Section: Respiratory Medicine

Research

A STUDY OF CORRELATION BETWEEN SEVERITY SCORE OF HRCT CHEST AND CLINICAL PARAMETERS OF ADULT PATIENTS ADMITTED WITH COVID-19AT MEDICAL COLLEGE, NORTH GUJARAT, INDIA

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Abstract

Background: COVID-19 disease is caused by highly infectious respiratory virus SARS-CoV-2, affecting 228 countries and territories worldwide. COVID-19 disease has wide spectrum of presentation from asymptomatic carrier stage to severe pneumonia with ARDS requiring ICU admission. A noncontrast high-resolution computed tomography of chest (HRCT) plays an important role in the early disease detection, assessing disease severity and predicting outcome. This study is planned to describe correlation of severity score on HRCT scan and clinical and laboratory parameters of patients with COVID-19 disease. **Materials and Methods:** It was a retrospective data analysis of patients admitted from 1st January 2021 to 31st May 2021at medical college, Visnagar, North Gujarat, India. Clinical, laboratory and radiological data collected for patients in which COVID-19 disease was confirmed by RTPCR test and who underwent HRCT scan. Data was collected in google form and entered in SPSS software for statistical analysis. **Result:** Total 270 patients were included in study with following data: age, gender, presence of comorbidities, laboratory tests including lymphocyte count, CRP, d-dimer and ferritin levels, maximum O2 requirement, need for intubation, Ward/ICU admission, length of hospital stay (LOS), and final outcome (expired, improved & discharged). The mean age was 54.44 years and 63.7% were males and 36.3% were female. HRCT scan showed mild severity score in 60 (22.22%) patients, moderate in 142 (52.59%) patients and severe in 68 (25.18%) patients, with male predominance among moderate and severe categories. HRCT severity score was found to be positively correlated with lymphopenia, increased serum CRP, d-dimer, and ferritin levels ($p < 0.0001$). The oxygen requirement and length of hospital stay were increasing with the increase in HRCT scan severity. **Conclusion:** HRCT scan is important tool for assessing disease severity and play a key role in assisting physician in management plan and predicting outcome. HRCT severity score positively correlates with inflammatory lab parameters, length of hospital stay, oxygen demand in patients with COVID-19 disease.

INTRODUCTION

Coronavirus disease-19 (COVID-19) is the infectious disease caused by novel coronavirus SARS-CoV-2. The first case of COVID-19 was reported to the world health organization (WHO) by Chinese authorities on December 31 2019 as a result of patient suffering from pneumonia in Wuhan city, Hubei province, China. Following a rapid spread in China, new outbreaks occurred in northern Italy and in several European countries. On march 12th 2020 WHO

announced COVID-19 outbreak as global pandemic.[1]

Up to now the Covid 19 pandemic has affected 228 countries and territories worldwide and cause 64 crore cases and 66 lakh death worldwide. India is having the second highest numbers of covid-19 case just being after USA with 4.46 crore case and 5.4 lakh death.[2]

Clinical presentation of novel corona virus disease COVID-19 is nonspecific, and may vary from asymptomatic carrier with sign & symptoms like other viral infection to patients with severe pneumonia requiring ICU admission and ventilatory support.[3]

Corona Virus disease-19(COVID-19) can be confirmed by isolating virus from diseased patient. RTPCR test from nasopharyngeal swab used as standard reference test to confirm COVID-19. The RTPCR test is robust detection tool to confirm COVID-19, however there is small but significant proportion of false negative results reported. [4,5]

A noncontrast high-resolution computed tomography of chest (HRCT) plays an important role in the early disease detection, especially in patients with false-negative RT-PCR results, as well as in monitoring the disease progression. [6,7] Moreover, the disease severity can also be confirmed from high-resolution CT chest imaging findings, supporting the clinicians in their clinical judgment and ensuring effective and timely management.[8]

Numbers of studies have been done about pulmonary involvement on chest CT image using software or visual assessment. Our study is planned to describe correlation of severity score on HRCT and clinical and laboratory parameters of patients with COVID-19 disease in town of north Gujarat, India.

MATERIALS AND METHODS

It was a retrospective study conducted at Nootan medical college and research center, Visnagar.

Ethical approval was obtained from Institutional Ethics committee. The informed consent was waived off as per approval form Ethics committee. We collected clinical, laboratory and radiological data from medical record department of the hospital for patients admitted from 1st January 2021 to 31st May 2021.Data was collected for patients in which COVID-19 disease was confirmed by RTPCR test and who underwent HRCT scan. Data was collected in google form and entered in the SPSS software for statistical analysis.

All HRCT scan were performed using Siemens 32 slice CT scan machine. Patients were placed in supine position with single breath holding. Scanning parameters were as follow: scan direction craniocaudally, tube voltage 110kv, tube current 100-600ma, slice collimation 32*0.600, pitch 1.50, rotation time 1s, scan length 128-1535.

