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Long-Term Effect of Post-Covid-19 Syndrome on Respiratory Parameters in Iraqi People

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Abstract **Background:** The long-term sequelae of COVID-19 are thought to be a novel area of research due to variances in the epidemiology and therapy. Nevertheless, the follow-up time interval (6 or 12 months) was excessively long, and the time point of the follow-up period varied from 3 to 24 months in the prior research. More research is required to understand better COVID-19's effects, including their long-term effects on the lungs and how they may affect pulmonary function. Therefore, this study aims to investigate the long-term impact of post-COVID-19 syndrome on pulmonary function tests. **Methods:** This research was a case-control study conducted from 13 October 2023 to 13 November 2023 at the Al-Sader Teaching Hospital in Maysan City. There are fifty-eight patients and fifty-eight controls included. This study comprised patients who visited a pulmonary consulting clinic and had COVID-19 symptoms, matched by controls who were chosen at random. The controls had to meet the same criteria as the cases, with the exception that they did not have COVID-19 disease. The most popular kind of breathing or pulmonary function test is spirometry, spirometry was used to measure: FVC, FEV, and FEV1/FVC ratio. **Result:** sixty-six post covid19 syndrome with ages (34.1 ± 9.8) years and sixty-seven controls were enrolled. The results of FVC and FEV parameters indicate a significant difference ($P<0.05$) between cases and control groups. However, no significant differences existed between groups for the FEV1/FVC ratio. In the comparison of lung function tests between cases and control across different age groups (18-29, 30-39, 50-65) years, we found that mean FVC is significantly lower for the age group 18-29 years than for 30-39 and 50-65 years, and the mean FEV is significantly lower for the age group 18-29 years than for 30-39. **Conclusion:** After COVID-19, a significant number of patients continue to have symptoms, with respiratory symptoms accounting for the majority of complaints. Patients with continuing symptoms were younger and presented a significantly lower FVC and FEV.

Key Words coronavirus disease 2019 (COVID-19), lung function test, long covid. post COVID-19, pulmonary function test, spirometry

1. Background

Coronavirus 19 is a highly contagious disease caused by a newly discovered strain of coronavirus called the severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2). The World Health Organization first reported the outbreak in December 2019 in Wuhan, China [1]. This has led to widespread illness and death across the globe [2]. The first case of COVID-19 in Iraq was recorded on February 24, 2020, in Al-Najaf City. As of April 9, 2020, confirmed cases have increased significantly to 1232 [3].

When SARS-CoV-2 infects type two alveolar cells in the lung, it attaches to specific angiotensin-converting enzyme 2 (ACE2) receptors, and multiplies inside the cell. It causes an inflammatory response that includes vasodilatation, necrosis of endothelial cells, increased pulmonary capillary permeability, and in more severe cases, acute systemic inflammatory responses and cytokine production [4]. The virus causes multiple organ failure by getting into the bloodstream, primarily in organs with ACE2 receptors like the heart and kidneys. Inflammatory cell infiltration, fluid accumulation inside the alveoli, alveolar wall disintegration, and lung fibrosis all contribute to the infection of lung tissue that was exposed during autopsy [5].

People who have the SARS-CoV-2 virus may experience symptoms similar to pneumonia, such as fever, weariness, coughing, breathing difficulties, the production of sputum, and muscular discomfort [6]. The respiratory issues caused by the SARS-CoV-2 virus progress over time and can lead to consequences such as acute respiratory distress syndrome (ARDS), septic shock, and/or multiple organ failure. Invasive mechanical ventilation (IMV) and vasopressor therapy for low blood pressure and acute hypoxemic respiratory failure are two conditions for about 5% of COVID-19 cases that require extended mechanical ventilation support. Usually, hospitals keep these patients under close observation in the intensive care unit (ICU) [7].

