Journal of Advances in Medicine and Medical Research

34(12): 16-26, 2022; Article no.JAMMR.86118
ISSN: 2456-8899
(Past name: British Journal of Medicine and Medical Research, Past ISSN: 2231-0614, NLM ID: 101570965)

Correlation of CT Severity Index with Clinical Severity of COVID-19 Pneumonia and it's Relation to Disease Outcome

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMMR/2022/v34i1231369

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/86118

Original Research Article

Received 20 March 2022
Accepted 23 April 2022
Published 30 April 2022

ABSTRACT

Background and Objectives: Since the first case of Covid – 19 infection in Kerala, it has spread rapidly throughout the country. The COVID-19 infection is caused by SARS-CoV-2 virus. Fever, cough and breathlessness are the most common symptoms of infected individuals. An in-depth understanding of the modes of spread, clinical features, triage of infected patients at presentation, immediate appropriate treatment and containment measures to minimize transmission of infection are cornerstones of pandemic control. The present study attempts to correlate chest CT Severity Index with clinical severity of Covid-19 infection and its outcome in infected individuals.
Materials and Methods: This was a retrospective, cross – sectional, descriptive study. Study group consisted of 97 adults who tested Covid positive with RT-PCR and had positive findings on chest CT scan at our Hospital.
Results: There was a statistically significant association between CT Severity Index and clinical

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severity of Covid – 19 Pneumonia in the study patients; as well as between CTSI and outcome of Covid – 19 Pneumonia in terms of favourable and adverse outcomes.
Interpretation and Conclusion: Since the CTSI correlates significantly with clinical severity of Covid - 19 infection and it's outcome, its inclusion in the CT report is invaluable in rapidly triaging the patient, initiating early appropriate treatment and providing a reasonably accurate prediction of future course and outcome of the infection. By significantly cutting down time spent in triaging a patient in the ER, it saves time and minimizes need for large skilled workforce of medical personnel in limited resource settings.

Keywords: CTSI; Covid Pneumonia; significant association; clinical severity; outcome.

1. INTRODUCTION

The first cases of COVID-19 infection in India were reported on 30 January 2020 in three towns of Kerala among three Indian medical students who had returned from Wuhan in China, which was then the epicenter of the pandemic [1,2]. Since then, it has spread like wildfire throughout the country and simultaneously engulfed the entire world, taking a heavy toll on the lives of countless individuals and exhausting healthcare resources globally.

The Novel Coronavirus disease 2019, abbreviated as COVID-19, is caused by the Severe Acute Respiratory Syndrome Coronavirus type-2 (SARS-CoV-2) which belongs to the family of beta coronaviruses [3]. This is an enveloped, single-stranded RNA virus [2].

Severe acute respiratory illness with fever, cough and breathlessness comprise the most common symptoms of individuals infected with the SARS-CoV-2 virus [4]. Isolated upper respiratory tract symptoms such as runny nose and sore-throat have also been reported in isolation [4]. Gastrointestinal symptoms such as diarrhoea has been reported in about 2-40% of infected patients. Taste or olfactory disorders are noted in up to 53% of the cases; and recent onset anosmia is being considered as a unique symptom warranting testing of patients. Recent case series from foreign countries describe neurological symptoms such as ischaemic or haemorrhagic stroke, dizziness, headache, musculoskeletal disturbances, altered mental state, Guillain-Barré syndrome, or acute necrotising encephalopathy, in patients infected with the virus [4]. Cardiovascular events associated with covid-19 infection include myocardial injury, especially in patients with severe infections, myocarditis and pericarditis with reduced systolic function, cardiac arrhythmias,and congestive cardiac failure. Covid-19 is also associated with a hypercoagulable state thereby increasing the risk for venous thromboembolism including pulmonary embolus [4]. The "Gold Standard" test for diagnosis of COVID-19 infection is the "Reverse Transcription Real-Time Fluorescence Polymerase Chain Reaction" (RT-PCR) test performed on specimens obtained from the upper respiratory tract or blood of suspected individuals [3]. An in-depth understanding of the modes of spread of the disease, plethora of clinical features, triaging of infected patients at presentation, immediate institution of appropriate treatment and measures to contain person to person transmission of the infection are the cornerstones of control of the pandemic. The present study attempts to correlate the various findings on CT Scan study of the Chest and the CT Severity Index with clinical severity of Covid-19 infection and its relationship with outcome of the disease in infected individuals.

