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Impact of COVID-19 Infection on Pulmonary Function Tests in Patients 6-8 Weeks After Recovery

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ABSTRACT— This study aimed to investigate the effect of COVID-19 on pulmonary function tests after 6-8 weeks of recovery, to confirm the necessity of the test to follow up the patients after recovery and to find out the possibility to use it as a workable procedure to indicate the severity of the previous infections. This a randomized-control study The study was conducted in Basrah City. Three groups of patients were divided based on the severity of the previous infection, Group 1 included the patients with previously severe infection; group 2 were the patients with previously mild infection and group 3 who never infected. Pulmonary function tests (PFTs) were measured in all groups using a spirometer. Data analysis showed that group 1 had a significant change in some PFT,6-8 weeks after recovery and this change was in form a restrictive pattern, while group 2 showed non- significant changes compared to group 3. COVID-19 might affect PFT after recovery in a way depended on the severity of the infection. This study pointed to the necessity of following up the previously infected patients and that measurement was workable test to indicate the severity of the previous infection.

KEYWORDS: pulmonary function test, COVID- 19

1. INTRODUCTION

Since the World Health Organization (WHO) has declared that the coronavirus is a pandemic on the11th of March, the interest to study all aspects of this infectious disease has increased, especially with the increasing number of infections and death over the world [1]. Coronavirus disease is caused by a novel virus, a sever acute respiratory syndrome Corona virus [2], [3]. This infection disease has appeared in 2019, that is why known as COVID-19, then has spread from China to other countries in December 2019 [4- 7]. The rapid transmission of COVID-19 from an individual to the other made it one of the most concerning in the whole world till moment. The studies are continuous to get effective control way and treatment [8]. The clinical effect dramatically varies among individuals from asymptomatic signs to respiratory impairment and multi - organ failure [9]. The patients with COVID-19 are known to have a fever, cough, headache, loss of smell and deterioration of the gastrointestinal system [10]. People infected after the entry of the virus through the nose or mouth mainly and begins to cause injury to the respiratory system [11]. Although it could involve many organs, lung injury represents one of the most clinical signs [18]. Due to the increased cases of lung injuries that are recorded in the discharged patients, more attention was kept a focus on the evaluation and assessment of lung injuries [12], [13]. A previous study stated that discharged coronavirus patients with pneumonia still have some abnormalities related to computed topography(CT) scan of the chest and ground-glass opacity [14], as well as they still have some lung function disorders with limited function to do the activities, which may last for many months depending on the severity of their cases [15-17]. Another pervious study found that respiratory impairment and pulmonary function disorders might last for 30 days and even for 6 weeks post hospital discharge [18]. In this study, we aimed to investigate the

effect of COVID- 19 on pulmonary function tests after a full recovery, in about 6-8 weeks of recording a negative test for the infection as well as to confirm the necessity of measuring the lung test to follow up the patients after recovery as well as to find out the possibility to use pulmonary function tests as a procedure that may indicate to the severity of the previous infections.

Pulmonary function tests: Forced Expiratory Volume at the first second of expiration (FEV1); Forced Vital Capacity(FVC)the ratio of FEV1/FVC (FEV1/FVC%); Peak Expiratory Flow (PEF)and Estimated Lung Age (ELA) were used to evaluate the respiratory function. These tests are very workable to evaluate and monitor the efficiency of respiratory system as well as diagnose any disorder that could occur due to the infection [19]. FEV1, FVC, and FEV1/FVC are considered cornerstone pulmonary physiology outcomes for describing a population with different respiratory abnormalities; evaluating the response to the treatment in different clinical trials, and characterizing populations in epidemiologic studies. This agrees with what was stated by the ATS/ERS which characterizes spirometry as a fundamental measurement in respiratory disorders [20].

2. PATIENTS AND METHODS

2.1 Patients

The study included 193 adult individuals from both sexes (71 females and 122 males), with the age range 38-72 yrs. These individuals were divided into three groups according to their health status and the differences in the severity of COVID- 19 infection. These groups are: Group 1 which included 64 patients (23 females and 41 males) who experienced severe signs and symptoms of the disease such as having pneumonia according to the radiographic test and oxygen saturation percentage > 90% at rest, with hospitalization period for 20-29 days.