Teaching faculties of radiology department evaluated the HRCT image to determine disease severity score in each patient. The scan was first assessed whether negative or positive for typical finding of COVID-19 pneumonia like bilateral, multilobe involvement, posterior peripheral ground glass opacities, as defined by the RSNA consensus statement.[9]. Severity was assessed by visual assessment of each lobe using following scoring system. [Table 1 and 2]

Table 1: Individual lobar scores based on percentage of involvement

Lobar involvement	Score
5% or less	1
6% to 25%	2
26% to 49%	3
50% to 75%	4
more than 75%	5

Table 2: Sum of the individual lobar score to indicate overall severity of lung

Total score	Severity (category)
1-15	Mild
16-25	Moderate
>25	Severe

The analysis was performed using SPSS software. Descriptive statistics of patients' demographics, clinical and laboratory results were reported as numbers and relative frequencies. Frequencies of HRCT scores were calculated and compared with other clinical variables.

The Pearson chi square test was used for correlations, and p value less than 0.05 was defined as statistically significant.

RESULTS

Baseline Information

Our study population involves patients with acute respiratory infection suspected to have COVID-19 infection. Infection with SARS-CoV-2 was confirmed by reverse transcriptase-polymerase chain reaction (RT-PCR) test from nasopharyngeal swab. All patients who have RTPCR confirmed COVID-19 and who underwent HRCT test were included in study.

106 patients were excluded from the study as per the following exclusion criteria: patients less than 18 years old, patients with negative RTPCR test, discharge to another facility, inconclusive HRCT scan due to significant motion artefacts, or CT with atypical findings for COVID-19 pneumonia.

Finally, 270 patients were included with the following information been collected: age, gender, presence of comorbidities/ risk factors, laboratory tests including lymphocyte count, CRP, d-dimer and ferritin levels, maximum O2 requirement, need for intubation, Ward/ICU admission, length of hospital stay (LOS), and final clinical outcome (expired, improved & discharged)

The mean age was 54.44 years (range 19–87 years; 172 males (63.7%), 98 females (36.3%)). The age was further classified into 6 groups: <30, 30–39, 40–

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49, 50–59, 60–69, and >70 years. Most common age group was that between 50 to 59 years(28.5%).
Comorbidity considered are hypertension, diabetes mellitus, ischemic heart disease, COPD and chronic kidney disease. No any comorbidity found in 140(51.85%), one comorbidity found in 113 patients (41.85%), two comorbidities in 16 patients (5.92%) and three or more in only one patient (0.37%).
Laboratory results shows lymphopenia in 227 (84.07%) patients, elevated CRP in 258(95.91%), high D dimer in 215 (80.52%) and elevated ferritin in 203(81.85%) patients.
Out of 270 patients 93(34.44%) patients did not require any oxygen support. Remaining 177 patients required oxygen support as below: 49(18.14%) patients required nasal cannula,65(24.07%) patients required oxygen via non rebreathing mask,, 54(20%) patients required bilevel positive airway pressure and nine(3.33%) patients required intubation and mechanical ventilation. ICU admission was required in 177 (65.55%) patients out of which male and female patients were 125(70.62%) & 52(29.37%) respectively.
Regarding hospital stay 46(17.03%) patients stayed in hospital for 5 days or less, 165(61.11%) patients stayed for 6-10 days and 59(31.85%) patients stayed for 11-15 days. In terms of clinical outcome, 23(9.30%) patients were expired and 247(90.70%) patients were improved and discharged from the hospital.

CT Severity score and clinical parameter

Our result showed significant correlation between HRCT score and male gender, raised inflammatory marker, higher oxygen requirement in form of NRBM mask& BiPAP/Intubation, duration of hospital stay ,need for ICU admission and intubation.
HRCT scan showed mild disease in 60(22.22%) patients(50% male,50% female), moderate in 142(52.59%) patients(66.19% male,33.80% female) and severe disease in 68(25.18%) patients(70.58% male,29.41% female).
The mild severity seen in mainly 30-39 years age group (n=31,51.66%) and least in > 70 years of age group(n=2,3.33%), moderate disease severity was mainly seen in 50-59 years of age group (n=72,50.70%) and least in 30-39 years of age group (n=6,4.22%), severe scans results were mainly seen in 50-59 years of age group(n=29,42.64%) and least in < 30 years of age group(n=3,4.41%).

