

## COMPARISON OF HEMATOLOGICAL, BIOCHEMICAL AND RADIOLOGICAL PROFILE OF PATIENTS WITH COVID-19 INFECTION BASED ON SEVERITY

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### Abstract

**Background:** COVID-19 is one of the fastest spreading infectious disease recorded in the history of mankind after Spanish flu. This study mainly focuses on the hematological, biochemical and radiological changes in COVID-19 patients. These changes can prove to be a useful marker for COVID-19 infection and its severity. To quantitatively estimate CBC, CRP, peripheral smear, RBC indices, D-Dimer, and their corresponding radiological and clinical parameters in COVID-19 positive patients and compare them on the basis of the severity of infection. **Materials and Methods:** All the cases who (presented with Breathlessness, cough, fever) were then tested positive for COVID-19 by RT-PCR between 3 June 2021 And 3 July 2021. These cases were then divided into categories based on comprehensive guidelines for management of covid19 patients by the directorate general of health services, MoHFW, Government of India. **Result:** A total of 178 patients were chosen, the cases were further divided into four groups, consisting of 51 of asymptomatic, 33 of mild, 33 of moderate, 61 of severe depending on the severity. The Male to female ratio was noted to be 1.28:1. Breathlessness was most common presenting symptom, noted in 122 cases, followed by cough (119 cases) and fever (98 cases). Hypertension was more common (22 cases) as compared to diabetes (13 cases). 11 cases of coronary heart disease, 2 cases of tuberculosis and 1 case with thalassemia were seen. Neutrophilia was noted in moderate and severe patients, Lymphocytopenia was noted in Moderate and severe cases. Slightly elevated RDW-CV, RDW-SD and PWD was noted. Elevated levels of D-Dimer, CRP levels and serum ferritin were noted in all the cases. Total protein, albumin, globulin and A/G ratio were seen to be lower in severe cases. Creatinine and urea levels were seen to be higher in severe cases. In CT scan (HRCT scan) there were patchy predominantly areas of, ground glass opacities with interlobular septal thickening seen scattered in bilateral lungs. **Conclusion:** The present study gives a better understanding about COVID-19 and haematological and radiological reports-based on which further treatment of patient can be done.

## INTRODUCTION

Corona Virus Disease 2019 (COVID-19) was declared as a global pandemic on 11 march 2020, affecting almost 1.7 billion people as of June 2021 in the world, out of which about 28 million in India, wiping about 3.7 million population of world and 370 thousand in India.<sup>[1]</sup> It is one of the fastest spreading infectious disease recorded in the history of mankind after Spanish flue. The number of COVID-19 cases are increasing in spite of regular

efforts by the government and health care workers. Common presenting symptoms of COVID-19 include fever, dry cough, and fatigue.<sup>[2,3]</sup> The patients affected with COVID-19 infection initially present with pneumonia and acute respiratory tract infection which further progresses to acute respiratory distress syndrome, acute respiratory failure, or other severe secondary complications in some patients.<sup>[4]</sup> The changes in biochemical parameters directly points to the severity level of COVID-19 cases. Different studies demonstrate

various biochemical, hematological and radiological parameters like Complete Blood Count(CBC), Differential Leucocyte Count(DLC), C-Reactive Protein(CRP) levels and D-dimer status that point to severity of COVID-19 cases.<sup>[5,6]</sup> According to a study even CT severity scores have proved to be of great help in analysing the patient severity and are repeatedly used in patient management.<sup>[7]</sup> In spite of this there is a knowledge gap between comparing all the information at once and coming to a conclusion for better treatment of the patient. This study mainly focuses on the hematological, biochemical and radiological changes in COVID-19 patients. These changes can prove to be a useful marker for COVID-19 infection and its severity. Most of the hematological and biochemical investigations are economically viable and easy to have in short notice. These findings can also be easily available at small COVID-19 centers and comparing all of them will result in better management of the patient. Hence this study was conducted to quantitatively estimate CBC, CRP, peripheral smear, RBC indices, D-Dimer, and their corresponding radiological and clinical parameters in COVID-19 positive patients and compare them on the basis of the severity of infection.

