*Original Research Article*

# Correlation of CT Scan Chest Severity score with Serum Ferritin In COVID-19 disease: A Retrospective Study


**Abstract :**

Background**:** COVID-19 disease is due to SARS-CoV-2 Virus with its rapid progression causing severe and fatal complications like Pneumonia. CT scan chest and inflammatory biomarkers like serum ferritin, helpful in screening, clinical management and prevention of serious complications of the Covid-19 disease are to be investigated and assessed.

Aims and Objectives: This study is aimed to assess the association between the CT Scan Chest severity score and the Serum Ferritin levels in COVID -19 disease in predicting clinical severity with categorization into different risk groups to identify patients at risk of fatal complications to ensure optimal resource allocation.

Materials and Methods: This retrospective observational study in a Govt. Medical college attached Tertiary care hospital for COVID –19 disease in Andhra Pradesh from 1st to 31st October 2020 included 76 patients of Covid-19 disease of > 20 years of age admitted with laboratory confirmed RT PCR diagnosis of Covid – 19 disease. Data was collected from the hospital records of the patients on demography, radiological imaging of CT scan chest severity score and laboratory measurements of Serum Ferritin levels and tabulated with the results expressed as mean ± SD. The disease severity was classified as mild (1-8), moderate (9-15) and severe (16-25) based on CT scan chest Severity scoring. Then the association between CT scan chest severity score and serum ferritin levels was studied, assessed and correlated.

Results:
Study data of a total of 76 COVID –19 positive patients was analysed and summarized. 54 patients (71%) were Males and 22 patients (29 %) were Females. Mean age (Years) of the patients was 52 ±13.2 years with males and females as 53.11±13.45 and 50.18 ±11.71, respectively. Based on the 25 point CT scan chest severity score, 50 % (38 patients) were in the mild grade (1 -8) with a mean ±SD of 4.74±2.44, 43.42% (33 patients) were in the moderate grade (9 - 15) with a mean ±SD of 11.31 ± 2.06 and 6.58% (5 patients) were in the severe grade (16 -25) with a mean ±SD of 18.4 ± 3.29. The mean ±SD values of Serum Ferritin were 261.22±377.12ng/ml, 431.14 ±284.69ng/ml and 870.8±928.06ng/ml with mild, moderate and severe grade of CT chest severity score respectively. Statistically significant correlation was found between between the CT Chest Severity Score and Serum Ferritin levels.

Conclusion:
Serum ferritin levels were observed to be high in the CT scan chest positive group and so the serum ferritin levels measured at the time of admission predict radiological severity. This positive correlation between the CT Chest Severity Score and Serum Ferritin levels can predict clinical severity of Covid -19 disease with categorization into different risk groups helping in the clinical management, prevention of serious complications and disease outcome.


**1. Introduction:**

**Comment [A1]:** The main idea of the article is to assess correlation between CT scores and Ferritin levels; however, this is not statistically supported. What defines this correlation and its strength?

**Comment [A2]:** I recommend rewriting this paragraph

**Comment [A3]:** I recommend splitting the sentence to make it more understandable

**Comment [A4]:** What defines this significance?

**Comment [A5]:** Typo

A novel infectious disease reported first in Wuhan, Hubei province, China in December 2019 and later found as coronavirus infection (2019-nCov), which has spread rapidly all over the world was named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The World Health Organization (WHO) announced the disease name as Coronavirus disease-19 (COVID-19) and eventually declared it as global pandemic on 11 March 2020 with significant impacts upon the healthcare delivery systems [1-3].

SARS-CoV-2 virus spreads between people when an infected person is in close contact with another person [4, 5]. The incubation period (from the infection to the onset of first symptoms) is 2-14 days with a median of 5 days [6-8]. The COVID – 19 disease with its unpredictable clinical course can rapidly develop, causing severe and fatal complications. The COVID-19 disease clinical picture is broad spectrum with a wide range of symptoms and with asymptomatic carriers to severe pneumonia patients requiring ventilator support and ICU admissions with increased mortality [9-11].

The RT-PCR (Reverse transcription-polymerase chain reaction) test, a nucleic acid amplification test through molecular identification of SARS-Cov-2 with Nasopharyngeal swab samples is the Gold standard test for the diagnosis of COVID-19 disease [12,13] but, there are reports of significant small proportion of false negative tests [14].

