

To Determine Role of C-reactive Protein Test and Computerised Tomography Scan of Lung in Diagnosis of COVID-19

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Abstract

The outbreak of novel Coronavirus Disease 2019 (COVID-19) has led the entire world to limp. The virus is causing the severe acute respiratory syndrome, with increasing morbidity and mortality. The WHO declared COVID-19 as a pandemic or public health emergency because of its morbidity and mortality. Several inflammatory markers have been used in the initial diagnosis, as well as prognostic markers in disease progression. One of the inflammatory markers is C reactive protein. The other markers that help in prognosis are ferritin, neutrophil-lymphocyte ratio, CT scan of the lung, IL6 (interleukin 6), RT PCR is reliable diagnostic evidence. Aim of the study: 1. The aim is to determine the C-reactive protein, CT (Computerised Tomography) scan of the lung, RT PCR (Reverse Transcriptase Polymerase Chain reaction) in COVID-19 patients. 2. To compare CRP & CT scan values of the lung in various age groups. A cross-sectional study was done from September 2020 to January 2021 and the results were analysed. Out of 704 covid positive patients, the maximum number of patients were in the age group between 31 to 70. The RT PCR showed COVID positive results in 689 (97.8%) patients. The CRP values were found to be >25mg/l from 31-50 (34.7%) years and in 51-70 years of age (52%). In comparison of CT scan with CRP changes, CRP values were found to be raised when there is 25-50% (24.5%) and >50% (27.6%) involvement of lung by COVID. CT scan lung involvement was >50% in the age group between 31-50 (38.9%) and 51-70 (50%), respectively. High CRP values of >25mg/l were observed with the same age group 34.7% with the group of 31-50 and 52% with the group of 51-70, respectively. CRP correlated with the advancing age group and was found to be a good predictor of disease progression.

Keywords: C reactive protein, CT lung, RT PCR

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INTRODUCTION

The Coronavirus Disease 2019 (COVID-19) was reported first in Wuhan, China, in December 2019.¹ The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is an enveloped RNA virus that is grouped under SARS (Severe acute respiratory syndrome) virus. The disease started to spread so rapidly that by March 6, 2020, we figured around 80,651 cases and 3070 deaths were noted across the mainland of China.² Outside China, SARS-CoV-2 started to spread around the world, especially in South Korea, Iran, Italy and India etc.³ In the present scenario we have come across 70,00,000 cases reported as on February 11, 2021. Now, the mutant strain has risen and led to a lockdown in many countries. The World Health Organisation (WHO) gave a clear indication of the risk of spread and the impact of COVID-19 to be extremely high at a global level on February 28, 2020. Several preventive measures were taken across the world with a heavy campaign to reduce the spread of virus and also to decrease the mortality. This pandemic has paralysed the whole world and continues to be even now. The symptoms arising from COVID-19 infection at the initial phase generally include fever, dry cough, and malaise that are non-specific. Unlike human coronavirus infections, upper respiratory symptoms are notably infrequent. We encounter common laboratory findings on admission to hospital such as lymphopenia and bilateral ground-glass opacity or consolidation in chest CT scans besides positive RT-PCR. We should be able to assess them initially with the laboratory parameter to improve the morbidity.⁴ In general in the affected patient population, >20% of the people infected with SARS-CoV-2 develop life-threatening complications. The systemic inflammatory response to the SARS-CoV-2 infection is a hallmark of 2019, and most hospitalized patients with COVID-19 have abnormal inflammatory biomarkers.⁵ Several inflammatory markers help in early pickup of severely affected patients. C-reactive protein (CRP) is an acute-phase protein synthesized by the liver whose level rises in inflammation. CRP levels are usually raised in bacterial infection mainly than in viral infection. Elevated CRP concentrations were associated with cardiovascular disease, surgical patients with severe infection, autoimmune disorders like rheumatoid arthritis, thromboembolism, and deep

vein thrombosis. Elevated CRP levels have been found in viral infections like H1N1 influenza, acute respiratory syndrome like Middle East Respiratory syndrome. CT scan of the lung played an important role in assessing the severity of disease in case RT PCR is negative.⁴ In our study we assessed the correlation between CRP, lung lesion based on CT scan besides RT PCR to assess the severity and in management and prognosis of the disease.

