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Correlation of CT severity grade with laboratory findings in COVID-19 patients

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ABSTRACT

Introduction: CT chest is strongly recommended for evaluation in COVID-19 cases as it involves the respiratory system. In the current study, we correlate the CT chest with the most commonly encountered laboratory abnormalities in COVID-19 patients based on their CT severity grade. *Materials and methods:* This was a retrospective study, conducted in a designated COVID center in 123 hospitalized patients who were confirmed COVID-19 positive. The research was conducted over three months (August 2020 to October 2020). Patient demographics, chest CT findings with CT severity scores of the affected lung parenchyma, and laboratory values like serum D-dimer, CRP, ferritin, and lymphocyte count were reported. The association between the severity of a chest CT scan and the levels of laboratory parameters was investigated. Before the study, the local ethics committee granted its approval. *Results:* There were total of 123 cases, out of which 86 (30.1%) study subjects were males and 37 (69.9%) were females. There was no discernible link between gender and severity score. A positive correlation was seen between the CT imaging findings and serum D-dimer, CRP, and ferritin levels; however, a negative correlation was seen with lymphocyte count. *Conclusion:* A significant correlation is seen between the CT severity score with laboratory values and the disease severity. Chest CT score is an important signal of the amount of systemic inflammation and can help speed up the diagnostic procedure in symptomatic patients.

Keywords: COVID-19, Computed tomography (CT), CT severity score, Reverse Transcriptase - Polymerase Chain Reaction (RT-PCR).

1. INTRODUCTION

SARS-CoV-2 is a beta-coronavirus that belongs to Coronaviridae family. The term coronavirus has been named the word Corona, which represents "crown-like" glycoprotein spikes. The virus was transmitted to humans via intermediate zoonotic sources, which have been identified (Shereen et al., 2020). In December 2019, the first case was heard in Wuhan, China. The bats were identified as the intermediate host behind its transmission (Chatterjee et al., 2020). The World Health Organization (WHO) classified COVID-19 as a pandemic on March 11, 2019 (Rubin et al., 2020). The index case in India was

reported on 30th January 2020 as a student returning from China. The use of RT-PCR kits and Rapid antigen test kits have been approved and validated and are also being used for surveillance purposes by the ICMR in India. Maximum testing of symptomatic patients to detect positive patients with efforts to increase awareness with help of social media platforms has been used as a strategy to control the spread of infection (Pal and Yadav, 2020). The RT-PCR helps in the detection of the virus. For assessment of disease severity, prognosis, management strategies, and therapeutic monitoring, the use of in vitro diagnostic testing is prevalent (Lippi and Plebani, 2020).

In the early stages, chest radiographs may lead to false negatives, whereas even before the beginning of symptoms, CT abnormalities could be seen. CT findings have proven important in cases where patients had initial false-negative results on RT-PCR test. Thereafter ample amount cases were published to define the typical imaging characteristics on CT for COVID-19 pneumonia. There was a significant overlap in imaging findings with other causes of acute lower respiratory tract infections and organizing pneumonia, making it difficult to characterize "COVID-19". However, the progression of imaging features over time can help us to differentiate COVID-19 from other causes (Salehi et al., 2020).

In response to inflammation, there is a rise in serum CRP (C-reactive protein) level, which is an inflammatory response protein. A coagulation cascade gets initiated which in turn activates the complement system leading to the formation of thrombi (Zhu et al., 2020). The severity of bacterial infections is evaluated by the neutrophil-to-lymphocyte ratio (NLR). Higher levels of serum ferritin levels, according to recent studies, contribute to an increase in the amount of cytokines. It is important to timely control the level of cytokines with help of proper immunomodulators and cytokine antagonists to reduce inflammatory response which improves the outcome and survival chances of patients with COVID-19 (Gandini et al., 2020).

Even if the signs and symptoms of COVID-2019 infection have been understood, the laboratory findings are still not known as far as we can tell. Laboratory medicine plays a significant role in early detection, diagnosis and management, which has an impact on the patient's outcome. As a result, the goal of our research is to offer a quick overview of the most common laboratory abnormalities seen in COVID-19 patients, categorized by CT severity grade.