## MATERIALS AND METHODS

All the cases who (presented with Breathlessness, cough, fever) were then tested positive for COVID-19 by RT-PCR between 3 June 2021 And 3 July 2021 were taken into consideration for the study. The cases were then categorised into Category I that is Asymptomatic (SPO2  $\geq$ 95%), Category II that is Mild (SPO2 $\geq$ 94%), Category III that is Moderate (SPO2 93-90%), and Category IV(SPO2 $<$ 90%), that is severe based on their SPO2 saturation (according to the comprehensive guidelines for management of covid19 patients by the directorate general of health services, MoHFW, Government of India).

The clinical, haematological, biochemical and radiological parameters of the cases were collected from the case records. These data were then tabulated according to the severity and then compared and analysed using statistical analysis (ANOVA).

## RESULTS

A total of 178 patients were chosen for the study. All these cases were tested positive for COVID-19 by RT PCR. The cases were further divided into four groups, consisting of 51 of asymptomatic, 33 of

mild, 33 of moderate, 61 of severe depending on the severity of the infection. The age of the patients ranged from 6 to 87 Yrs. (Mean age: 47.67 yrs.). The Male to female ratio was noted to be 1.28:1 with 100 males and 78 females. Among these patient's breathlessness was most common presenting symptom, noted in 122 cases, followed by cough (119 cases) and fever (98 cases).<sup>34</sup> Out of 178 cases had comorbidities, of which hypertension was more common (22 cases) as compared to diabetes (13 cases). 11 cases of coronary heart disease, 2 cases of tuberculosis and 1 case with thalassemia were seen. [Table 1]

On analysis of Complete blood count of the cases, Total WBC count was seen to be significantly elevated in sever patients while the Asymptomatic, Mild and moderate cases showed within the normal limits. Further on, on analysing the differential counts, it was observed that Neutrophilia was noted in moderate and severe patients, while in mild and asymptomatic patients were within normal limits. Similarly, lymphocytopenia was noted in Moderate and severe cases, while the lymphocyte count was normal in Asymptomatic and mild cases.

Slightly elevated RDW-CV, RDW-SD and PWD was noted and elevated in moderate patients followed by severe, mild and asymptomatic.

No significant findings were noted among the cases in the platelet, RBC counts, Haemoglobin, RBC indices and haematocrit. [Table 2]

Inflammatory marker was also evaluated in all the cases which showed significant differences in the four groups. Elevated levels of D-Dimer, CRP levels and serum ferritin were noted in all the cases, but the values of D- Dimer, and Serum ferritin and CRP levels were significantly highly in the severe group, as compared to moderate, mild and asymptomatic.

Total protein, albumin, globulin and A/G ratio were seen to be lower in severe cases as compared to moderate, mild and asymptomatic.

Similarly, Creatinine and urea levels were seen to be higher in severe cases as compared to moderate, mild and asymptomatic.

CT scan (HRCT) was done in all the 178 cases and the severity score as well as CORADS score was given to each patient. As per Table 4 it was noted that the patients with severe disease showed a higher CT score and CORADS score as compared to the other groups. (TABLE 4)

There were patchy predominantly areas of, ground glass opacities with interlobular septal thickening seen scattered in bilateral lungs, predominantly in bilateral lower lobes these findings were more in patients with severe infection followed by moderate, mild and asymptomatic.

**Table 1: Symptoms and comorbidities present in the present study population**

| Parameters       | Category I | Category II | Category III | Category IV |
|------------------|------------|-------------|--------------|-------------|
| Breathlessness   | 22         | 21          | 24           | 55          |
| Cough            | 33         | 21          | 27           | 38          |
| Fever            | 29         | 22          | 16           | 31          |
| Diabetes Melitus | 5          | 4           | 0            | 4           |

|               |    |   |   |   |
|---------------|----|---|---|---|
| Heart Disease | 2  | 1 | 0 | 8 |
| Hypertension  | 10 | 3 | 0 | 9 |
| Tuberculosis  | 0  | 0 | 2 | 0 |
| Thalassemia   | 1  | 0 | 0 | 0 |

