

**CORRELATION OF CT SEVERITY SCORE AND LABORATORY PARAMETERS
WITH CLINICAL OUTCOME AND COMPLICATIONS IN COVID 19 PATIENTS**

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Abstract

Introduction: Corona virus disease 2019(COVID-19) is an infectious acute disease associated with significant morbidity and mortality. The disease threatened the whole world in 2020 and 2021 and new cases are reported till date. CT is invaluable in assessing no of bronchopulmonary segments involved in the lung as conventional chest X ray is not sensitive. Several cytokines are released during pathogenesis of the disease which play a pivotal role in dictating the disease outcome. In this study, we aimed to study the correlation between CT score, inflammatory markers with patient's outcome.

Materials and Methods: A retrospective hospital based study conducted at Sri Manakula Vinayagar medical college and hospital (SMVMCH), tertiary care center located at Madagadipet in rural Puducherry, India. Adult patients who got admitted in SMVMCH with proven COVID 19 infection were chosen as study participants. The study was carried out after obtaining Institutional ethics committee (IEC) clearance. Data pertaining to CT severity score (CTSS), inflammatory markers, duration of hospital stay till discharge or death is collected from all such patients.

Results: CT score was correlated using Pearson Correlation. Sample size (N) was taken as 117. CT score of 7 or less was classified as mild, was seen in 29 patients (24.8%). Moderate Covid was classified at a score of 8-17, was seen in 71 patients (60.7%). Severe Covid score of 18 or greater was seen in 17 out of the 117 patients (14.5%). Out of the 117 patients 51.3% of patients stayed in hospital for 7 days, 33.3% stayed in hospital for 14 days, 8.5% stayed in hospital for 21 days, 6.8% stayed in hospital for 31 days. Patients with increased values of CTSS and C reactive protein (CRP) had higher length of hospital stay and increased mortality compared to other

patients. 49 patients were observed in intensive care for an average duration of 3 days till their oxygen saturation got stabilized at 95% or more and were shifted to ward care.

Conclusion: Increased CTSS was associated with increased duration of hospital stay and increased mortality. CRP was the marker which had a strong correlation with patient's outcome and CTSS.

Key Words: COVID 19, CT severity score, CRP, Outcome.

INTRODUCTION

Corona virus disease 2019 (COVID-19) is an infectious acute disease caused by a novel corona virus called severe acute respiratory syndrome coronavirus 2 (SARS –COV 2).¹ Cases were first detected in Wuhan city, China in December 2019. The epidemic has escalated and spread rapidly around the world affecting 229 countries and territories. India is one of the country worst affected with the pandemic with 4,50,03,055 cases and 5,33,306 deaths detected till date.

COVID 19 definitive diagnosis is done by reverse transcriptase polymerase chain reaction (RT PCR). Though RT PCR is highly specific (which is always negative in those without COVID 19 infection), several studies^{2,3} raised concern about the sensitivity of this test.² Hence an alternative investigation was required to minimize chance of missed diagnosis. COVID 19 reporting and data system (CO-RADS) provides level of suspicion for pulmonary involvement of COVID 19 based on features seen on non contrast chest CT.⁴ The level of suspicion increases from very low (CO RADS 1) to very high (CORADS 5).

CT severity score tells the number of bronchopulmonary segments involved in both lungs in COVID 19 infection. COVID 19 infection is associated with numerous complications like acute respiratory distress syndrome (ARDS), acute liver injury, secondary infection, septic shock. Some conditions predispose to the development of severe COVID 19 illness including chronic kidney disease, chronic obstructive pulmonary disease, morbid obesity, sickle cell disease, type 2 diabetes. Several inflammatory markers have been reported to be significantly associated with high risk of development of severe COVID-19 infection which include serum ferritin, D dimer, LDH, procalcitonin (PCT), erythrocyte sedimentation rate (ESR), C reactive protein (CRP) and interleukin 6.⁵ These markers help in assessing prognosis and need for close follow up in patients with severe COVID 19 infection.

