Functional Assessment and Exercise Capacity in Post-Covid Patients, An Observational Study

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Abstract

Background: The salient feature of Post-acute COVID-19 is a syndrome is the persistence of clinical symptoms more than four weeks from the beginning of acute symptoms. Multiorgan effects of COVID-19, includes clinical manifestations related to the cardiovascular, pulmonary, renal, and neuropsychiatric systems, although the duration of these multiorgan system effects is unclear. On the other hand effects of COVID-19 treatment/hospitalization, includes post-intensive care syndrome (PICS), resulting in extreme weakness and post-traumatic stress disorder.

Aim of Study: To assess prevalence of Post COVID symptoms, pulmonary and cardiac complication, and there relation to infection severity. This study included 50 post Covid-19 patients with different severities. Each patient was subjected to full history taking about Covid illness and post covid symptoms as dyspnea, Fatigue, palpitation, and sleep and mood disturbances. Also they underwent 6MWD (after 1 and 3 months), spirometry, HRCT and echo 3 months post COVID infection.

Results: The post COVID symptoms (dyspnea, Fatigue, palpitation and sleep and mood disturbances) were more prevalent in moderate and Severe COVID infections, also abnormalities in 6MWD, spirometry and HRCT were related to COVID severity, but echocardiography didn't show any difference post infection.

Conclusion: Moderate and Severe COVID infections are more associated with persistence of post covid symptoms than mild infection especially dyspnea and fatigue. Also, they are associated with abnormalities in 6MWD, Spirometry and HRCT 3 months post infection, while mild cases are not.

Key Words: *Post Covid – 6MWD – Spirometry – HRCT – Echocardiography.*

Introduction

THE salient feature of Post-acute COVID-19 is a syndrome is the persistence of clinical symptoms more than four weeks from the beginning of acute symptoms.

Multiorgan effects of COVID-19, includes clinical symptomsrefers to the cardiovascular, pulmonary, renal, and neuropsychiatric systems, the duration of these multiorgan system effects is unclear. On the other side effects of COVID-19 treatment/ hospitalization, includes post-intensive care syndrome (PICS), resulting in marked weakness and posttraumatic stress disorder [1].

The pathophysiology of post-acute COVID-19 syndrome is not totally known and considered multifactorial especially considering the affection of different organsin the body. SARS CoV-2 infection in patients with underlying comorbidities or immunocompetent conditions may lead to a gush of cytokine release called "cytokine storm". Prolonged cytokine release results in ARDS, hypercoagulable state, maladaptation of the ACE2 pathway, hypoperfusion to end-organs, septic shock, multiorgan failure, and may even lead to death. So long duration of inflammation can be considered the main pathogenesis of most post-COVID manifestations [2].

Patients with post-COVID-19 syndrome develop an abnormal form of immune response, with increased interferon-γ, interleukin-2, B-cell, CD4+ and CD8+ T-cells, and appear to have effect or T-cell activation with pro-inflammatory features. Some patients may have aberrant innate response to interferons and/or macrophage activity, and even a genetic predisposition [3].

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Abbreviations:
6MWD: 6 minute walk distance.
HRCT : High resolution computed tomography.

The inflammatory reaction can target the endothelium of vessels (endothelitis), the myocardium (myocarditis) and the central nervous system (neuroinflammation), among other systems. An augmented inflammatory response can hit previous pathologies and also promote thrombotic complications [1].

Since neuropsychiatric symptoms appears frequently in post-covid syndrome, it was found that it is mainly due to profound increase of circulating cytokines, and particularly IL-6, which can penetrate the blood-brain barrier, may happen and result in central nervous system complications [4].

Aim of work:

To assess prevalence of Post COVID symptoms, pulmonary and cardiac complication, and there relation to infection severity.

Patients and Methods

The present study was conducted in the Pulmonology Department in collaboration with Cardiology Department, Kasr El-Aini Hospital in the period from October 2021 to March 2022.This prospective cross-sectional study included 50 patients (simple random sample) recovered from covid-19 virus infection 1 month before participating in the study.

This study performed after obtaining Ethical approval Committie letter.

IRB: Ms-473-2021

Inclusion criteria:

Post covid patients (recovered) diagnosed by PCR, turned to be PCR negative at time of study, who had infection 1 month before participation in the study.

Exclusion criteria:

Severely ill patients who cannot perform PFT or who are severely debilitated and become oxygen dependant due to infection with covid-19 virus. or

- PCR positive patients.

- Patients who did not come for follow up after 3 months.