**Table 2: Haematological parameters in the present study population**

| Parameters            | Category I  | Category II | Category III | Category IV | F Stat |
|-----------------------|-------------|-------------|--------------|-------------|--------|
| Total WBC Count       | 8.23±4.38   | 9.56±3.45   | 9.57±4.74    | 11.93±5.64  | 5.83   |
| Neutrophils           | 6.43±5.08   | 7.00±2.46   | 12.3±2.6     | 11.03±4.26  | 0.67   |
| Lymphocytes           | 1.67±1.14   | 1.22±0.73   | 0.99±0.66    | 0.83±0.50   | 10.78  |
| Monocytes             | 0.26±0.12   | 0.25±0.14   | 0.20±0.15    | 0.37±0.24   | 6.96   |
| Eosinophils           | 0.10±0.11   | 0.07±0.11   | 0.04±0.06    | 0.06 ±0.11  | 2.46   |
| Basophils             | 0.06±0.07   | 0.05±0.06   | 0.04±0.05    | 0.13 ± 0.30 | 2.60   |
| Immature Granulocytes | 0.15±0.17   | 0.23 ±0.25  | 0.27±0.29    | 0.64±1.75   | 2.43   |
| RBC Count             | 4.72±0.71   | 4.40±0.81   | 4.74±1.18    | 4.61±0.72   | 1.20   |
| Haemoglobin           | 12.34±2.06  | 12.28±1.68  | 12.42±2.48   | 12.56±3.28  | 0.11   |
| Haematocrit           | 40.81±6.34  | 40.21±5.38  | 41.25±7.96   | 40.96±6.12  | 0.16   |
| MCV                   | 85.79±14.40 | 90.10±8.92  | 83.78±18.30  | 89.37±8.96  | 2.12   |
| MCH                   | 26.19±3.98  | 28.92±8.36  | 27.17±5.20   | 27.66±7.26  | 1.28   |
| MCHC                  | 30.12 ±1.82 | 30.52±0.59  | 30.06±1.51   | 30.04±2.31  | 0.60   |
| RDW-CV                | 15.60±2.23  | 14.85 ±1.02 | 16.50±2.47   | 16.09±4.04  | 2.09   |
| RDW-SD                | 54.65±8.57  | 53.48±6.24  | 59.10±10.13  | 55.19±10.71 | 2.31   |
| Platelet Count        | 236 ±102.45 | 247±74.17   | 221±115.10   | 229±92.58   | 0.46   |
| PCT                   | 0.16±0.06   | 0.16±0.05   | 0.15±0.07    | 0.16±0.06   | 0.21   |
| MPV                   | 7.13±0.59   | 6.97±0.97   | 7.26±0.60    | 7.21±1.00   | 0.81   |
| PDW                   | 18.09±1.76  | 18.77±0.76  | 18.35±1.25   | 18.77±0.84  | 3.53   |

