

## Original Research Article

# **The Diagnostic and Prognostic Role of Non-Contrast Chest CT in COVID-19 Primary Infected Patients**

### **Abstract**

**Background:** Chest computed tomography (CT) has shown to have a significant role to help in diagnosis of coronavirus disease 2019 (COVID-19) also assessing the disease progression and monitoring the response to treatments since it is less expensive, readily accessible, safe and saves time. This research objects to evaluate the diagnostic and prognostic role of non-contrast chest CT in COVID-19 primary infected patients. This prospective research involved 100 COVID-19 infected patients as proven by polymerase Chain Reaction (63 females and 37 males). Initial and follow up CT scans were performed.

**Results:** There was a positive significant correlation between CT severity score and diabetes mellitus, malignancy, and other immune-compromised disease. There was a positive significant correlation between CT severity score and age ( $r=0.830$ ,  $p<0.001$ ) and smoking ( $r=0.231$ ,  $p=0.020$ ). Age, smoking and CT severity score were significant predictors for incidence of fibrotic changes.

**Conclusion:** This study confirmed the great significance of chest CT for the differentiation between pulmonary changes occurred during infection and follow up and predict the risk factors that can affect the prognosis of the disease.

**Keywords:** Diagnostic, Prognostic, Non-Contrast Chest CT, COVID-19, Primary Infected Patients

### **Introduction:**

In December of 2019, a highly contagious illness caused severe respiratory distress syndrome in Wuhan, China. It was subsequently determined that the condition was caused by a new coronavirus. On March 11, 2020, the World Health Organization designated the illness Coronavirus disease 2019 (COVID-19) and proclaimed it a pandemic. In the weeks that followed, the illness swiftly spread throughout the majority of the world's nations, generating a worldwide health crisis. As of April 14, 2020, the overall number of cases has surpassed 1.8 million, with over 110 thousand fatalities<sup>[1]</sup>.

Chest computed tomography (CT) has shown to have a significant role to help in diagnosis of this deadly disease also assessing the disease progression and monitoring the response to treatment as it is less expensive, readily accessible, safe and saves time<sup>[2]</sup>.

Various investigations have documented a broad range of CT results associated with COVID-19. It is including bilateral multifocal patchy areas of ground glass opacities (GGO), consolidation with air bronchogram, crazy pavement appearance that mostly present sub pleural and predominantly involving the lower lung lobes and posterior segments & other different signs that vary depending to illness stage, disease severity, and related comorbidities<sup>[3]</sup>.

COVID-19 is yet to reveal its long-term effects. According to studies, some individuals with viral lung infections caused by COVID-19 exhibit symptoms of overall improvement after recovery<sup>[5]</sup>. In other cases, they show irreversible pulmonary dysfunction and demonstrate residual imaging include worsening GGOs or consolidations, fibrotic band formation, and organizing pneumonia<sup>[6]</sup>.

This research objects to evaluate the diagnostic and prognostic role of Non Contrast chest CT in COVID19 primary infected patients

### **Patients and Methods:**

This prospective research involved 100 COVID-19 infected patients as proven by Polymerase Chain Reaction (PCR) (63 females and 37 males) who were referred to Radio-diagnosis and Medical Imaging Department at the local institution. Their ages ranged from 27 to 75 years old. Initial and follow up CT scans were performed. Lung changes and CT extent scores were recorded from March 2021 to May 2022. This research was conducted after the approval of the institutional ethical committee. Informed written consent was obtained from all patients.

We included moderate to severe cases of COVID-19 that tested positive by PCR. (Patients were categorized according to Ministry of Health and Population protocol definition of moderate and severe cases. Moderate cases have COVID pneumonia manifestations on chest CT associated with clinical symptoms &/Or leucopenia or lymphopenia. Severe cases have increased respiratory rate, decreased Oxygen saturation % in room air and more progressive chest CT findings), Patients who have significant travel history or have close contact with person who has infected by COVID-19.

Exclusion criteria were pregnant females, patients less than 18 years and who refuse undergo chest CT.

All subjects underwent complete history taking include:

Personal history: as regards the name, age and gender, residence and phone number, Clinical data for any complain as (fever, cough, dyspnea, sore throat, fatigue, loss of smell and taste, abdominal pain, nausea, vomiting, diarrhea, body aches, headache, runny nose, skin rash, redness of the eye), history of any comorbidities such as systemic hypertension, diabetes mellitus, tobacco smoke and others.

**Clinical examination and evaluating vital signs such** as heart rate, respiratory rate, body temperature, blood pressure and oxygen saturation in room air. **Laboratory investigations including:** Hemoglobin level (Hb), Hematocrit level (HCT), white blood cells count (WBCs

count), lymphocyte count, platelet count, C-reactive protein (CRP), D-dimer, aspartate transaminase (AST) and alanine transaminase (ALT) levels.

Non contrast Multi-Detector CT (MDCT) chest examination during infection and follow up CT scan after 3 months from symptoms' onset.

### **The Chest CT Examination:**

#### **The MDCT equipment**

MDCT was performed with a 128 Slice CT scanner (Optima CT660, GE healthcare) using 120 KV and slice thickness 5 mm. The non-enhanced chest CT was acquired from the thoracic inlet to the diaphragm. Acquisition will be achieved in the axial plane with coronal and sagittal reconstruction.

#### **MDCT imaging protocol**

- The examination is initially explained to the patient. The complete immobilization of the patient throughout the test is crucial.
- The patients were positioned in the supine, head-first posture.
- A single breath-hold scan is planned from the level of the lung apex to the end of both costophrenic angles.
- All patients underwent follow up non-contrast chest CT examinations after 3 months from symptoms onset with the same scanners used for initial CT scans.
- The CT images were evaluated for each Patient regarding lesion distribution and the presence of typical findings of COVID-19 pneumonia (sub pleural unilateral or bilateral GGO in the lower lobes with a peripheral or posterior distribution), presence of consolidation or other possible associated findings including interlobular septal thickening, crazy-paving pattern, air bronchogram sign, halo sign and others.

