (E JOURNAL AUG 2021-18-23, n.d.); whereas in various European studies, data revealed 66.2-88% patients getting anosmia and gustatory dysfunctions but about 25.5% of them had fully recovered. (Ciaa525, n.d.; Lechien et al., 2020). So, the symptoms have their own geographical variations across the globe. Neuropsychiatric disturbances were observed in as many as 16% patients as insomnia, irritability or low mood disorders in our survey. In line with earlier studies, several of the patients experienced neuropsychiatric issues such as anxiety, depression, and new-onset headaches as well as concentration or memory deficits, sleeplessness or insomnia or hypersomnia even 20 weeks after infection. In a meta-analysis including 55 peer-reviewed studies, the prevalence of depression, anxiety, and insomnia was reported as 15.97%, 15.15%, and 23.87% in COVID-19 patients, respectively. (Kayaaslan et al., 2021; Lechien et al., 2020)[17,22]. Headache (4%) and anxiety (4%) were both slightly more prevalent in females. Shortness of breath and low blood oxygen levels are probably responsible for the connection to mental distress and higher stress reactivity leading to neuropsychological symptoms. (Pai, 2021).

Exertional Dyspnea was noted in 5% cases in present study. Studies have reported dyspnea in post COVID-19 patients ranging from 7% to 43.4%(Kumar, 2021; Mahmud et al., 2021). COVID-19 may result in persistent lung issues such fibrosis, bronchiectasis, and cough. For some of the patients, the dyspnea may not totally improve. Our study also revealed certain cutaneous manifestations such as skin rashes in 8% of patients during recovery. Freeman et al. found a prevalence of urticaria (16%) in their series of 716 cases of post COVID-19 patients. (Qin et al., n.d.).

New onset HTN was seen in 1.2% of hospitalized patients similar to finding of other studies. (Mahmud et al., 2021). 20.4% of them had at least one co-morbid conditions among hypertension, diabetes mellitus, coronary artery disease, hypothyroidism & asthma. With 9% of hospitalized patients having severe comorbidities, 4 deaths (1.6%) were documented during the convalescence period. In the pathophysiology of cardiovascular problems, high levels of circulating cytokines and mediators of toxic response, such as IL-6, TNF-, and nitric oxide, have been observed(Pai, 2021; Qin et al., n.d.).

Risk factors associated with development of post COVID-19 symptoms elicited in our study were age>60 years, high BMI, poor vaccination status and long duration of illness (>14 days). Age and disease duration have a substantial correlation; gender and illness duration as well. Males tend to be sicker for longer than females. Patients under 50 years old typically experience illnesses for a longer period of time. In a study by Mahmud et al. respiratory distress, lethargy, long duration of illness, and moderate severity of the disease were predicted as the risk factors. A similar study by M. Augustin et al. showed a lower SARS-CoV-2 IgG titre at the beginning of the observation period was associated with a higher frequency of PCS. (Augustin et al., 2021; Mahmud et al., 2021).

The main strength of the study is in discovering the post COVID-19 symptomatology in mild to moderate illness patients, which was not apparent in previous studies as they mostly included severely ill hospitalized patients. Elevation of auto-antibodies following mild or asymptomatic infection dysregulates the immune system and results in long haul COVID-19 symptoms.

The study has few limitations. This study is based on patient's self-declaration. There could be variations in how patients' symptoms were perceived, expressed, or treated.96 were drop outs by the end of 6th month which might have diluted the incidence of PCS slightly. Lastly it was conducted in a single center, thus proportion of complications may not be applicable to the whole population.

CONCLUSION

Long COVID is the parallel pandemic which needs to be addressed and assessed properly by continuous monitoring of patients especially ones with co-morbidities. Our findings demonstrated that a significant percentage of COVID-19 patients continued to experience symptoms up to 6 months following mild-to-moderate illness. While some patients visited the outpatient clinics specifically for respiratory or cardiovascular issues, patients with neuropsychiatric symptoms may have been less conscious of their symptoms and choose to ignore them. Patients should be enlightened about the long-term effects of COVID-19 and awareness about post recovery follow-up should be raised. Post COVID-19 OPD Clinics must be set to evaluate patients even after recovery and spread awareness in public to seek healthcare facilities. Continuous Follow- up visits till 6 months after COVID-19 illness is recommended for all high-risk category patients. A systematic, multidisciplinary rehabilitation programme that includes specific suggestions for physical activity, diet, psychiatric treatment, along with routine follow-up seems to be necessary.