1.1 Aims and Objectives

1. To correlate the Chest CT Severity Index with clinical severity of Covid-19 pneumonia.
2. To determine the relationship between Chest CT Severity Index and outcome of Covid-19 pneumonia in infected individuals.

2. MATERIALS AND METHODS

2.1 Study Design

This was a retrospective, cross – sectional, descriptive, hospital based research study. The source population consisted of 103 adult patients (male and female) who tested positive for Covid-19 infection with RT-PCR test of their upper respiratory tract specimens and who underwent CT scan study of the chest at MVJ Medical College and Research Hospital, Hoskote from July 2020 to April 2021. Among them, 97

patients had positive findings on CT Chest study and were selected as the study group.

Techniques and Data Collection: CT scans of the chest were performed using a 16-slice Multi Detector Row CT Scanner - GE Brivo model 385. Patients were scanned in supine position, in cranio-caudal direction and single breath hold images at end inspiration were obtained. Segmented CT scan images were aquired wherever patients were breathless or could not hold breath for sufficiently long time. Children and severely tachypneic adult patients who could not hold their breath for sufficient length of time were excluded from the study. After acquisition, the CT images were retrospectively reconstructed in HRCT kernel using high spatial frequency algorithm, 1.25mm slice thickness at 1.25mm intervals covering the entire thorax from the level of thoracic inlet cranially to just below domes of diaphragm caudally. An X-ray Tube Current of 80 – 100 mA and tube voltage of 120 to 140 kVpwere the scanning parameters used in the study. The acquired images were reconstructed using lung and mediastinal windows. After completion of Chest CT scans for COVID positive patients,the rooms were sanitized using standard disinfection regimens at the end of each day. The CT Scan images were reviewed and imaging findings including the CTSI (CT Severity Index) for each patient were documented as per the study proforma. The information regarding clinical severity of COVID-19 pneumonia in each patient and outcome of the infection was recorded from the case sheets retrospectively.

Inclusion Criteria: All adult patients of both sexes who

1. Had a positive RT-PCR test for Covid-19 infection.
2. Underwent CT scan study of the chest at MVJ Medical College and Research Hospital, Hoskote from July 2020 to April 2021.
3. Had positive findings on CT Chest study.
4. Whose Chest CT Scans were of diagnostic quality to allow objective interpretation of images.

2.2 Exclusion Criteria

1. Children less than 18 years of age.
2. Patients who tested RT-PCR Positive but could not undergo the chest CT Scan due to inability to hold breath either due to breathlessness or restlessness.
3. All patients who required ventilatory support and who were in critical pneumonia with ARDS and / or septic shock or Multi Organ Dysfunction Syndrome and could not undergo the Chest CT Scans.
4. Patients who tested RT-PCR Positive and underwent the chest CT Scan but had no findings or negative findings pertaining to Covid – 19 pneumonia.

Review and analysis of CT Scan images: The CT Scan images were interpreted and evaluated to determine the disease severity score by a radiologist with more than 8 years experience. All the patients' Chest CT images were reviewed for the presence or absence of Ground Glass Opacities, Consolidation, Crazy – Paving appearance, Vascular Dilatation in the involved lobes, Subpleural Bands, Traction Bronchiectasis, Architectural Distortion and Parenchymal Bands. Specifically, the morphological appearance and distribution of these opacities (multiple, confluent, multilobar and multifocal ground glass opacities and consolidation) considered as typical or diagnostic of Covid-19 pneumonia as defined in the RSNA consensus statement were first assessed, whether present or absent [5].

In each patient, the C.T Severity Index was then calculated using the 25 – point CT Severity Score [5]. This score is computed depending upon the visual assessment of extent of involvement of each lobe of both lungs (3 lobes on the right and 2 lobes in the left lung) [6]. Each lobe was assessed visually for the presence and extent of Ground Glass opacities (with or without crazy -paving), Consolidation, and combination of the two; and a five point scale was given as follows: 0 to 5% involvement of a lobe by the above opacities – 1; 5 to 25 % involvement of a lobe by the above opacities – 2; 26 to 49% involvement of a lobe by the above opacities – 3; 50 to 75% involvement of a lobe by the above opacities – 4; and 76 to 100% involvement of a lobe by the above opacities – 5 [6].

The scores thus obtained in each individual lobe were then added together to give a single overall CT score of severity of Covid – 19 pneumonia in the patient. The pneumonia was then graded as – Mild, if the overall CT Severity Score was 0 to 7; Moderate if the overall score was 8 to 17; and Severe if the overall score was 18 to 25 [6].

