International Journal Dental and Medical Sciences Research
Volume 3, Issue 1, Jan-Feb 2021 pp 161-169 www.ijdmsrjournal.com ISSN: 2582-6018

Prevalence of fatigue in individuals from Pune city after 6 weeks of Mild and Moderate grade COVID-19 infection.

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Date of Submission: 15-12-2020 Date of Acceptance: 30-12-2020

ABSTRACT: BACKGROUND**:** Coronavirus disease (COVID-19) caused by SARS-CoV-2 virus was declared as a global pandemic by the WHO in March 2020. India is the second worst hit by the pandemic in which Maharashtra records highest number of infected cases with highest number of patients in Pune city. Most of patients belonged to mild and moderate category of COVID-19. A concern about persistence of fatigue was raised in COVID-19 patients during and after the course of infection.
OBJECTIVE: Fatigue affects the physical as well as psychological well being of the patient. Thus, it is essential to find out the prevalence of fatigue after 6 weeks in these individuals from Pune city by using Fatigue Severity Scale.
METHODS AND MATERIALS: A cross sectional observational study was conducted among 25-60 years old males and females suffering from mild and moderate COVID-19 infection. This cross sectional observational study was carried out during the period from August to October 2020 on individuals, who had tested positive before 6 weeks. A telephonic interview by qualified physiotherapist was done that comprised of Fatigue Severity Scale.
RESULTS: After the statistical analysis, it was found that 31% (n=38) participants complained of presence of fatigue after 6 weeks of infection subjectively. When fatigue was assessed objectively using the Fatigue Severity Scale, it was found that only 7% (n=9) participants had problematic fatigue and rest of the 93% (n=112) did not show presence of fatigue.
CONCLUSION**:** There is no significant prevalence of fatigue post 6 weeks among individuals suffering from mild and moderate grade of COVID- 19 infection in Pune region.
KEYWORDS: Mild grade COVID 19, Moderate grade COVID-19, Fatigue, Pune.

I. INTRODUCTION

In late 2019, infection with a novel betacoronavirus, subsequently named SARS-CoV-2, was reported in people who had been exposed to a market in Wuhan, China, where live animals were sold. Since then, there has been rapid spread of the virus, leading to a global pandemic of COVID-19.[(1)] India has been no exception to this pandemic, and there is a widespread infection prevalent India as well. The state of Maharashtra is leading in number of COVID-19 cases (17,84, 361) as on 26th October 2020. The city of Pune has shown rising trend in the number of corona cases, from 677 positive COVID--19 cases in the month of April 2020 to as high as 1,61,844 positive COVID-19 cases in October 2020.[(2)]

Diagnosis of COVID-19 is made by detection of SARS-CoV-2 RNA by PCR testing of a nasopharyngeal swab or other specimens which includes saliva. Antigen tests are generally less sensitive than PCR tests but are less expensive and can be used at the point of care with rapid results. Evaluation and management of COVID-19patients depend on the severity of the infection. Patients with mild disease usually recover at home, whereas patients with moderate disease should be monitored closely and sometimes hospitalized.[(1)]

According to algorithms designed in India, Mild Disease cases present with fever and/or upper respiratory tract illness (Influenza Like Illness). They may also present with dry cough, nasal congestion, sore throat, change in sense of taste or smell, headache, muscle pain, and malaise. It is also characterized by the absence of serious symptoms such as dyspnea.[(1,2,3,4)] The majority (81%) of COVID-19 cases are mild in severity.[(5)]

Moderate Disease cases present with clinical or radiographic evidence mild pneumonia (with respiratory rate 15 to 30/minute,SpO2> 90% on room air).The patients may also present with

International Journal Dental and Medical Sciences Research
Volume 3, Issue 1, Jan-Feb 2021 pp 161-169 www.ijdmsrjournal.com ISSN: 2582-6018

respiratory symptoms of cough, shortness of breath, and tachypnea.[1,2,3,6,7]