2. MATERIALS & METHODS

Data collection

After permission from the Institutional Ethics Committee, a retrospective study was conducted in a designated COVID center. This included 123 hospitalized patients who were confirmed COVID-19 positive status with RT-PCR test or Rapid Antigen test. The study duration was for a period of 3 months (August 2020 to October 2020). The clinical and laboratory data such as D-dimer, CRP, and lymphocyte count, and Sr. Ferritin levels were collected.

Inclusion criteria

Symptomatic and asymptomatic patients, irrespective of age group and co-morbid conditions, tested COVID-19 positive by RAT or RT-PCR.

Exclusion criteria

Pregnant patients were not included in the study due to the harmful effects of radiation exposure to the developing embryo or fetus. Patients with negative RAT and RT-PCR tests for COVID-19.

Imaging technique & protocol

With all precautionary measures, undertaken arrangements were made for all COVID-19 positive cases to limit its spread while undergoing CT scan. Toshiba Activion 16; 16 slice helical MDCT scan machine was used for all examinations. CT scan was performed by keeping the patient in the supine position on the CT table. Scanning parameters were kept the same as the manufacturer's standard recommended pre-setting. Scanning parameters were: scan direction (caudocranially), tube voltage (120KV), tube current (100-600 mA)-smart mA dose modulation, slice collimation (16 × 0.625 mm), width (0.625 × 0.625 mm), pitch (1), rotation time (0.5 s), scan length (60.00 – I300.00 s). 2-mm slice thickness images were reconstructed. Multiplanar images in the coronal and sagittal sections were reconstructed.

Imaging analysis

Concerning Fleischner society defined various terms related to disease which included ground-glass opacity (GGO), crazy-paving pattern, and consolidation. In keeping in mind various publications, diagnosis of suspect COVID-19 pneumonia was given based on

the following CT patterns: GGO, crazy-paving, and consolidation. The score was calculated considering the extent of lung involvement as per each of the five lobes. The total of each lobar score was calculated which was out of 25 and was graded subsequently into the mild, moderate, and severe category as follows. Table 1 shows CT severity score according to percentage of each lobe involvement. Lobe with no involvement was give 0 score, with <5% score of 1 was given, with 5-25% score of 2 was given, for 25-50% score of 3 was given, for 50-75% score of 4 was given and if the lobe involvement was >75%, score of 5 was given.

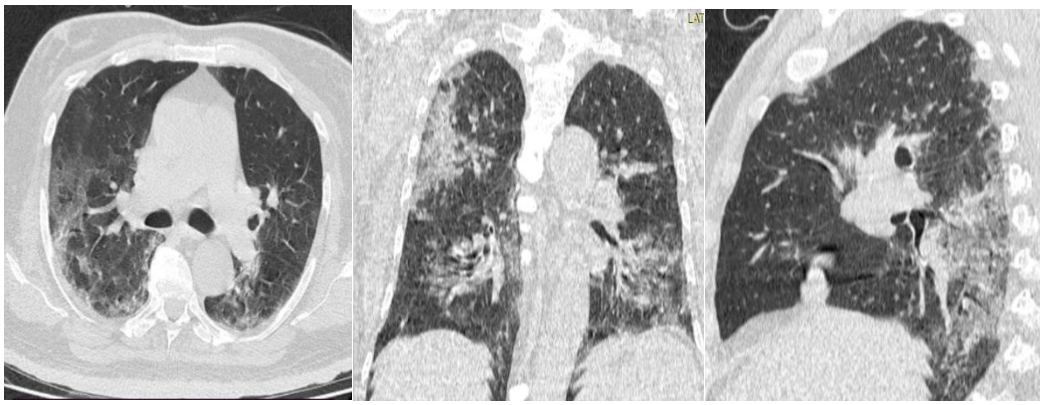
Table 1 CT severity score calculation according to percentage of lung involved.

Percentage of lobar involvement	CT severity score
0	0
<5%	1
5-25%	2
25-50%	3
50-75%	4
>75%	5

Table 2 shows classification according to severity grading according to score. Score of less than 7 was classified in mild category, score between 8 to 15 was classified in moderate category and score above 15 was classified in severe category. The results of the scans were initially classed as typical and atypical COVID19 pneumonia findings. Then, depending on the evaluation of each lobe involved, classification into distinct groups was done. CT images in axial, coronal and sagittal sections in COVID 19 positive patients showing severity of disease in different patients (Figure 1 and 2).