2.3 Statistical Analysis

The variables collected and analysed in this study were – patient demographics (age and sex distribution), CT Chest findings of Ground Glass Opacities, Consolidation, Crazy – Paving appearance, Vascular Dilatation in the involved lobes, Subpleural Bands, Traction Bronchiectasis, Architectural Distortion and Parenchymal Bands. The CT Severity Index of each patient was documented using the above described method. The information regarding clinical severity of Covid – 19 pneumonia and final outcome of the infection in each patient was also recorded from the case sheets.

Statistical analysis was performed using IBM SPSS version 22 software. Descriptive statistics of patients' demographics,CT chest findings, and CT Severity Indices were reported as numbers and relative frequencies. Frequencies of CT Severity Index were compared with the variables of clinical severity of Covid – 19 pneumonia and disease outcome.

The Chi Square and Fisher's Exact test were used for correlation of these variables, and a *p* value of less than 0.05 was defined as being statistically significant.

The clinical severity of Covid – 19 pneumonia was retrospectively obtained from the case sheets of the study patients who were treated in our hospital and was graded based on the prevalent updated WHO Document of interim guidance published under the Title "Clinical Management of Covid – 19" released on 27th May 2020 [7] as follows:

Mild Disease (Grade 1) - Symptomatic patients meeting the case definition for COVID-19 without evidence of viral pneumonia or hypoxia i.e., with Respiratory rate of < 24 per minute and SpO2 of > or = 94% on room air.

Moderate pneumonia (Grade 2) - Adult with clinical signs of pneumonia (fever, cough, dyspnoea, mild tachypnoea) but no signs of severe pneumonia, including SpO2 ≥ 90% on room air and Respiratory rate of 24 to 30 per minute.

Severe pneumonia (Grade 3) - Adult with clinical signs of pneumonia (fever, cough, dyspnoea, fast breathing) plus one of the following: respiratory rate > 30 breaths per minute; severe respiratory distress; or SpO2 < 90% on room air.

Critical Disease (Grade 4) – Adults who manifest with one or more of the following complications within 1 week of a known clinical insult (i.e. pneumonia) or new or worsening respiratory symptoms: ARDS, Sepsis, Septic shock, and the other acute, life threatening complications outlined in the WHO document [7].

The outcome of patients with Covid – 19 pneumonia in the study group was divided into 4 categories as follows: Category 1 – Improved and discharged; Category 2 – Death; Category 3 – Referred to higher Centre; Category 4 – DAMA (Discharged Against Medical Advise).

Outcome of the pneumonia was considered favourable if the patients improved and were discharged (Category 1) whereas adverse outcomes were indicated by death and Referral to higher centre (categories 2 and 3).

3. RESULTS

Our study population consisted of 103 adult patients who tested positive for Covid-19 infection using the RT-PCR test and who underwent CT Scan study of the Chest at MVJ Medical College and Research Hospital Hoskote from July 2020 to April 2021.

In our study group, 75 patients (77.4%) were maleand 22 patients (22.6%) were female (Table 1 and Fig. 1). The 61 to 65 years age group constituted the highest percentage (18.5%) of patients in our study, followed by 41 to 45 year age group (15.5%), represented in Table 2 and Fig. 2. The number and percentage of characteristic CT Chest findings in the study group is represented in Table 3 and Fig. 3.