A non-contrast high-resolution CT scan chest is an effective and essential method in COVID-19 disease in early diagnosis, disease course and management, especially in false-negative RT-PCR tests [15]. Studies of Li K. et al and Zhang H et al reported the lungs involvement in the CT scan chest images using both visual and software quantitative severity assessment of the CT scan chest images that determines the percentage of affected lung volumes in Covid-19 disease [16, 17].The CT chest image findings help in the clinical evaluation of the COVID-19 disease severity with effective management [18-20]. In the studies of Guan W et al. and Guan W.J et al., Ground-Glass Opacity and Consolidation were the main CT chest findings in COVID-19 disease especially with the severity of the disease [21, 22]. Studies of Song F et al and Sun Q et al. reported that an increase in the extent of consolidation, present in the early and follow-up CT chest scans alert the clinicians in the management of COVID-19 patients [23, 24].The study of Yuan et al. reported that there was a higher frequency of consolidation in patients died of the disease than in the survived [25].

Inflammatory Biomarkers commonly evaluated to assess severity of COVID–19 diseases are D–Dimer, serum ferritin, LDH, pro-calcitonin (PCT), C-reactive protein (CRP), interleukin-6 (IL-6), and interleukin-10 (IL-10) and are helpful in screening, categorization, clinical course, management, prognosis and prevention of serious complications of the disease due to its rapid progression [22, 26]. Studies of Qin C et al. and Xiao KH et al. reported that numerous inflammatory markers are elevated in COVID-19 disease with severe infection or in the intensive care unit relative to milder infection [27, 28].

Serum ferritin, a degradation product of haem is an inflammatory mediator of immune dysregulation causing cytokine storm in COVID –19 infections with fatal outcome and so those with elevated ferritin have high probability to develop serious complications. Studies of Xiong Y et al. and Salehi S et al. investigating the laboratory parameters of COVID-19 disease reported high Ferritin values [29, 30]. Studies of Feng Y et al., Zhou F et al. and Wu C et al. reported that serum ferritin levels were higher with severe COVID-19 than in a mild infection [31-33].

This study was aimed to investigate, assess and correlate the association between the CT Scan Chest severity score and Serum Ferritin levels in COVID-19 disease and then to predict the

clinical severity, to categorize the COVID-19 disease patients in the clinical management and prevention of serious complications and to identify patients at risk of fatal complications.

**Comment [A6]:** I recommend rewriting the sentence. How were the scores assessed?

**2. Materials and Methods:**

**2.1Study design**

**Study type**:

This was a retrospective and observational study conducted in a Govt. Medical college attached Tertiary care hospital for the diagnosis and treatment of COVID-19 disease in Andhra Pradesh.

Study Data Collection:

Data was collected retrospectively from the hospital record of patients in terms of demography i.e. Age, Sex, CT Scan radiological imaging of Chest and laboratory measurements of serum ferritin.

Study Population:

The study subjects were a total of 76 patients admitted in the period from 1st to 31st October, 2020

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Subjects Data Selection:

**Inclusion criteria:**

1. Age ≥ 20 years
2. Patients tested positive for Covid-19 disease by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) tests with nasopharyngeal swab samples
3. Covid-19 positive patients who have undergone both CT scan of chest and Serum Ferritin level estimation

**Exclusion criteria:**

1. Age <20 years
2. COVID-19 positive patients who have not under gone CT scan chest and Serum Ferritin estimation
3. COVID-19 positive patients with co-morbidities like Diabetes. Hypertension etc.

Study was approved by the institutional ethical committee.

**Comment [A7]:** What about informed consent?

**2.2 Research protocol**

The study data taken at the time of admission into the hospital was collected from the hospital information system. The diagnosis of COVID-19 pneumonia was done in accordance with the clinical criteria. The CT scan chest images were evaluated using the Picture Archiving and Communication Systems (PACS).