According to reports, COVID-19 survivors who were hospitalized continue to experience symptoms, radiographic abnormalities, and physiological impairments even months after their initial illness [8]. There are a significant number of patients who require treatment with high-flow nasal oxygen and/or mechanical ventilation, especially those recovering from COVID-19-related acute respiratory distress syndrome [9], The individual displays long-term lung complications confirmed by pulmonary function testing (PFT) and chest computed tomography (CT). According to recent reports by Berlin et al. (2020), the most common functional abnormality observed is impaired diffusion capacity. A less frequent incidence of pulmonary dysfunction was discovered through a decrease in forced vital capacity (FVC) [10]. Following a CT scan of the chest, the most commonly seen radiographic effects are ongoing ground-glass opacity and the subsequent progression of fibrotic changes [11]. Nonetheless, considering the severity of cases and conditions in many individuals, it is crucial to take into account the possible long-term impacts of the COVID-19 virus [12]. The World Health Organization (WHO) has recently established a clinical case definition for what is known as the "post-COVID-19 condition." Nevertheless, other organizations have used different terminology to describe the long-term impacts of SARS-CoV-2 infection [13]. Prolonged exposure to SARS-CoV-2 increases the risk of respiratory problems, including disorders that affect the functioning of the lungs [14]. The impact of post-COVID-19 symptoms is more pronounced in older patients with a higher body mass index (BMI), particularly in males compared to females, those who are already ill, and those who require mechanical ventilation [15]. While the virus is commonly associated with respiratory symptoms, new data suggests that it can impact multiple bodily systems. These include gastrointestinal, musculoskeletal, neurological, vascular, hematological, and other functions [16], [17]. Many individuals who have recovered from COVID-19 may continue to experience symptoms that persist for days, weeks, or even months after being released from the hospital. These symptoms can have lasting impacts on various organs within the body, such as the heart, kidneys, and liver. However, it is mainly the respiratory system that is impacted by the SARS-CoV-2 virus, which can result in a reduction in lung capacity [18]. It has been reported that adults may experience a long-term decline in their lung function. The spirometry test is a frequently used pulmonary function test that should be conducted with safety precautions to prevent infection. The spirometer measures lung function and provides information on the Forced Expiratory Volume in 1 second (FEV1), Forced Vital Capacity (FVC), and the ratio between FEV1 and FVC [19]. The results of a spirometry test can be highly indicative of the severity of a COVID-19 infection. Extended follow-up data on COVID-19 survivors has not yet been released, despite short-term radiological outcomes and decreased lung function noted in patients upon hospital discharge being recorded. Our aim, then, was to describe the long-term effects of COVID-19 on lung function in survivors.

2. Methods

A. Participants and Study Design

This research was a case-control study conducted from 13 October 2023 to 13 November 2023 at the Al-Sader Teaching Hospital in Maysan City. There are fifty-eight patients and fifty-eight controls included. This study comprised patients who visited a pulmonary consulting clinic and had COVID-19 symptoms, matched by controls who were chosen at random. The controls had to meet the same criteria as the cases, except that they did not have COVID-19 disease.

B. The Inclusion Participants Include

1) All treated and recovered cases of COVID-19 cases of all ages, admitted in the indoor unit have been enrolled in the study.
2) Recovered cases of COVID-19 irrespective of the duration of admission were enrolled in the study.
3) Recovered cases of COVID-19 irrespective of oxygen saturation were enrolled in the study.
4) Recovered cases of COVID-19 cases willing to undergo spirometry tests were enrolled in the study.

C. The Exclusion Participants from this Study Include

1) Recovered cases of COVID-19 cases not willing to undergo spirometry test
2) Recovered cases of COVID-19 cases not able to perform a spirometry test
3) Recovered cases of COVID-19 cases with neurological issues like hemiparesis or hearing difficulty and having coordination or cooperation problems during spirometry
4) Recovered cases of COVID-19 cases with tachypnea or tachycardia.
5) Recovered cases of COVID-19 in pregnant females (any trimester was excluded).
6) Patients with a history of restrictive and obstructive lung diseases before their COVID-19 illness.
7) Recovered cases of COVID-19 with smoking and drinking habit.
8) Recovered cases of COVID-19 with comorbidities other than prior lung diseases.