CT severity score and Laboratory results

In mild CT severity score group normal lymphocyte count was seen in 29(48.33%) and lymphopenia was seen in 31(51.66%) patients. In patients with moderate scans normal lymphocyte count was seen in 13(9.15%) patients and decreased lymphocyte count was seen in 129(90.84%) patients. Only one patients(1.47%) with severe scan showed normal lymphocyte count and 67(98.52%) patients showed lymphopenia.
This shows that lymphopenia was more commonly seen in moderate and severe HRCT scan results and is statistically significant(chi square value 62.536 and p value 0.000)
CRP results was done for 269 patients. In patients with mild scan CRP level was normal < 6mg/L in 8(13.6%) patients and elevated in 51(86.4%). In patients with moderate scan group CRP level was normal in 2(1.4%) patients and elevated in 140(98.6%) and in patients with high CT severity score CRP level was normal in only one (1.4%) and 67 patients (98.6%) were having elevated CRP level. These finding were found to have statistically significant correlation with CT severity score. (Chi square value 17.2822 and p value 0.000177)
D dimer test results were available for 267 patients. In patients with mild category D dimer level was normal in 29 patients. In patients with moderate scan results D dimer were normal in 22(15.6%) patients and elevated in 119(84.39%) patients. In patients with severe scan group D dimer level was normal in 1(1.47%) and elevated in 67(98.52%) patients. In moderate and severe CT severity score category patients higher level of D dimer was commonly seen and there is statistically significant association. (Chi square value 49.864 and p value 0.000)
Ferritin levels was assessed in 248 patients. In mild category group ferritin level was normal in 22(42.30%) and elevated in 30(57%). In patients with moderate scan results ferritin level were normal in 22(16.92%) and elevated in 108(83.07%) patients. In patients with severe CT scan score ferritin levels were normal in 5 (7.57%) and elevated in 60(90.90%) patients. As CT severity score increase from mild to severe category ferritin level also increase from normal to high level. (Chi square 23.2336 and p value <0.00001)

CT severity score and Oxygen requirement & outcome

In mild CT severity score category 35 (58.33%) patients did not require any oxygen,16(26.66%) required oxygen with nasal cannula,7(11.66%) required oxygen via non rebreathing mask, two(3.33%) required BiPAP and no any patients required intubation.
46(32.39%) of patients with moderate CT severity score finding did not require any oxygen support,24(16.90%) required oxygen with nasal cannula,38(26.76%) required non rebreathing mask,30(21.12%) required BiPAP and four (2.81%) patients required intubation.
12 (17.64%)patients with severe CT scan results did not require any oxygen support,9(13.23%) required nasal cannula,20(29.41%) required oxygen with non rebreathing mask,22(32.35%) required ventilatory support with BiPAP and 5 (7.35%) patients required intubation and mechanical ventilation.[Table3]

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Table 3: Oxygen requirement according to HRCT severity category

Category		No oxygen	Nasal cannula	NRBM mask	BiPAP	Mechanical Ventilation	Total
Mild	Number	35	16	7	2	0	60
	% within category	58.33	26.66	11.66	3.33	0.00	100
	% of total	12.96	5.92	2.59	0.74	0.00	22.21
Moderate	Number	46	24	38	30	4	142
	% within category	32.39	16.09	26.76	21.12	2.81	100
	% of total	17.03	8.88	14.07	11.11	1.48	52.57
Severe	Number	12	9	20	22	5	68
	% within category	17.64	13.23	29.41	32.35	7.35	100
	% of total	4.44	3.33	7.40	8.14	1.85	25.16
Total		93	49	65	54	9	270

This trends shows that oxygen requirement through nasal cannula and NRBM mask is increase from mild to severe category of CT severity score and same trend is seen in requirement of BiPAP and intubation as CT severity category changes from mild to severe.

In case of length of stay in hospital,17(36.95%) patients with mild scan,24(52.17%) patients with moderate scan and five(10.86%) patients with severe finding required hospital admission for <= 5 days.

66 (40%) patients stayed in hospital for 6-10 days from mild category,89(53.93%) from moderate scan category and 10(6.06%) patients from severe scan category stayed in hospital for 6-10 days.

20 (33.89%) patients stayed in hospital for 11-15 days from mild category,27(45.76%) from moderate category and 12(20.33%) from severe scan category stayed in hospital for 11-15 days.

The mean duration of stay in hospital was 8.75 days and one patients with severe category stayed in hospital for highest 33 days. The length of hospital stay and CT severity scores were found to have statistically significant correlation (chi square value 9.9084 and p value 0.04199).

35(58.33%) patients with mild CT severity score required admission in general ward, while 25(41.66%) required admission in Intensive care unit. In patients with moderate category 46(32.39%) were admitted in ward while 96(67.60%) were admitted in ICU.In severe category only 12(17.64%) patients were admitted in ward while most of patients 56(82.36%) were admitted in ICU.