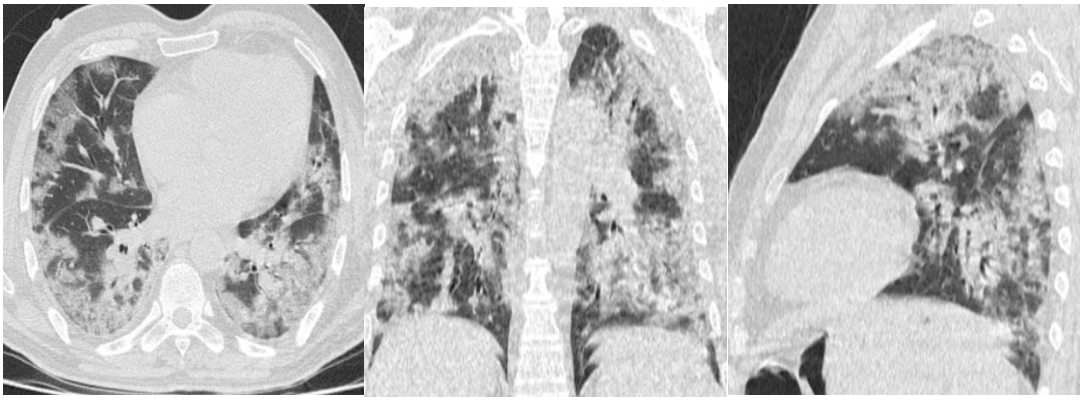
Table 2 Grading according to CT severity score.

CT severity score	CT severity grade
<7	MILD
8-15	MODERATE
>15	SEVERE



(a) (b) (c)

Figure 1 Axial (a) thin-section of HRCT scan shows pleural based ground glass opacities involving right upper lobe and left lower lobe. Coronal (b) thin-section shows the moderate involvement of right upper and lower lobes and left lower lobe. Sagittal (c) thin-section shows involvement of right lower lobe, suggestive of moderate disease severity.



(a) (b) (c)

Figure 2 Axial (a) thin-section of HRCT chest scan shows multiple pleural based peripheral areas of ground glass opacities involving bilateral lower lobes. Coronal (b) thin-section shows the severe involvement of bilateral upper and lower lobes with diffuse crazy paving and few peripheral areas of consolidation. Sagittal (c) thin-section shows involvement of left upper and lower lobe, suggestive of severe disease.

Statistical analysis

Statistical analysis was done using Microsoft Excel and Epi info software. The description of the data such as patient's demographics was done in the form of arithmetic mean +/- standard deviation for quantitative data while in the form of frequencies (%) for qualitative (categorical) data. P-values of less than 0.05 were considered significant. For co-relation of categorical variables (i.e. to understand the associations between different variables), Pearsons' correlation co-efficient test (2 tailed test) was used and a p-value of less than 0.01 was defined as statistical significant.

3. RESULTS

Our study comprised 123 individuals who had a nasopharyngeal swab confirmed positive by an RT-PCR or RAT test. Patients who tested positive for COVID-19 underwent HRCT chest. Eventually, 123 cases had been included with the following information acquired: age, gender, laboratory tests including d-dimer, CRP, lymphocyte count, and ferritin levels. The average age was 49.03 years [range 24-76 years], 86 (30.1%) study subjects were males and 37 (69.9%) were females. Patients were further divided into 6 age groups: 21 to 30, 31 to 40, 41 to 50, 51 to 60, 61 to 70, and 71 to 80 years.

Age wise distribution

Maximum i.e. 30 (24.4%) belonged to age group of 51-60, followed by 24 (19.5 %) in age group 21-30 years, 23(18.7%) belonged to 61-70 years, 19(15.4%) study subjects belonged to 41-50 years age group, 18(14.6%) belonged to 31-40 years and minimum 9 (7.3%) in 71-80 years (Table 3). Patients were divided according to age into different categories and were further classified as per severity of involvement of lung parenchyma into mild, moderate and severe category. Patients with younger age group had predominantly mild disease whereas severe disease was predominantly observed in older age group (Table 4).

Table 3 Age wise distribution of study subjects

AGE		
Age	Frequency	Percent
21-30	24	19.5
31-40	18	14.6
41-50	19	15.4
51-60	30	24.4
61-70	23	18.7
71-80	9	7.3
Total	123	100.0

Table 4 Prevalence of age categories for each CT severity score.