Table 1. Showing sex distribution of patients in the study

Sex	No. of patients	Percentage
Male	75	77.4
Female	22	22.6
Total	97	100

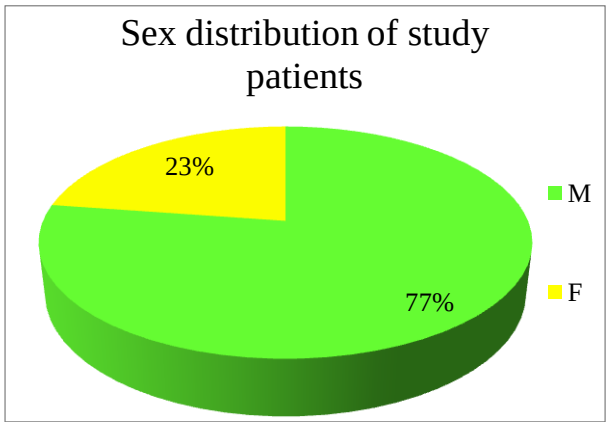

Fig. 1. Diagram showing sex distribution of patients in the study

Table 2. Showing age distribution of patients in the study

Age group	No. of patients	Percentage
< 25 yrs	2	2.0
26 - 30 yrs	6	6.2
31 - 35 yrs	11	11.4
36 - 40 yrs	8	8.3
41 - 45 yrs	15	15.5
46 - 50 yrs	13	13.5
51 - 55 yrs	7	7.2
56 - 60 yrs	4	4.1
61 - 65 yrs	18	18.5
66 - 70 yrs	8	8.2
71 - 75 yrs	4	4.1
76 - 80 yrs	0	0.0
> 81 yrs	1	1.0
Total	97	100.0

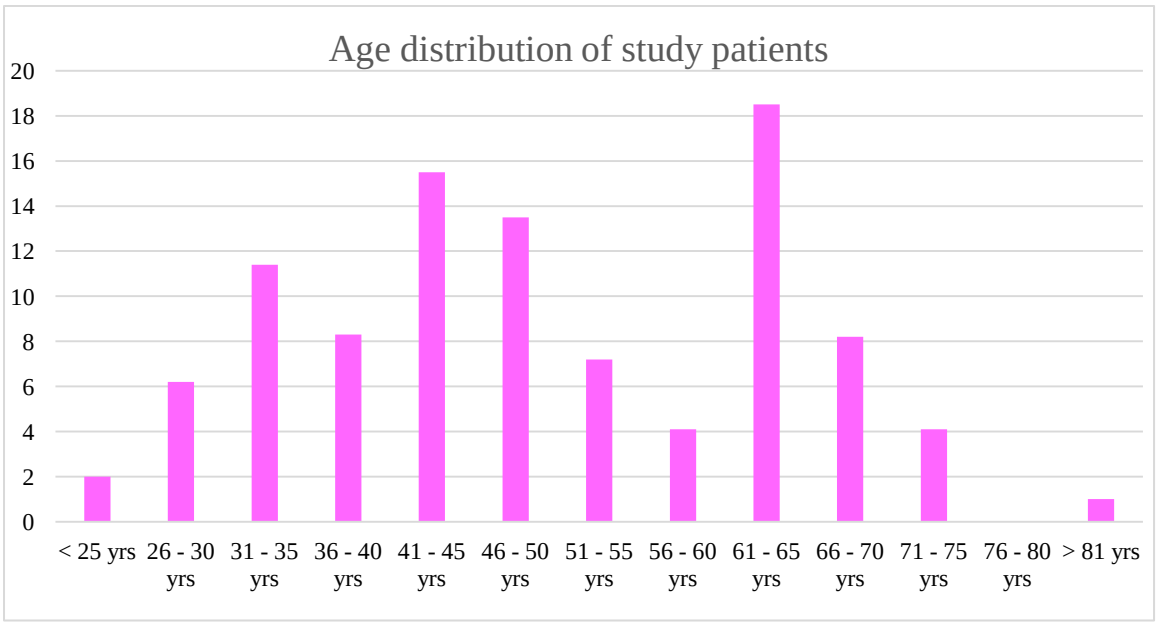

Fig. 2. Graph diagram showing age distribution of patients in the study

Table 3. showing Summary of characteristic features on CT Chest of study patients. (G.G.O. – Ground Glass Opacities)

CT features	CT features	No. of patients	Percent
Ground Glass Opacities (G.G.O)		74	76.2
Consolidation		89	91.7
Crazy-paving		45	46.4
Vascular dilatation		75	77.3
Traction bronchiectasis		8	8.2
Subpleural bands		51	52.5
Architectural distortion		32	32.9
Parenchymal bands		36	37.1