#### **Post processing:**

On a workstation, image reconstruction and alteration were conducted. Multiplanar reconstruction with axial, sagittal and coronal images were done in both mediastinal and lung windows. Nonetheless, examination of the axial source pictures remains a key component of the evaluation.

### **Chest CT severity score:**

Using a simple CT score, the degree of lung involvement in each patient was examined. Each lobe could receive a CT score ranging from 0 to 5 depending on the percentage of involvement, which was classified as score 0 (0% or none), score 1 (1-5% or minimal), score 2 (6-25% or mild), score 3 (26-49% or moderate), score 4 (50-75% or severe), and score 5 (greater than 75% or extensive). The total CT score for the five lobes was the sum of the individual lobar values and ranged from 0 (no involvement) to 25 (severe involvement) (maximum involvement). Total CT Score less than 7 is considered mild COVID-19, score from 8 to 16 is considered moderate COVID-19 and score from 17 to 25 is considered severe COVID-19. It was necessary to examine both lungs as a whole in axial, coronal, and sagittal reconstruction planes in order to precisely estimate the extent of the affection.

### **Statistical analysis**

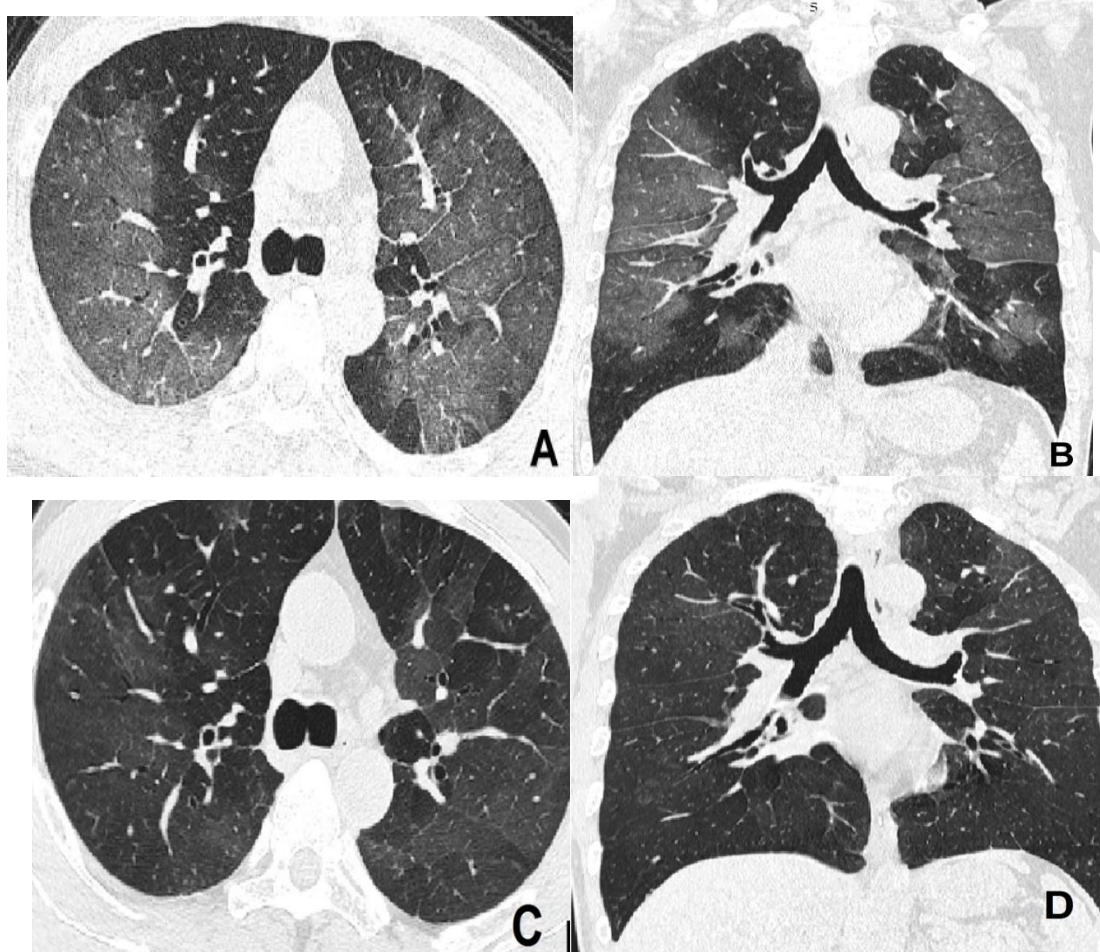
Statistical analysis was done by SPSS v28 (IBM Inc., Armonk, NY, USA). Quantitative variables were expressed as mean and standard deviation (SD). Qualitative variables were expressed as frequency and percentage and were analyzed utilizing the Chi-square test. Spearman coefficient to correlate between two normally distributed quantitative variables. Logistic regression is also used to estimate the relationship between a dependent variable and one or more independent variables.

### **Cases:**

#### **CASE 1:**

Clinical data: 43 years old male patient with coronavirus disease had no comorbidities.

Imaging findings: A, Axial and B, coronal chest CT images (lung window) obtained after the onset of symptoms show extensive GGO at both upper lung lobes. C, Axial and D, coronal scans obtained at follow up show marked regression of previously seen GGO. **Figure (1)**