Group 2 included 72 patients (27 females and 45 males) with mild symptom and no evidence to appear pneumonia. These patients stayed at home for medication and treatment. These two groups were documented to be infected with coronavirus by PCR and CT scan and were divided into separated groups depending on several criteria e.g., respiratory distress, percentage of oxygen saturation, respiratory rate (30 > (, mechanical ventilation demand [18].

The measuring of pulmonary function tests for the patients of these 2 groups were done after 6-8 weeks of recovery, when patients recorded negative results for the infection. The last group is group 3 which included 57 healthy individuals (21 females and 36 males) who never infected by a coronavirus. All individuals from the three groups showed no significant differences in the underlying diseases such as hypertension and Diabetic Mellitus and no significant differences in age and smoking status. Several criteria were excluded e.g. Patients with anatomical deformities and chest trauma, the individuals who kept on long term medication or who were chronically ill, the individual who were with a history of a chest or abdominal surgery, and obese individuals. The required information related each participant such as health status, smoking, drug taken and duration of the disease were all recoded via form of a questionnaire. The study was approved by ethical committee of College of Pharmacy, University of Basrah.

2.2 Pulmonary function tests measurement

Pulmonary function tests measurements were done to all participants using Micro Medical Lab Spirometer (MIR Spirol III Diagnostic Spirometer, Ltd. England). The procedure of measurement was done for all before 12:00 pm by a well-trained physician following the American Thoracic Society (ATS) guide. Each participant had to repeat the measurement at least three times in order to get the most suitable record of

pulmonary function tests, because this procedure depends on participants, cooperation. The function tests that were depended on to follow and diagnose the participants were FEV1: Forced Expiratory Volume; FVC: Forced Vital Capacity; percentage of FVC Percentage of FEV1, PEF: Peak Expiratory Flow and ELA: Estimated Lung Age.

2.3 Statistical analysis

Data were analyzed by using Statistical Package for the Social Sciences (SPSS) Statistical Software for Windows, Version 25.0 IBM (SPSS Inc, IL, USA). They were represented as means value ±standard deviation (SD). A least significant difference (LSD) of one-way analysis of variance (ANOVA) was used to test the differences among the groups. Qualitative data were represented as (%) tested using the Pearson Chi-square test. The result was considered significant at $p<0.05$. The study was conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki. It was registered in research registry with unique ID and hyperlink. The study was carried out with patients verbal and analytical approval before sample was taken. The study protocol, the patient information, and informed consent form were reviewed and approved by a local ethics committee of college of medicine, University of Basrah.

3. RESULTS

All of groups in the study showed no significant differences($p<0.05$) in general characteristics such as age, weight, height, BMI and gender dimorphism as shown in details table 1. On the other hand, when comparing pulmonary function tests among, the three groups there were significant changes in these parameters. Group 1 patients who recovered from severe infection revealed significant decline ($p>0.05$) in FVC, FVC% FEV1and FEV1/FVC%. As seen in table 2, FVC of group 1 (3.3425±0.33) was significantly lower than FVC of both group 2 and group 3 (3.8146±0.38 and 3.9337±0.32), $p >0.05$. FEV1 (2.6478±0.36) was also significantly lower than both group 2 and group 3(3.2700±0.38 and 3.3507±0.28), ($p >0.05$). The same result was found related to FEV1/FVC%, while there were no significant differences in each of PEF and ELA ($P < 0.05$), as seen in the table. Data revealed that there were significant differences in the percentage of the diagnostic cases .The percentage of obstructive cases in group 1 was (6.3%) which was significantly different from the obstructive cases of both group 2 and group 3,$p >0.05$.As well as there were increases in restrictive cases (26.6%) and combined cases (3.1%) in group 3 .It should be mentioned that the percentage restrictive cases was the highest one among the three groups (26.6% vs 11.1% and 8.8%) ,furthermore it is the highest percentage cases among the abnormal cases, as illustrated in table 3.There were no significant changes in the percentage of the diagnostic cases between group 2 and group 3.Both of them showed the highest percentage of the cases is the normal case 3 (86.1% and 91.2%) which were group 1 more than the normal cases.