Mild cases are managed mostly at a Covid Care Centre (CCC), community health centre (CHC), sub district and district hospitals. They are monitored continuously, given the possibility of detoriation. Symptomatic treatment (antipyretics, anti tussives, etc), adequate nutrition and hydration forms the basis of management in COVID-19 patients of mild severity. Moderate cases are managed at Dedicated Covid Health Centres (DCHC), district Hospitals or Medical College Hospitals. Symptomatic treatment (antipyretics, anti tussives, etc), adequate nutrition and hydration, oxygen support, awake proning, anticoagulation therapy (UFH or LMWH), corticosteroids, antiviral drugs and control of disease progression, etc forms the basis of management in COVID-19 patients of moderate severity [6,7]

Patients with pre-existing co-morbidities have a higher fatality rate. These co-morbidities include diabetes (7.3%), respiratory disease (6.5%), cardiovascular disease (10.5%), hypertension (6%), and oncological complications (5.6%). Patients without co-morbidities have a lower fatality rate (0.9%). Other risk factors for severe Covid—19 infection are older age (>60 years), obesity (BMI >30 kg/m^2), sickle cell disease and chronic kidney disease.[8]

Fatigue is defined as sense of physical tiredness or exhaustion and lack of energy. It is different from sadness or weakness. It is a major issue that warrants clinical attention considering its association with decrease in patient's health related quality of life. Fatigue affects the physical as well as psychological well being of the patient. [9] It has been proved that fatigue is a consequence of various viral and non viral diseases. Mohammed F Islam, studied course of previous epidemics like SARS infection and H1N1infection and found that fatigue is one of the most potential health complication post viral infection which can linger for weeks or months, and SARS-CoV-2 has not been an exception to this. This is known as post-viral fatigue. The reason is ongoing inflammatory process and lack of physical activity. [10] Liam Townsend, et al raised out a concern that SARS-CoV-2 has the potential to trigger a post viral fatigue syndrome, and has concluded that there is a significant burden of fatigue at follow up of 10 weeks, with half of the patient reporting severe fatigue. [11]Very less research is available about fatigue lingering in mild and moderate grade COVID-19 infected patients after certain period of recovery.

Thus, it is essential to find out the prevalence of fatigue in individuals who suffered mild or moderate grade COVID-19 infection by using standard outcome measure. This is to prevent further deterioration of quality of life due to fatigue and to know who is in need of further attention and intervention for fatigue management. Thus, the present was undertaken.

II. METHODS AND MATERIALS:

This cross sectional observational study (N=121) was conducted after seeking the approval of College Ethical Committee. The study design was in accordance with the Declaration of Helsinki, revised in 1983. VERBAL Consent was taken from the participants over a telephone call.

The targeted population consisted of 121(Considering the mean score of 50 and standard deviation of 10 at type 1 error alpha of 0.001 and allowable error of 5%, minimum required sample size for estimation of score for Indian patients is 106) COVID-19 patients of mild and moderate severity (as per WHO guidelines) in Pune city. Simple Random sampling method was used

Both males and females of age ranging between 25-60 were included in the study. It was necessary that these participants have tested positive for COVID-19 by RT-PCR test before 6 weeks and have completed treatment by expert doctors for the symptoms of mild and moderate grade COVID-19 infection. They had to be tested negative or asymptomatic post treatment. Participants that needed mechanical ventilatory assistance during hospitalization, or those showing chest X ray infiltration anytime during the course of infection, or those receiving supplemental oxygen therapy at home were excluded from the study. Individuals undergone any major cardiac/ abdominal/ thoracic/ cranial surgeries in the past two years or those who have been diagnosed with a known respiratory/ neurological/ psychiatric disorders have also been excluded from the study

III. METHODOLOGY:

This study was carried out during the period from August to October 2020 on individuals, who had tested positive for mild or moderate grade of COVID-19 infection during the period of June to September 2020.Subjects fulfilling the inclusion criteria were identified.A telephonic interview by qualified physiotherapist was done that comprised of Evaluation form (annexure A) and Fatigue Severity Scale (Hindi / English Annexure B).