The present study aims to analyze outcome and complications of COVID 19 infection in relation with CT severity score and laboratory parameters.

OBJECTIVES

1. To estimate CT severity score in patients with proven COVID 19 infection.

2. To estimate values of various inflammatory markers like D dimer in all such patients
3. To correlate clinical outcome and complications of all such patients with CT score and inflammatory markers.

MATERIALS AND METHODS

Study setting: Hospital based study conducted in August and September 2021 at SMVMCH, and data was collected from patients who got admitted from April to July 2021 during the second covid wave in the country.

Study design: The present study is a retrospective analytical study.

Study participants: Adult patients (Age 18-80) of both sexes who got admitted in SMVMCH with proven COVID 19 infection (With RT PCR)

Exclusion criteria

- Microbiologically confirmed pulmonary tuberculosis
- Proven malignant tumour of lung
- Biopsy proven interstitial lung disease

Study duration: The duration of this study was 2 months from the date of approval.

Sampling method: This was done by simple random sampling

Sample size: Sample size for this study was calculated to be 108 by using open epi software version 3.0 based on the presence of peripheral ground glass opacities and consolidation in 86 patients with COVID 19 infection based on a previous study.⁶

Methodology:

Patients with proven COVID 19 infection who got admitted in the hospital were selected. Demographic and clinical characteristics of patients including comorbidities were collected. CT severity score (Maximum score 25) and values of D dimer, LDH, serum ferretin, CRP collected from all such patients. CT score and inflammatory markers were correlated with the clinical outcome and complications (which includes total no of days of stay in the hospital, development of complications like ARDS and discharge/death of patient) and data analyzed.

Statistical Analysis

Data was entered using the software Epi Info version 7.2.2.6 and analysis was done using the software SPSS version 24.0. Description of categorical variables like gender was done in frequency and percentage and that of continuous variables like age using mean and standard deviation. 2 tailed test and Pearson correlation were used to assess the significance.

RESULTS

A total of 117 patients (89 males and 28 females) were included in the study. A total of 58 and 41 patients had diabetes mellitus (DM) and hypertension (HTN) respectively (Tables 1 and 2). The relationship of CTSS with duration of stay and final outcome is depicted in tables 3 and 4 respectively. The relationship of D dimer, LDH, Serum ferretin and CRP with duration of stay in

hospital and final outcome is depicted in 5,6,7,8 respectively. The relationship of CTSS with each of the inflammatory markers and its statistical significance is shown in 9,10,11,12 respectively. Diagram 1 shows ROC curve describing relationship between final outcome of patient with CTSS.

Table 1: DM * Gender

		GENDER		Total
		Male	Female	
DM	No	45	14	59
	Yes	44	14	58
Total		89	28	117

Table 2: HTN * Gender

		GENDER		Total
		Male	Female	
	No	56	20	76
	Yes	13	2	15
Total		89	28	117

Table 3: CTSS with duration of stay

Count						
		CTSS				Total
		<=7	8-12	13-17	>=18	
Duration	1-7 days	19	24	10	7	60
	8-21 days	10	18	13	8	49
	22-31 days	0	3	3	2	8
Total		29	45	26	17	117

2 tailed value: 0.019

Table 4: CTSS with final outcome

Count				
		Outcome		Total
		Death	Alive	
CT score	<=7	1	28	29
	8-12	5	40	45
	13-17	6	20	26
	>=18	5	12	17
Total		17	100	117