**Table 3: Biochemical parameters in the present study population**

| Parameters         | Category I  | Category II | Category III | Category IV | F Stat |
|--------------------|-------------|-------------|--------------|-------------|--------|
| D-Dimer            | 283±350.45  | 297±295.23  | 418±321.23   | 827±598.00  | 18.09  |
| CRP                | 3.74±4.71   | 4.99±5.27   | 8.56±7.48    | 26.38±98.94 | 2.15   |
| ALT                | 29.88±25.80 | 28.48±17.22 | 26.24±15.01  | 47.96±83.65 | 1.92   |
| AST                | 36.17±36.38 | 34.09±35.01 | 27.03±14.97  | 39.90±36.98 | 1.08   |
| ALP                | 103±68.63   | 84.90±36.28 | 90.00±57.29  | 100±50.50   | 0.98   |
| Total Bilirubin    | 0.67±0.38   | 1.3±0.77    | 0.64±0.35    | 0.70±0.44   | 1.48   |
| Direct Bilirubin   | 0.3020±0.21 | 0.23±0.10   | 0.35±0.17    | 0.37±0.25   | 3.82   |
| Indirect Bilirubin | 0.36±0.23   | 0.28±0.16   | 0.32 ±0.21   | 0.33±0.21   | 0.91   |
| Total Protein      | 6.76±0.56   | 6.56±0.68   | 6.56±0.80    | 6.02±1.25   | 6.75   |
| Albumin            | 3.72±0.46   | 3.56±0.48   | 3.51±0.43    | 3.25 ±0.63  | 7.86   |
| Globulins          | 3.03±0.33   | 3.06 ±0.34  | 3.05±0.49    | 2.97 ±0.91  | 0.20   |
| A/G Ratio          | 1.24±0.19   | 1.28±0.49   | 1.15±0.19    | 1.04 ±0.42  | 4.60   |
| Creatinine         | 0.82 ±0.35  | 0.81 ±0.18  | 0.74±0.18    | 1.54±1.81   | 6.30   |
| Uric Acid          | 4.21±1.75   | 3.63±1.10   | 3.59±1.39    | 4.50±2.18   | 2.80   |
| Urea               | 27.00±13.08 | 23.93±8.03  | 23.82±13.11  | 47.85±31.81 | 15.67  |
| Serum Ferritin     | 431±498.38  | 302±228.12  | 752±106.39   | 812±604.92  | 6.34   |

**Table 4: Radiological parameters in the present study population**

| Parameters | Category I | Category II | Category III | Category IV  | F Stat |
|------------|------------|-------------|--------------|--------------|--------|
| CT-Score   | 9.94±4.23  | 11.33±3.30  | 12.87±5.13   | 15.5082±5.32 | 14.25  |
| ICO-RADS   | 4.66±1.08  | 4.87±0.54   | 4.87±0.48    | 5.00±0.00    | 2.37   |

## DISCUSSION

COVID-19 is an acute disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-COV-2). The first case of COVID-19 was noticed on 17 November 2019, a 55-year-old individual from Hubei province in china.<sup>[8]</sup> The first case in India being on 27 January 2020, a 20-year-old female from Thrissur, Kerala.<sup>[9]</sup> And the first case in Karnataka being 40-year-old software professional on march 1 2020.<sup>[10]</sup> On 11 march 2020, WHO declared novel coronavirus disease (COVID-19) outbreak as a pandemic and reiterated the call for countries to take immediate action and scale up responses to treat, detect and reduce transmission to save people's lives.<sup>[11]</sup> COVID-19 virus spreads via

respiratory droplets and contact. SARS-COV-2 with the help of its spike glycoprotein(s) antigen binding with the host cell receptor, enters into the host cell. In the COVID-19 patients there is damage to type 2 alveolar cells their function to produce pulmonary surfactant which reduces the alveolar surface tension is hindered, now the alveoli tend to collapse. To prevent this, muscles in the airway becomes hyperactive that results in increased lung volume in the interstitial space attracting liquid contributing to oedema in the lungs. The presence of SARS-COV-2 in the lungs stimulates an uncontrolled immune reaction causing a cytokine storm.<sup>[12]</sup> The infection can vary in people from asymptomatic to a very severe state, asymptomatic where a total absent/negligible symptom either a respiratory rate of 12-16 per minute and spo2 being greater than or