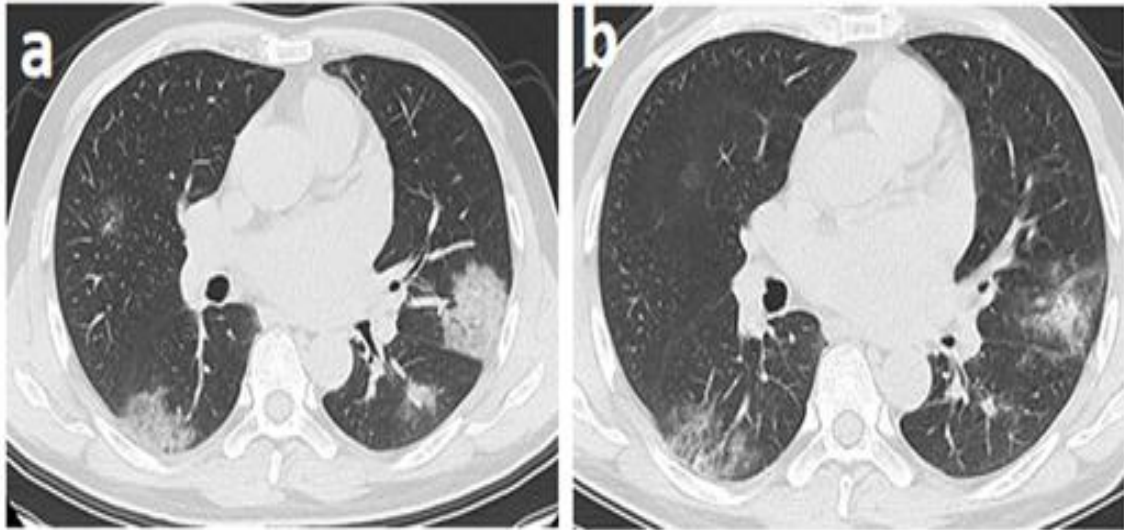
**Figure (1): A, C Axial and B, D coronal chest CT images (lung window).**

## Case 2

Clinical data: a 57 years old female patient with coronavirus disease and has history of malignancy.

Imaging findings: chest CT scans show (a) Axial image obtained after the symptom onset exhibits bilateral GGO and consolidation at lower lung lobes. (b) Axial image obtained after recovery show obvious regression of previously seen opacities with still seen small residuals.

**Figure (2)**



**Figure (2): (a and b) axial chest CT images (lung window).**

**Results:**

Baseline characteristics are presented at **Table 1**

Laboratory investigations are presented at **Table 2**

Lung involvement and Pattern of distribution of lung opacities in the studied patients **Table 3**

Main Chest findings and other associated chest CT during infection and chest CT score of the studied patients are presented at **Table 4**

There was a significant difference between severity of COVID-19 infection and comorbidities as diabetes mellitus (DM), malignancy, and other immunocompromised disease ( $P < 0.05$ ). There was an insignificant difference between severity of COVID-19 infection and hypertension. Most of cases of DM, malignancy, and other immunocompromised disease had Severe CT score while cases of hypertension had mild and moderate CT score. **Table 5**

There was a positive significant correlation between CT severity score and DM ( $r = 0.302$ ,  $P = 0.002$ ), malignancy ( $r = 0.251$ ,  $P = 0.012$ ), and other immune-compromised disease ( $r = 0.253$ ,  $P = 0.011$ ). There was a positive significant correlation between CT severity score and age ( $r = 0.830$ ,  $p < 0.001$ ) and smoking ( $r = 0.231$ ,  $p = 0.020$ ). **Table 6**

Regarding the chest CT findings of the studied patients at 3 month follow up scan, complete radiological resolution of previous opacification occurred in 39 (39%) patients, partial regression with residual opacifications occurred in 27 (27%) patients and fibrotic like changes occurred in 34 (34%) patients. **Table 7**

There was a significant relationship between fibrotic changes and age, smoking and CT severity score >17. Cases with old age >50 had fibrotic changes (85.3%) higher than younger age <50 (14.7%) (P<0.001). Smoker had fibrotic change (58.82%) higher than non-smoker (41.17%) (P<0.001). Cases with CT severity score >17 had fibrotic changes (70.58%) higher than cases with CT severity score<17(29.41%) (P<0.001). **Table 8**

Age, smoking and CT severity score were significant predictors for incidence of fibrotic changes (P<0.05). **Table 9**

#### **Discussion:**

This study aimed to evaluate the role of chest CT in COVID-19 primary infected cases during and after convalescence.

Female COVID-19 cases were more prevalent in our research than males; with 63% of the study patients were females and 37 % of the study patients were males. This was going with Nabahati et al. <sup>[10]</sup> who found that of 173 COVID-19 included patients, 57 (32.9%) were male and others were female.

Concerning comorbidities, among the studied patients, there were 26 (26%) patients had no comorbidities, 22(22%) patients were diabetic, 19 (19%) had malignancy, 17 (17%) had hypertension and 16 (16%) had other immune-compromised diseases (chronic kidney disease, collagen diseases). This was similar to Ding et al. <sup>[11]</sup> who reported that COVID-19 cases with chronic diseases as hypertension, diabetes, autoimmune diseases, chronic renal disease, and cancer were commonly found COVID-19 hospitalized patients.

Regarding clinical complain of the studied patients, 74 (74%) patients had fever, 60 (60%) patients had cough, 42 (42%) patients had dyspnea, 30 (30%) patients had sore throat, 17 (17%) patients had runny nose, 36 (36%) patients had smell and taste disorders, 38 (38%) patients had fatigue , 31 (31%) had muscle or body aches, 18 (18%) patients had headache , 20 (20%) patients had abdominal pain, 28 (28%) patients had diarrhea , 18 (18%) had nausea , 19 (19%) patients had vomiting, 6 (6%) patients had skin rash and 5 (5%) patients had redness of the eye. Our result is supported by Dawoud et al. study.<sup>[12]</sup>

This comes consistent with what was previously described that severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) shares symptoms with SARS-COV and Middle East respiratory syndrome (MERS), including fever, coughing, and shortness of breath<sup>[9, 13, 14]</sup>.

In this research, WBCs ranged from  $4.5 - 9.7 \times 10^3$  cells/ $\mu$ l with a mean of  $7.1 \pm 1.55 \times 10^3$  cells/ $\mu$ l, and lymphocytes ranged from  $0.8 - 3.5 \times 10^3$  cells/ $\mu$ l with a mean of  $2.1 \pm 0.78 \times 10^3$  cells/ $\mu$ l. This tendency towards relative lymphopenia was in congruence with Wu et al.<sup>[15]</sup>who found that pooled ORs of lymphopenia were significantly associated with hospitalization due to COVID.