2 tailed value: 0.008

Table 5: D-dimer * Hospital duration* Outcome

Hospital duration			Outcome		Total
			Death	Alive	
1-7 days	D-dimer	Normal (<0.5)	5	42	47
		Abnormal (>=0.5)	2	11	13
	Total		7	53	60
8-14 days	D-dimer	Normal (<0.5)	5	22	27
		Abnormal (>=0.5)	2	10	12
	Total		7	32	39
15-21	D-dimer	Normal (<0.5)	1	6	7
		Abnormal (>=0.5)	0	3	3
	Total		1	9	10
22-31 days	D-dimer	Normal (<0.5)	1	2	3
		Abnormal (>=0.5)	1	4	5
	Total		2	6	8
Total	D-dimer	Normal (<0.5)	12	72	84
		Abnormal (>=0.5)	5	28	33
	Total		17	100	117

2 tailed value: 0.566

2 tailed value: 0.172

Table 6: LDH * Hospital duration* Outcome

Hospital duration	Outcome	Total
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			Death	Alive	
1-7 days	LDH	Normal (142-280)	4	46	50
		Abnormal (>=281)	3	7	10
	Total		7	53	60
8-14 days	LDH	Normal (142-280)	5	25	30
		Abnormal (>=281)	2	7	9
	Total		7	32	39
15-21	LDH	Normal (142-280)	1	7	8
		Abnormal (>=281)	0	2	2
	Total		1	9	10
22-31 days	LDH	Normal (142-280)	0	4	4
		Abnormal (>=281)	2	2	4
	Total		2	6	8
Total	LDH	Normal (142-280)	10	82	92
		Abnormal (>=281)	7	18	25
	Total		17	100	117

2 tailed value: 0.265

2 tailed value: 0.002

Table 7: Ferritin * Hospital duration* Outcome

Hospital duration			Outcome		Total
			Death	Alive	
1-7 days	Ferritin	Normal	4	43	47
		Abnormal	3	10	13
	Total		7	53	60
8-14 days	Ferritin	Normal	4	23	27
		Abnormal	3	9	12
	Total		7	32	39

		Total	7	32	39
15-21	Ferritin	Normal	1	7	8
		Abnormal	0	2	2
	Total		1	9	10
22-31 days	Ferritin	Normal	1	3	4
		Abnormal	1	3	4
	Total		2	6	8
Total	Ferritin	Normal	10	76	86
		Abnormal	7	24	31
	Total		17	100	117

2 tailed value: 0.001

2 tailed value: 0.561

Table 8: CRP * Hospital duration* Outcome

Hospital duration			Outcome		Total
			Death	Alive	
1-7 days	CRP	Normal	0	29	29
		Abnormal	7	24	31
	Total		7	53	60
8-14 days	CRP	Normal	2	9	11
		Abnormal	5	23	28
	Total		7	32	39
15-21	CRP	Normal	0	2	2
		Abnormal	1	7	8
	Total		1	9	10
22-31 days	CRP	Abnormal	2	6	8
	Total		2	6	8
Total	CRP	Normal	2	40	42
		Abnormal	15	60	75
	Total		17	100	117