	Grades			
Age	Negative	Mild	Moderate	Severe
21-30 years	16	7	0	1
31-40 years	2	8	5	3
41-50 years	1	2	11	5
51-60 years	2	5	17	6
61-70 years	0	4	6	13
71-80 years	0	4	5	0

Gender wise distribution

Gender wise distribution of study subjects, 86 (30.1%) study subjects were males and 37 (69.9%) were females (Table 5). Association between gender and CT severity score: No significant relationship was seen with mean of 10.23 in male patients and 9.29 in female patients (Table 6).

Table 5 Gender wise distribution of patients

SEX		
Sex	Frequency	Percent
Male	86	69.9
Female	37	30.1
Total	123	100.0

Table 6 Gender wise Mean and SD of CT severity score

Gender	Mean and SD of CT severity score	P value 0.504265 df-1
Male	10.23 ± 7.15	
Female	9.29 ± 7.11	

Laboratory values

Laboratory results showed reduced lymphocyte count (normal: 1500 to 4000/microlitre) in 37(30.1%) cases, raised C-Reactive Protein (50 mg/L) in 236 cases (40.3%), raised D-dimer (>1 mcg/mL) in 46(37.4%) patients and raised ferritin levels (>+00ng/mL) in 55 cases(44.7%). 37 patients (30.1%) had low lymphocyte count, 45 patients (36.6%) had normal lymphocyte count while 41 patients (33.3%) had increased lymphocyte count (Table 7). 77 patients (62.6%) had normal D-dimer levels, while 46 patients (37.4%) had increased D-dimer levels (Table 8).

Table 7 Distribution of study subjects according to lymphocyte count

Lymphocyte		
	Frequency	Percent
Low	37	30.1
Normal	45	36.6
High	41	33.3
Total	123	100.0

Table 8 Distribution of study subjects according to D-dimer

D DIMER		
	Frequency	Percent
Normal	77	62.6
High	46	37.4
Total	123	100.0

68 patients (55.3%) had normal Ferritin levels while 55 patients (44.7%) had abnormal ferritin levels (Table 9). Mean value of CRP was highest (2.73) in severe group of patients while it was lowest (0.31) for negative group (Table 10). Mean value of ferritin 520.8 was highest and mean value CRP 0.40 was lowest in mild group. Similarly, mean value of ferritin 456 was highest and mean value of CRP 1.13 was lowest in moderate group. In severe group, mean value was highest for ferritin 1141.5 and mean value was lowest for CRP 2.73 (Table 11). Association between CT severity grade and D-dimer: CT severity score and D Dimer are positively co-related with p value < 0.01 (Table 12). Association between CT severity grade and CRP: Positive association of CT severity grade with CRP was seen with p-value< 0.01. Higher CRP values were seen in cases with higher CT severity score (Table 13).

Table 9 Distribution of study subjects according to their ferritin level

FERRITIN		
	Frequency	Percent
Normal	68	55.3
Abnormal	55	44.7
Total	123	100.0

Table 10 Mean and SD of CRP according to severity

Grade	Mean and SD of CRP
NA	0.31 ± 1.43
Mild	0.4 ± 1.58
Moderate	1.13 ± 1.57
Severe	2.73 ± 1.64

Table 11 Mean and SD of D-dimer, CRP, ferritin and lymphocyte according to severity

	Mean and SD			
Grade	D-DIMER	CRP	FERRITIN	LYMPHOCYTE
Mild	0.75 ± 1.53	0.40 ± 1.58	520.8 ± 447.39	3.95 ± 2.01
Moderate	1.4 ± 1.51	1.13 ± 1.54	456±455.38	3.05±1.98
Severe	2.75 ± 1.69	2.73 ± 1.64	1141.5±471.77	1.74±2.02

Table 12 Association between CT severity grade and d-dimer

Correlations			
		CT SEVERITY SCORE	D-DIMER
CT SEVERITY SCORE	Pearson Correlation	1	.678**
	Sig. (2-tailed)		.000
	N	123	123
D-DIMER	Pearson Correlation	.678**	1
	Sig. (2-tailed)	.000	
	N	123	123
**. Significant correlation at the 0.01 level. (2-tailed).			

