Post Covid-19 Dyspnea

Asmaa Abdou Atta Mohamed*[a], Alaa Rashad Mahmoud[a], Eptehal Mohammed Dongol[a], Haggagy Mansour Mohamed[a]

[a]Chest diseases and tuberculosis Department, Faculty of Medicine, South Valley University, Qena, Egypt

Abstract

Background: Post-COVID-19 dyspnea is a complex condition characterized by persistent and distressing shortness of breath after recovery from acute COVID-19 infection.

Objectives: This study aims to identify the possible causes and key factors contributing to post-COVID-19 dyspnea.

Patients and methods: A cross sectional study was done at Qena University Hospital including 100 patients with post-COVID-19 dyspnea. The patient demographic data, ABG, CBC, 6MWT, spirometry, ECG, echocardiography and CT results were collected. Ct was done was done at acute COVID-19 phase, after 3 months and after 6 months.

Results: The mean age of the study cohort was (60.06 years). Interstitial lung disease (51%) and ischemic heart disease (20%) were the main causes. Positive correlations were found between the dyspnea grade using mMRC and both ECG abnormalities, EF, CRP, TLC, lung abnormalities (bilateral ground glass opacities, CORAD IV), and interstitial pattern (diffuse intestinal thickening, honey combing), While there were negative correlations were seen with LVEDD, and serum Vit D.

Conclusion: This study sheds light on the complexity of post-COVID-19 dyspnea, emphasizing the need for a multidisciplinary approach in the effective management of this condition.

Keywords: COVID-19; Dyspnea; Lung; CT chest.

DOI: 10.21608/SVUIJM.2023.230808.1663

***Correspondence**: asmaaabdou12101993@gmail.com

Received: 1 August,2023.

Revised: 27 August,2023.

Accepted: 4 September,2023.

Published: 17 August, 2024

Cite this article as: Asmaa Abdou Atta Mohamed, Alaa Rashad Mahmoud, Eptehal Mohammed Dongol, Haggagy Mansour Mohamed.(2024). Post Covid-19 Dyspnea. *SVU-International Journal of Medical Sciences*. Vol.7, Issue 2, pp: 409-418.

Introduction

The "Post Coronavirus Disease-19 Syndrome" is observed in individuals who have a history of probable or confirmed SARS-CoV-2 infection, typically occurring about 3 months after the onset of COVID-19 symptoms and lasting for at least 2 months **(Pierce et al., 2022).**

Post-COVID-19 dyspnea is a complex condition characterized by persistent and distressing shortness of breath after recovery from acute COVID-19 contagion. Its diverse manifestations, including chest tightness and limited exercise tolerance, significantly impact patients' quality of life **(Harenwall et al., 2022).** The underlying causes involve inflammation, lung injury, fibrosis, and microvascular issues, necessitating a comprehensive understanding. Certain risk factors, such as age, pre-existing respiratory conditions, and the severity of the acute infection, contribute to vulnerability **(Yong et al., 2022).**

Chest computed tomography (CT) is essential in the COVID-19 post-recovery period. Fibrotic lung disease, a recognized sequela of COVID-19 infection, must be ruled out **(Parry et al., 2021).** The frequency of this consequence is likely to grow as the number of current patients rises with fresh waves of contagion, making chest CT a critical diagnostic tool **(Honarmandpour et al., 2022).**

The aim of this study is to identify the possible causes and key factors that contribute to post COVID-19 dyspnea.

Patients and methods

The research is a cross sectional study undertaken at Qena University Hospital's Department of Chest Diseases and Tuberculosis. The research included 100 patients who had post-COVID-19 dyspnea and met the following inclusion criteria: age over 18 years, proven COVID-19 infection through positive PCR test with at least 3 months after the beginning of COVID-19 symptoms, and symptom persistence. We excluded patients with specific respiratory illnesses and cardiovascular disorders.