In our study due to unavailability of the software, the CT scan Chest severity scores were calculated on the visual assessment of area involved in each lobe of the lung (3 on right and 2 on left. It was graded according to the percentage of each lobar involvement of 5 lobes with GGOs, consolidation, crazy paving on the basis of the area involved as: 0 (no involvement), 1 (<5% involvement), 2 (5–25% involvement), 3 (26– 50% involvement), 4 (51–75% involvement) and 5 (>75% involvement). A score of 1-25 was used to evaluate the extent of inflammatory pulmonary lesions quantitatively for each of the five lung lobes and the total CT scan score of both lungs was equal to the sum of the scores of the five lobes, with a maximum total score of

**Comment [A8]:** Who calculated the scores?

**Comment [A9]:** I think you mean each lobe is give a score from 1-5 and total lung score is between 1-25?

25 points. The severity was further classified based on the total cumulative severity score. CT Scan Chest Severity score of 1 -25 was graded based on the extent of involvement of lung damage due to infection as, Mild (1-8), Moderate (9-15) and Severe (16-25) as cited in the study of Pan F et al [34].

Serum ferritin was estimated by fully automated biochemical analyser according to the instructions provided in the kit by the manufacturer. Normal range of Serum Ferritin is 20 - 250ng/ml provided in the kit by the manufacturer.
Then correlation between CT chest severity score with serum ferritin levels was studied.

**2.3 Statistical analysis:**

Comment [A10]: How can you support the correlation statistically?

A total of 76 patients > the age of 20 years with COVID-19 PCR-positive test admitted in the hospital during the month of October 1st to 31st 2020 were included in the study. Data of age, sex, presence of CT Scan Chest Score and laboratory test of serum ferritin level was collected and compiled in MS Excel. Data was summarized and analysed by using simple mathematical means. Data results were represented in terms of number (N), percentage (%) and mean ± standard deviation.

**3. Results:**

In the table 1), study group of 76 cases age was classified into 7 groups ;>20-30, >30-40, >40-50, >50-60, >60-70, >70-80, >80 yrs. The age range is of 24 - 86 years (males 24 – 86 yrs and females 26-72 years). The most common age groups were that between 60 - 70 yrs (21/76; 27.63%) with the males of 18/76 and females of 3/76) and 40-50 years (20/88; 26.32%) with the males of 13/76 and females of 7/76.

**Table-1): AGE Distribution of Cases**

| Age (Years) | Males | Females | Total | Percentage |
|---|---|---|---|---|
| > 20-30 | 3 | 1 | 4 | 5.263 |
| ➢ 30-40 | 9 | 4 | 13 | 17.11 |
| ➢ 40-50 | 13 | 7 | 20 | 26.32 |
| ➢ 50-60 | 8 | 6 | 14 | 18.42 |
| ➢ 60-70 | 18 | 3 | 21 | 27.63 |
| ➢ 70-80 | 2 | 1 | 3 | 3.95 |
| ➢ 80-90 | 1 | 0 | 1 | 1.31 |
| Total | 54 | 22 | 76 | 100 |

In the Table 2), the study group of 76 cases are with 54 (71%) males and 22 (29%) females. The mean age of the study group was 52 ±13.2 yrs (males 53.11±13.45 yrs and females 50.18 ±11.71 yrs). The mean CT Score of the study group was 8.58 ± 4.66 (males 9.67 ± 4.83 and females 6.46 ±3.81). The mean serum ferritin of the study group was 380.08 ± 417.91(males 448.16 ± 393.16 and females 228.21 ± 442.68)

**Table-2): Sex Wise Distribution of Mean ± SD of Age, CT Score and Serum Ferritin**

| Sex | No. | Percentage (%) | Mean Age (Years) | CT Score (No.) | Ferritin (ng/ml) |
|---|---|---|---|---|---|
| Males | 54 | 71 | 53.11 ±13.45 | 9.67 ± 4.83 | 448.16 ± 393.16 |
| Females | 22 | 29 | 50.18 ±11.71 | 6.46 ±3.81 | 228.21 ± 442.68 |
| Total | 76 | 100 | 52 ±13.2 | 8.58 ± 4.66 | 380.08 ± 417.91 |

In the table 3), based on the 25 point CT scan chest severity score, CT severity score was with a mean ±SD of 11.48 ±2.59 of 76 patients with 50 % (38 patients) were in the mild grade (1 - 8) with a mean ±SD of 4.74±2.44, 43.42% (33 patients) were in the moderate grade (9 - 15) with

a mean ±SD of 11.31 ± 2.06 and 6.58% (5 patients) were in the severe grade (16 -25) with a mean ±SD of 18.4 ± 3.29. The mean ±SD values of Serum Ferritin were with a mean ±SD of 521.1 ± 529.96 of 76 patients with 261.22±377.12ng/ml, 431.14 ±284.69ng/ml and 870.8±928.06ng/ml with mild, moderate and severe grade of CT chest severity score respectively.