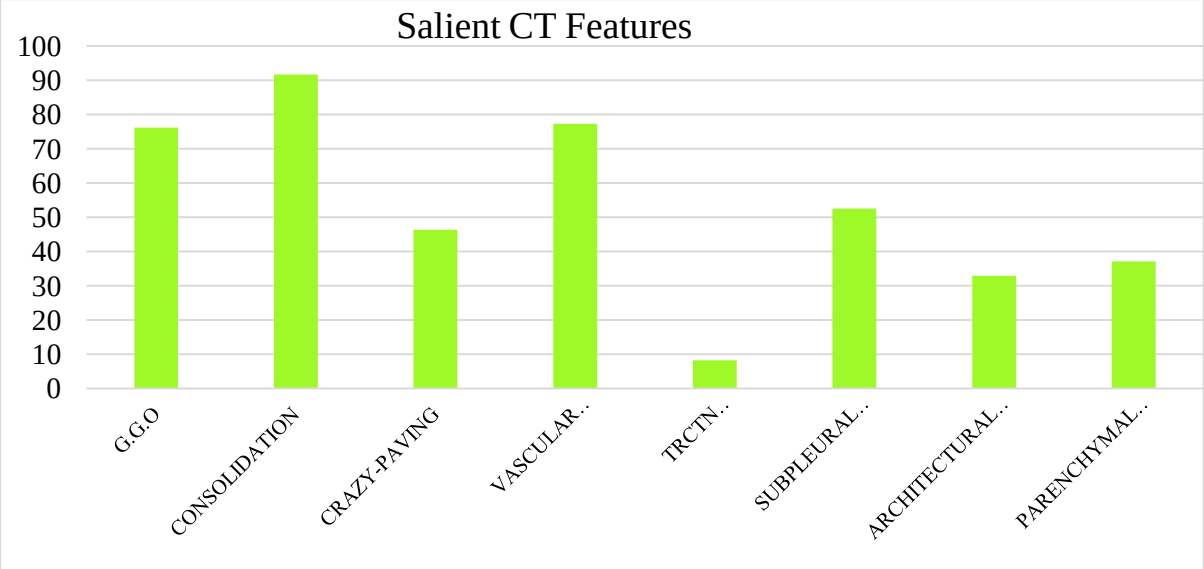

Fig. 3. Showing the Salient CT Features of Covid-19 Pneumonia in the study patients

From Table 3 and Fig. 3, we can infer that the most common finding of Covid Pneumonia in the study patients was Consolidation (in 92% of patients) followed by Ground Glass opacities (in 76% of patients) associated with minimal Vascular Dilatation (in 77% of patients) in the involved segments of the lung parenchyma. Subpleural bands and Crazy-paving were the next frequent findings seen in about 53 and 46% of patients respectively.

The results of statistical correlation between CT Severity Index and clinical severity of Covid – 19 Pneumonia are as given in Table 4 and Fig. 4.

From the above table and figure, we can infer that there is a statistically significant correlation between the CT Severity Index and clinical severity of Covid – 19 Pneumonia in the study patients (Chi square score: 17.73, p value: 0.0013).

The results of statistical correlation between CT Severity Index and outcome of study patients with Covid – 19 Pneumonia are as given in Table 5 and Fig. 5.

4. DISCUSSION

The results of our study show that amongst the salient CT features of Covid – 19 pneumonia, Consolidation was the most common finding followed by Ground Glass Opacities, with peripheral subpleural bands being the next most common. These findings are in agreement with several published studies on the subject [8,9,10].

Our study showed a statistically significant association between CT Severity Index and clinical severity of Covid – 19 Pneumonia in the study patients with a p value of 0.0013 (Table 4 and Fig. 4). From table and Fig. 5 we can also infer that there is a statistically significant

association between CT Severity Index and outcome of Covid – 19 Pneumonia in the study patients in terms of favourable and adverse outcomes as described earlier in the section on Statistical Analysis, with a p value of 0.007.

Table 4. Showing the Statistical significance of correlation between CT Severity Index and clinical severity of Covid – 19 Pneumonia in the study patients

CTSI Grades	Clinical Severity			Total Number of patients
	1 – Mild Disease	2 – Moderate Pneumonia	3 – Severe Pneumonia	
Grade 1 (CTSI Score 0 to 7)	2	13	1	16
Grade 2 (CTSI Score 8 to 17)	20	41	10	71
Grade 3 (CTSI Score 18 to 25)	0	8	8	16
Total	22	62	19	103
Chi square : 17.73, df:4, p value : 0.0013				