The significant decline in the pulmonary tests of group 1could be confirmed by the comparison between the real age and the estimated lung age (ELA) of the individual. ELA of group 1 was significantly more than the real age (57.19± 10.58 vs55.19±9.87), $p>0.05$. While this change did not occur in group 2 and group 3. They reveal no significant changes between the real age and ELA, $P< 0.05$, as seen in table 4. However, ELA can reflect the impairment in spirometeric tests parameters because it is inversely related to these parameters. Table 5 showed that ELA had inverse correlations with FEV1 and FEV1/FVC, (r=-0.282 and -0.414 respectively, $p>0.05$), as illustrated in figure 2, 3. While it was not a significant correlation with FVC inspite of the inverse correlation (r= -0.084), $p <0.05$. (figure 1).

Table 1: Characteristics of the groups

	Group 1	Group 2	Group3	Total	*P value

Groups	(N=64)	(N=72)	(N=57)	(N=193)	
Parameter					
Age	55.19±9.87	55.38±9.50	55.19±8.97	55.26±9.42	0.991
weight	84.11±5.431	84.90±5.49	85.21±7.01	84.73±5.95	0.571
height	176.08±6.07	175.92±6.63	177.18±7.00	176.34±6.55	0.517
BMI	27.17±1.86	27.49±2.00	27.23±2.74	27.31±2.20	0.667
Gender:					
Male(%)	41 (64.1%)	45 (62.5%)	36 (63.2%)	122 (63.2%)	0.982
Female (%)	23 (35.9%)	27 (37.5%)	21 (36.8%)	71 (36.8%)	

*Data were considered a significant at p> 0.05

Table 2: Comparison of pulmonary function tests among the three groups

group	Group 1 N=64	P value Difference Between group 1 &(2, 3)	Group 2 N=72	P value Difference Between group 2 & 3	Group 3 N=57	Total N=193
parameter						
FVC(L)	3.3425±0.33	*0.003 **<0.001	3.8146±0.38	0.055	3.9337±0.32	3.6932±0.43
FVC%	83.6774±7.62	*0.01 **0.001	86.8617±7.19	0.374	87.9919±6.52	86.1396±7.33
FEV1(L)	2.6478±0.36	*0.005 **<0.001	3.2700±0.38	0.190	3.3507±0.28	3.0875±0.46
FEV1/FVC %	79.2026±7.05	**<0.001 **<0.001	85.6502±6.45	0.806	85.3842±4.26	83.4336±6.78
PEF	6.63±0.85	0.061 0.093	7.7581±0.82	0.958	7.7500±0.90	7.0485±1.31

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ELA	57.19±10.58	0.460 0.450	55.94± 9.46	0.953	55.84±9.17	56.33±9.47

FVC, Forced Vital Capacity; FEV1, Forced Expiratory Volume at the first seconds; PEF: Peak Expiratory Flow, ELA: Estimated lung age
* statistically significant at p <0.05.
** Highly significant: p < 0.001

Table 3: The percentage of diagnosed cases in the three groups

Diagnosis	**Group1**	**P value** **Between group 1&(2,3)**	**Group2**	**P value** **Between Group 2&3**	**Group3**	**Total**
Normal	41 (64.1%)	*0.027	62 (86.1%)	***0.604	52 (91.2%)	155 (80.3 %)
Obstructive	4 (6.3%)	**0.004	1 (1.4%)		0 (0%)	5 (2.6%)
Restrictive	17 (26.6%)		8 (11.1%)		5 (8.8%)	30 (15.5 %)
Combined	2 (3.1%)		1 (1.4%)		0 (0%)	3 (1.6%)
Total	64		72		57	193

Data were represented as: No. (%), Chi-square test use to test the difference between the groups.
P* value significant difference (0.027) between severe and mild groups
P** value significant difference (0.004) between severe and control groups
P*** value no significant difference (0.604) between mild and control groups

Table 4: Comparison between the real age and ELA of the three groups.