D. Ethical Issues

By ethical standards, the study groups were chosen. The data were collected after receiving approval from the Department of Medical Physiology at the University of Kufa/College of Medicine and the Maysan Health Directorate to conduct the study in Al-Sader Teaching Hospital. A practical supervisor was also appointed in the hospital to oversee the workflow. The study was entirely voluntary, and participants were free to leave at any time if they so desired. Pulmonary function tests were not conducted until after informed consent was obtained and fulfilled. The examinations that were conducted were non-invasive procedures with minimal hazards. As can be observed with any maneuver involving particular blowing techniques, dyspnea may have developed. During pulmonary function tests, syncope may occur in rare instances. The pulmonary function tests were conducted by the participants while seated in an arm-supported chair to minimize risk. Falling or getting hurt was no longer a possibility.

E. Clinical Assessment

A detailed history was taken from each person (case and control) including age, name, gender, telephone number, work, workplace, height, and weight, as the history of chronic diseases such as diabetes, hypertension, and other diseases, habits of the patient (if cigarette smoking or alcohol drinker or not). History of COVID-19 infection focusing on symptoms such as fever, cough, headache, loss of sense of smell and taste, vomiting, diarrhea, runny nose, shortness of breath, pain in the chest, and others have been taken. Also the duration of the illness and the type of treatment or vaccine that is used for this disease.

F. Pulmonary Function Tests

1) Spirometry Test

The most popular kind of breathing or pulmonary function test is spirometry. This test gauges how much air can be taken in and expelled from the lungs, as well as how quickly and easily can do so. Based on the standards of the European Respiratory Society/American Thoracic Society (ERS/ATS), spirometry was used to measure: Forced vital capacity (FVC), Forced expiratory volume in one second (FEV1), FEV1/FVC ratio, Peak expiratory flow rate (PEF), and Forced expiratory volume from 25-75

2) Spirometry Technique

Before the test began, the operator ensured that the participants were comfortable and gave them an explanation of what to expect. While performing spirometry, the operator explained and encouraged the participants to close their mouths for the entire duration of the test while ensuring there was no obstruction at the mouthpiece, for example, the tongue. At the start of the procedure, the participants were instructed to breathe through the mouthpiece. During the test, the patient will be sitting upright. The patient has a clip applied to their nose, and they are given a plastic mouthpiece attached to the spirometry machine. To help the participants become accustomed to the machine, they were told to breathe through the mouthpiece multiple times. The participants were instructed to take a full, fast breath without a pause at maximal inspiration, followed by a forced expiration with a last maximal inspiration signifying the completion of the maneuver. Upon completing an attempt, click the "calculate results" button to end the exam. Different colors were used to illustrate each attempt. Between each try, there was a one-minute rest time. Testing will be done at least three times with this maximum effort to get the best results. The optimal outcome was determined by adding the highest FEV1 and FVC. The operator provided coaching to the participants in between tries to guarantee maximum effort and precise results.

G. Statistical Analysis

Statistical analyses were done using the SPSS program (version 26). Categorical variables were presented as percentages and frequencies while continuous variables were presented as means ± standard deviations. The chi-square test was used to assess the association between categorical variables (age groups, gender, and BMI). An independent t-test was used to compare the means between cases and controls. Error bars of means and standard deviations were used to compare lung function parameters according to age groups and gender. The P values less than 0.05 will be considered statistically significant results.

3. Results

A. Patient Characteristics

The baseline demographics data between post-COVID-19 infection(cases) and healthy controls are shown in Table 1. The mean age and mean BMI of post-COVID-19 infection and healthy controls were 34.1±9.8 and 35.9±11.7 years, 29.4±8.01 and 28.6±6.1 (Kg/m2), respectively. The table indicates no significant differences ($P > 0.05$) in age, BMI, and sex between groups.