The Fatigue Severity Scale is a 9-item scale which measures the severity of fatigue and its

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effect on a person's activities and lifestyle in patients with a variety of disorders. The items are scored on a 7 point scale. The minimum score=9 and maximum score possible=63. More common way of scoring is mean of all the scores with minimum score being 1 and maximum score being 7. Mean (SD) FSS scores for healthy individuals; 2.3 (0.7). Cut-off score of 4 or more considered indicative of problematic fatigue. Administration time is less than 5 mins. The scale was scored and interpreted according to the norms.[12] Data was analysed by descriptive statistics using Windows Excel.

IV. RESULTS

The table I represents demographic data of the study population.

Sr. No.	Parameter	Subtype	Percentage Value (%)
1	Age Distribution Mean age=41.5 years (graph I-a)	20-30(n=27) 31-40(n=29) 41-50(n=34) 51-60(n=31)	22 24 28 26
2	Sex	Male (n=55) Female (n=66)	45 55
3	Morbidity profile (graph I-b)	Co-morbidity present (n=35) No co-morbidity present (n=86)	29 71
4	Co-morbidity Distribution (graph I-c)	Diabetes Mellitus(n=12) Systemic Hypertension(n=16) DM+HTN(n=3) Hypothyroidism(n=3) Hypothyroid + HTN(n=1) None(n=86)	10 13 2 3 1 71
5	Grade of COVID-19 infection (graph I-d)	Mild (n=88) Moderate (n=33)	73 27

The mean age of the study population is 41.5 years. Out of 121 COVID-19 patients screened 45% were males(n=55) and 55% were females (n=66).

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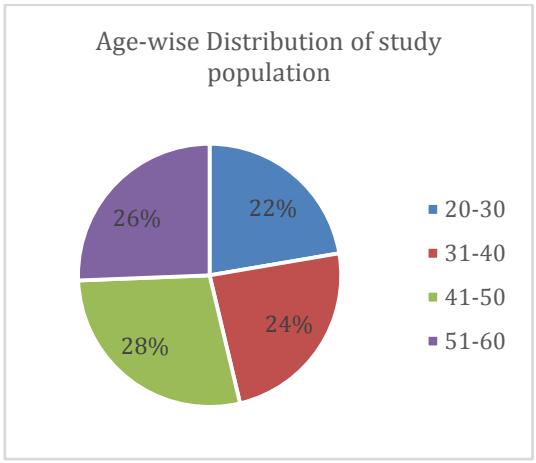
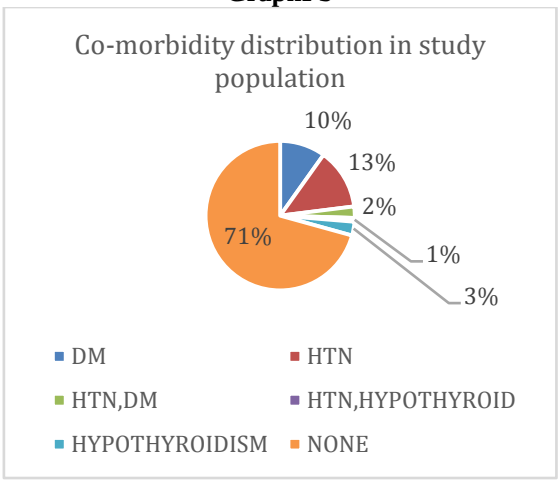


Graph I a

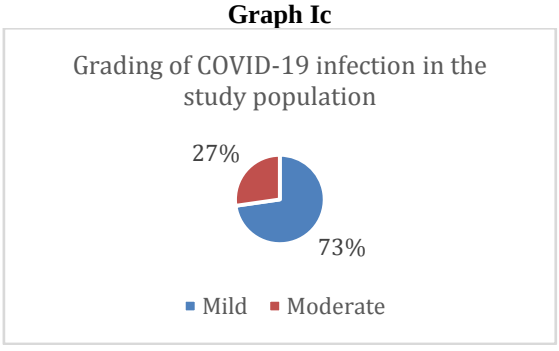
About 29% (n=35) of the population presented with co morbidities like Type 2 Diabetes mellitus, systemic hypertension and hypothyroidism, whereas, 71% (n=86) of the participants did not have any co morbidities out these (graph I-b).