All the patients were subjected to:

- **Full history taking** including age, gender, and BMI, smoking status. as well as comorbidities including diabetes, hypertension, asthma, COPD, and cardiovascular illnesses.
- **Assessment of dyspnea**
  The Modified Medical Research Council Dyspnea Scale was used to determine the severity of the dyspnea.
- **Physical examination** including pallor, cyanosis, jaundice, and lymph node enlargement.
- **Vital data** (blood pressure, temperature, heart rate, respiration rate).
- **Several diagnostic tests** were used in the research to assess the participants' health. ABG. ABG was performed using ABL800 FLEX blood gas analyzer, Denmark. Oximetry was used to determine resting oxygen saturation.
- **Spirometry** (PO Box6, Rochester from Micro Medical Limited - England) was employed to examine lung function including FEV1 (Forced Expiratory Volume in 1 second) and FVC (Forced Vital Capacity).
- **ECG (Electrocardiogram) and echocardiography** were used to check cardiac health. ECGs were taken at several stages during the procedure, including diagnosis, evaluation, and follow-up as required. Echocardiography: the measured parameters including: Ejection fraction (EF), interventricular septal defect (IVSD), left ventricular end-diastolic

diameter (LVEDD), pulmonary artery systolic pressure (PASP), tricuspid regurgitation (TR), and dilated cardiomyopathy (DD) grading.

- **Laboratory investigations:** including complete blood count (CBC), the inflammatory marker (C-reactive protein), and serum Vitamin D levels were all tested in the lab. CRP levels were determined by turbidimetric analysis. Commercial ELIZA kits were used to determine serum Vitamin D levels.

HRCT: CT chest evaluations were conducted utilizing a GE 1835CT01 machine, USA, employing multi-detector computed tomography technology with a 4-slice CT scanner. These chest CT examinations were carried out using 128 slice spiral CT scanners, positioning patients in a head-first supine orientation. The scanned region spanned from the superior thoracic aperture to the lung base, and specific scanning parameters included a tube voltage of 120 kV, automatic tube current, a layer thickness of 2 mm, interlamellar spacing of 1 mm, and a matrix size of 512×512. Ct was done was done at acute COVID-19 phase, after 3 months and after 6 months.

Ethical Consideration: SVU-MED-CHT019-1-22-2-338

Statistical analysis

IBM SPSS version 21(Statistical Package for Social Science) software program (SPSS Inc., Chicago, IL) was used to input and analyze the data. Qualitative descriptive statistics used numbers and percentages. Person correlation was used for data association.

Results

This study included 100 cases with their mean age of the patients was 60.06 years 75% of them were female. The mean BMI was 33.01±5.96 kg/m2. Diabetes mellitus was present the most prevalent comorbidity in our cohort (54% of cases). Regarding the dyspnea grading, the majority of the cases were classified as Grade III (51%) while, 36% were categorized as Grade IV.

The demographic and baseline characteristics were shown in (**Table.1**).

Table 1. Demographic and the basal characteristics of the study population

Variables	(N = 100)
Age (Years)	60.06 ± 15
Sex	
• Male	25 (25%)
• Female	75 (75%)
BMI (Kg/m^2)	33.01 ± 5.96
Active Smokers	17 (17%)
Comorbidities	
• DM	54 (54%)
• HTN	41 (41%)
Causes of Post COVID Dyspnea	
• Fibrosis	51 (51%)
• IHD	20 (20%)
• Others	29 (29%)
Grade of dyspnea grade at the presentation	
• I	5 (5%)
• II	8 (8%)

• III	51 (51%)
• IV	36 (36%)

BMI: Basal Metabolic Index, HTN: Hypertension, DM: Diabetes Mellitus.

ABG and Lab data of included subjects was shown in (**Table .2).**

Table 2. ABG and Lab data of the study cohort

Variables	**(N = 100)**
ABG	
PH	7.47 ± 0.13
PCO2 (mmHg)	33.96 ± 7.08
PO2 (mmHg)	66.26 ± 18.52
SO2 (%)	88.14 ± 8.52
Laboratory data	
CRP (mg/L)	42.26 ± 45.93
TLC (*10^3Cells/ µL)	9.98 ± 4.02
Hb (g/dl)	12.56 ± 2.14
PLT (*10^3Cells/ µL)	258.12 ± 119.34
RBCs (*10^6Cells/ µL)	4.38 ± 0.71
Serum Vit. D (ng/ml)	20.01 ± 7.26
6MWT	
Distance (m)	182.78 ± 72.47
Termination (m)	9.75 ± 4.33
Pause (Number)	2.62 ± 1.41
Respiratory assessment	
Resting Saturation (%)	87.94 ± 8.27
FVC (L)	1.93 ± 0.86
FV1 (L)	1.69 ± 0.75
FEV1/FVC	88.68 ± 10.54
Cardiac assessment	
ECG	
Inverted T wave	21 (21%)
Sinus Tachycardia	28 (28%)
ST depression	8 (8%)
Echocardiography	
EF (%)	62.62 ± 11.02
IVSD (Cm)	1.1 ± 0.47
LVEDD (Cm)	4.5 ± 0.87
PASP (mmHg)	33.83 ± 10.97
TR detection	66 (66%)
TR Degree	
Mild	42 (42%)
Moderate	16 (16%)
Severe	8 (8%)
DD Grade	