2 tailed value: 0.000

2 tailed value: 0.014

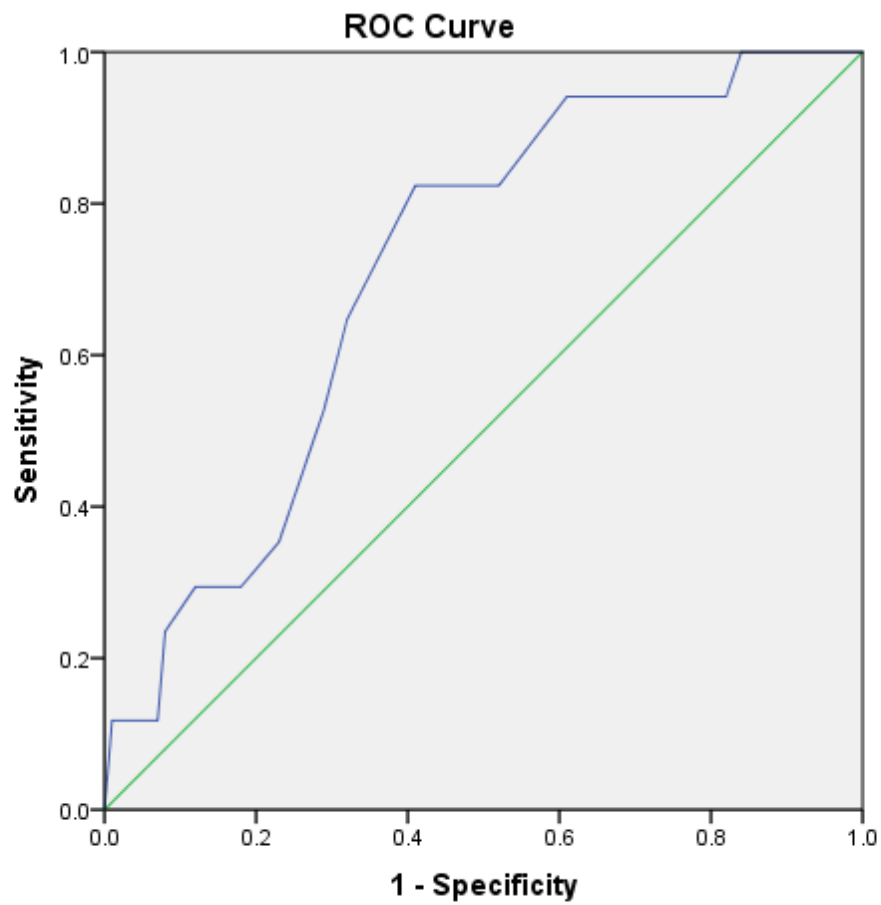
Correlations: Table 9			
		CT-Score	D DIMER
CT-CHEST	Pearson Correlation	1	.108
	Sig. (2-tailed)		.247
	N	117	117
D DIMER	Pearson Correlation	.108	1
	Sig. (2-tailed)	.247	
	N	117	117

Correlations: Table 10			
		CT-Score	LDH
CT-CHEST	Pearson Correlation	1	.165
	Sig. (2-tailed)		.076
	N	117	117
LDH	Pearson Correlation	.165	1
	Sig. (2-tailed)	.076	
	N	117	117

Correlations: Table 11			
		CT-Score	CRP
CT-CHEST	Pearson Correlation	1	.278**
	Sig. (2-tailed)		.002
	N	117	117
CRP	Pearson Correlation	.278**	1
	Sig. (2-tailed)	.002	
	N	117	117

Correlations: Table 12			
		CT-Score	FERRITIN
CT-CHEST	Pearson Correlation	1	.135
	Sig. (2-tailed)		.148
	N	117	116
FERRITIN	Pearson Correlation	.135	1
	Sig. (2-tailed)	.148	
	N	116	116

Diagram 1: ROC curve



Diagonal segments are produced by ties.

Area Under the Curve

Test Result Variable(s): CT-CHEST			
Area	Std. Error ^a	Asymptotic Sig. ^b	Asymptotic 95% Confidence Interval

			Lower Bound	Upper Bound
.711	.060	.005	.594	.829

The positive actual state is death. The test result variable(s): CT-CHEST has at least one tie between the positive actual state group and the negative actual state group.

DISCUSSION

Pneumonia cases of unknown origin were first reported in Wuhan, China in December 2019 and a history of exposure to seafood market was considered. Since then the disease spread rapidly and WHO declared it a pandemic on March 11 2020. CT chest performed on patients during the initial days when cases were first reported in China reported abnormalities in all patients.⁷ In COVID 19, there is a phenomenon of an extreme inflammatory response, in which inflammatory cytokines are rapidly secreted in a massive amount in response to infection⁸. Several studies performed earlier^{9, 10} highlighted the importance of these inflammatory markers during pathogenesis and outcome in COVID 19 infection. The present was done to assess the prognostic significance of CT and several inflammatory markers in COVID 19 patients.