Objective

1. The aim of this study is to determine the C-reactive protein value, CT scan lung score, RT PCR in COVID-19 patients at a tertiary care teaching hospital.
2. To compare the CRP value and CT scan involvement of the chest in different age groups.

MATERIALS AND METHODS

The study was done at a tertiary care teaching hospital from September 2020 to January 2021.

Ethical clearance was obtained from the institution.

Study population

The population included in this study were all patients who came with symptoms suggestive of COVID-19 and above the age of 5 years.

Inclusion criteria

All patients who were tested positive for COVID-19 (either RT PCR or Based on CT chest) and also those above the age of 5 years.

Exclusion criteria

All patients who were found to be tested negative for COVID-19 were excluded from the study. Note in our results, ND denotes not detected in that particular test but would have been found to be COVID positive by other tests.

Duration of the study

From September 2020 to January 2021. Study is a cross sectional survey.

Statistical Methods

The statistical analysis was done by Descriptive and inferential statistical analysis. Results on continuous measurements were presented on Mean \pm SD (Min-Max) and results on categorical measurements were presented in Number (%). Significance was assessed at 5 % level of significance. The following assumptions

on data were made, Assumptions: 1. Dependent variables should be normally distributed, 2. Samples drawn from the population should be random, and Chi-square/ Fisher Exact test was used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis. Fisher Exact test was used when cell samples were exceedingly small⁶⁻⁹.

CRP is a passive agglutination test. The test was done according to the instructions given by the kit insert. (Aspen laboratories, Himachal Pradesh, India). The results observed were qualitative which correspond to 6mg/dl. Semi-quantitative analysis was done by dilution of the serum and the results were expressed by multiplying with the dilution factor and expressed in mg/l. RT-PCR was done by extraction of the RNA virus from the sample of nasal swab and oropharyngeal swab (2 swabs), the amplification of the curve was observed, and the CT value was (threshold cut-off value) expressed as positive or negative. Note: The threshold cut-off value varies with the kit insert. (Meril Diagnostics Pvt Ltd., Andheri East, Mumbai, India) is used in our lab. This is a qualitative assay. In addition, CT scan assessed the changes in the lung and CT scores were given based on the involvement of the lung. The reporting of chest CT patients suspected to be having COVID-19 were categorised based on

CT score. In CT scan, each lobe of the lung is given a CT score ranging from 1 to 5. In the right lung, there are 3 lobes: upper, middle and lower. Left lung has only two lobes, upper and lower. The CT scan scores are given as follows. When there is 5% involvement the score is —1, 5- 25% involvement the score is 2, 25 - 50% involvement the score is -- 3, 50-75% involvement the score is 4, 75% involvement the score is 5, showing disease severity.

RESULTS

In our study, we received samples from 704 patients. The samples were received from patients who got tested positive for COVID-19 either by RT-PCR or CT scan of the lung. We received 8 (1.1%) patients below 10 years of age (between 6 to 10), 175 (24.8%) patients in 11 - 30 years of age, 276 (39.2%) patients in 31 - 50 years of age, 213 (30.2%) patients in 51 - 70 years of age, 32 (4.5%) patients in 71- 90 years of age. The highest number of samples were received in the age group from 31 to 70 years. (Table 1). There were 426 (60.5%) male patients and 278 (39.4%) female patients. (Figure 1) The results of RT PCR showed positive results in 689 (97.8%) patients and were not detected in 15 patients (2.2%). (Table 2). The CT scan involvement of the lung took place in the following manner: There was no involvement (not detected) in 423 (60%) patients, <25% of involvement in 154 (21.8%) patients. 25 - 50% involvement in 92 (13.0%), > 50% involvements in 35 (8.3%) patients. (Table 3). This shows that RT-PCR was a more sensitive and reliable parameter in detection of COVID-19. We determined CRP values in various