0	25 (25%)
1	47 (47%)
2	28 (28%)

PCO2 (partial pressure of carbon dioxide), PO2 (partial pressure of oxygen), SO2 (oxygen saturation), TLC (total leukocyte count), Hb (hemoglobin), Plt (platelet count), RBCs (red blood cells), EF (ejection fraction), IVSD (interventricular septal thickness in diastole), LVEDD (left ventricular end-diastolic dimension), PASP (pulmonary artery systolic pressure), TR: Tricuspid Regurgitation, DD: Diastolic Dysfunction.

CT chest Findings was shown in (**Table .3).**

Table 3. CT chest Findings

Variables	(N = 100)
At time of Acute COVID-19 attack	
➢ Normal	6 (6%)
➢ Bilateral ground glass opacities	80 (80%)
➢ Bilateral ground glass opacities and consolidation	14 (14%)
➢ CORAD Grade	
• CORAD III	72 (72%)
• CORAD IV	22 (22%)
At time of assessment	
• Diffuse intestinal thickening	40 (40%)
• Diffuse intestinal thickening and Honey combing	3 (3%)
• Honey combing	51 (51%)
• Normal	6 (6%)
Follow up	
• Normal	62 (62%)
• Diffuse interstitial thickening	18 (18%)
• Honey combing	20 (20%)

(Table .4) illustrated that there were a considerable positive correlation between the dyspnea severity using mMRC and both (6MWT Termination, 6MWT Pause, Inverted T wave, ST Depression, EF, TLC, HB, RBCs, CRP, Bilateral ground glass opacities , CORAD IV at the time of the acute COVID-19, Diffuse intestinal thickening at time of assessment, honey combing the time of assessment and honey combing at follow up while there were negative correlation between the dysnea severity grading with both PO2, SO2, resting saturation, serum vitamin D, 6MWT distance and LVEDD ($p < 0.05$).

Table 4. Correlation between the dyspnea severity and the patient parameters

Variables	**Dyspnea Grade**	
	r	P. Value
ABG		
• PH	0.10452	0.30072
• PCO2	0.04017	0.69149
• PO2	-0.674	0.0001
• SO2	-.0697	0.0001
6MWT		

• Distance	-0.352	0.00033
• Termination	0.362	0.00021
• Pause	0.375	0.00012
• Resting Saturation	-0.610	0.0001
Spirometry		
• FVC1	-0.07107	0.48227
• FV1	-0.07075	0.48423
ECG		
• Inverted T wave	0.259	0.0093
• Sinus Tachycardia	0.08457	0.40281
• ST Depression	0.310	0.00168
Echocardiography		
• EF	0.206	0.03996
• IVSD	0.04645	0.64633
• LVEDD	-0.336	0.00062
• PASP	0.013	0.89784
• TR detection	0.00325	0.9744
• Mild	0.11541	0.25287
• Moderate	0.03919	0.69864
• Severe	-0.257	0.00977
• DD Grade		
• Grade 0	-0.19258	0.05491
• Grade 1	0.09099	0.36793
• Grade 2	0.08457	0.40281
Laboratory parameters		
• TLC	0.205	0.04048
• HB	0.528	0.0001
• PLT	-0.18669	0.06291
• RBCs	0.380	0.0001
• Serum Vitamin D	-0.477	0.0001
• CRP	0.255	0.01047
CT Findings		
• **At time of Acute COVID-19 attack**		
• Normal	-0.653	0.0001
• Bilateral ground glass opacities	0.244	0.015
• Bilateral ground glass opacities and consolidation	0.166	0.98
• CORAD		
• CORAD III	-0.17029	0.09028
• CORAD IV	0.559	0.0001
• **At time of assessment**		
• Diffuse intestinal thickening	0.293	0.00306
• Diffuse intestinal thickening and Honey combing	0.185	0.06537