**Table-3): Severity Wise Distribution of Mean ± SD of Age, CT Score and Serum Ferritin**

| Severity | No. | Percentage (%) | Mean Age (Years) | CT Score (No.) | Ferritin (ng/ml) |
|---|---|---|---|---|---|
| Mild | 38 | 50.0 | 51.74 ± 13.02 | 4.74 ± 2.44 | 261.22 ± 377.12 |
| Moderate | 33 | 43.42 | 52.3 ± 13.4 | 11.31± 2.06 | 431.14 ± 284.69 |
| Severe | 5 | 6.58 | 56.2 ± 11.4 | 18.4 ± 3.29 | 870.8 ± 928.06 |
| Total | 76 | 100 | 53.42 ± 12.61 | 11.48 ±2.59 | 521.1 ± 529.96 |

**4. Discussion:**

The present study shows the association and correlation of the CT scan chest imaging and serum ferritin levels in the COVID-19 RT PCR test positive patients admitted to our tertiary level Govt. hospital with the aim to assess the clinical severity of Covid – 19 disease.

World Health Organization (WHO) declared COVID-19 outbreak as a public health emergency of international concern on 30 January 2020 and as pandemic on March 11, 2020, after the first report of Coronavirus disease 2019 (COVID-19) in December 2019 in Wuhan, China [1,2]. The RT-PCR (Reverse transcription-polymerase chain reaction) test with nasopharyngeal swab is the standard test for the diagnosis of COVID-19 disease c [35]. WHO advised CT scan chest imaging as a diagnostic test of COVID-19 disease whenever RT-PCR testing is not available, in delayed test results or in a clinical suspicion of COVID-19 with early negative RT-PCR test [36]. CT scan is useful in the assessment of the disease severity [37]. Similarly, Serum Ferritin, an inflammatory mediator of immune dysregulation is closely related to the disease severity [38].

In the present study, a total of 76 COVID-19 positive patients, who have undergone both CT Scan of Chest and Serum Ferritin estimation in the month of October 2020 were included. Visual assessment of each of the 5 lung lobes severities was used for classification as grades of mild (1– 8), moderate (9 -15) and severe (16 – 25) based on the total cumulative severity score.The main CT features in this study were Ground Glass Opacities, consolidation, crazy-paving pattern, and linear opacities, as in the study of Li K et al. [39].

Our study group of 76 cases was of 54 (71%) males and 22 (29%) females in the age range of 24 - 86 years (males 24 – 86 years and females 26-72 years) similar to the study of Gurung A et al [40], with age range from 19-89 years. The most common age groups were that between 60 - 70 years (21/76; 27.63%) with males of 18/76 and females of 3/76 and 40-50 years (20/88; 26.32%) with males of 13/76 and females of 7/76, similar to the study of Gurung A et al [40] in the age group of 50-59 years (25.8%).

Our study mean age was 52 ±13.2 years (males 53.11±13.45 years and females 50.18 ±11.71 years) similar to the studies of Gurung A et al [40] of 47.8 years and Tan C et al [41] of 48.89 ±18.47 years. Sex distribution of the study group of 76 patients showed CT Severity score of 8.58 ± 4.66 (males 9.67 ± 4.83 and females 6.46 ±3.81) and serum ferritin of 380.08 ± 417.91(males 448.16 ± 393.16 and females 228.21 ± 442.68).

**Comment [A11]:** In your discussion you are viewing the results again

**Comment [A12]:** In the discussion you are mainly comparing your results with other literature. It would be more valuable to analyse results and elaborate on pathophysiology and clinical significance of your results, for example.

When patients were divided according to the age (with a range of 24 -86 years), the extent of pulmonary involvement (severity scores) was significantly higher in patients with higher levels of ferritin. Age was not related to ferritin levels but males displayed significantly higher levels.

