Original article:

Study of Inflammatory Markers and its relation to mortality and severity in covid 19 positive patients at tertiary care centre

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Abstract:

Background: This study aims to retrospectively analyze the clinical features, inflammatory markers, and CT scores of COVID-19 patients to identify factors associated with disease severity and prognosis.

Methods: This single-centered, retrospective, observational study was conducted at a tertiary care hospital. Ethical approval was obtained, and informed consent was acquired from participants. The study included 100 COVID-19 patients who were categorized based on disease severity using clinical, laboratory, and radiographic criteria. Inflammatory markers (CRP, D-dimer, IL-6, creatinine, AST, ALT, procalcitonin, LDH) were correlated with CT severity scores. Complications, treatments, and outcomes were also analyzed.

Results: The study population consisted of 100 patients (65.7% males, median age 59.6 years). Most common symptoms were fever (84.2%), dry cough (52.6%), and dyspnea (44.7%). CT severity scores were positively correlated with inflammatory markers (CRP, D-dimer, IL-6, LDH), age, and oxygen requirement. Severe cases were associated with complications including shock, acute cardiac injury, acute respiratory distress syndrome, liver dysfunction, acute kidney injury, and acute heart failure. Treatment modalities correlated with disease severity. Most patients (94.7%) were discharged, while 5.2% died, all of whom were severe cases.

Conclusion: Inflammatory markers, CT severity scores, age, and oxygen requirement are valuable indicators of COVID-19 severity and prognosis. This study emphasizes the significance of employing non-contrast high-resolution CT imaging and inflammatory markers to aid in clinical decision-making and disease management. Early intervention and tailored treatment strategies based on disease severity can potentially improve patient outcomes.

Keywords: COVID-19, Inflammatory markers, Disease severity

Introduction:

Patients infected with SARS-CoV-2 have a series of clinical manifestations, including fever, cough, myalgia or fatigue, dyspnoea, even acute respiratory distress syndrome (ARDS), acute cardiac injury and secondary infection, and a lot of severe patients had to been admitted to the intensive care unit (ICU)Clinically, most individual patients showed the changes of neutrophil count (NC), D-dimer, blood urea nitrogen, and creatinine levels and lymphocyte counts (LC)[1] besides the positive viral nucleic acid analysis and the representative pulmonary CT findings (bilateral distribution of patchy shadows and ground glass opacity). A non-contrast high-resolution CT chest imaging plays a pivotal and essential role in the early disease detection, particularly in patients with false-negative RT-PCR results, as well as in managing and monitoring the course of disease. [2,3,4]Moreover, the disease severity can be ascertained from the imaging findings, significantly supporting the clinicians in their clinical judgment and ensuring effective and timely management. Prognosis can also be affected by the severity of the disease in the critically ill patients allowing appropriate selection of early involvement of the intensive care However, the correlation between the inflammatory markers and the disease severity is still not completely clear.[5,6] Therefore, this study retrospectively analysed clinical features of covid-19 patients, blood inflammation indicators among severe and non -severe patients, additionally also the CT scores in patients which may help to identify severe or critical patients early and perform clinical intervention early.[7,8,9]

Material and methods:

The research study was carried out at a tertiary care hospital. Prior to commencing the study, the necessary ethical committee approval was obtained to ensure that the research adhered to ethical standards. Informed consent was acquired from all the patients who participated in the study, guaranteeing their awareness and agreement to be a part of the research.

The study targeted a particular population—individuals who had been officially diagnosed with COVID-19 and had been admitted to the tertiary care hospital during the stipulated study duration. In order to gather relevant information, data was collected through established methods.

A total of 100 patients were included in the study. To be included, patients needed to test positive for COVID-19 through RT-PCR and/or RAT testing. Moreover, individuals with varying degrees of COVID-19 severity—ranging from mild to moderate, severe, and critical—were incorporated in the study, provided they were 13 years of age or older. Even COVID-19 positive patients with pre-existing chronic illnesses were considered for inclusion, as long as they granted their consent to participate.