• Honey combing	0.534	0.0001
• Normal	-0.653	0.0001
• **Follow up**		
• Normal	-0.13638	0.17606
• Diffuse interstitial thickening	-0.17498	0.08164
• Honey combing	0.334	0.0007

EF (ejection fraction), IVSD (interventricular septal thickness in diastole), LVEDD (left ventricular end-diastolic dimension), PASP (pulmonary artery systolic pressure), TR: Tricuspid Regurgitation, DD: Diastolic Dysfunction, TLC (total leukocyte count), HB (hemoglobin), PLT (platelet count), RBC (red blood cells).r: Pearson Correlation

The causes of Post COVID Dyspnea causes were illustrated in **(Fig.1).**

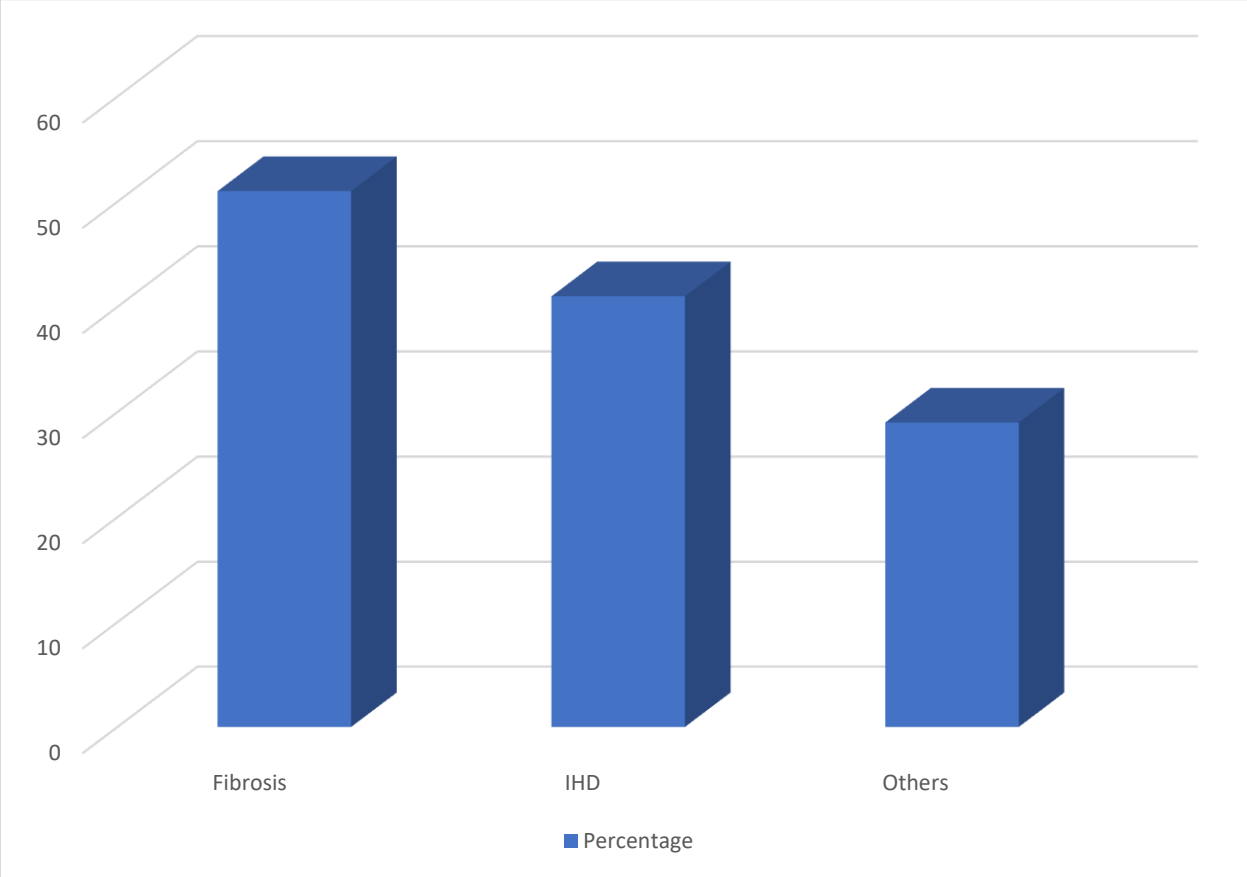

Fig.1. Causes of post COVID-19 dyspnea causes among the study cohort

Discussion

This study included 100 cases with their mean age of the patients was 60.06 years 75% of them were female. The mean BMI was 33.01±5.96 kg/m2. Diabetes mellitus was present the most prevalent comorbidity in our cohort (54% of cases). The greater prevalence in older individuals may stem from weakened immune systems and pre-existing conditions. Hormonal and immunological differences, as well as ACE2 receptor expression, may contribute to the higher proportion of females experiencing post-COVID dyspnea. Behavioral and social factors could also play a role, with women potentially seeking medical attention earlier

(Menges et al., 2021; Sathyamurthy et al., 2021).

In accordance with our study, **Carfì et al. (2020),** studied 143 post-COVID-19 patients, with a slightly younger average age, comprising 90 males and 53 females, and a similar proportion of females. However, they reported a higher incidence of comorbidities. Additionally, **Goërtz et al. (2020)** considered a larger cohort of 2113 patients, with a significantly younger average age (47 years) and a higher representation of females (1803), though specific comorbidity data were not provided.

Our study disclosed that post-COVID dyspnea predominantly resulted from interstitial pulmonary fibrosis (51% of cases), emphasizing the significant role of lung involvement in respiratory symptoms post-recovery. Ischemic heart disease (IHD) accounted for 20% of cases, while 29% had other contributing causes including vitamin D deficiency and psychological elements. Most patients experienced moderate-to-severe dyspnea, with 51% classified as Grade III and 36% as Grade IV, highlighting the substantial burden of