In the context of the biochemical analysis, the current work demonstrated that CRP was increased in all cases, with a range of 10 – 45 mg/L and a mean of  $28.8 \pm 10.1$  mg/L. Several studies shown that CRP level may act as a predictor of illness severity<sup>[7, 14, 16]</sup>.

In our research, we also revealed that the hospitalized COVID-19 cases had high D-dimer levels with the levels ranged from 0.4 – 2  $\mu$ g/mL, and the mean was  $1.2 \pm 0.49$   $\mu$ g/mL. In accordance, Kaftan et al.<sup>[17]</sup>found that elevated D-dimer was associated with an increased hospitalization due to COVID-19.

The AST ranged from 19 – 54 U/L with a mean of  $34.97 \pm 9.87$  U/L, and the ALT ranged from 15 – 62 U/L with a mean of  $36.3 \pm 13.55$  U/L. Our result is similar to Dawoud et al.<sup>[12]</sup>study that showed that some COVID-19 patients had elevated AST and ALT levels.

In this work, we performed CT evaluation for the study patients, which showed that bilateral lung involvement occurred in 88 (88%) patients whereas unilateral lung involvement occurred in 12 (12%) patients. The pattern of distribution of lung opacities in studied patients was mainly sub pleural (52% of patients). Similar to Haseli et al. <sup>[18]</sup> study, our research showed that, Lower lobes of the lungs were affected more often.

Regarding the chest CT score for assessment of severity of pulmonary involvement, most of the patients had moderate disease (46%) or severe disease (36%). This high percentage is due to we recruited our sample from patients indicated hospitalization. Given the shortage of available beds during the pandemic, they were kept for the more severe cases. Similar to Teima et al. <sup>[19]</sup> study, our study showed that dyspnea, cough, fatigue and muscle or body ache were significantly elevated in severe cases.

In this research, GIT signs was significantly elevated in severe cases. The most common reported GIT symptom was diarrhea. Our result is strongly supported the study of Kumar et al. <sup>[20]</sup>.

In consistency with our findings, Bersanelli<sup>[22]</sup> reported that cancer is one of the most widespread and well-known illnesses that impair the immune system and increase disease severity. Concerning the chronic renal disease, Bigdelou et al. <sup>[23]</sup>, in their recent study stated that chronic kidney disease is associated with oxidative stress and elevated expression of ACE-2 and cytokines, including interleukin 6 (IL-6) and CRP.

The present study revealed that patients with severe disease by the CT severity score were significantly older in age. These findings go in consistency with several studies that demonstrated deteriorating results among ageing people<sup>[24-26]</sup>.

Regarding the chest CT findings of the studied patients at 3 month follow up scan, complete radiological resolution of previous opacification occurred in 39 (39%) patients, partial regression with residual opacifications occurred in 27 (27%) patients and fibrotic like

changes occurred in 34 (34%) patients. our findings are comparable with Solomon et al.<sup>[27]</sup> who described that More than fifty percent of previously hospitalized survivors of SARS-CoV-2 infection will exhibit abnormalities on CT, with parenchymal or subpleural bands, reticular abnormality, indications of fibrotic abnormality, and air trapping being the most prevalent.

Our study demonstrated that there was a significant relationship of the CT severity score, the patients' age, and smoking with the follow-up fibrotic changes. In line with these findings. Also, Nabahati et al.<sup>[10]</sup> found that elevated CT severity scores at admission were associated with elevated risk of fibrotic abnormalities observed at 3-month CT follow-up. Ali & Ghonimy<sup>[28]</sup> declared that older age, cigarette smoking, and elevated CT severity score were predictors of post COVID-19 fibrotic changes. Multiple studies indicate smoking to be a risk factor for lung fibrotic alterations after COVID-19 infection.<sup>[29-31]</sup> This is likely attributed to what has been proposed by Rai et al.<sup>[32]</sup> that Compared to nonsmokers, smokers are 1,4 times more likely to have severe COVID-19 symptoms and 2,4 times more likely to need intensive care unit admission and mechanical ventilation or die. Each of all these factors increases the risk for developing pulmonary fibrosis.

The same results for age, and CT severity score were observed in Han et al.<sup>[33]</sup> as well. Sansone et al.<sup>[34]</sup> who stated that following MERS and SARS-CoV 2, the risk of developing pulmonary fibrosis among the elderly is higher. Our research has limitations including the following: First, the interval between CT scans was just three months. To assess if fibrotic-like alterations are persistent, progressive, or reversible, patients with fibrotic-like changes need extended follow-up. Second, the lack of knowledge on pulmonary function testing.

**Conclusion:** This study confirmed the great significance of chest CT for the differentiation between pulmonary changes occurred during infection and follow up and predict the risk

factors that can affect the prognosis of the disease as well as identify the relation between severity of the infection and other associated clinical findings and comorbidities.

**List of Abbreviations:**

**ALT:** Alanine transaminase.

**AST:** Aspartate transaminase.

**COVID-19:** Coronavirus disease 2019.

**CRP:** C-reactive protein.

**CT:** Computed tomography.

**DM:** Diabetes mellitus.

**GGO:** Ground glass opacities.

**GIT:** Gastrointestinal tract.

**Hb:** Hemoglobin.

**HCT:** Hematocrit.

**IL-6:** Interleukin 6.

**MDCT:** Multi-Detector CT.

**MERS:** Middle East respiratory syndrome.

**PCR:** Polymerase Chain Reaction.

**SARS-CoV2:** Severe acute respiratory syndrome coronavirus 2.

**WBCs:** White blood cells.

**References:**

1. Hui DS, E IA, Madani TA, Ntoumi F, Kock R, Dar O, et al. (2020) The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health - The latest 2019 novel coronavirus outbreak in Wuhan, China. *Int J Infect Dis* 91:264-266. 10.1016/j.ijid.2020.01.009