**Comment [A13]:** What defines this significance? Is it P-value? Or just from observation of results?

Our study CT severity score was 11.48 ±2.59 of 76 patients with, 50 % (38 patients) in the mild grade of 1-8 (4.74±2.44), 43.42% (33 patients) in the moderate grade of 9 – 15 (11.31 ± 2.06) and 6.58% (5 patients) in the severe grade of 16 -25(18.4 ± 3.29), similar to the study of Gurung A et al [40], Chest CT Scan severity score with 11-15 in 92 (48.3%) cases with maximum 24 (12.6%) cases with a score of 12.

Based on the 25 point CT scan chest severity score of our study group of 76 patients, mean ±SD values were of CT score 11.48 ±2.59 and Serum Ferritin 521.1 ± 529.96. Serum Ferritin level was elevated in the studies of Gurung A et al [40], Banerjee D et al [42] and Guo W et al [43] study which is similar to our study findings.

Our study Serum Ferritin was 521.1 ± 529.96 of 76 patients with 261.22±377.12ng/ml, 431.14 ±284.69ng/ml and 870.8±928.06ng/ml with mild, moderate and severe grade of CT chest severity score respectively similar to the studies of Gurung A et al [40] and Canovi S et al [44] which showed elevated Ferritin levels correlating with the chest CT scan severity score. Our study showed CT severity score with increased serum ferritin levels was 50% of mild cases followed by 43.42% of moderate cases similar to the study of Gurung A et al [40], showing 46.4% cases followed by moderate cases 37.5%, and also to the study of by Kappert K et al [45].

Our study showed stronger and significant association of raised Serum Ferritin with severity of lung involvement (based on HRCT chest) of disease. The studies of Ghufran Aref Saeed et al and Atkan Yilmaz et al [46, 47} observed high serum ferritin levels in the CT-positive group and have moderate positive correlation with CT severity. The study of Gupta et al [48] reported that the Severity of lung involvement according to HRCT chest findings was greater in patients with raised values of ferritin. This study results are similar to the studies of Ghufran Aref Saeed et al, Atakan Yilmaz et al. and Prakhar Gupta et al.[46,47, 48], which reported positive correlation of CT scan chest severity score with serum ferritin levels.

**Comment [A14]:** Again, what defines this strength?

Our study and other studies suggested the positive correlation of serum ferritin level to the CT scan severity and so, with the clinical severity of the Covid-19 disease. Hence, the serum ferritin levels measured at the time of admission of the Covid-19 disease patients predict the severity of the Covid-19 disease radiologically and clinically. High serum ferritin levels in the CT scan chest positive group with a positive correlation with CT chest severity score indicate that serum ferritin level is related to the radiological severity and clinical severity of the COVID–19 disease.

**Comment [A15]:** There was no proper clinical assessment in this study. i.e., Symptoms, oxygen saturation, ...

Based on this significant association of inflammatory biomarkers with the severity of lung involvement, the assessment of levels of inflammatory biomarkers helps in categorization of patients into different risk groups following diagnosis, to ensure optimal resource allocation, especially in places where CT scan chest facilities are not readily available.

**5. Conclusion:**

The present study of CT scan chest severity score and Serum Ferritin values of the COVID-19 positive patients showed high serum ferritin levels in CT Scan Chest positive Covid-19 patients. High ferritin levels, a potential predictor of CT severity suggests the clinical severity of COVID-19 disease. As the clinical severity of COVID-19 disease have association with serum ferritin

levels, serum ferritin levels measured at the time of admission of the Covid-19 disease patients can predict radiological severity.

This study positive correlation between the CT chest severity score and Serum ferritin level in Covid-19 disease helps to screen and categorize the COVID-19 disease positive patients into different risk groups in the clinical management and prevention of serious complications. This has a pivotal role to assist physicians in the management plan as an indicator for disease severity and possible outcome especially when CT scan chest facilities are not available. However, more research is needed to further clarify the value of correlation of chest CT and serum ferritin levels in COVID-19 disease in patient outcome.

**6. Limitations:**

This study results have some limitations. First, the results are not generalized to all the patients in this region, as it is the only tertiary level Govt. hospital admitting Covid -19 positive patients. Second, the information about the patients who are asymptomatic and do not present to the hospital is not known. So, the study findings are confined to the patients diagnosed with Covid-19 positive disease. Finally, it is primarily a retrospective observational study conducted in a single centre with a small sample size. So, the studies of large sample sizes at multiple centres are needed to increase the accuracy of the findings for further evaluation of Covid-19 disease.

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