

# CO-RELATION OF CHEST CT GRADE BY COVID-RADS AND LABORATORY BIOMARKERS IN SUSPECTED CORONA VIRUS (COVID-19) PNEUMONIA PATIENTS - OUR EXPERIENCE AT A TERTIARY CARE HOSPITAL

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## ABSTRACT

**BACKGROUND:** Its been more than a year that the world has been suffering from corona virus disease as it has become a global pandemic. There's not a single diagnostic test for the corona virus because of high false positive rates. So we have to correlate the clinical, laboratory and radiological findings for the diagnosis and management of the patients. CT chest findings in COVID-19 have been simplified through various reporting systems for assessment of severity of COVID pneumonia. **OBJECTIVE:** We intend to evaluate the relationship between biomarkers (C- reactive protein (CRP), lactate dehydrogenase (LDH), D-dimers & ferritin) & CT scan chest grade (COVID-RADS). **METHODS:** All patients with suspected COVID-19 pneumonia who went through CT scan chest in Liaquat National Hospital from April 2020 to November 2020 were included in the study. We retrospectively collected the data from their electronic medical records for the levels of laboratory biomarkers and CT findings were analyzed using the COVID-19 imaging reporting and data system (COVID-RADS) for grading of CT findings into five grades. **RESULTS:** In total, 80 patients, including 60 males and 20 females with COVID-19 pneumonia, were part of our study. Serum LDH and ferritin levels were elevated in 69 (90.8%) and 63 (81.8%) patients respectively. C-reactive protein was elevated in 34 (45.3%) patients. 57 (82.6%) patients had elevated D- dimer levels. 65 (81.3%) and 52 (72.5%) patients presented with typical and atypical chest findings respectively. Most of the patients had grade 2B chest findings 62 (77.5%). 3 (76.8%) and 11 (15.9%) patients had raised LDH level in grade 2B and 3 respectively. 51 (81%) and 9 (14.3%) patients had raised ferritin in grade 2B and 3 respectively. D-dimer was elevated in 44 (77.2%) and 8 (14%) patients in grade 2B and 3 respectively. 26 (76.5%) and 6 (17.6%) patients had raised C-reactive protein in grade 2B and 3 respectively. **CONCLUSION:** We found no association of laboratory biomarkers with CT chest COVID-RADS grading so there can be a possibility that the patients have raised lab biomarkers but it doesn't correlate with the grade of COVID-RADS.

**Keywords:** Coronavirus disease, COVID-19, CT, pneumonia, SARS-CoV-2, COVID-RADS, biomarkers

## Introduction

On January 30, 2020, the World Health Organization (WHO) stated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak as a global health emergency. 66 243 918 confirmed cases and 1,528,984 deaths have been reported at the time of

writing this article (December 7, 2020).<sup>1</sup>

SARS-CoV-2 infection in humans can cause mild respiratory symptoms to severe acute respiratory syndrome.<sup>2,3</sup>

Many biological markers can be used to monitor the

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progression of the disease.<sup>4</sup> We can initially categorise patients into mild, severe or critical based on clinical symptoms & laboratory biomarkers thus allowing for earlier intervention.<sup>5</sup>

Reverse transcription polymerase chain reaction (RT-PCR) of SARSCoV-2 genes are recommended for the confirmation of COVID-19 according to the WHO.<sup>6</sup> Some patients COVID-19 infection might have initial negative RT-PCR results.<sup>7</sup> COVID-19 pneumonia abnormalities may be revealed earlier than RT-PCR testing. We can use high resolution CT as one of the main tools for screening, primary diagnosis, and evaluation of disease severity.<sup>8</sup>

CT is chosen as the first-line imaging tool in highly suspected cases and is useful for observing imaging changes during treatment.<sup>9</sup> It has potential for recognizing those patients who have negative RT-PCR results but the clinical suspicion of COVID-19 is high.<sup>10,11</sup>

We aim to describe epidemiological, clinical, laboratory, and radiological characteristics in suspected COVID-19 patients who underwent chest CT scan in our department.

We aim to evaluate the relationship between biomarkers (C-reactive protein (CRP), lactate dehydrogenase (LDH), D-dimers & ferritin) & CT scan chest grade (COVID-RADS).

## Material and Methods

We retrieved the electronic medical records of 80 patients who had high suspicion of COVID-19 pneumonia & underwent CT chest scan in the above mentioned time period. These patients were diagnosed by Infectious Control department by using the real-time reverse transcription polymerase chain reaction (RT-PCR) assay with nasopharyngeal or oropharyngeal swab.

Patient related details like age, gender, clinical symptoms, laboratory results were reviewed.

We conducted this study after approval from the Institutional review board. Informed consent was waived as this is a retrospective study.

CT chest was done at the end-inspiration level with patients in supine position and arms raised. CT system in our setup has the following details: TOSHIBA 16 slicer ACTIVION, 5mm section thickness for reconstruction.