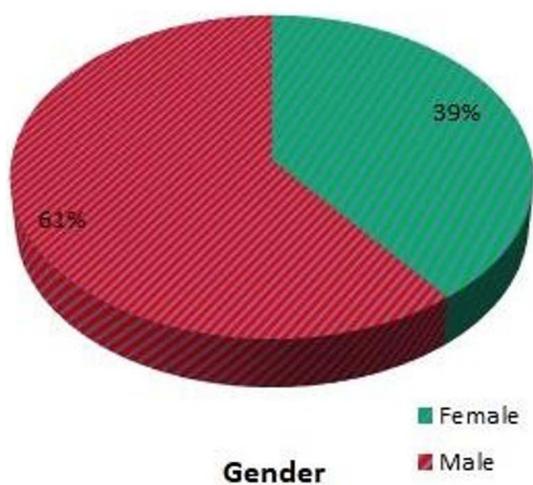


Fig. 1. Gender distribution of COVID-19 patients

Table 1. Age wise distribution of patients in COVID 19 patients

Age in Years	No. of Patients	%
<10		1.1
11-30	175	24.8
31-50	276	39.2
51-70	213	30.2
71-90	32	4.5
Total	704	100.0

Mean ± SD: 43.45+16.29

age groups and the results were expressed in mg/l. 8 patients had CRP in the range of <5mg/l and there were no patients with values > 25mg/l in the age group of less than 10 years. In the age group of 11 - 30 years 152 (31.39%) patients had CRP in the range of < 5mg/l and 5 (5.1%) patients had in the range of > 25mg/l. As the age advanced CRP with values > 25mg/l was seen in the age group 31 - 50 years 34 (34.7%), and also in 51 - 70 years 51 (52.7%). We had more patients in the age group from 31 - 70 years. (Table 4). CT scan changes involving lungs were also seen more in the same age groups. CT scan involvement of the lung involving > 50% was seen in the age group between 31 - 50 (38.9%) years and 51 – 70 (50%) years. (Table 5). When we compared CT scan with CRP changes, we found CRP values were found to be increased when there is involvement of the lung from 25 - 50% (24.5%) and > 50% (27.6%) respectively. (Table 6).

DISCUSSION

Globally it is a fact that large number of patients have been affected with COVID-19 which is rapidly increasing and asymptomatic

patients are also the source of infection. (10) Early determination of key indicators were an important basis to guide treatment strategies to prevent morbidity and mortality.¹¹ The most common laboratory findings on admission to hospital include lymphopenia and bilateral ground-glass opacity or patchy changes in chest CT scans. The main pathological changes are damages involving lungs that cripples the patient. It causes damage to the immune complex too. CT dynamic monitoring is done to assess the involvement of the lungs. Most of the time when RT-PCR is negative, the results suggestive of COVID was correlated with the CT scan.¹² We can see multiple ground glass appearance involving both the lobes of the lungs when there is > 50% damage. If you find a 50% increase in lung X-ray findings within 24 to 48 hours, this was considered an early warning indicator of severity of the disease. CT scan can sometimes predict the prognosis of a patient.¹³ According to Zhong Nanshan's latest research, the sensitivity of COVID-19 diagnosis with CT scan alone was 76.4%, and the application of CT scan in COVID-19 was evaluated as useful.¹⁴ Studies by Chen Lin et al all suggested the correlation of

Table 2. Reverse Transcriptase Polymerase Chain Reaction (RTPCR) distribution in COVID 19 patients

RT PCR	No. of Patients (n=704)	%
Positive	689	97.8
Negative	0	0.0
ND	15	2.2

Table 3. Computerised Tomography scan of lung distribution in patients of COVID

CT-SCAN	No. of Patients (n=704)	%
25%	154	21.8
25-50%	92	13.0
50%	35%	8.3
ND	423	60.0

Table 4. Correlation of Age distribution with C reactive protein in patients of COVID