GraphI b



The ordinal scale prepared by the WHO[13] for assessing the clinical progression of the illness over a period of time was used to grade the severity of COVID-19 infection in the study individuals. This scale revealed that, out of 121 individuals, 73%(n=88) were mildly infected and 27% (n=33) were moderately infected (graph I-c).

Graph Ic



Fever (69%), Fatigue (61%), cough (35%), body ache (23%), breathlessness (20%), anosmia(20%), nasal congestion (14%), ageusia (9%), sore throat (7%) were the major symptoms

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reported by the individuals during the acute infection phase of COVID-19, as depicted in Table II(a). as shown in graph II, 2% (n=3) individuals reported having dizziness, leg pain, nausea and loss of appetite. After 6 weeks, 56% (n=68) individuals did not report any persistent symptom, whereas, in the remaining 44% (n=53), the most frequently reported symptom was of fatigue (31%) followed by breathlessness (17%), leg pain (11%), cough (7%), body ache (3%), chest pain (3%), joint pain(3%), headache(2%), Dizziness(1%)(Table II(b). If the symptoms are compared as shown in graph II, symptoms such as fever, anosmia, ageusia, nausea, loss of appetite, sore throat are completely absent after 6 weeks of infection.

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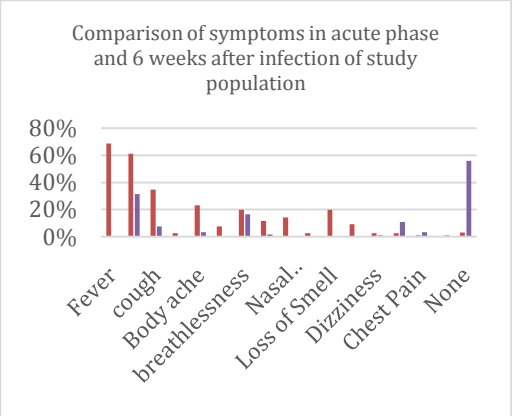

Table II: Physical symptoms as reported by Individuals (a) during Acute COVID-19 infection, (b) 6 weeks after infection

N=121				
Symptom	**(a) Acute COVID-19 (graph 2.1)**		**(b) After 6 weeks of infection (graph 2.2)**	
	n	**%**	**n**	**%**
Fever	83	69%	0	0
Fatigue	74	61%	38	31%
Cough	42	35%	9	7%
Loss of Appetite	3	2%	0	0
Body ache	28	23%	4	3%
Sore throat	9	7%	0	0%
breathlessness	24	20%	20	17%
Headache	14	12%	2	2%
Nasal congestion	17	14%	0	0%

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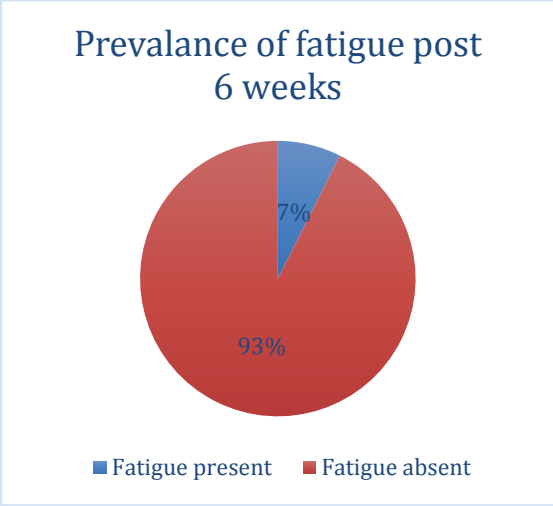
Nausea	3	2%	0	0%
Loss of Smell	24	20%	0	0%
Loss of Taste	11	9%	0	0%
Dizziness	3	2%	1	1%
Leg Pain	3	2%	13	11%
Chest Pain	1	1%	4	3%
Joint pain	0	0%	1	1%
None	4	3%	68	56%



Graph II-a

To highlight about the fatigue symptom, 61% (n=71) individuals reported fatigue in the acute phase of infection, but only half of them, that is 31% (n=38) complained of presence of fatigue even after 6 weeks of infection subjectively, when asked on the telephonic interview. However, when fatigue was assessed objectively using the Fatigue Severity Scale, it was found that only 7% (n=9) participants reported the score of 4 or more, indicating the presence of problematic fatigue. (graph II-a). Rest of the 93% (n=112) who scored less than 4 on FSS did not qualify for presence of fatigue.