- For every patient the following was done:

Clinical data with particular attention to:

- Age and Co-morbidities (e.g diabetes, hypertension, cardiac disease, ..etc).

- Severity of COVID infection. Classification of study participants was done as the following Mild infection (non-pneumonic infection), moderate (pneumonic infection without hypoxia) then severe infection which includes hypoxia, dyspnea and >50% of lung affection in computed tomography imaging [5].

- Assessment of Post-Covid symptoms after 1 month especially those which are related to pulmonary and cardiac function e.g. dyspnea, fatigue, chest pain, palpitations, sleep and mood disturbance. The previous symptoms were assessed as the following:

- Degree of dyspnea according to mMRC scale.

- Degree of fatigue according to fatigue severity scale, each question is graded from 1 to 7 according to patient, a score of less than 36 indicates that patient is not suffering from fatigue while a score of 36 or more highlights that he may need further assessment by a physician [6].

   • Chest pain, Sleep disturbance includes insomnia and hypersomnia, Mood disturbance includes anxiety or depression.

   Investigations were done after 3 months: (Prior to investigations, participants were confirmed COVID PCR –ve):

- High resolution computed tomography of chest (HRCT), Echocardiography, 6MWD (after 1 and 3 months), spirometry (according to ATS /ERS guidelines 2005) [7].

Statistical methods:

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 28 (IBM Corp., Armonk, NY, USA). Data was summarized using mean, standard deviation, median, minimum and maximum for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. For comparing categorical data, Chi square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5, Chan, [8]. *p*-values less than 0.05 were considered as statistically significant.

Results

Table (1): Demographic data of studied population.

	Mean	SD
Age	45.44	16.53
	Number	Percentage
Sex:		
Male	29	42%
Female	21	58%
Comorbidities:		
No	39	78%
Diabetic	4	8%
Hypertensive	2	8%
Diabetic and hypertensive	5	10%
Cardiac:		
Yes	9	18%
No	41	82%
Covid Severity:		
Mild	12	24%
Moderate	18	36%
Severe	20	40%

Table (2): Prevalence of post COVID symptoms after 1 and 3 months regardless COVID severity.

	1st month		3rd month	
	Number	%	Number	%
Dyspnea	37	74	10	20
Fatigue	49	98	19	38
Chest pain & palpitations	19	38	5	10
Sleep & mood disturbace	26	52	8	16

Table (3): Post-Covid symptoms after 1 month in relation to COVID severity.

	Covid severity						p-value
	Mild		Moderate		Severe		
	Count	%	Count	%	Count	%	
Dyspnea:							
Yes	1	8.3	16	88.9	20	100.0	<0.001
No	11	91.7	2	11.1	0	0.0	
Fatigue:							
Yes	11	91.7	18	100	20	100	0.240
No	1	8.3	0	0.0	0	0	
Chest pain and palpitation:							
Yes	5	41.7	5	27.8	9	45.0	0.537
No	7	58.3	13	72.2	11	55.0	
Sleep and Mood disturbances:							
Yes	8	66.7	8	44.4	10	50	0.478
No	4	33.3	10	55.6	10	50	

Table (4): Comparative statistical analysis as regards 6MWD post-COVID after 1 month and 3 months in different COVID severities.

	Covid severity						p-value
	Mild		Moderate		Severe		
	Number	%	Number	%	Number	%	
6 MWD after 1 month:							
Desaturation	0	0.0	3	16.7	20	100.0	<0.001
Nodesaturation	12	100.0	15	83.3	0	0.0	
6 MWD after 3 month:							
Desaturation	0	0	0	0	13	65	<0.001
No desaturation	12	0	18	0	7	35	

Table (5): Comparative statistical analysis as regards HRCT after 3months in different COVID severities.

	Covid severity						p-value
	Mild		Moderate		Severe		
	Number	%	Number	%	Number	%	
Spirometry after 3 month:							
Normal	11	91.7	11	61.1	1	5.0	<0.001
Restrictive	1	8.3	3	16.7	11	55.0	
Restrictive, obstructive	0	0.0	2	11.1	7	35.0	
Obstructive	0	0.0	2	11.1	1	5.0	
HRCT after 3 month:							
Residual lesion	0	0	1	5.6	19	95	<0.001
Normal	12	100	17	94.4	1	5	
Echocardiography after 3 month:							
Normal	11	91.7	17	94.4	13	65	<0.049
Abnormal	1	8.3	1	5.6	7	35	

Discussion

In our study comparative statisticalanalysis of age and comorbidities of study population in different COVID severities, showed that old age represented 42% of our study population, 71% of them had severe COVID infection and rest of group had moderate COVID infection, while young age (<50yrs) represented 56% of population, 41% had mild infection, 41% had moderate infection and 17% had severe COVID infection.While regarding comorbidities 81% of our study population who had comorbidities had severe COVID infection So, there is a tight relation between old age and comorbidities and severity of disease which is close to study done by Zhou et al., [9] in which 100% of his study population who had severe COVID infection were old age and had comorbidities.