Two experienced radiologists with many years of clinical experience in radiology reported the CT chest findings. They followed the COVID-19 imaging reporting and data system (COVID-RADS), which was formulated from the CT chest findings of 37 published studies that included total of 3647 patients.<sup>12</sup> This COVID-RADS categorized typical and atypical CT features into five grades (Tab. 1). The suspicion for pulmonary involvement increased as the grade progressed.<sup>12</sup>

According to current literature majority of the patients have typical chest CT findings of COVID-RADS 3 which includes peripheral and multifocal ground glass pattern.<sup>13,14</sup>

CT findings	Description	COVID RADS grade	level of suspicion
Normal Chest CT		0	Low
Atypical findings (Inconsistent with COVID-19)	<ul style="list-style-type: none"> <li>- Pleural effusion</li> <li>- Cavity</li> <li>- Pulmonary nodule(s)</li> <li>- Nodular pattern</li> <li>- Lymphadenopathy</li> <li>- Peribronchovascular distribution</li> <li>- Halo sign</li> <li>- Tree-in-bud sign</li> <li>- Bronchiectasis</li> <li>- Airway secretions</li> <li>- Pulmonary emphysema</li> <li>- Pulmonary fibrosis</li> <li>- Isolated pleural thickening</li> <li>- Pneumothorax</li> <li>- Pericardial effusion</li> </ul>	1	Low
Fairly typical findings	<ul style="list-style-type: none"> <li>- Single GGO (early)</li> <li>- Consolidation without GGO (late/complicated)</li> <li>- Focal pleural thickening</li> <li>- Vascular enlargement</li> <li>- Air bronchogram</li> <li>- Bronchial wall thickening</li> <li>- White lung stage (late/complicated)</li> <li>- Parenchymal fibrotic bands (late/remission)</li> </ul>	2A	Moderate
Combination of atypical findings with typical/fairly typical findings		2B	Moderate
Typical findings	<ul style="list-style-type: none"> <li>- Multifocal GGO</li> <li>- GGO with superimposed consolidation</li> <li>- Consolidation predominant pattern (late/complicated)</li> <li>- Linear opacities (late/complicated)</li> <li>- Crazy paving pattern (late/complicated)</li> </ul>	3	High

**Table 1:** Coronavirus disease 2019 (COVID-19) imaging reporting and data system (COVID-RADS) CT findings.<sup>12</sup>

Statistical analyses of the data was performed using SPSS version 23.0. Quantitative data was presented as mean and standard deviation (SD). Categorical variables were presented as frequency and percentages and association between CT chest findings and biomarkers was compared by chi-square or Fisher exact test. T-test was used to determine mean difference between two groups. The differences were considered statistically significant at  $p \leq 0.05$ .

## Results

In total, 80 patients (mean age,  $57.04 \pm 13.7$  years; range, 17-92 years), including 60 males (mean age,  $56.22 \pm 13.03$  years; range, 17-92 years) and 20 females (mean age,  $59.50 \pm 15.63$  years; range, 20-86 years) with COVID-19 pneumonia, were included in our study. (Tab. 2)

The most prevalent presenting symptoms in order of frequency were fever 63 (78.8%), dry cough 45 (56.3%), dyspnea 43 (53.8%), myalgia 4 (5%) and expectoration 3 (3.8%) (Tab. 2).

The level of laboratory biomarkers were as follows: serum LDH and ferritin levels were elevated in 69 (90.8%) and 63 (81.8%) patients respectively. D-dimer was elevated in 57 (82.6%) patients. 34 patients (45.3%) had elevated C-reactive protein levels (Tab. 2). Most of the patients 53 (66.3%) had positive real-time reverse transcription polymerase chain reaction (RT-PCR) assay with nasopharyngeal or oropharyngeal swab. (Tab. 2)

Majority of the patients 65 (81.3%) had typical chest findings with multifocal GGO as predominant CT finding seen in 50 (62.5%) of patients. 61 (76.3%) patients had atypical findings with typical/fairly typical chest findings. 58 (72%) patients presented with atypical chest findings with pleural effusion in 26 (32.5%) of patients. (Tab. 3)

53 (76.8%) and 11 (15.9%) patients had raised LDH levels in grade 2B and 3 respectively. 51 (81%) and 9 (14.3%) patients had raised ferritin in grade 2B and 3 respectively. D-dimer was elevated in 44 (77.2%) and 8 (14%) patients in grade 2B and 3 respectively. 26 (76.5%) and 6 (17.6%) patients had raised C-reactive protein in grade 2B and 3 respectively. (Tab. 4)

	Frequency n(%)
<b>Gender</b>	
Male	60 (75)
Female	20 (25)
<b>Symptoms</b>	
Fever	63 (78.8)
Dry cough	45 (56.3)
SOB	43 (53.8)
Myalgia	4 (5.0)
Productive cough	3 (3.8)
<b>C-reactive protein levels</b>	
Normal <10mg/L	41 (54.7)
High >10mg/L	34 (45.3)
Missing	5 (6.3)
<b>LDH levels</b>	
Normal <140-280 U/L	7 (9.2)
High > 280 U/L	69 (90.8)
Missing	4 (5)
<b>Dimer levels</b>	
Normal <0.5	12 (17.4)
Positive >0.5	57 (82.6)
Missing	11 (13.8)
<b>Ferritin levels</b>	
Normal <12-300ng/ml	14 (18.2)
High >300ng/ml	63 (81.8)
Missing	3 (3.8)
<b>PCR</b>	
Positive	53 (66.3)
Negative	27 (3.8)
<b>COVID-RADS CT Chest Grades</b>	
Low	2 (2.5)
Low	3 (3.8)
Moderate 2A	2 (2.5)
Moderate 2B	62 (77.5)
High	11 (3.8)