dyspnea on daily activities and overall well-being. The fibrosis prevalence may be due to severe lung damage and scarring from the immune response to SARS-CoV-2, influenced by infection severity, immune responses, comorbidities, and genetic factors. Pre-existing lung conditions like asthma or COPD may increase vulnerability to post-COVID fibrosis and dyspnea **(Antony et al., 2023; Bugra et al., 2022).**

In accordance with our study, **Beaudry et al., (2022)** disclosed that post Covid 19 dyspnea was associated with obstructive and restrictive lung disease, heart failure (HF) and pulmonary hypertension, they concluded that dyspnea is attributed to; impaired gas exchange, dynamic hyperinflation (early critical tidal volume mechanical constraint), and/or elevated pulmonary vascular pressures. Similarly, **McGroder et al., (2021)**, conducted their studies on 76 COVID-19 patients with dyspnea. The most common radiographic abnormality was fibrosis with patterns of ground glass opacities (43%), followed by reticulations (39%) and traction bronchiectasis (28%). Fibrotic-like patterns were more common in those who were mechanically ventilated compared with those who were not (72% vs 20%, p=0.001). In contrary to our study, **Scaramuzzo et al., (2022)** stated that cardiopulmonary testing does not show significant alterations in COVID-19 patients with dyspnea.

In this study, there were a considerable positive correlation between the dyspnea severity using mMRC and both (6MWT Termination, 6MWT Pause, Inverted T wave, ST Depression, EF, TLC, HB, RBCs, CRP, Bilateral ground glass opacities , CORAD IV at the time of the acute COVID-19, Diffuse intestinal thickening at time of assessment, honey combing the time of assessment and honey combing at follow up while there were negative correlation between the dysnea severity grading with both PO2, SO2, resting saturation, serum vitamin D, 6MWT distance and LVEDD ($p < 0.05$).

In harmony with this study, **Grewal et al., (2023), summarized that** patients with dyspnea had a lower percent-predicted 6-min walk distance (91±15% vs 102±16%; p=0.01) compared to patients without dyspnea. Furthermore, the most common PFT abnormality in dyspneic patients was a decreased DLCO, which was present in 16 patients (46% of those with dyspnea).

However, our study had limitations including its small sample size, it is a single center study.