Comparative statistical analysis as regarding sex in different COVID severities, This study showed that 55% of males in our study population had severe COVID infection while 19% of females had severe infection and majority of females had moderate and mild infection. These results are matching with results of study done by Jin et al. [10], which showed that males tended to have more serious COVID infection and complication than females with 70% vs 29%.

Nine (18%) of our study population had cardiac history from this group 7(77.8%) had severe COVID infection, this result was matching study done by Kong et al. [11] in which 95% of his study population had history of cardiac disease and subsequently a severe COVID infection. This difference was because his study included much more participants than ours, also most of his participants had history of cardiac disease.

We assessed prevalence of post COVID symptoms after 1 month and 3 months, our study showed persistence of symptoms after 3 months in 28% of our study population and it was found thatdyspnea and fatigue aremost common persisting symptoms in 20% and 38% respectively in our study population after 3 months. These results are matching with the study done by Goertz et al., [12] which showed persistence of both dyspnea and fatigue in 71% and 87% respectively in his study population.

As regarding the prevalence of post covid symptoms after1 month in relation to severity, it is showed that 41% from mild cases, 83% form moderate cases and 100 % of severe cases (overall 80% from study population) experienced post covid symptoms after 1 month. These results are matching with the study done by Carfi et al., [13] in which they found

that 82% of their study population with different covid severities experienced post covid symptoms during1st month post infection. There is a relation between incidence of various post-COVID symptoms and infection severity. Our study showed that dyspnea was the most common post covid symptom in 74% of study population (8% of those with mild infection, 88% of those with moderate infection and 100% of those with severe infection), those findings are matching with study done by Ferandez et al., [14] in which 74% of his study population of his study population experienced dyspnea post COVID and most of his study population had severe COVID infection. Regarding fatigue, it was reported that 98% of ourstudy population experienced fatigue as a post COVID symptom fromwhich 22% had had mild infection, 36% had had moderate infection and 40% had dsevere infection, this result was matching with study done by Rao et al., [15] in which he found that >50% of his study population experienced fatigue post infection and most of them has severe infection. Regarding palpitations, This study showed that 38% of population experienced palpitations from which 47% had severe infection, 26% had moderate infection and 26% had mild infection, these results are not matching with the study done by Dewland et al., [16] that showed that 92% of his study population experienced palpitations, this difference because in this study most of population >80% had severe COVID infection which is more than that of my study.

Sleep and mood disturbance were also reported in this study as post covid symptoms, it was found that 52% of our study population experienced them post infection from which 38% had severe infection 30% had moderate infection and 30% had mild infection. These results match with the study done by Giuntella et al., [17] in which 65% of his study population experienced sleep and mood disturbance post COVID infection.

In this study we reassessed post covid symptoms after 3 months from infection, we found persistence of post covid symptoms in 56% of patients who had severe infection while 5.6% in those who had moderate infection (overall 28% from our study population) and for those who had mild infection they were free from symptoms after 3 months. These results match with the study done by Augustin et al., [18] in which they found persistence of post covidsymptoms in 30% in their study population who had different infection severities after 3 months from infection.

Our study assessed pulmonary function of study population post COVID infection through

various methods. Firstly, 6 minute walking distance (6MWD) was performed 1 month post infection. The test showed desaturation in 16% of patients who had moderate infection and 100% in patients who had severe infection, and desaturation in all patients with mild infection and 84% of patients with moderate infection. While when 6MWD was performed 3 months post infection, desaturation occurred in 65% of patients with severe infection and no desaturation in all patients with mild, moderate infection and 35% of patients with severe infection. These results are matching with the study done by Wong et al., [19] which showed that patients with moderate or severe COVID-19 had a lower 6 MWD compared to patients with mild disease 1 month post infection and follow-up after 3 months showed improvement in moderate cases and some of severe cases.