B. Lung Function Test between Cases and Control

The comparison of spirometry results including FVC, FEV1, and FEV1/FVC between cases and controls is shown in Table 2. The results of FVC and FEV parameters indicate a significant difference ($P<0.05$) between cases and control groups. The mean of FVC in cases is (3.4±0.7) and it decreases significantly ($P < 0.004$) in comparison with the control mean (3.8±0.8). The cases also have a low FEV mean (2.7±0.7) in comparison with the mean of control (3.2±0.7). However, no significant differences existed between groups for the FEV1/FVC ratio ($P > 0.05$).

C. Comparison of the Lung Function Tests between Cases and Control Across Different Age Groups (Years)

Table 3 and Figure 1 indicates that the FVC and FEV parameters have a significant difference between cases and control ($P <0.05$) for the age group (18-29) years, but the

Variable	Subgroup	Group		Total	P
		Cases (n=66) No.(%)	Controls (n=67) No.(%)		
Age group (years)	18-29	29 (43.9%)	24(35.8%)	53(39.8%)	0.2
	30-39	17(25.8%)	25(37.3%)	42(31.6%)	
	40-49	13(19.7%)	7(10.4%)	20(15.0%)	
	50-65	7(10.6%)	11(16.4%)	13(13.5%)	
Mean age(years) ±SD		34.1±9.8	35.9±11.7		0.3
Sex	Male	38(57.6%)	42(62.7%)	80(60.2%)	0.5
	Female	28(42.4%)	25(37.3%)	53(39.8%)	
BMI	Normal	15(22.7%)	17(25.4%)	32(24.1%)	0.8
	Overweight	26(39.4%)	28(41.8%)	54(40.6%)	
	Obese	25(37.9%)	22(32.8%)	47(35.3%)	
Mean BMI (Kg/m2)±SD		29.4±8.01	28.6±6.1		0.6

Table 1: Demographic data of study population

Lung function test	Cases (n=66) Mean ±S D	Controls(n=67) Mean ± SD	P value
FVC	3.4±0.7	3.8±0.8	0.004
FEV	2.7±0.7	3.2±0.7	0.0001
FEV/FVC	79.6±15.7	81.6±9	0.4

Table 2: Lung function test in cases and controls

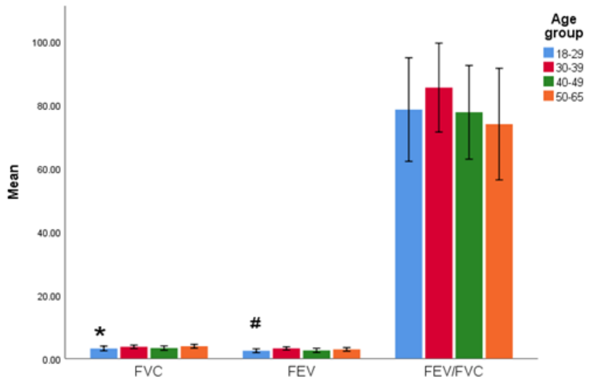

Figure 1: Comparison of the lung function tests between cases and control across different age groups (years), * Mean FVC is significantly lower for the age group 18-29 years than for 30-39 and 50-65 years. Mean FEV is significantly lower for the age group 18-29 years than for 30-39

FEV/FVC ratio increases insignificantly between cases mean (78.4±16.3) and control mean (84.3±10.4) (P > 0.05) for the same age group. The FVC, FEV, and FEV/FVC parameters of another age group (30-39, 40-49, 50-65) years show no significant difference between cases and control (P > 0.05).

D. Lung Function Test Differences between Males and Females in Cases and Control

Table 4 and Figure 2shows that the FVC and FEV parameters of males have significant differences in cases and controls, the mean of FVC in cases (3.8±0.6) decreased significantly compared to the control mean (4.2±0.6), while the FEV/FVC ratio have no significant difference between two groups (p= 0.7). In females, The FEV parameters decrease significantly in cases mean (2.2±0.4) than in control (2.6±0.4). However,