This was a single-centered, retrospective, and observational study. It concentrated on patients who had been hospitalized due to confirmed cases of COVID-19 in a tertiary care setting.

Results:

The study population included 100 hospitalized patients with laboratory-confirmed COVID-19 (Table 6) (Figure 11-19). The median age was 59.6 years (IQR, 48.0–68.0), and 24 (31.5%) were females. Hypertension (28 [36.8%]), diabetes (12 [15.7%]), coronary heart disease (11 [14.4%]), and cerebrovascular diseases (5 [6.5%]) were the most common coexisting conditions. Fever (84.2%), dry cough (52.6%), fatigue (51.3%), anorexia (43.4%), dyspnoea (44.7%), and chest discomfort (42.1%) were the most common symptoms, whereas dizziness

(6.5%), nasal obstruction (3.9%), abdominal pain (1.3%), haemoptysis (1.3%), headache (3.9%), vomiting (2.6%), shiver (2.6%) were less common. The median durations from first symptoms to dyspnoea and hospital admission were 5.5 days (IQR, 0–8.0), and 9.0 days (IQR, 5.0–12.0) respectively

Table 1 – CT scores and patient's severity

Severity (n=76)	CT score
Mild	0
Moderate	33
Severe	35

Table 2: Co relation between inflammatory markers and CT score severity

Marker	Range	Non severe (Mean±SD)	Severe (Mean± SD)	Total (Mean ±SD)	P value
CRP	0-10	10.0(7-17.5)	40 (10-8.0)	15.1(9-50.9)	0.0023
D-dimer	0-243	122 (75-254)	222(132.5-529)	168(92-393.5)	0.004
IL-6	0-7.0	11.8 (3.3-27.5)	33 (13.1-69.2)	18.7(7.7-46.4)	<0.0001
Creatinine	0-24	17 (15-22.5)	18.0(15.8-20)	17 (15-21)	0.696
AST	15-40	31(22.5-49.5)	38(26-59)3	33.24.5 (25-52.8)	0.0810
ALT	9-50	22 (15.5-37.5)	27(20-39.0)	24 (17.3-37.8)	0.1227
Procalcitonin	0.00-0.5	0.07 (0.03-0.16)	0.005 (0.03-0.009)	0.09 (0.06-0.23)	<0.0001
LDH	109-225	245.5(194.3-319.8)	225 (184-303)	275 (212-318.2)	0.0041
CT severity score	14.1±4.1	12.21±6.1	17.1±3.2	14.1±4.1	<0.0001

Table 3- Complications, treatment and outcomes of patients with COVID-19

Characteristics	Total (N = 100)	Non-severe(n=53)	Severe (n = 47)	P value
Complications, No./total No. (%)				
Shock	11/100	0/53	11/47	< 0.0001
Acute-cardiac injury	15/100	02/53	13/47	0.001
Acute respiratory distress syndrome	13/100	0/53	13/47	< 0.0001
Liver dysfunction	9/100	01/53	08/47	0.0011
Acute kidney injury	1/100	00/53	01/47	0.0565
Acute heart failure	14/100	02/53	12/47	0.0002
Treatment, No./total No. (%)				
Administration-of oseltamivir	60/100	31/53	29/47	0.4019
Administration of antibiotics	73/100	39/53	34/47	0.0956
Use of antifungal medications	08/100	01/53	07/47	0.0001

Administration of systemic corticosteroid	40/100	15/53	25/47	< 0.0001
Oxygen inhalation	52/100	28/53	24/47	0.0141
Noninvasive ventilation	09/100	0/53	09/47	< 0.0001
Invasive mechanical ventilation	06/100	0/53	06/47	0.0005
Clinical outcomes, No./total No. (%)				
Discharge from hospital	72/100	41/53	31/47	0.0040
Death	04/100	0/53	04/47	0.0040