Conclusion

Our study reveals that post-COVID-19 dyspnea stems from multiple factors, predominantly lung fibrosis and ischemic

heart disease. Assessments such as ABG, 6MWT, and respiratory evaluations suggest potential respiratory issues and inflammation, while cardiac assessments identify ECG abnormalities and cardiac involvement. CT chest findings underscore lung involvement and fibrosis. This study sheds light on the complexity of post-COVID-19 dyspnea, emphasizing the need for a multidisciplinary approach in the effective management of this condition.

References

- **Antony T, Acharya KV, Unnikrishnan B, & Keerthi NS (2023).** A silent march-Post covid fibrosis in asymptomatics–A cause for concern?. Indian Journal of Tuberculosis, 70(2): 249-252.
- **Beaudry RI, Brotto AR, Varughese RA, de Waal S, Fuhr DP, Damant RW, et al (2022).** Persistent dyspnea after COVID-19 is not related to cardiopulmonary impairment; a cross-sectional study of persistently dyspneic COVID-19, non-dyspneic COVID-19 and controls. Frontiers in Physiology, 13(1): e917886.
- **Bugra KERGET, Gizem CIL, Omer ARAZ, Fatih ALPER, Metin AKGUN (2022).** When and how important is anti-fibrotic therapy in the post-COVID-19 period?. Bratislava Medical Journal/Bratislavske Lekarske Listy, 123(9).
- **Carfì A, Bernabei R, Landi F (2020).** Persistent symptoms in patients after acute COVID-19. Jama, 324(6): 603-605.
- **Goërtz YM, Van Herck M, Delbressine JM, Vaes AW, Meys R, Machado FV et al (2020).** Persistent symptoms 3 months after a SARS-CoV-2 infection: the post-COVID-19 syndrome?. ERJ open research, 6(4).
- **Grewal JS, Carlsten C, Johnston JC, Shah AS, Wong AW, Ryerson CJ (2023).** Post-COVID dyspnea: prevalence, predictors, and outcomes in a longitudinal, prospective cohort. BMC Pulmonary Medicine, 23(1): 1-9.
- **Harenwall S, Heywood-Everett S, Henderson R, Smith J, McEnery R, Bland AR et al (2022).** the interactive effects of post-traumatic stress symptoms and breathlessness on fatigue severity in post-COVID-19 syndrome. Journal of Clinical Medicine, 11(20): e6214.
- **Honarmandpour F, Jahangirimehr A, Tahmasbi M, Khalighi A, Honarmandpour A (2022).** Follow-up the severity of abnormalities diagnosed in chest CT imaging of COVID-19 patients: A cross-sectional study. Health Science Reports, 5(5): e818.
- **McGroder, C. F., Zhang, D., Choudhury, M. A., Salvatore, M. M., D'Souza, B. M., Hoffman, E. A., et al. (2021).** Pulmonary fibrosis 4 months after COVID-19 is associated with severity of illness and blood leucocyte telomere length. Thorax, 76(12): 1242-1245.
- **Menges D, Ballouz T, Anagnostopoulos A, Aschmann HE, Domenghino A, Fehr JS et al (2021).** Burden of post-COVID-19 syndrome and implications for healthcare service planning: A population-based cohort study. PloS one, 16(7): e0254523.
- **Parry AH, Wani AH, Shah NN, Jehangir M (2021).** Medium-term chest computed tomography (CT) follow-up of COVID-19 pneumonia patients after recovery to assess the rate of resolution and determine the potential predictors of persistent lung changes. Egyptian Journal of Radiology and Nuclear Medicine, 52(1): 1-9.

- **Pierce JD, Shen Q, Cintron SA, Hiebert JB (2022).** Post-COVID-19 syndrome. *Nursing research*, *71*(2): 164-174.
- **Sathyamurthy P, Madhavan S, Pandurangan V (2021).** Prevalence, pattern and functional outcome of post COVID-19 syndrome in older adults. Cureus, 13(8).
- **Scaramuzzo G, Ronzoni L, Campo G, Priani P, Arena C, La Rosa Rvet al (2022).** Long-term dyspnea, regional ventilation distribution and peripheral lung function in COVID-19 survivors: a 1 year follow up study. BMC Pulmonary Medicine, 22(1): 408.
- **Yong SJ (2021).** Long COVID or post-COVID-19 syndrome: putative pathophysiology, risk factors, and treatments. Infectious diseases, 53(10): 737-754.