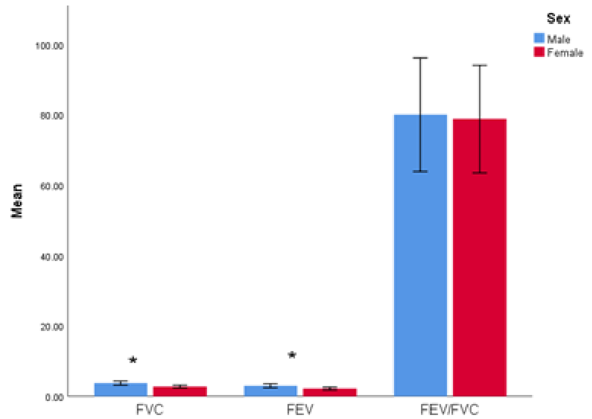

Figure 2: Lung function parameters in male and female, *Mean of FVC and FEV increase significantly in male than in female

there is no significant decrease in FVC and FEV/FVC mean in cases (2.8±0.4, 78.8±15.3) and control (3.1±0.6, 82.3±8.8) respectively.

4. Discussion

Regarding long-term sequelae in patients affected with COVID-19 infection, many questions were raised by the COVID-19 pandemic. We studied the long-term effects of post-COVID-19 syndrome on pulmonary function test parameters of post-hospital discharge when compared to control. We discovered that the post-COVID-19 groups' spirometry data, including the means of FVC and FEV1, were significantly lower than those of the controls. However, the FEV1/FVC ratio had no significant differences between the groups.

According to our research, the post-COVID-19 group had reduced lung function as determined by spirometry as compared to the control group. Our results were supported by the previous studies showing a significant decrease in post-COVID-19 spirometric parameters (FVC and FEV1) compared to controls after three to six months of recovery [20], [21]. An increase in FEV1/FVC values (although not statistically significant, (p = 0.4) despite decreased FEV1

Age group (Years)	Lung function test	Cases (n=66) Mean ±SD	Controls(n=67) Mean ±SD	P value
18-29	FVC	3.1±0.8	4.02±0.7	0.0001
	FEV	2.4±0.7	3.5±0.6	0.0001
	FEV/FVC	78.4±16.3	84.3±10.4	0.2
30-39	FVC	3.7±0.5	3.5±0.9	0.4
	FEV	3.2±0.5	2.9±0.7	0.2
	FEV/FVC	85.4±14	81.2±8.03	0.2
40-49	FVC	3.3±0.7	3.6±0.7	0.4
	FEV	2.6±0.7	2.9±0.5	0.3
	FEV/FVC	77.6±14.8	79.4±8.9	0.8
50-65	FVC	3.9±0.6	4.1±0.9	0.6
	FEV	2.9±0.6	3.3±0.7	0.2
	FEV/FVC	73.8±17.6	77.9±6.8	0.5

Table 3: Comparison of the lung function tests in cases and control across different age groups (years)

Sex	Lung function test	Cases (n=66) mean±SD	Controls(n=67) mean±SD	P value
Male	FVC	3.8±0.6	4.2±0.6	0.007
	FEV	3.05±0.6	3.6±0.6	0.0001
	FEV/FVC	80.1±16.1	8101±9.2	0.7
Female	FVC	2.8±0.4	3.1±0.6	0.06
	FEV	2.2±0.4	2.6±0.4	0.002
	FEV/FVC	78.8±15.3	82.3±8.8	0.3