2. Zhao W, Zhong Z, Xie X, Yu Q, Liu J (2020) Relation Between Chest CT Findings and Clinical Conditions of Coronavirus Disease (COVID-19) Pneumonia: A Multicenter Study. *AJR Am J Roentgenol* 214:1072-1077. 10.2214/ajr.20.22976
3. Kolta MF, Ghonimy MBI (2020) COVID-19 variant radiological findings with high lightening other coronavirus family (SARS and MERS) findings: radiological impact and findings spectrum of corona virus (COVID-19) with comparison to SARS and MERS. *Egyptian Journal of Radiology and Nuclear Medicine* 51:1-8.
4. He JL, Luo L, Luo ZD, Lyu JX, Ng MY, Shen XP, et al. (2020) Diagnostic performance between CT and initial real-time RT-PCR for clinically suspected 2019 coronavirus disease (COVID-19) patients outside Wuhan, China. *Respir Med* 168:105980. 10.1016/j.rmed.2020.105980
5. Shaw B, Daskareh M, Gholamrezanezhad A (2021) The lingering manifestations of COVID-19 during and after convalescence: update on long-term pulmonary consequences of coronavirus disease 2019 (COVID-19). *Radiol Med* 126:40-46. 10.1007/s11547-020-01295-8
6. Machnicki S, Patel D, Singh A, Talwar A, Mina B, Oks M, et al. (2021) The Usefulness of Chest CT Imaging in Patients With Suspected or Diagnosed COVID-19: A Review of Literature. *Chest* 160:652-670. 10.1016/j.chest.2021.04.004
7. Wang K, Kang S, Tian R, Zhang X, Zhang X, Wang Y (2020) Imaging manifestations and diagnostic value of chest CT of coronavirus disease 2019 (COVID-19) in the Xiaogan area. *Clin Radiol* 75:341-347. 10.1016/j.crad.2020.03.004
8. Canovi S, Besutti G, Bonelli E, Iotti V, Ottone M, Albertazzi L, et al. (2021) The association between clinical laboratory data and chest CT findings explains disease severity in a large Italian cohort of COVID-19 patients. *BMC Infect Dis* 21:157. 10.1186/s12879-021-05855-9

9. Shabrawishi M, Al-Gethamy MM, Naser AY, Ghazawi MA, Alsharif GF, Obaid EF, et al. (2020) Clinical, radiological and therapeutic characteristics of patients with COVID-19 in Saudi Arabia. *PLoS One* 15:e0237130. 10.1371/journal.pone.0237130
10. Nabahati M, Ebrahimpour S, Khaleghnejad Tabari R, Mehraeen R (2021) Post-COVID-19 pulmonary fibrosis and its predictive factors: a prospective study. *Egyptian Journal of Radiology and Nuclear Medicine* 52:1-7.
11. Ding L, She Q, Chen F, Chen Z, Jiang M, Huang H, et al. (2020) The Internet Hospital Plus Drug Delivery Platform for Health Management During the COVID-19 Pandemic: Observational Study. *J Med Internet Res* 22:e19678. 10.2196/19678
12. Dawoud MM, Dawoud TM, Ali NYA, Nagy HA (2020) Chest CT in COVID-19 pneumonia: a correlation of lung abnormalities with duration and severity of symptoms. *Egyptian Journal of Radiology and Nuclear Medicine* 51:1-12.
13. Livingston E, Bucher K (2020) Coronavirus Disease 2019 (COVID-19) in Italy. *Jama* 323:1335. 10.1001/jama.2020.4344
14. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. (2020) Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 395:507-513. 10.1016/s0140-6736(20)30211-7
15. Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, et al. (2020) A new coronavirus associated with human respiratory disease in China. *Nature* 579:265-269. 10.1038/s41586-020-2008-3
16. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. (2020) Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med* 382:1708-1720. 10.1056/NEJMoa2002032
17. Kaftan AN, Hussain MK, Algenabi AA, Naser FH, Enaya MA (2021) Predictive Value of C-reactive Protein, Lactate Dehydrogenase, Ferritin and D-dimer Levels in Diagnosing

COVID-19 Patients: a Retrospective Study. *Acta Inform Med* 29:45-50.  
10.5455/aim.2021.29.45-50

18. Haseli S, Khalili N, Bakhshayeshkaram M, Sanei Taheri M, Moharramzad Y (2020) Lobar Distribution of COVID-19 Pneumonia Based on Chest Computed Tomography Findings; A Retrospective Study. *Arch Acad Emerg Med* 8:e55.

19. Teima AAA, Amer AA, Mohammed LI, Kasemy ZA, Aloshari SH, Ahmed MM, et al. (2022) A cross-sectional study of gastrointestinal manifestations in COVID-19 Egyptian patients. *Ann Med Surg (Lond)* 74:103234. 10.1016/j.amsu.2021.103234

20. Kumar A, Arora A, Sharma P, Anikhindi SA, Bansal N, Singla V, et al. (2020) Gastrointestinal and hepatic manifestations of Corona Virus Disease-19 and their relationship to severe clinical course: A systematic review and meta-analysis. *Indian J Gastroenterol* 39:268-284. 10.1007/s12664-020-01058-3

21. Boettler T, Marjot T, Newsome PN, Mondelli MU, Maticic M, Cordero E, et al. (2020) Impact of COVID-19 on the care of patients with liver disease: EASL-ESCMID position paper after 6 months of the pandemic. *JHEP Rep* 2:100169. 10.1016/j.jhepr.2020.100169

22. Bersanelli M (2020) Controversies about COVID-19 and anticancer treatment with immune checkpoint inhibitors. *Immunotherapy* 12:269-273. 10.2217/imt-2020-0067

23. Bigdelou B, Sepand MR, Najafikhoshnoo S, Negrete JAT, Sharaf M, Ho JQ, et al. (2022) COVID-19 and Preexisting Comorbidities: Risks, Synergies, and Clinical Outcomes. *Front Immunol* 13:890517. 10.3389/fimmu.2022.890517

24. Mahase E (2020) Covid-19: death rate is 0.66% and increases with age, study estimates. *Bmj* 369:m1327. 10.1136/bmj.m1327

25. Verity R, Okell LC, Dorigatti I, Winskill P, Whittaker C, Imai N, et al. (2020) Estimates of the severity of coronavirus disease 2019: a model-based analysis. *Lancet Infect Dis* 20:669-677. 10.1016/s1473-3099(20)30243-7