equal to 95%, mild being the patients with symptoms, may have loss of taste and smell and anoxia/nausea/vomiting with no breathlessness and respiratory rate less than 24 and spo2 being greater than or equal to 94%, moderate being those patients being patients with all symptoms including high fever and breathlessness where respiratory rate increased to 24-30 and spo2 reduced to 90-93% and severe patients being those which have all the symptoms with severe fever, headache, weakness and breathlessness, where respiratory rate increased to more than 30 and SpO2 reduced to less than 90%.<sup>[13]</sup> The study mainly focusses on the markers like d-dimer, CRP levels and serum ferritin, etc for their effects on lungs and analysing them for the better management of COVID-19 patients. The study took place in Gadag institute of medical sciences, Gadag. 178 patients were chosen for the study, they were further divided into 4 categories.<sup>[14]</sup> All the patients were tested positive for reverse transcriptase- polymerase chain reaction. RT-PCR detects the virus in the upper respiratory tract and separates the positive patients from the negative patient's PCR proves to be a useful and promising test in covid19 patients.<sup>[14]</sup> But in some studies, it is proven to give a false positive also.<sup>[15]</sup> In this study it male to female ratio was 1.28:1. Similar to the studies which have also have taken almost equal(1.2:1) male and female for the study.<sup>[16]</sup> This and other studies showed males are at more risk than females for the COVID-19 infection. Even the males are more prone to have a severe infection then compared to females.<sup>[17]</sup> COVID-19 infection presents with the symptoms like breathlessness, cough, fever, diarrhoea.<sup>[18]</sup> In this study breathlessness was noted to be the most common symptom. Where as in other studies cough is also noted to be common,<sup>[19]</sup> and in other fever to be common.<sup>[20]</sup> Studies also shows that breathlessness is the symptom which can be present in patients even after their discharge from the hospital.<sup>[21]</sup> The study also shows the presence of comorbidities in patients with COVID-19 infections. There are studies that prove the presence of comorbidities and diabetes in the patients of COVID-19 infections.<sup>[22]</sup> Diabetes is a common and risky comorbidity and is also associated with the severity of COVID-19 infection and hypertension was also found to be common in these patients.<sup>[23]</sup> These comorbidities can be treated with ACE inhibitors.<sup>[23]</sup> Tracking comorbidities is important for the better management of patients.<sup>[24]</sup> The blood CBC reports in patients with infection shows increase in in the WBC count,<sup>[25]</sup> lymphocytopenia, neutrophilia. These are important biochemical reports for tracking the progress in the infection in the COVID-19 patients. This also serves as a marker for the severity of the infection. Out of all the haematological parameters that were tested there were no changes in the value of RBC count, and RBC Indices (MCH, MCV, HGB, HCT, MCHC), this is also reported in some studies.<sup>[26]</sup> In these

CBC reports there was a surprisingly increase in the RDW-SD, RDW-CV which was also noted in some studies.<sup>[27]</sup> In addition to this there was an increase in the PDW levels as in other studies also.<sup>[28]</sup> On analysing the inflammatory markers there was increase in the d-dimer levels which has proved to be an important marker for analysing the severity of patients with covid19 infections.<sup>[29]</sup> In some studies d-dimer was showed to be higher in non-survivor's patients then in the survivors. In addition to D-dimer, CRP levels were also higher in the patients under the study. CRP levels have proved to be a promising in the managements of COVID-19 patients. Serum ferritin is also an inflammatory marker seen to be higher in the patients with COVID-19 infection.<sup>[30]</sup> Serum ferritin hence can also be used a biomarker for the severity of the infection.the patients with infection also showed decrease in the total proteins and the albumin levels. This is also showed in the other studies done on the COVID-19 infection.<sup>[31]</sup> COVID-19 infection was also related to increase in the serum creatinine and urea levels as also seen in some studies these also throw some light on the acute kidney infections in covid19 patients.<sup>[32]</sup> On the radiological aspect CT scores and CORADS score proved to be another confirmatory and important test for management of asymptomatic, mild, moderate severe patients,<sup>[33]</sup> based on ground glass opacity seen in the covid19 patients the health care workers can get an idea of fibrosis and inflammation in the lungs of a COVID-19 affected patients.<sup>[34]</sup> These CT findings proved to be similar to the that of SARS COV and MARS COV giving an evolutionary aspect of novel corona virus. But these ground glass opacities cannot be taken as the only marker for the severity of infection, but if other symptoms of the COVID-19 infection are present or a positive RT-PCR report should alert the radiologist.<sup>[34]</sup> Comparing the sensitivity of RT-PCR and the CT scan reports(CT score and the CORADS score) , CT scan proves to be more sensitive.

## CONCLUSION

The current study shows the significance of basic diagnostic tests and routine investigations to assess the severity of the COVID-19 as well as to monitor its prognosis when compiled together. This in-turn will aid in the better management of the patient and alert the treating clinician regarding deterioration of the patient condition.

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