Graph III shows the percentage of individuals who were physically active/ inactive before and after COVID 19 infection

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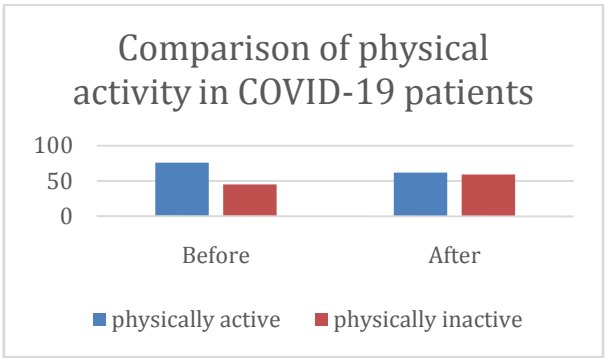

Graph III

V. DISCUSSION

In 2020, the entire world was challenged in many ways causing a large void in the health and medical field, as people had to face the COVID-19 pandemic. Since this was a novel virus, very less literature was available, which made the management in this pandemic even more challenging.

This cross-sectional observational study has made it evident that 31% population(graph 2) experienced fatigue in Pune city, 6 weeks post COVID-19 infection, but only 7% of the population had problematic (FSS Score>4) fatigue when assessed using FSS.(graph I-e)

Viral infections demonstrate decreased lymphocyte counts, higher leukocyte counts with an elevated neutrophil-to-lymphocyte ratio (NLR) in addition to decreased percentages of monocytes, eosinophils and basophils. It has also been reported that there is a decline in the levels of both helper and suppressor T cells in SARS-CoV-2 infection. In COVID-19 infection, patients have increased level of IL-2, IL-7, IL-6, granulocyte-colony stimulating factor, etc like several immune factors. This develops a pattern of hyper-inflammation which has been associated with complications in COVID -19 infection. It is also associated with a delayed expression of type 1 interferon signalling, which is a crucial part of the innate defence against viral infection. In response to viral nucleic acids , the subsequent intracellular reactions promotes the synthesis of interferons (IFN) and this plays a key role in the 'cytokine storm' found in COVID-19 patients.[10] Increased level of cytokines have found to be acting on central nervous system. These inflammatory signals bring about activation of immunologically responsive cells such as microglia and cytokine expression in brain. Production of IFNs results in fatigue like behaviour by suppression of serotonergic system, thus leading to fatigue in COVID-19 patients. It is already evident that the levels of IL-6 and interferons are significantly elevated in the blood of severely ill patients, compared to patients with mild illness. The level of IL-6 in the blood of the severe group was 76 % higher than that of the mild group (30 %)[14]. Present study did not show prevalence of problematic fatigue, as individual recovered from mild and moderate grade of COVID 19 infection were included in the study. Also, proportion of study population recovered from mild grade infection was more as compared to moderate grade infection (graph I-d).

However, recently, a study by Liam Townsend, et al. [11] concluded that there is a significant level of fatigue reported by the COVID-19 patients at a follow up of 10 weeks, with half of the patient's cohort reporting severe fatigue. This persistent impact could be due to inclusion of patients of different grades of severity of infection. The current study includes only the mild and moderate severity, unlike the quoted study.

Another reason for non significant rise in Fatigue severity score in the present study could be the regular supervised exercise regimen (aerobic light intensity exercise) the study population underwent during their stay at Covid Care Centres and Dedicated Covid Hospitals. Thus, keeping these patients physically active and consistent mobility exercise neutralised the possibility of development of long term fatigue in the study population. Also, 63% of the study participants (n=76) were physically active before the COVID-19 infection. (graph II). Regular physical activity changes fibre type, enhanced enzyme activity, regulation of ionic balance and changes in the muscle activation reduces muscle fatigue during high-intensity exercises, depending on the type, intensity, frequency,and duration of the training programme[15]. Aerobic exercises cause significant changes such as improvement in the metabolism; decrease in the levels of epinephrine, nor epinephrine, cholesterol and triglycerides; boosting of the immune system; and, improvement in

endorphin secretion, mood and mental status[16]. In other words, when the musculoskeletal system is inactive, the duration of oxidation reduces, and this is an important factor in the incidence of fatigue, negatively affecting the daily activities.