26. Dowd JB, Andriano L, Brazel DM, Rotondi V, Block P, Ding X, et al. (2020) Demographic science aids in understanding the spread and fatality rates of COVID-19. *Proc Natl Acad Sci U S A* 117:9696-9698. 10.1073/pnas.2004911117
27. Solomon JJ, Heyman B, Ko JP, Condos R, Lynch DA (2021) CT of Post-Acute Lung Complications of COVID-19. *Radiology* 301:E383-e395. 10.1148/radiol.2021211396
28. Ali RMM, Ghonimy MBI (2021) Post-COVID-19 pneumonia lung fibrosis: a worrisome sequelae in surviving patients. *Egyptian Journal of Radiology and Nuclear Medicine* 52:1-8.
29. Marvisi M, Ferrozzi F, Balzarini L, Mancini C, Ramponi S, Uccelli M (2020) First report on clinical and radiological features of COVID-19 pneumonitis in a Caucasian population: Factors predicting fibrotic evolution. *Int J Infect Dis* 99:485-488. 10.1016/j.ijid.2020.08.054
30. Aul DR, Gates DJ, Draper DA, Dunleavy DA, Ruickbie DS, Meredith DH, et al. (2021) Complications after discharge with COVID-19 infection and risk factors associated with development of post-COVID pulmonary fibrosis. *Respir Med* 188:106602. 10.1016/j.rmed.2021.106602
31. Lee I, Kim J, Yeo Y, Lee JY, Jeong I, Joh JS, et al. (2022) Prognostic Factors for Pulmonary Fibrosis Following Pneumonia in Patients with COVID-19: A Prospective Study. *J Clin Med* 11. 10.3390/jcm11195913
32. Rai DK, Sharma P, Kumar R (2021) Post covid 19 pulmonary fibrosis. Is it real threat? *Indian J Tuberc* 68:330-333. 10.1016/j.ijtb.2020.11.003
33. Han X, Fan Y, Alwalid O, Li N, Jia X, Yuan M, et al. (2021) Six-month Follow-up Chest CT Findings after Severe COVID-19 Pneumonia. *Radiology* 299:E177-e186. 10.1148/radiol.2021203153
34. Sansone A, Mollaioli D, Ciocca G, Limoncin E, Colonnello E, Vena W, et al. (2021) Addressing male sexual and reproductive health in the wake of COVID-19 outbreak. *J Endocrinol Invest* 44:223-231. 10.1007/s40618-020-01350-1

UNDER PEER REVIEW

**Table:**

**Table 1: Demographic data and comorbidities, smoking status and clinical complain of the studied patients of the studied patients**

|                                  |  | N=100                           |              |
|----------------------------------|--|---------------------------------|--------------|
| <b>Age (years)</b>               | <b>Mean ± SD</b>                         | 56.4 ± 8.98                     |              |
|                                  | <b>Range</b>                             | 27 - 75                         |              |
| <b>Sex</b>                       | <b>Male</b>                              | 37 (37%)                        |              |
|                                  | <b>Female</b>                            | 63 (63%)                        |              |
| <b>Comorbidities</b>             | <b>None</b>                              | 26 (26%)                        |              |
|                                  | <b>Diabetes mellitus</b>                 | 22 (22%)                        |              |
|                                  | <b>Malignancy</b>                        | 19 (19%)                        |              |
|                                  | <b>Hypertension</b>                      | 17 (17%)                        |              |
|                                  | <b>Other immune-compromised disease:</b> | <b>1-chronic kidney disease</b> | 16 (16%)     |
|                                  |  | <b>2-collagen diseases</b>      |              |
| <b>Smoking</b>                   | <b>Smokers</b>                           | 26 (26%)                        |              |
|                                  | <b>Non-smokers</b>                       | 74 (74%)                        |              |
| <b>Fever</b>                     |  | 74 (74%)                        |              |
| <b>Cough</b>                     |  | 60 (60%)                        |              |
| <b>Dyspnea</b>                   |  | 42 (42%)                        |              |
| <b>Sore throat</b>               |  | 30 (30%)                        |              |
| <b>Runny nose</b>                |  | 17(17%)                         |              |
| <b>Smell and taste disorders</b> |  | 36 (36%)                        |              |
| <b>Fatigue</b>                   |  | 38 (38%)                        |              |
| <b>Muscle or body aches</b>      |  | 31 (31%)                        |              |
| <b>Headache</b>                  |  | 18 (18%)                        |              |
| <b>Abdominal pain</b>            |  | 20 (20%)                        |              |
| <b>Diarrhea</b>                  |  | 28 (28%)                        |              |
| <b>Nausea</b>                    |  | 18 (18%)                        |              |
| <b>Vomiting</b>                  |  | 19 (19 %)                       |              |
| <b>Skin rash</b>                 |  | 6 (6%)                          |              |
| <b>Redness of the eye</b>        |  | 5 (5%)                          |              |
| <b>Vital signs</b>               | <b>Heart rate (beat/minute)</b>          | <b>Mean ± SD</b>                | 90.3 ± 14.01 |
|                                  |  | <b>Range</b>                    | 62 – 118     |
|                                  | <b>Respiratory rate (breath /minute)</b> | <b>Mean ± SD</b>                | 21.7 ± 5.44  |
|                                  |  | <b>Range</b>                    | 12 – 30      |
|                                  | <b>SBP (mmHg)</b>                        | <b>Mean ± SD</b>                | 124.6 ± 9.21 |
|                                  |  | <b>Range</b>                    | 110 – 140    |
|                                  | <b>DBP (mmHg)</b>                        | <b>Mean ± SD</b>                | 74.3 ± 9.12  |
|                                  |  | <b>Range</b>                    | 60 – 90      |
|                                  | <b>Oxygen saturation % in room air</b>   | <b>Mean ± SD</b>                | 94.6 ± 2.03  |
|                                  |  | <b>Range</b>                    | 92 – 98      |

Data is presented as frequency (percentage), mean± SD and range, SBP: systolic blood pressure, DBP: diastolic blood pressure.