REFERENCES

1. Augustin, M., Schommers, P., Stecher, M., Dewald, F., Gieselmann, L., Gruell, H., Horn, C., Vanshylla, K., Cristanziano, V. di, Osebold, L., Roventa, M., Riaz, T., Tschernoster, N., Altmueller, J., Rose, L., Salomon, S., Priesner, V., Luers, J. C., Albus, C., … Lehmann, C. (2021). Post-COVID syndrome in non-hospitalised patients with COVID-19: a longitudinal prospective cohort study. The Lancet Regional Health - Europe, 6. https://doi.org/10.1016/j.lanepe.2021.100122
2. CDC. (2021). COVID-19 Real Time Learning Network.
3. ciaa525. (n.d.).
4. E JOURNAL AUG 2021-18-23. (n.d.).
5. Goërtz, Y. M. J., van Herck, M., Delbressine, J. M., Vaes, A. W., Meys, R., Machado, F. V. C., Houben-Wilke, S., Burtin, C., Posthuma, R., Franssen, F. M. E., van Loon, N., Hajian, B., Spies, Y., Vijlbrief, H., van 't Hul, A. J., Janssen, D. J. A., & Spruit, M. A. (2020). Persistent symptoms 3 months after a SARS-CoV-2 infection: the post-COVID-19 syndrome? ERJ Open Research, 6(4), 00542–02020. https://doi.org/10.1183/23120541.00542-2020
6. Jason, L. A., Cotler, J., Islam, M. F., Sunnquist, M., & Katz, B. Z. (2021). Risks for Developing Myalgic Encephalomyelitis/Chronic Fatigue Syndrome in College Students Following Infectious Mononucleosis: A Prospective Cohort Study. Clinical Infectious Diseases : An Official Publication of the Infectious Diseases Society of America, 73(11), e3740–e3746. https://doi.org/10.1093/cid/ciaa1886
7. Kayaaslan, B., Eser, F., Kalem, A. K., Kaya, G., Kaplan, B., Kacar, D., Hasanoglu, I., Coskun, B., & Guner, R. (2021). Post-COVID syndrome: A single-center questionnaire