This shows that there is significant association between place of admission and HRCT severity score. Those with mild involvement of lung as determined by HRCT chest were managed in ward as compared to moderate and severe involvement were commonly admitted in ICU.(chi square value 23.9388 and p value is <0.005)

Of mild category no any patient were expired and all patients 60 (100%) were improved and discharged. 11(7.7%) patients with moderate category were expired while 131(92.3%) patients were improved and discharged. Among severe scan group 12(17.6%) patients were expired and 56(82.4%) were improved. This shows that best outcome were associated with mild category while death rate was increased among those with severe scan results and this association is statistically significant. (chi square value 12.967 and p value is 0.002)

DISCUSSION

To diagnose a patients with suspected to have COVID-19 disease various test are available like RTPCR test from nasopharyngeal swab, imaging study like HRCT chest, laboratory tests. The WHO advised to use HRCT chest to diagnose COVID-19 disease whenever RTPCR results are pending or not available or when strong clinical suspicion of COVID-19 disease but primarily negative RTPCR results.

HRCT chest also can be useful tool to quantify extent of involvement of lung and disease burden in patients with COVID-19. The extent of involvement of lung can be confirmed by direct visualization method as in our study or by software that confirms the extent of involvement of lung volumes using deep learning algorithms.

In this study, radiologist used direct visualization and assessment of each of lobe of lung. Individual lobar scores based on percentage of involvement were calculated. The sum of individual lobar score indicates the overall severity of lung.

A number of existing studies showed that present of comorbidities, especially hypertension, diabetes mellitus, ischemic heart disease and chronic kidney disease, carries poor prognosis and even worst outcome when multiple comorbidities are present. However, our study did not find statistically significant correlation between CT severity score and presence of comorbidities, although significant correlation present between ICU admission and presence of comorbidities (p< 0.0001).

Our study showed lymphopenia in 84% of patients, mainly in moderate and severe HRCT severity score category and it is statistically significant. Similar results of decreased lymphocyte count and lymphocyte ratio were obtained by Yun H, Sun Z,Wu J, et al. in data analysis of novel corona virus screening in 2510 patients.[10] Tavakolpour S, Rakhshandehroo T, Wei, et al. hypothesize following possiblecauses for lymphopenia observed in severe COVID-19 patients, inflammatory cytokine storm,

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exhaustion of T cell, direct infection of T cell with SARS-CoV2,interference with T cell expansion by SARS-CoV2.[11]

Our results showed that CRP level had significant correlation with severity of HRCT score.98.6% patients with severe score had elevated CRP levels. Ali N found that the elevated levels of CRP might be linked to the overproduction of inflammatory cytokines in severe patients with COVID-19. Cytokines fight against the microbes but when the immune system becomes hyperactive, it can damage lung tissue. Thus, CRP production is induced by inflammatory cytokines and by tissue destruction in patients with COVID-19.[12,13]

As a mediator of cytokine storm, a form of extreme immune dysregulation associated with fatal outcomes, ferritin level is usually ordered as a part of a panel along with other inflammatory markers. Many studies have correlated high ferritin levels with severe COVID disease. Para O, Caruso L,Pestelli G,et al. shared physio-pathogenic basis between COVID-19 and Hyperferritinemic Syndromes in a study involving 200 patients showed that highly elevated ferritin level were independently associated with bad outcome.[14] Similarly, severe involvement of lung in HRCT scan and high ferritin level found in this study.

D dimer can be used as one of the prognostic indicator, where high level are seen in more critical conditions. In moderate and severe CT severity score category patients in this study showed higher level of D dimer and there is statistically significant association. Systematic review and meta-analysis by GungorB,AticiA, BaycanOF,et al. involving 5750 non-severe and 2063 severe patients showed D-dimer levels were significantly higher in patients with severe clinical status and non-surviving patients had significantly higher D-dimer levels compared to surviving patients.[15,16]

The data analysis of this study found that there was increased requirement of oxygen with increasing severity score on HRCT. Similarly, study done by Kohli A, Jha T, & Pazhayattil AB on 740 patients found that significant positive correlation with oxygen requirement, place of admission and death.[17,18]

Average duration of stay in this study was 8.75 day,61.11% patients stayed for 6-10 days and 31.85% patients stayed for 11-15 days. One patient stayed for highest 30 days in hospital. Length of hospital stay depends on multiple factors like admission and discharging criteria, demand for bed and its availability and time course of pandemic of COVID-19.[19]

Death rate in our study was significantly increased among severe CT severity score category which is comparable to death rate by other studies.[20]

There are several limitations of the study. First, assessment of severity score on HRCT scan can be subjective. This can be reduced by assessing severity of disease by experienced reader, considering multiple opinion to reach consensus. Second, need for larger multicentric cohort to increase accuracy of finding. Third, other factors that might contribute to disease severity like comorbidities and life style should also be focused, so further investigation and researches are needed.

CONCLUSION

HRCT scan is important tool for assessing disease severity and play a key role in assisting physician in management plan and predicting outcome. HRCT severity score positively correlates with inflammatory lab parameters, length of hospital stay, oxygen demand in patients with COVID-19 disease.

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