**Table 2: Laboratory investigation of the studied patients**

|   |                  | <b>N=100</b> |
|---|------------------|--------------|
| <b>Hb (gm/dL)</b>                             | <b>Mean ± SD</b> | 11.4 ± 0.7   |
|   | <b>Range</b>     | 9.5 – 13     |
| <b>HCT (%)</b>                                | <b>Mean ± SD</b> | 39.1 ± 5.69  |
|   | <b>Range</b>     | 30.7 - 49.7  |
| <b>WBCs (x 10<sup>3</sup>cells/μl)</b>        | <b>Mean ± SD</b> | 7.1 ± 1.55   |
|   | <b>Range</b>     | 4.5 - 9.7    |
| <b>Lymphocyte (x 10<sup>3</sup> cells/μl)</b> | <b>Mean ± SD</b> | 2.1 ± 0.78   |
|   | <b>Range</b>     | 0.8 - 3.5    |
| <b>Platelets(x 10<sup>3</sup>cells/μl)</b>    | <b>Mean ± SD</b> | 250.2 ± 55.8 |
|   | <b>Range</b>     | 145 – 350    |
| <b>CRP (mg/L)</b>                             | <b>Mean ± SD</b> | 28.8 ± 10.1  |
|   | <b>Range</b>     | 10 – 45      |
| <b>D-dimer (μg/mL)</b>                        | <b>Mean ± SD</b> | 1.2 ± 0.49   |
|   | <b>Range</b>     | 0.4 – 2      |
| <b>AST (U/L)</b>                              | <b>Mean ± SD</b> | 34.97 ± 9.87 |
|   | <b>Range</b>     | 19 – 54      |
| <b>ALT (U/L)</b>                              | <b>Mean ± SD</b> | 36.3 ± 13.55 |
|   | <b>Range</b>     | 15 – 62      |

Data is presented as mean± SD and range, Hb: Hemoglobin, HCT: Hematocrit, WBCs: White blood cells, CRP, C-reactive protein, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase

**Table 3: Lung involvement and Pattern of distribution of lung opacities in the studied patients**

|  |                         | <b>N=100</b> |
|--|-------------------------|--------------|
|  | <b>Bilateral</b>        | 88 (88%)     |
|  | <b>Unilateral</b>       | 12 (12%)     |
| <b>Pattern of distribution of lung opacities</b> | <b>Sub pleural</b>      | 52 (52%)     |
|  | <b>Diffuse</b>          | 12 (12%)     |
|  | <b>Peribronchial</b>    | 5 (5%)       |
|  | <b>Mixed</b>            | 31 (31%)     |
| <b>Right upper lobe</b>                          | <b>Apical</b>           | 32 (32%)     |
|  | <b>Posterior</b>        | 66 (66%)     |
|  | <b>Anterior</b>         | 36 (36%)     |
| <b>Right middle lobe</b>                         | <b>Lateral</b>          | 55 (55%)     |
|  | <b>Medial</b>           | 20 (20%)     |
| <b>Right lower lobe</b>                          | <b>Superior</b>         | 79 (79%)     |
|  | <b>Posterior</b>        | 84 (84%)     |
|  | <b>Medial</b>           | 41 (41%)     |
|  | <b>Anterior</b>         | 33 (33%)     |
|  | <b>Lateral</b>          | 71 (71%)     |
| <b>Left upper lobe</b>                           | <b>Apico-posterior</b>  | 60 (60%)     |
|  | <b>Anterior</b>         | 31 (31%)     |
|  | <b>Superior lingula</b> | 39 (39%)     |
|  | <b>Inferior lingula</b> | 35 (35%)     |
| <b>Left lower lobe</b>                           | <b>Superior</b>         | 77 (77%)     |
|  | <b>Antero-medial</b>    | 28 (28%)     |
|  | <b>Lateral</b>          | 76 (76%)     |
|  | <b>Posterior</b>        | 81 (81%)     |

Data is presented as frequency (percentage).

**Table 4: Main Chest findings and other associated chest CT during infection and chest CT score of the studied patients**

|   |                                      | <b>N=100</b> |
|---|--------------------------------------|--------------|
| <b>Ground glass opacities</b>                         |                                      | 62 (62%)     |
| <b>Consolidation</b>                                  |                                      | 14 (14%)     |
| <b>Mixed ground glass opacities and consolidation</b> |                                      | 24 (24%)     |
| <b>Interlobular septal thickening</b>                 |                                      | 35 (35%)     |
| <b>Subpleural fibrotic line</b>                       |                                      | 34 (34%)     |
| <b>Air bronchogram sign</b>                           |                                      | 30 (30%)     |
| <b>Crazy paving pattern</b>                           |                                      | 24 (24%)     |
| <b>Mosaic pattern</b>                                 |                                      | 22 (22%)     |
| <b>Pleural thickening</b>                             |                                      | 20 (20%)     |
| <b>Pleural effusion</b>                               |                                      | 15 (15%)     |
| <b>Reticular pattern</b>                              |                                      | 14 (14%)     |
| <b>Nodule</b>   |                                      | 13 (13%)     |
| <b>Bronchiectasis</b>                                 |                                      | 12 (12%)     |
| <b>Bronchial wall thickening</b>                      |                                      | 11 (11%)     |
| <b>Halo sign</b>                                      |                                      | 10 (10%)     |
| <b>Mediastinal lymphadenopathy</b>                    |                                      | 10 (10%)     |
| <b>Pericardial effusion</b>                           |                                      | 5 (5%)       |
| <b>Chest CT score</b>                                 | <b>Score less than 7 (Mild)</b>      | 18 (18%)     |
|   | <b>Score from 8 to 16 (Moderate)</b> | 46 (46%)     |
|   | <b>Score from 17 to 25 (Severe)</b>  | 36 (36%)     |

Data is presented as frequency (percentage).