It is extremely important to identify patients who become severely ill during the course of illness. A total of 17 patients expired in the present study due to covid related complications. Out of them, 1 patient had a CTSS of ≤ 7 (5.8%), 5 patients had CTSS of 8-12 (29%), 6 patients had a CTSS of 13-17 (34.8%) and 5 patients had a CTSS of more than 18 (29%). In the group of patients who survived, 28 (28%), 40 (40%), 20 (20%) and 12 (12%) patients had a CTSS of less than 7, 8-12, 13-17 and 18 or more respectively. A 2 tailed p of 0.008 was obtained which was statistically significant suggesting that increasing CTSS score correlated with increased mortality in COVID 19 patients. Increased CTSS was also associated with increased length of stay in hospital, with a 2 tailed value of 0.019 which was significant. These results are consistent with several earlier studies^{11, 12, 13} where increased CT score was associated with poor outcome. However not all patients with a higher CT score succumbed to complications and a total of 17 patients with a score of ≥ 18 got discharged from the hospital. These findings suggest that presence of comorbidities like diabetes, hypertension have an important role in deciding patient's outcome.

Elevated CRP was associated with poor outcome in the present study. 2 tailed values of 0.000 and 0.014 for duration of stay and final outcome respectively which was statistically significant. An

earlier study done in Newyork¹⁴ suggested that elevated CRP was strongly associated with increased incidence of venous thromboembolism, acute kidney injury and mortality in COVID 19. An important role is played by CRP in inflammatory processes and host responses to infection including the complement pathway, apoptosis, phagocytosis, nitric oxide (NO) release, and the production of cytokines, particularly interleukin-6 and tumor necrosis factor- α . CRP plays a role in the recognition and clearance of foreign pathogens and damaged cells by binding to phosphocholine, phospholipids, histone, chromatin, and fibronectin. Elevated serum ferretin was associated with increased length of hospital stay but not with mortality. Elevated LDH was associated with increase in mortality but not with no of days of stay in hospital. However no statistical significance was found between D dimer with duration of stay in hospital and mortality of patients in the present study. These results are contrary to several earlier studies done earlier^{15,16,17} where there was a strong correlation between D dimer and outcome.

Each of the inflammatory markers was again corelated with CTSS for final outcome (discharge/death) of patients and significance assessed. There was a statistically significant relationship between CRP and CTSS (2 tailed value of 0.002). However no significant relationship was found between CTSS and values of D dimer, Serum ferretin and LDH.

A single patient who initially presented to hospital in a stable condition with CTSS of 2 gradually developed respiratory distress and were shifted to ICU for close monitoring and succumbed to death despite adequate treatment. 3 patients with CTSS of 8-12 admitted in a stable condition gradually deteriorated during hospital stay and expired. On the other hand, a good no of patients who had tachypnea with tachycardia during admission gradually improved and got discharged from the hospital. This probably signifies the role of good immunity in combating infection against COVID 19. The adverse impact of poor nutrition on the immune system, including its inflammatory component, may be one of the explanations for the higher risk of more severe outcomes from infection with SARS-CoV-2 seen in older people.¹⁸ Both cell mediated immunity and antibody response help in containing viral infections.¹⁹ It was observed that the longer stay in hospital was seen among patients with Type 2 Diabetes, hypertension and among patient >65 years of age. Those with age >50, poor glycemc control, associated heart failure and chronic kidney disease were found to be deciding factors in guiding prognosis in many patients.

CONCLUSION

The present study emphasizes initial evaluation of all covid 19 patients with Non contrast CT chest and and CRP. CT scans can have a pivotal role in assisting diagnosis, evaluating treatment strategies and work as an indicator for disease severity and possible outcome. Those Patients with a CTSS of more than 7 and elevated CRP should be closely monitored throughout the

hospital stay. Good nutrition along with addressing co morbidities during the stay in hospital can play a definite role in improving outcome in COVID 19 patients.

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