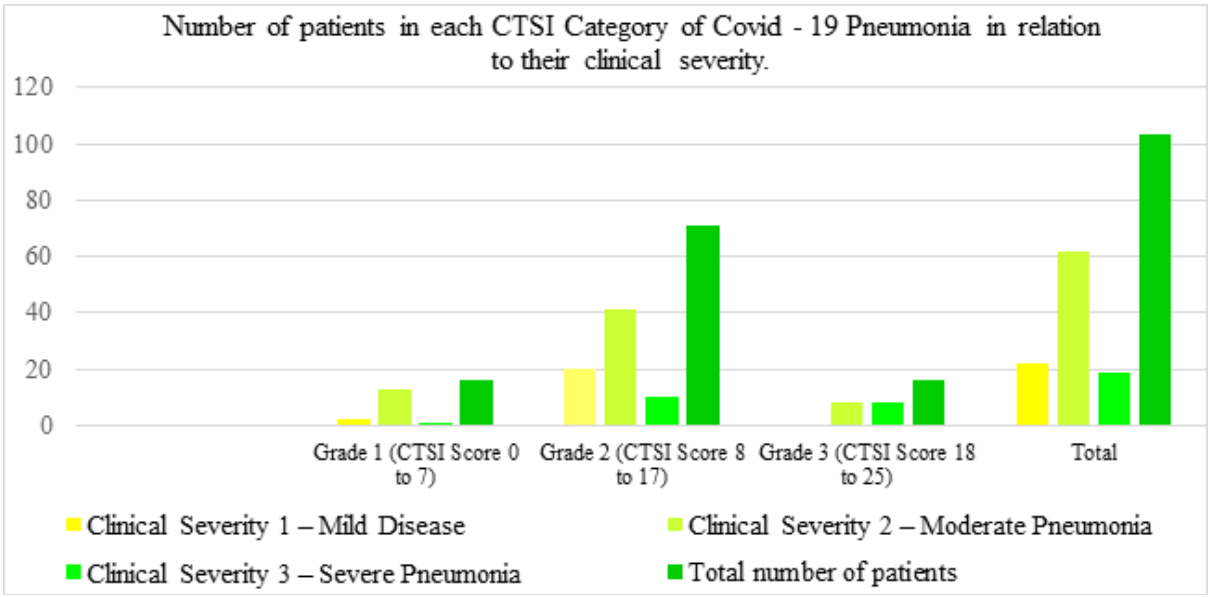

Fig. 4. Bar graph showing the Number of patients in each CTSI Category of Covid - 19 Pneumonia in relation to their clinical severity

Table 5. Showing the Statistical significance of correlation between CT Severity Index and outcome of study patients with Covid – 19 Pneumonia

Disease Outcome Codes	CTSI Code			Total
	1 – Mild disease	2 – Moderate pneumonia	3 – Severe Pneumonia	
1.0 – Improved and Discharged	16	68	12	96
2.0 - Death	0	0	2	2
3.0 - Referred	0	3	1	4
4.0 – Discharged Against Medical Advice	0	0	1	1
Total	16	71	16	103
Pearson Chi-Square :17.884,df : 6, p value : 0.007.				

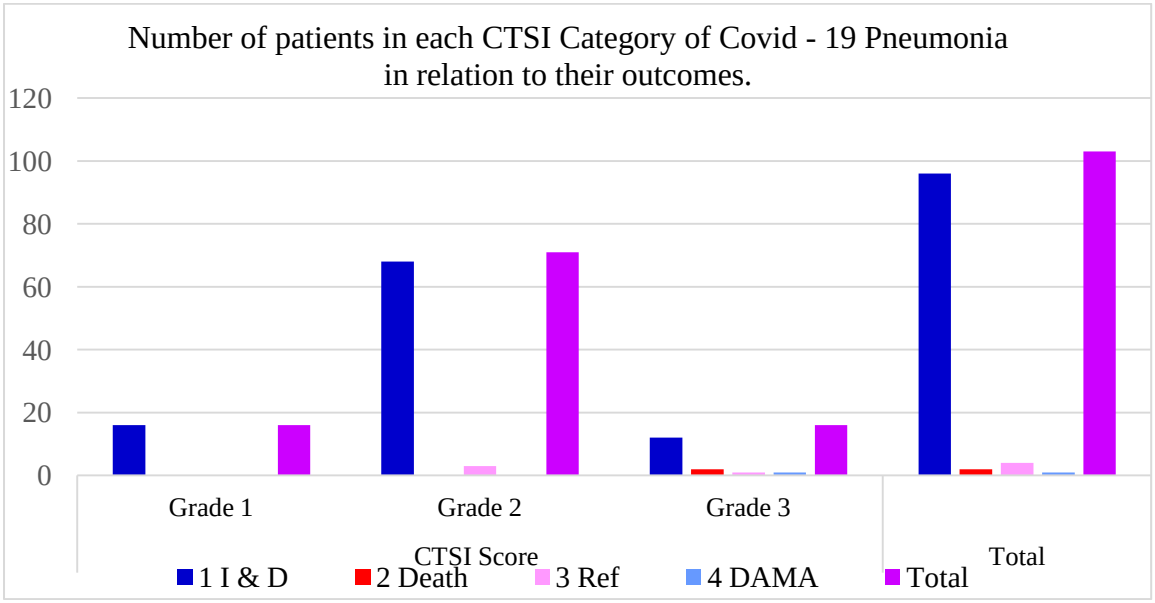

Fig. 5. Bar graph showing the Number of patients in each CTSI Category of Covid - 19 Pneumonia in relation to their disease outcome