Parameter **Group**	**Age (years) Mean ± SD**	**ELA (years) Mean ± SD**	**P value**
Group 1	55.19±9.87	57.19±10.58	0.014*
Group 2	55.38±9.50	55.94± 9.46	0.613
Group 3	55.20±8.97	55.84±9.17	0.578

*A significant at p> 0.05

Table5: Correlation between ELA and spirometric parameters. (Bivariate correlation test)

		FVC	FEV1	FEV1/FVC
ELA	r	-0.084	-0.282	-0.414
	p	0.243	<0.001	<0.001

ELA: Estimated lung age; r: correlation coefficient; Correlation is significant at p>0.05

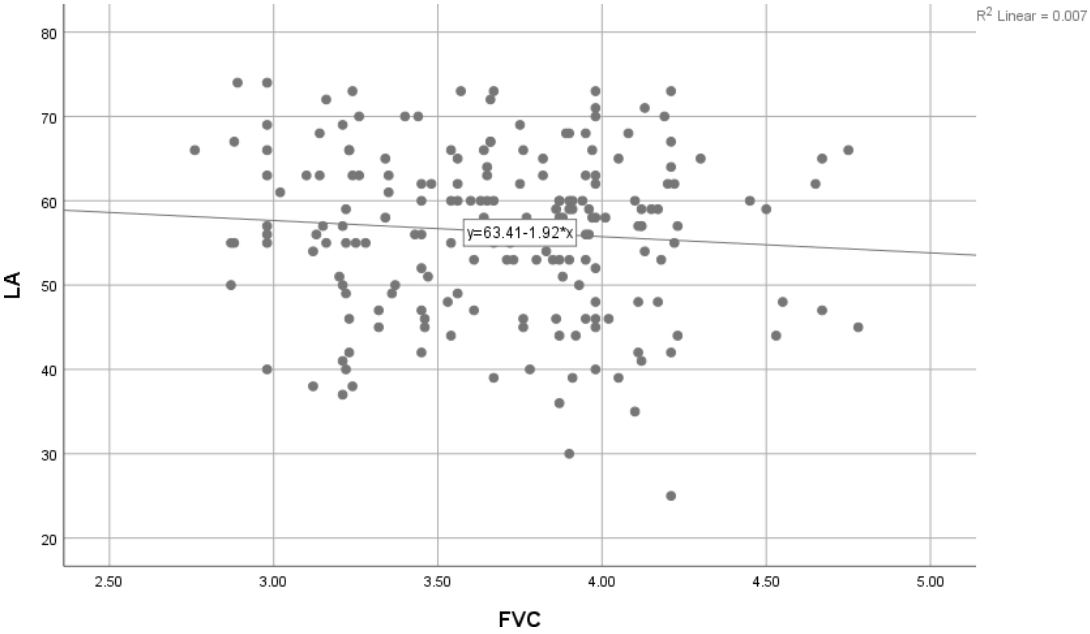

Figure 1: Correlation between FVC and ELA

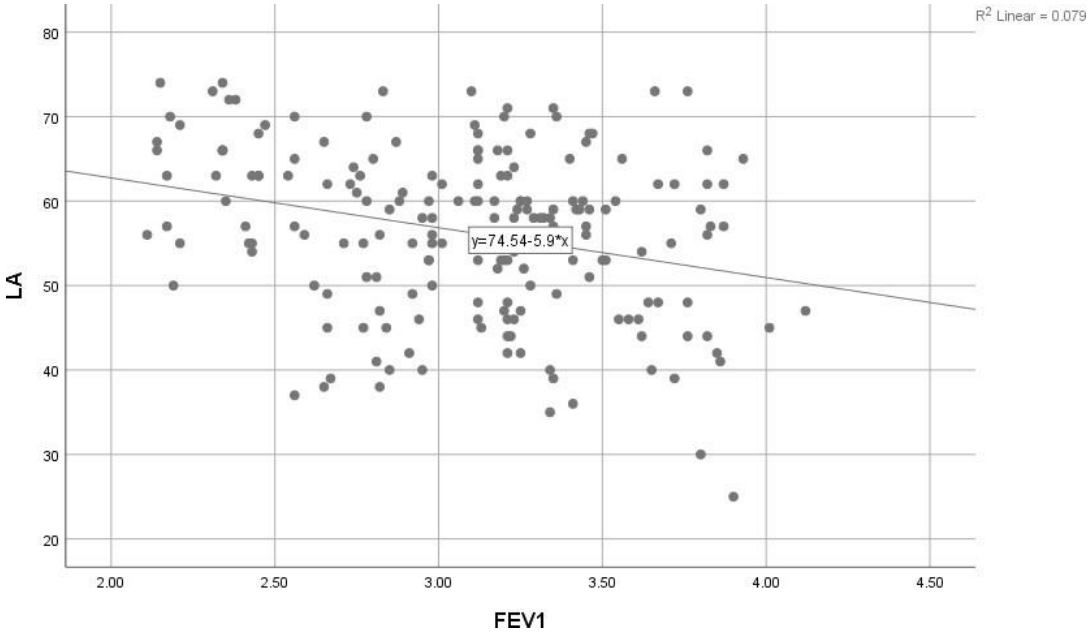

Figure 2: Correation between FEV1 and ELA

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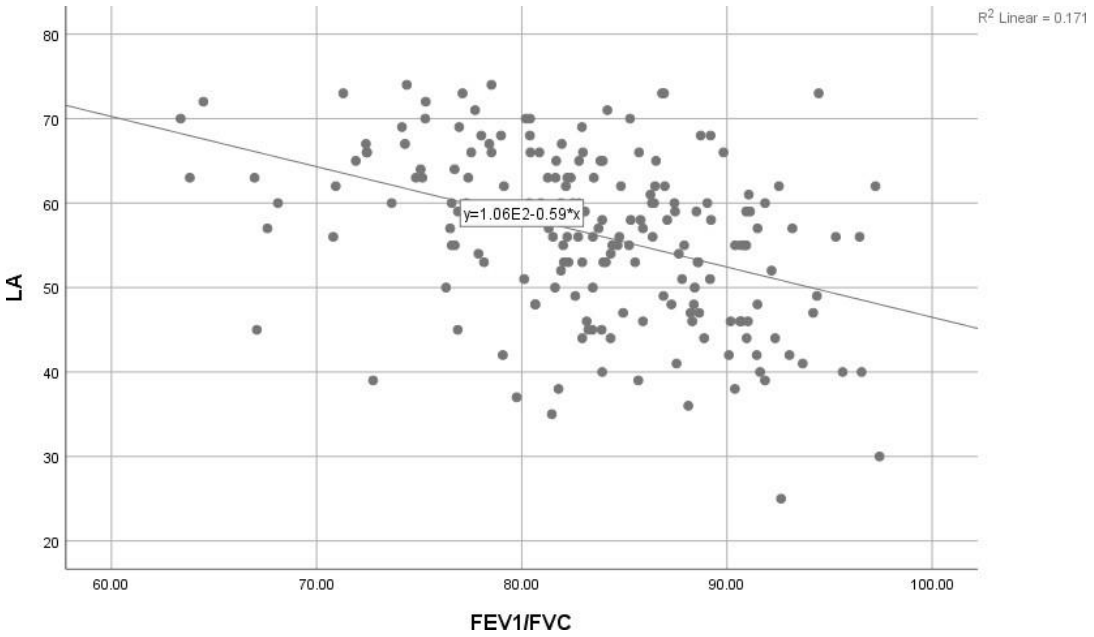