Table 13 Association between CT severity grade and CRP

Correlations			
		CT SEVERITY SCORE	CRP
CT SEVERITY SCORE	Pearson Correlation	1	.660**
	Sig. (2-tailed)		.000
	N	123	123
CRP	Pearson Correlation	.660**	1
	Sig. (2-tailed)	.000	

	N	123	123
**. Significant correlation at the 0.01 level. (2-tailed).			

Association between CT severity grade and lymphocyte count: Negative correlation was seen between CT severity score and lymphocyte count with p value >0.01 (Table 14). Association between CT severity score and Ferritin level: Positive association was noted between CT severity grade and Ferritin level with p value < 0.01. Patients with higher CT severity score had increased Ferritin levels (Table 15).

Table 14 Association between CT severity grade and lymphocyte count

CORRELATIONS			
		CT SEVERITY SCORE	LYMPHOCYTE
CT SEVERITY SCORE	Pearson Correlation	1	-.125
	Sig. (2-tailed)		.169
	N	123	123
LYMPHOCYTE	Pearson Correlation	-.125	1
	Sig. (2-tailed)	.169	
		123	124

Table 15 Association between CT severity grade and ferritin levels

Correlations			
		CT SEVERITY SCORE	FERRITIN
CT SEVERITY SCORE	Pearson Correlation	1	.600**
	Sig. (2-tailed)		.000
	N	123	123
FERRITIN	Pearson Correlation	.600**	1
	Sig. (2-tailed)	.000	
	N	123	123
**. Significant correlation at the 0.01 level. (2-tailed).			

4. DISCUSSION

Chest imaging is advised by WHO whenever RT-PCR testing is unavailable or when there are symptoms related to COVID-19. The work of clinicians and radiologists should go hand in hand to improve diagnostic and treatment efficacy (Saeed et al., 2021). In our study, most of the study subjects with severe disease were males. Old studies have indicated that disparity which can be because of multiple factors like behaviour, hormonal protective effects. Disease with maximum severity was found in the older age group (61-70 years). Different factors like co-morbid conditions such as diabetes mellitus, hypertension along with the functioning of the health care system could be held responsible (Dangis et al., 2020; Zhang et al., 2020; Mallapaty, 2020). The majority of the data demonstrate that D-dimer levels are related to clinical outcome in the form of disease severity (Yao et al., 2020).

The amount of serum CRP and the severity of the CT scan were shown to have a significant relationship in our study. With help of CRP levels, treatment can be initiated in the early stages. CRP thus can be used as a predictive marker for the progression of the disease. However, there are not enough studies to prove the association of CRP with disease progression. Decreased lymphocyte count was well correlated with the increase in CT severity score. Inflammatory cytokine storm was related to the presence of decreased lymphocyte count. Previous studies have shown the relation of low serum iron which was directly proportional to disease severity (Zhao et al., 2020). Decreased lymphocyte count was well correlated with the increase in CT severity score. Inflammatory cytokine storm was related to the presence of decreased lymphocyte count. Previous studies have shown the relation of low serum iron which was directly proportional to disease severity.

In our study, D-dimer, C reactive protein, and serum ferritin levels were significantly increased with low lymphocyte count in severe grade patients, which are consistent with the previous studies. Chest CT scoring can help us in classifying patients into different categories according to the severity which thus can be helpful so that patients in the severe group can get intensive care and close observation. Chest CT findings in association with laboratory parameters can help us in predicting disease progression thus helping in its management.

5. CONCLUSION

The clinical laboratory biomarkers must be determined to diagnose COVID-19 infection early and predict disease severity based on imaging data. As a result, laboratory data can be used to assess COVID-19 patients early on.

Abbreviations

COVID-19(corona virus disease), CRP(C-reactive protein), CT(computed tomography), SARS-CoV-2 (severe acute respiratory syndrome coronavirus-2), GGO(ground glass opacity), HRCT (high-resolution computed tomography), RT-PCR (reverse transcription polymerase chain reaction).

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Authors Contribution

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Ethical Approval

The study was approved by Medical Ethics Committee of NKP Salve Institute of Medical Sciences and Research Centre with the letter number: (NKPSIMS &RC & LMH/IEC/5/2020).

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Conflicts of interest

The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are present in the paper.

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