**Table 5: Relation between severity of COVID-19 infection and clinical findings and some comorbidities**

|                                  | <b>N=100</b>           | <b>Mild</b>                | <b>Moderate</b>          | <b>Severe</b>  |
|----------------------------------|------------------------|----------------------------|--------------------------|----------------|
| <b>Fever</b>                     | 74 (74%)               | 25%                        | 29%                      | 20%            |
| <b>Cough</b>                     | 60 (60%)               | 15%                        | 19%                      | 26%            |
| <b>Dyspnea</b>                   | 42 (42%)               | 3%                         | 13%                      | 26%            |
| <b>Sore throat</b>               | 30 (30%)               | 8%                         | 17%                      | 5%             |
| <b>Runny nose</b>                | 17(17%)                | 9%                         | 6%                       | 2%             |
| <b>Smell and taste disorders</b> | 36 (36%)               | 12%                        | 14%                      | 10%            |
| <b>Fatigue</b>                   | 38 (38%)               | 9%                         | 10%                      | 19%            |
| <b>Muscle or body aches</b>      | 31 (31%)               | 6%                         | 9%                       | 16%            |
| <b>Headache</b>                  | 18 (18%)               | 10%                        | 5%                       | 3%             |
| <b>Abdominal pain</b>            | 20 (20%)               | 3%                         | 6%                       | 11%            |
| <b>Diarrhea</b>                  | 28 (28%)               | 4%                         | 10%                      | 14%            |
| <b>Nausea</b>                    | 18 (18%)               | 11%                        | 5%                       | 2%             |
| <b>Vomiting</b>                  | 19 (19 %)              | 4%                         | 6%                       | 9%             |
| <b>Skin rash</b>                 | 6 (6%)                 | 0                          | 2%                       | 4%             |
| <b>Redness of the eye</b>        | 5 (5%)                 | 0                          | 2%                       | 3%             |
|                                  | <b>Mild<br/>(n=18)</b> | <b>Moderate<br/>(n=46)</b> | <b>Severe<br/>(n=36)</b> | <b>P value</b> |
| <b>DM</b>                        | 2 (11.11%)             | 6 (13.04%)                 | 14 (38.89%)              | 0.009*         |
|                                  |                        |                            |                          | P1=0.883       |
|                                  |                        |                            |                          | P2=0.031*      |
| <b>Malignancy</b>                | 2 (11.11%)             | 5 (10.87%)                 | 12 (33.3%)               | 0.047*         |
|                                  |                        |                            |                          | P1=0.512       |
|                                  |                        |                            |                          | P2=0.024*      |
|                                  |                        |                            |                          | P3=0.012*      |

|  |            |             |             |           |
|--|------------|-------------|-------------|-----------|
| <b>Hypertension</b>                    | 3 (16.67%) | 14 (30.43%) | 0 (0.0%)    | 0.262     |
| <b>Other immunocompromised disease</b> | 1 (5.56%)  | 5 (10.87%)  | 10 (27.78%) | 0.047*    |
|  |            |             |             | P1=0.512  |
|  |            |             |             | P2=0.049* |
|  |            |             |             | P3=0.048* |

Data is presented as frequency (percentage),\*: significant as p value <0.05, P1: p value between mild and moderate cases, P2: p value between mild and severe cases, P3: p value between moderate and severe cases, DM: Diabetes mellitus.

**Table 6: Correlation between CT severity score and DM, malignancy, other immune-compromised disease, age, smoking**

|   | CT severity score |         |
|---|-------------------|---------|
|   | R                 | P value |
| <b>DM</b>                               | 0.302             | 0.002*  |
| <b>Malignancy</b>                       | 0.251             | 0.012*  |
| <b>Other Immuno-compromised disease</b> | 0.253             | 0.011*  |
| <b>Age</b>                              | 0.830             | <0.001* |
| <b>Smoking</b>                          | 0.231             | 0.020*  |

r: spearman correlation, \*: significant as P value <0.05, CT: Computed tomography, DM: Diabeted mellitus

**Table 7: Chest CT findings of the studied patients at 3 month follow up scan**

|   | <b>N=100</b> |
|---|--------------|
| <b>Complete radiological resolution of previous opacification</b> | 39 (39%)     |
| <b>Partial regression with residual opacifications</b>            | 27 (27%)     |
| <b>Fibrotic like changes</b>                                      | 34 (34%)     |

Data is presented as frequency (percentage). CT: Computed tomography.

**Table 8: Comparison between age, smoking and CT severity score based on the Chest CT findings of the studied patients at 3 months' follow-up scan**

|                          |                    | <b>Fibrotic like changes (n=34)</b> | <b>No fibrotic like changes (n=66)</b> | <b>P value</b> |
|--------------------------|--------------------|-------------------------------------|--|----------------|
| <b>Age</b>               | <b>&gt;50</b>      | 29 (85.3%)                          | 21 (31.18%)                            | <0.001*        |
|                          | <b>&lt;50</b>      | 5 (14.7%)                           | 45(68.81%)                             |                |
| <b>Smoking</b>           | <b>Smoker</b>      | 20 (58.82%)                         | 6 (9.09%)                              | <0.001*        |
|                          | <b>Non- smoker</b> | 14 (41.17%)                         | 60(90.90%)                             |                |
| <b>CT severity score</b> | <b>&gt;17</b>      | 24(70.58%)                          | 12(18.18%)                             | <0.001*        |
|                          | <b>&lt;17</b>      | 10(29.41%)                          | 54 (81.81%)                            |                |

Data is presented as frequency (percentage), \* significant as P value < 0.05, CT: Computed tomography.

**Table 9: Logistic regression of different variables for prediction of incidence of fibrotic changes**

|                          | <b>Coefficient</b> | <b>Std. Error</b> | <b>r<sub>partial</sub></b> | <b>t</b> | <b>P</b> |
|--------------------------|--------------------|-------------------|----------------------------|----------|----------|
| <b>Age</b>               | 0.01262            | 0.002501          | 0.4543                     | 5.048    | <0.0001* |
| <b>Smoking</b>           | 0.8250             | 0.08583           | 0.6966                     | 9.612    | <0.0001* |
| <b>CT severity score</b> | 0.03183            | 0.007907          | 0.3767                     | 4.026    | 0.0001*  |

\* significant as P value < 0.05, CT: Computed tomography.

UNDER PEER REVIEW