Age in Years	CRP					Total
	ND	<5mg/l	5-10mg/l	10-25mg/1	>25mg/l	
=10	0(0%)	8(1.7%)	0(0%)	0(0%)	0(0%)	8(1.1%)
11-30	0(0%)	152(31.9%)	14(14.1%)	4(13.3%)	5(5.1%)	175(24.9%)
31-50	0(0%)	192(40.3%)	39(39.4%)	11(36.7%)	34(34.7%)	276(39.2%)
51-70	1(100%)	107(22.5%)	40(40.4%)	14(46.7%)	51(52%)	213(30.3%)
71-90	0(0%)	17(3.6%)	6(6.1%)	1(3.3%)	8(8.2%)	32(4.5%)
Total	1(100%)	476(100%)	99(100%)	30(100%)	98(100%)	704(100%)
h4ean + SD		39.97 +15.88	48.23 +15.04	48.50 +14.23	53.87 +14.05	43.43 +16.29

PM.001**, Significant, Student t Test

Table 5. Computerised Tomography Scan of lung Changes in different age groups

Variables	CT SCAN				Total	P Value
	-	<25%	25-50%	>50%		
Age in Years						
≤ 10	8(1.9%)	0(0%)	0(0%)	8(1.1%)		
11-30	142(33.6%)	24(15.6%)	8(8.8%)	1(2.8%)	8(1.1%)	
31-50	149(35.2%)	71(46.1%)	42(46.2%)	14(38.9%)	276(39.2%)	
51-70	105(24.8%)	53(34.4%)	37(40.7%)	18(50%)	213(30.3%)	<0.001**
71-90	19(4.5%)	6(3.9%)	4(4.4%)	3(8.3%)	32(4.5%)	

Table 6. Comparison of C- Reactive protein and Computerised Tomography of lung changes in COVID-19

Variables	CRP					Total	P Value
	ND	<5mg/l	5-10mg/l	10-25mg/l	>25mg/l		
CT SCAN							
ND	0(0%)	352(73.9%)	22(22.2%)	11(36.7%)	38(38.8%)	423(60.1%)	<0.001**
<25%	0(0%)	104(21.8%)	38(.4%)	3(10%)	9(9.2%)	154(21.9%)	<0.001**
25-50%	0(0%)	18(3.8%)	38(38.4%)	11(36.7%)	24(24.5%)	91(12.9%)	<0.001**
>50%	1(100%)	2(0.4%)	1(1%)	5(16.7%)	27(27.6%)	36(5.1%)	<0.001**

the CT scan in the diagnosis and evaluation of COVID-19.⁴ CRP is a type of protein and is found to be raised in response to inflammation. Generally, CRP level is found to be on an increased level in bacterial infections than in viral infections. To our surprise, many COVID-19 patients in this study showed raised CRP levels mostly in the age group between 31 - 70 years, in addition to CT changes involving > 50% involvement of the lungs in the same age groups. It is consistent with Wang et al study.¹⁵ It is an important index for the diagnosis and assessment of severe pulmonary infectious diseases.¹⁶ Moreover, critical cases in this study showed significantly raised levels of CRP than non-critical patients, which suggested that CRP may be a serum marker of disease severity in COVID-19 patients. The logistic regression analysis demonstrated that CRP was indeed related to disease progression. Patients presenting with pneumonia were found to have raised CRP level.¹⁷ In Matsumoto's study we found raised levels of CRP levels in severe pneumonia. His study showed that CRP levels and the area of increased lung lesion increased as the disease progressed.¹⁸ which was correlating with our study.

CONCLUSIONS

Early intervention is required to prevent

mortality among severe COVID-19 patients. Raise in CRP level values could be used as a valuable marker initially to start the treatment early. As the disease progresses, CRP can be used as a prognostic marker to assess the severity which is correlating with our study. This was observed from the CT score involvement of the lung. However, a large sample size is required to confirm these results. We need to focus to assess the patient initially based on clinical findings and carry out relevant investigations to prevent morbidity and mortality.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

FUNDING

None.

DATA AVAILABILITY

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

ETHICS STATEMENT

The study was approved by the Institutional Ethics Committee, A.C.S. Medical College Hospital, Chennai, India (No.98/2020/1EC/ACSMCH Dt. 16.12.2020).

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