Discussions

This retrospective study describes the   basic demographic characteristics like age, gender, signs and symptoms, laboratory findings, radiological findings, CT score of covid-19 patients admitted in a tertiary care hospital during the study period. Additionally, this study also recorded the complications, Interventions being carried out and the survival rates or outcomes of patients. We divided the patients based on clinical, laboratory and radiographic findings as into severe and non- severe cases, the non- severe cases were then sub-classified into mild and moderate cases and the severe ones included severe and critical cases, based on Ministry of health and Family welfare guidelines, Government of India. Based on CT score, the patients were further classified as mild cases, moderate cases and severe cases.[10,11]

A total of 100 patients were included in the study, of which 34.2% were females and 65.7%were males. Of which, 53.9% included non- severe cases (mild and moderate) and 46.05% included severe cases (severe and critical ones). The incidence of males was higher when compared to females, accounting for 65.7% of the total cases. Majority of the patients survived well and were discharged, accounting for 94.7% of all the total cases. Only few patients died, this accounted for 5.2% of the total cases. All the patients who died were amongst the severe group. [12] Most severe patients were older and had more underlying conditions. Common symptoms at onset of illness were fever, dry cough, fatigue, dyspnoea, and chest discomfort. Local and/or bilateral patchy shadowing was a typical hallmark of CT imaging for COVID-19. Lymphopenia and elevated levels of neutrophil count, C-reactive protein, interleukin 6, D-dimer, creatinine, lactate dehydrogenase, cTnT, and NT-proBNP were more commonly seen in severe cases. During hospitalization, the prevalence of new onset hypertension, acute heart injury, and heart failure was significantly higher in severe patients.

During hospitalization, the morbidity of new onset hypertension, acute heart injury, and heart failure was significantly higher in severe patients. Increased level of myocardial enzymes and cTnT was found dead cases. These findings suggest a higher possibility of cardiovascular complications in severe patients with COVID-19. Outcomes of patients with COVID-19 may be improved by prevention of the development and progression of associated cardiac complications. [13,14]

The WHO advised the use of chest imaging as part of diagnostic workup of COVID-19 disease whenever RT-PCR testing is not available, in case of delayed test results or when there is a clinical suspicion of COVID-19 with initial negative RT-PCR testing. [15] Clinicians should work hand in hand with the radiologists in order to make the proper choice of imaging modality. CT scan can be a useful tool in evaluating the individual disease burden[2,4,5]. The quantitative severity can be assessed using a visual method (as in our study) or software that determines the percentage of affected lung volumes using the deep learning algorithm. [7]

In this study, and due to unavailability of the software, the visual assessment of each of the 5 lung lobes. The severities were further classified based on the total cumulative severity score

Furthermore, our results showed that the serum CRP level had significant correlation with CT severity. Studies have also suggested that early treatment at early disease stage can be considered using CRP as a predictive marker for likelihood of disease progression[2]. D-dimer likewise can be used as a prognostic indicator, where higher levels are seen in more critical conditions. However, there is lack of evidence regarding the causal effect. It is not yet clear whether this increase is related to the direct effect of the virus or the systemic inflammatory response.[4]

In our study, we corelated the CT severity score with the levels of inflammatory markers. IL-6 showed positive corelation with CT severity score which was statistically significant. Procalcitonin was negatively associated with CT severity score. Similar findings were reported in a study done by Samuel Bogdan et al[6]

As expected, and found in our data, oxygen requirements increase with the increasing CT severity. i.e., progressive increase in oxygen requirement can be due to the direct damage of the lung by the virus causing inflammatory changes in alveolar wall that limit oxygen exchange, leading to acute respiratory distress, pulmonary fibrosis, and eventually death. Moreover, significant pulmonary thromboembolic effects were also found on autopsies from patients who died from COVID-19 disease[7-9]. Death rate in our cohort was significantly increased among patients with severe CT findings, as noted in other studies.

Conclusion:

An increase in these inflammatory markers is an early indicator of cytokine storm in these patients, which is a harbinger of a relatively poor prognosis and is associated with higher mortality in covid-19 patients. CT scans can have a pivotal role in assisting physicians in the management plan and work as an indicator for disease severity and possible outcome. CT severity score is positively correlated with inflammatory lab markers, increased age and oxygen requirement in patients with COVID-19 infection.

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