Other method of assessing pulmonary residual affection post COVID is radiological assessment of lung through performing HRCT after 3 months post infection. This study showed residual lesion in the form of ground glass opacities in 5.6% of patients with moderate infection and 95% of patients with severe infection and rest of study population had normal HRCT post infection. These results are matching with the study done by Zhao et al. [20] in which follow-up radiology was done 3 months post infection and showed residual lesion in 50% of cases from which 40% had severe COVID infection.

Spirometry is also performed 3 months post infection, We found restrictive pattern was predominant specially in severe cases of COVID where 15 (30%) of patients from which 11 (73%) had severe infection, 3 (20%) had moderate infection and 1 (8%) had mild infection, while 9 (18%) patients showed mixed restrictive and obstructive pattern from which 7 (77%) had severe infection and 2 (33%) had moderate infection. These results are matching with the study done by Castro et al., [21] which showed restrictive pattern in 59% in patients and 16% patients showed obstructive pattern, most of those patients were hospitalized due to severe covid infection.

Finally, last method to assess cardiac affection in post COVID patients is echocardiography, it was done 3 months post infection.

Abnormal echocardiographic findings were found in 8 (16%) of study population, but it should be noticed that those abnormal findings are related to previous cardiac disease not related to COVID infection. These results are not matching with study done by Dweck et al., [22] in which this study showed abnormal new echocardiographic findings

in 55% of study population, even in those with out previous cardiac history there was echoabnormalities in 46% of them. The difference between two studies is due to selection of patients as our study has only 9 patients with previous cardiac disease while the other study has total 1216 patients from which 667 (55%) had already previous cardiac disease beside severe COVID infection.

Conclusion: The results of the study showed that old age and comorbidities are more associated with severe COVID infection rather than mild and moderate cases with statistically significant difference. Also, persistence of post COVID symptoms occurred more in moderate and severe cases. Abnormalities were detected in 6MWD, spirometry and HRCT were related to severe and moderate cases not mild one with statistically significant difference.

Persistence of post COVID symptoms in 28% of study population regard less COVID severity. Dyspnea and fatigue were most common post COVID symptoms persisted in our study after 1 month represented 74% and 98% respectively and represented 20% and 38% respectively of our study population after 3 months.

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التقييم الوظيفى والقدرة على ممارسة الرياضة لدى مرضى ما بعد كوفيد، دراسة قائمة على الملاحظة

مقدمة: السمة البارزة لمتلازمه ما بعد كوفيد COVID 19 الحاد هى استمرار الأعراض السريرية لأكثر من أربعة أسابيع من بداية الأعراض الحادة. تشمل التأثيرات أعضاء متعددة متعلقة بالقلب والأوعية الدموية والرئة والكلى والطب النفسى والعصبى، على الرغم من أن مدة وكيفية التأثيرات على اعضاء الجسم المختلفه هذه غير واضحة. من ناحية أخرى، تشمل آثار علاج كوفيد١٩ متلازمة ما بعد العناية المركزة، مما يؤدى إلى الضعف الشديد واضطراب ما بعد الصدمة.

يهدف هذا العمل إلى تقييم انتشار أعراض ما بعد COVID، والمضاعفات الرئوية والقلبية ، وعلاقتها بشدة العدوى. شملت هذه الدراسة ٥٠ مريضاً ما بعد Covid –١٩ بدرجات شدة مختلفة. تعرض كل مريض للتاريخ الكامل حول مرض Covid وأعراض ما بعد covid مثل ضيق التنفس والتعب والخفقان واضطرابات النوم والمزاج. أيضا، خضعوا لاختبار المشى لستة دقائق 6MWD (بعد ١ و٣ أشهر)، وقياس التنفس، واشعه مقطعيه عالية التباين (HRCT)، موجات تليفزيونيه على القلب (Echo) بعد ٣ أشهر من الإصابة بفيروس كورونا.

النتائج: كانت أعراض ما بعد كوفيد (ضيق التنفس، والتعب، والخفقان، واضطرابات النوم والمزاج) أكثر انتشاراً فى الاصابات بكوفيد المتوسطه والشديدة، كما كانت القصور فى 6MWD وقياس التنفس وHRCT مرتبطة بشدة الاصابه، لكن الموجات الصوتيه على القلب لم يظهر أى فرق بعد الإصابة.

الاستنتاج: ترتبط عدوى COVID المعتدلة والشديدة باستمرار أعراض ما بعد كوفيد أكثر من العدوى الخفيفة وخاصة ضيق التنفس والتعب. أيضا، ترتبط بتشوهات فى 6MWD ، قياس التنفس وHRCT بعد ٣ أشهر من الإصابة، فى حين أن الحالات الخفيفة ليست كذلك.