**Table 2:** Descriptive statistics of Covid-19 patients under study

## Discussion

COVID-19 is a rapidly spreading pandemic increasing the stress and work load on health department. Various biomarkers are important in COVID-19 infection for

	Frequency n(%)
<b>Atypical findings (Inconsistent with COVID-19)</b>	58 (72.5)
Pleural effusion	26 (32.5)
Lymphadenopathy	25 (31.3)
Pulmonary fibrosis	25 (31.3)
<b>Fairly typical findings</b>	
Vascular enlargement	8 (10)
Air bronchogram	15 (18.8)
<b>Typical findings</b>	
Multifocal GGO	50 (62.5)
GGO with superimposed consolidation	16 (20)
Consolidation predominant pattern	2 (2.5)
<b>Combination of atypical findings with typical/ Fairly typical findings</b>	61 (76.3)

**Table 3:** Chest CT scan findings using COVID-RADS

Biomarkers	Grading levels					p-value
	Low n (%)	Low n (%)	2A Moderate n (%)	2B Moderate n (%)	High n (%)	
<b>C-reactive protein levels</b>						
Normal <10mg/L	1 (2.4)	1 (2.4)	2 (4.9)	32 (78)	5 (12.2)	± 0.856
High >10mg/L	1 (2.9)	1 (2.9)	0 (0)	26 (76.5)	6 (17.6)	
<b>LDH levels</b>						
Normal <140-280 U/L	1 (14.3)	0 (0)	0 (0)	6 (85.7)	0 (0)	± 0.340
High >280 U/L	1 (1.4)	2 (2.9)	2 (2.9)	53 (76.8)	11 (15.9)	
<b>Dimer levels</b>						
Normal <0.5	0 (0)	0 (0)	1 (8.3)	8 (66.7)	3 (25)	± 0.501
Positive>0.5	2 (3.5)	2 (3.5)	1 (1.8)	44 (77.2)	8 (14)	
<b>Ferritin levels</b>						
Normal <12-300ng/ml	1 (7.1)	2 (14.3)	1 (7.1)	9 (6.3)	1 (7.1)	± 0.057
High >300ng/ml	1 (1.6)	1 (1.6)	1 (1.6)	51 (81)	9 (14.3)	

**Table 4:** Association of biomarkers with COVID-RADS grades

the treatment and monitoring of the patients.<sup>15</sup> So we studied 80 patients to determine the relationship between biomarkers (C-reactive protein (CRP), lactate dehydrogenase (LDH), D-dimers, ferritin) and CT scan chest grade (COVID-RADS).

We found out that fever was the most prevalent symptom seen in majority of the patients. Other common symptoms seen in majority of the patients were dry cough and difficulty in breathing.

One of the study showed that survivors had median

CRP values of approximately 40 mg/L, while non-survivors had median values of 125 mg/L, suggestive of a strong correlation with disease severity and prognosis. Other predictors of poor outcome include the serum ferritin and lactate dehydrogenase (LDH). Non-survivors have also shown higher levels of plasma D-dimers.<sup>16,17,18</sup>

Out of the biomarkers we studied, most of the patients had raised ferritin and LDH levels as also seen in many of the studies.

Chest CT showed high sensitivity in detecting GGO, which is considered a typical finding in COVID-19 pneumonia and, in some cases, may be the only alteration present in the early phases of the disease.<sup>19,20</sup> After reviewing CT chest findings according to COVID –RADS reporting system we found that the predominant finding in our study was multifocal ground glass opacity (GGO) as also seen in many of previous studies.

There are studies that showed association of biomarkers with COVID-19 disease progression but in this study we have associated the biomarkers with the COVID-RADS grades Majority of the patients 62 (77.5%) had grade 2B according to COVID-RADS. All the biomarkers were raised in grade 2B as compared to grade 3 so we did not find any association of the lab biomarkers with the chest CT grades (Tab.4).

There were few limitations in this study. First, the sample size is relatively small because this is a retrospective analysis of a new disease. Secondly this study has used a new COVID-RADS system of chest CT classification based on findings of many published articles so it may need modification and further work.

## Conclusion

From the results of our study we came down to the conclusion that laboratory markers that are raised in COVID pneumonia are not related to the severity of CT chest COVID RADS grading used in this study. To my knowledge there have been no work on association of biomarkers and CT chest grades so there may be a possibility that a patient has raised laboratory biomarkers but the CT chest findings are not that severe.

**Ethical approval:** Ethical approval was obtained

from Institutional Ethics Review Board of Liaquat National Hospital, Karachi.


**Patient's consent:** Written informed consent was waived by the Institutional Review Board.

**Conflict of Interest:** There is no conflict of interest

**Funding information :** No funding was required.

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