Table 4: Lung function parameters for males and females in cases and control

and FVC indicated that patients with COVID-19 may develop a restrictive form of lung disease. In comparison to the control group, a greater percentage of restrictive lung impairment was found in the post-COVID-19 group. These results have also been noted in previous research with a one-year follow-up [22]. Another study shows results different from ours, FEV1 exhibited a non-significant decrease, while FVC significantly reduced with disease severity ($p < 0.001$), and FEV1/FVC ratio increased with disease severity ($p = 0.033$), one-year follow-up shows a non-significant change in FVC, FEV1, FEV1/FVC ratio, compared with the 40-day measurement [23]. The group with severe/critical disease severity showed a continuous improvement in pulmonary function throughout a 12-month follow-up. After the first 12 months for each person, the improvement in pulmonary function started to decline in the group with moderate disease severity. In mild and moderate illness severities, this waning is probably due to less involvement of the lower respiratory tract and, thus, less damage to the lung parenchyma during the acute phase of the disease [24]. In hospitalized patients, Zhang et al. found a similar improvement in pulmonary function up to a year after disease onset [25]. According to the results of two studies on changes in lung function following SARS infection, the PFTs showed an improvement in the first year following discharge and a tendency of declining lung function from the one-year to the two-year follow-up [26]. It has been discovered that pulmonary fibrosis can last for months or even years following COVID-19 infection.

Following 3 years of a long COVID-19 infection, we observed in spirometric results that a percentage of participants still had restrictive lung function. This finding may be related to persistent radiological abnormalities that are consistent with pulmonary fibrosis [27], [28]. We were unable to determine the exact percentage of people in our study who had pulmonary fibrosis because we did not conduct a CT scan following recovery from an acute illness.

This current study demonstrates that several clinical and epidemiologic risk factors have been linked to an increased chance of developing post-COVID respiratory conditions. In particular, there were differences in lung function parameters between males, females, and different age groups in cases and control. However, our results indicated that FEV and FVC increased significantly in post-COVID males than females.

A previous observational study by Bursac, D. Petridis, D., highlighted that male sex was significantly associated with persistent COVID-19 symptoms [29]. These findings strengthen our results regarding the association of male sex with post-COVID conditions. The results of radiography and laboratory testing are linked to respiratory functions, and males are more affected than females. Consequently, this study implies that after COVID-19, sex has little effect on lung health. Short- and long-term COVID-19 illness symptoms have been linked to differences in sex hormones between men and women. For instance, it is well recognized that the male sex poses a significant risk for both mortality and severe acute illness. On the other hand, premenopausal women have been shown to exhibit lesser COVID-19 illness during the acute phase, which may indicate that female hormones are providing protection. As a result of this protection, Women would also have a lower chance of developing lung function impairments. However, female sex hormones have been suggested to partly be involved in the persistent symptoms seen in PACS [30].

The spirometric result shows no significant differences between the nonsevere and severe groups, younger patients exhibited considerably higher FEV1/FVC and significantly lower FEV1% and FVC% pred compared to older age groups [31]. These results support our study, the FVC mean is significantly lower for the age group 18-29 years than for 30-39 and 50-65 years, and the mean FEV is significantly lower for the age group 18-29 years than 30-39. Furthermore, as predicted with previous studies, we demonstrated that abnormal pulmonary function was mainly manifested in patients older than 50 years old because lung function naturally declines with aging, as evidenced by reductions in muscle strength and lung tissue's elasticity and function [32].

There are limitations in our study. First, the lack of a baseline of PFT data before the infection makes it difficult to compare with the results post-infection. The analysis of the effect of COVID-19 on lung function is still correct. Second, In this investigation, we did not perform CT images nor examine the relationship between them and the lung function parameter. This study only examined spirometric tests (FVC, FVE1, and FEV1/FVC Ratio). DLCO was not measured. Longer follow-up on COVID-19 patients should be made to determine the long-term dynamic variation of lung function following COVID-19 exposure. Additionally, more comorbid conditions can be compared, as well as new COVID variants, the study area can be expanded, and the sample size can be increased. Finally, additional contextual considerations may also be taken into account.

5. Conclusion

According to the study's findings, every post-COPD patient had differences in their various lung functions. While the BMI and FEV1/FVC values do not significantly differ among the group, the study suggests that there is a significant difference between age, gender, FVC, and FEV1. Long-term investigations are required to address whether these deficiencies are persistent. Pulmonary function tests should be performed in routine clinical follow-up for the detection of long-term sequelae of post-COVID-19 syndrome.

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Conflict of interest

The authors declare no conflict of interests. All authors read and approved final version of the paper.

Authors Contribution

All authors contributed equally in this paper.

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