A large scale retrospective study conducted by Ghufran Aref Saeed et al correlating the Chest CT Severity Scores with Clinical Parameters of Covid – 19 Pneumonia found that the CT severity score was positively correlated with lymphopenia, increased serum CRP, d-dimer, and ferritin levels. The oxygen requirements, length of hospital stay and death rate also increased significantly with increase in CT scan severity scores. They used the 25-point visual quantitative assessment method identical to the method used in our study [6].

Marco Francone et al conducted a retrospective single-centre study in which they correlated the semi-quantitative CT Chest Severity score in patients of COVID-19 pneumonia with clinical staging of disease and laboratory findings. They found that the CT Chest score was significantly higher in critical and severe than in mild stage and among late-phase than early-phase patients. Chest CT Severity score was significantly correlated with CRP and D-dimer levels as well. A CT score of ≥ 18 was associated with an increased mortality risk and was found to be predictive of death. They concluded that the Chest CTscore is significantly correlated with age of the patient, serum inflammatory markers, severity of clinical phase of the disease, and early or late stages. A Chest CT score of 18 and above was shown to be highly correlated with increased patient mortality on short-term follow-up. Their multivariate analysis demonstrated that Chest CT severity score may accurately represent short-term outcome, permitting direct visualization of extent of anatomic lung injury [11].

T. F. G Ribeiro et al conducted a large-scale retrospective, observational study on Covid-19 positive patients who underwent CT scans of the chest at admission between March 6 and April 6, 2020. CT scans were classified as positive, negative, or equivocal, and a radiological severity score (RAD-Covid Score) was assigned based on the percentage of lung involvement in each category of patients. Those patients with positive or equivocal CT Chest findings for Covid – 19 pneumonia were classified into mild, moderate and severe categories based on the extent of lung involvement (<25%, 25 to 50% and > 50% pulmonary involvement) and assigned a RAD-Covid score of 1, 2 or 3 respectively. Their study concluded that the RAD-Covid Score significantly correlated with clinical severity of the disease and high RAD-Covid Scores correlate positively with higher risk of progressing to severe clinical disease. The RAD-Covid Score was an independent predictor of disease severity, along with advanced age and comorbidities, and correlated well with risk of fatal outcome. Based on these observations, they suggested that the CT severity score must be included as part of the radiological report as a diagnostic supplement to aid clinicians in making treatment decisions [12].

Ran Yang et al conducted a retrospective study on 102 patients admitted to their hospital with

RT-PCR confirmed Covid – 19 infection to evaluate the value of Chest CT Severity Score in differentiating various clinical forms of the infection. The CT – Severity Score used in their study was derived by addingup the individual points from 20 regions of the lung parenchyma to obtain a single composite score. Thepoints were assigned for each region if parenchymal opacification involved 0% (0 points), less than 50% (1 point), or equal to or more than 50% (2 points)of each region. The relevant background clinical and laboratory values from the study patients were also collected, and patients were categorized clinically according to disease severity as per the prevalent National Health guidelines. They found that individual scores in each lung and the total CT-SS were significantly higher in severe COVID-19 pneumonia when compared with mild pneumonia. They derived an appropriate CT-SS threshold for identifying severe COVID-19 pneumonia as a score of 19.5 and higher. They concluded that the CT-Severity Score could be used to rapidly and objectively assess the severity of lung involvement in COVID-19 pneumonia [13].

Elmokadem AH et al conducted a retrospective study on 85 patients to compare the diagnostic performance and inter-observer agreement of five different CT chest severity scoring systems for COVID-19 to find the most precise one with the least interpretation time.Three readers were asked toscore the severity of pulmonary involvement in Covid – 19 pneumonia using five different systems - the chest CT Severity Score (CT-SS), chest CT score, Total Severity Score (TSS), modified total severity score (m-TSS), and 3-level chest CT Severity Score. The time taken to report each scoring system was calculated. In their study, all the chest CT scoring systems demonstrated excellent inter-observer agreement and reasonable performance to evaluate COVID-19 disease severity in relation to the clinical severity. Among all the scoring systems, they found that CT-SS and TSS had the highest specificity and least time for interpretation [14].