Figure 3: Correlation between FEV1/FVC and ELA

4. DISCUSSION

In this comparative study, despite that all participants of the three groups had non- significant variations in the characteristic details, underlying diseases or abnormalities; they revealed significant differences in the pulmonary function tests. Group 1 had a significant decline in each of FEV1, FVC, FVC% and FEV1/FVC% compared to the other groups. This result indicates to that pulmonary function tests disorders were among the consequences of previously infection with COVID 19 after 6-8 weeks of recovery and recording negative test results, the finding supports the fact that several clinical effects could persist even after the recovery which was reported by other studies [8], [21]. Our results were consistent with the results of other studies [22], [23] which found that coronavirus infection could result in different pulmonary complications such as pneumonia or acute respiratory syndrome. Furthermore, the recovered patients from coronavirus pneumonia can be left with damaged lunges [24]. As a result of damaged lung, pulmonary function disorders may develop and that may last for months or even years particularly in patient who infected with sever disease [25], and the impairment in the lung function depends on the severity of the infection [15], [26]. When the respiratory system infected by this virus, multiple infiltrates of both lunges may present [21] and several pathological events may take place by invasion the virus the lung cells, monocytes and endothelial cells of the vascular system leading to inflammatory changes including edema, degeneration and necrotic changes referred to pneumonia, which can be mild, moderate, severe and life threating [27]. The clinical evidence include shortness of breath, increased respiratory rate, decrease oxygen saturation as well as with higher serum lactate dehydrogenase (indicating tissue damage), C- reactive protein peaks (indicating inflammation) and lower counting of infection-fighting lymphocytes especially in severe illness [8]. These pathological evidence and inflammatory processes explain the decline in the pulmonary function in group 1 (table 2), as well as the defect in the ventilatory function which is represented by the increased percentage of abnormal diagnosis in the same group as illustrated in table3 that shows the percentage of the restrictive cases 26.6%, while obstructive percentage is 6.3% and the percentage of the combined cases is (3.1%). In group 1, all of the percentages of the abnormal diagnosis were significantly higher than those of both group 2 and 3. Among the most common abnormalities was impaired diffusion - capacity for carbon dioxide followed by restrictive ventilatory defect and decline in FEV1 /FVC ratio which are associated with the severity of the disease [28].

Pulmonary fibrosis usually occurs as a result of severe and/or prolonged assault to the lung [29]. This occurs due to dysregulation in one or more of the phases of wound healing: injury, inflammation and repair [30]. Acute lung injury attempt to repair by fibro proliferation and lung remodeling occur in COVID-19 disease lead to increase the risk of pulmonary fibrosis as a sequel to COVID-19 [12]. Moreover, the lung fibrosis cannot be cured because the scarred changes in the lung tissue do not regress [31]. Under normal physiological conditions, in the healthy normal individual, ELA is the same real age [32], [33]. While we found that ELA was significantly different when compared with the real age in group 1 and that ELA could reflect the defect and abnormality of lung function tests, it increases by the increase in the impairment of other pulmonary tests. The factors that could limit the study is the few numbers of participants in each group despite of the widespread of COVID 19 infection. The reason for the small groups were the exclusion of many cases such as smoking, obesity, comorbidities (hypertension and diabetes), other obstructive or restrictive lung diseases and any physical or anatomical abnormalities.

5. Conclusion

A severe infection with COVID 19 could leave the patients with a disorder in some pulmonary function tests even after 6-8 weeks of recovery, when patients record the first negative result for the infection, with the presence of varying percentages of abnormal pulmonary diagnosis. A restrictive pattern showed a higher percentage than other disorders. Furthermore, ELA of these patients was more than their real age. This result indicates that recovered patients from the severe infection need more tracking and follow up at least 6-8 weeks after recovery by measuring their pulmonary function tests as well as these tests could indicate the severity of the previous infections.

6. Data Availability

The quantitative data used to support the findings of this study are available from the corresponding author upon request.

Fund: Self-funded

Conflicts of Interest

The authors declare that there are no conflicts of interest.

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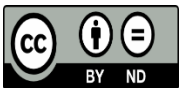

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