prevalence of fatigue increases with advancing age. The reason for this finding is attributed to poorer health, poorer sleep satisfaction, a down graph in the physical activity and functional status, and, deterioration in the psychosocial state which is an indirect effect of the degenerative changes that occur in various systems of the body advancing age[17,18]. In the present study, 74% (n=90) indviduals were of age group less than 50 years and rest 26% (n=31) individuals of age group more than 50 years. (graph I-a) i.e. majority of study population was in young adult age group thus reducing the effect of aging on fatigue.

In the present study population, 71% population (n=86) did not show the presence of any co-morbidities. (graph I-c). Presence of comorbidities in the patients of COVID-19 usually results in increased severity of the disease and worse prognosis. [19]

Thus, all of these previous study support finding of present study that most individuals (93%) from Pune region who suffered from mild and moderate grade COVID 19 infection does not show presence of problematic fatigue when assessed with standard outcome measure after 6 weeks of infection. This underlines the need for screening of Persistence of in this population fatigue by the use of standardized outcome measures.

During the data analysis it was found that, there was persistence of breathlessness among 17% of the studied population even after 6 weeks of COVID-19 (Table IIb). This could be because of reversal of conditioning effect gained after previous exercise regimen or lack of accurate home exercise programme prescribed by experts for improving the endurance or anxiety during exercise post COVID 19 infection.

This was a telephonic survey and Laboratory blood investigations were not taken into consideration for grading severity of COVID 19 infection. These factors may have hindered results of present study. In order to further expand the scope of study, it can be conducted on males and females separately, on different grades of COVID 19 infection; individuals along with different co morbidities and after different time intervals post recovery from COVID 19 infection.

VI. CONCLUSION:

This study concludes that though the individuals from Pune region who suffered from mild and moderate grade COVID 19 infection reported persistence of fatigue subjectively after 6 weeks but does not show significant fatigue when assessed using Fatigue Severity Scale.

Thus, there is no significant prevalence of fatigue post 6 weeks among individuals suffering from mild and moderate grade of COVID- 19 infection in Pune region.

VII. ACKNOWLEGDEMENTS:

We would like to express a heartfelt gratitude to Mr.Makarand Gokhale, administrative in-charge of the Garware COVID care centre, Pune and Dr. Kalyani Sant (BAMS) and to Dr. Pawan Shirsath (PT), Head of Physiotherapy Department in Sassoon General Hospital, Pune for their co-operation during the data collection. Special thanks to Dr. Birinder singh Paul, Professor Neurology, Dayanand Medical College and Hospital, Ludhiana, for letting us use the translated Hindi version of Fatigue Severity Scale, which was of utmost use in assessing fatigue in our study population by conquering all the language barriers.

We also wish to thank Dr.AparnaSadhale (PT), Principal, DES Brijlal Jindal College of Physiotherapy, Pune, for consenting us to conduct this study. We also extend our sincere thanks to Dr. Rajani Pagare (PT), HOD,Dr. Shreya Dhake (PT), Associate Professor, and Dr. Aditi Berry (PT), Assistant Professor, Cardiovascular PT department, DES Brijlal Jindal College of Physiotherapy, Pune, for their constant help in the review of literature. We wish to thank our colleagues, Dr. Supriya Raikwar (PT), Dr. Prajakta Bidkar (PT), Dr. Shrikant Sahu (PT), Dr. Jinal Kothari (PT) who were treating the COVID-19 Infected patients for their support during the data collection from the Sassoon General Hospital, Pune. We also thank Dr. Mrs. Swati Raje for helping us in statistical calculations necessary for the study.

Last but not the least, we would like to thank all the participants of this study for their co-operation and support during this study without whom this study would not have been possible. Lastly, we wish to thank all our colleagues, family and friends who have helped us directly or indirectly in completing this study successfully.

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