study on 1007 participants recovered from COVID-19. Journal of Medical Virology, 93(12), 6566–6574. https://doi.org/10.1002/jmv.27198
8. Kumar, U. (2021). Post-COVID-19 sequelae. Indian Journal of Respiratory Care, 10(4), 60. https://doi.org/10.4103/ijrc.ijrc_30_21
9. Lechien, J. R., Chiesa-Estomba, C. M., de Siati, D. R., Horoi, M., le Bon, S. D., Rodriguez, A., Dequanter, D., Blecic, S., el Afia, F., Distinguin, L., Chekkoury-Idrissi, Y., Hans, S., Delgado, I. L., Calvo-Henriquez, C., Lavigne, P., Falanga, C., Barillari, M. R., Cammaroto, G., Khalife, M., … Saussez, S. (2020). Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study. European Archives of Oto-Rhino-Laryngology, 277(8), 2251–2261. https://doi.org/10.1007/s00405-020-05965-1
10. Liu, Y., Ebinger, J. E., Mostafa, R., Budde, P., Gajewski, J., Walker, B., Joung, S., Wu, M., Bräutigam, M., Hesping, F., Rupieper, E., Schubert, A. S., Zucht, H. D., Braun, J., Melmed, G. Y., Sobhani, K., Arditi, M., van Eyk, J. E., Cheng, S., & Fert-Bober, J. (2021). Paradoxical sex-specific patterns of autoantibody response to SARS-CoV-2 infection. Journal of Translational Medicine, 19(1). https://doi.org/10.1186/s12967-021-03184-8
11. Mahmud, R., Rahman, M. M., Rassel, M. A., Monayem, F. B., Sayeed, S. K. J. B., Islam, M. S., & Islam, M. M. (2021). Post-COVID-19 syndrome among symptomatic COVID-19 patients: A prospective cohort study in a tertiary care center of Bangladesh. PLoS ONE, 16(4 April). https://doi.org/10.1371/journal.pone.0249644
12. Mandal, S., Barnett, J., Brill, S. E., Brown, J. S., Denneny, E. K., Hare, S. S., Heightman, M., Hillman, T. E., Jacob, J., Jarvis, H. C., Lipman, M. C. I., Naidu, S. B., Nair, A., Porter, J. C., Tomlinson, G. S., & Hurst, J. R. (2021). Long-COVID': A cross-sectional study of persisting symptoms, biomarker and imaging abnormalities following hospitalisation for COVID-19. Thorax, 76(4), 396–398. https://doi.org/10.1136/thoraxjnl-2020-215818
13. Nalbandian, A., Sehgal, K., Gupta, A., Madhavan, M. v., McGroder, C., Stevens, J. S., Cook, J. R., Nordvig, A. S., Shalev, D., Sehrawat, T. S., Ahluwalia, N., Bikdeli, B., Dietz, D., Der-Nigoghossian, C., Liyanage-Don, N., Rosner, G. F., Bernstein, E. J., Mohan, S., Beckley, A. A., … Wan, E. Y. (2021). Post-acute COVID-19 syndrome. In Nature Medicine (Vol. 27, Issue 4, pp. 601–615). Nature Research. https://doi.org/10.1038/s41591-021-01283-z
14. Nigro, E., Polito, R., Alfieri, A., Mancini, A., Imperlini, E., Elce, A., Krustrup, P., Orrù, S., Buono, P., & Daniele, A. (2020). Molecular mechanisms involved in the positive effects of physical activity on coping with COVID-19. In European Journal of Applied Physiology (Vol. 120, Issue 12, pp. 2569–2582). Springer Science and Business Media Deutschland GmbH. https://doi.org/10.1007/s00421-020-04484-5
15. Pai, M. & P. A. & C. B. & T. J. & P. Hong. (2021). Health Complications in Patients Recovering from COVID-19: A Narrative Review of Post-COVID Syndrome. Journal of Advances in Medicine and Medical Research. , 115–129.
16. Qin, C., Zhou, L., Hu, Z., Zhang, S., Yang, S., Tao, Y., Xie, C., Ma, K., & Shang, K. (n.d.). Dysregulation of immune response in patients with COVID-19 in Wuhan, China.
17. Raveendran, A. v., Jayadevan, R., & Sashidharan, S. (2021). Long COVID: An overview. In Diabetes and Metabolic Syndrome: Clinical Research and Reviews (Vol. 15, Issue 3, pp. 869–875). Elsevier Ltd. https://doi.org/10.1016/j.dsx.2021.04.007
18. Shah, S., Bhattarai, S. R., Basnet, K., Adhikari, Y. R., Adhikari, T. B., Bhatta, N., Chamlagain, R., Aryal, S., Sah, S. K., Bhandari, G., Bhandari, B., Poudel, S., Pant, P., & Das, S. K. (2022). Post-COVID syndrome: A prospective study in a tertiary hospital of Nepal. PLoS ONE, 17(8 August). https://doi.org/10.1371/journal.pone.0272636
19. Sudre, C. H., Murray, B., Varsavsky, T., Graham, M. S., Penfold, R. S., Bowyer, R. C., Pujol, J. C., Klaser, K., Antonelli, M., Canas, L. S., Molteni, E., Modat, M., Jorge Cardoso, M., May, A., Ganesh, S., Davies, R., Nguyen, L. H., Drew, D. A., Astley, C. M., … Steves, C. J. (2021). Attributes and predictors of long COVID. Nature Medicine, 27(4), 626–631. https://doi.org/10.1038/s41591-021-01292-y
20. Townsend, L., Dyer, A. H., Jones, K., Dunne, J., Mooney, A., Gaffney, F., O'Connor, L., Leavy, D., O'Brien, K., Dowds, J., Sugrue, J. A., Hopkins, D., Martin-Loeches, I., Ni Cheallaigh, C., Nadarajan, P., McLaughlin, A. M., Bourke, N. M., Bergin, C., O'Farrelly, C., … Conlon, N. (2020). Persistent fatigue following SARS-CoV-2 infection is common and independent of severity of initial infection. PLoS ONE, 15(11 November). https://doi.org/10.1371/journal.pone.0240784