Fausto Salaffi et al conducted a retrospective study across three different hospitals with the aim of determining the optimal cut-off value of a CT severity score that can be considered asan indicator of a severe/critical outcome.They used a composite CT Severity Scoring systemin which both the extent and nature of involvement were assessed at three levels in each lung, multiplied by each other; and a total score was obtained by adding the sum of the individual scores at all three levels in both lungs.The total score ranged from 0 to 96.They found that the mean CT severity score was 63.95 in the severe/critical group, 35.62 in the mild/typical group (P<0.001)anda CT severity score of 38 predicted the development of severe/critical symptoms. They therefore concluded that the CT severity score aids in the risk stratification of Covid-19 patients [15].

Chao Jin et al conducted a retrospective study from eight hospitals in China who underwent Chest CT Scans. CT findings in these patients were classified as - Pattern 0 (if no findings were present), Pattern 1 (bronchopneumonia pattern), Pattern 2 (organizing pneumonia pattern), Pattern 3 (progressive organizing pneumonia pattern), and Pattern 4 (diffuse alveolar damage pattern). Clinical findings were compared across these categories. Temporal evolution of these CT patterns and correlation with clinical outcomes, i.e., discharge or adverse outcome (admission to ICU, requiring mechanical ventilation, or death), with pulmonary sequelae (complete absorption or residuals) on CT after discharge were also analyzed.Their study results indicated that as disease evolves over 1 to 3 weeks and later, findings of Patterns 1 and 2 decreased significantly, while those of Patterns 3 and 4 increased. They suggested that classification of Covid – 19 patients based on the above CT pattern along with clinical characteristics within 2 weeks after symptom onset provides early prognostic indication of adverse outcome in COVID-19 pneumonia [16].

5. CONCLUSION

The Gold Standard diagnostic test for Covid – 19 infection is the RT-PCR performed on specimens obtained from the nasopharyngeal and / or oropharyngeal tract of suspected individuals. Of recent interest, scientists are in the process of designing a CRISPR target based Single guided RNA diagnostic kit for the detection of SARSCoV-2. However, computationally designed sgRNA requires to be tested in vitro to demonstrate its potential and efficiency in detecting this novel coronavirus [17]. CT Scans of the chest in Covid – 19 infection are a quick, non-invasive means of obtaining reasonably accurate estimation of the degree of pulmonary parenchymal involvement in the infective process.

Since the 25 point CT Severity Index correlates significantly with the degree of clinical severity of

Covid - 19 infection and it's outcome in an individual, its inclusion in the CT report is an invaluable diagnostic aid in rapidly triaging the patient in the ER, initiating appropriate treatment at the earliest and providing a reasonably accurate prediction of future course and outcome of the infection in an individual.

By significantly cutting down time spent in triaging a patient in the ER, it helps to initiate treatment faster, refer patients to higher centers where necessary;thereby saving precious time while minimizing the need for a large skilled workforce of medical and paramedical personnel in limited resource settings.

6. LIMITATIONS OF THE STUDY

There are many limitations in our study. First, this is a retrospective, cross-sectional study except for few patients who underwent follow-up CT Scans of the chest dictated by clinical needs. Hence, the radiological follow-up and assessment of temporal evolution of the pulmonary parenchymal opacities was not possible in most patients. Second, the patients who presented to our hospital were at different clinical stages and degrees of severity of pneumonia and this heterogeneity in time of presentation and disease stage may have a bearing on the outcome of the disease process. Third, many patients who were in the severe and critical stages of Covid – 19 pneumonia could not undergo CT Scans of the chest due to increased respiratory rate and need for intubation and ventilation and were therefore not part of the study. The long term clinical and radiological follow up of these patients could not be performed for technical and various other reasons including movement restrictions on patients and the general public during the pandemic at the time of this study.

DISCLAIMER

The products used for this research are commonly and predominantly used products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT AND ETHICAL APPROVAL

This study was approved by the Institutional Scientific and Ethical Review Committees vide letter number MVJMC & RH/PG/Synopsis/6/2021-22 dated 30-07-2021. Written informed consent from all the study patients was taken in English and local vernacular languages prior to commencement of the CT Scan study. All the personal information, imaging findings and clinical data collected from the study patients were kept strictly confidential.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/86118