

The Spectrum of Biochemical and Haematological Alterations in COVID-19 Patients Attending a Tertiary Care Hospital in Karnataka, India

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Severe Acute Respiratory Syndrome Coronavirus -2 (SARS-CoV-2), primarily acts on lungs. Most of these patients present with typical respiratory symptoms and signs. SARS-CoV-2, mainly detected by nasopharyngeal/oropharyngeal swab(s) of suspected subjects. The present study aimed at evaluating and discussing the alterations in biochemical and hematological parameters in COVID-19 patients in a tertiary care hospital. This observational study was conducted in a Tertiary care hospital, Coastal Karnataka, India. In this study, 124 COVID-19 patients were involved. Co-morbidities, such as hypertension was observed in 98 (79%), diabetes in 91 (73.3%), cardiovascular disease in 20 (16.1%), chronic kidney disease in 4 (3.2%) and liver disease in 2 (1.6%) cases. Hypertension and diabetes were more common. Symptoms such as fever was found in 109 cases (87.9%), dry cough in 102 (82.2%), fatigue in 89 (71.7%), chest tightness in 79 (63.7%), myalgia in 67 (54%) and mild shortness of breath in 46 (37%) cases. In this study, hemoglobin (9.4 ± 1.7 %) and platelets (240.1 ± 89.7) were decreased and erythrocyte sedimentation rate (ESR) (50.7 ± 15.7) significantly increased in severe cases. Mean values of random blood sugar (RBS) was 245.6 ± 126.9 mg/dl, HbA1c 7.9 ± 2.8 %, serum urea 82.8 ± 25.2 mg/dl, Creatinine 3.2 ± 1.5 mg/dl, Uric acid 6.8 ± 1.5 mg/dl, Total Bilirubin 1.2 ± 0.6 mg/dl, Alkaline Phosphatase 135.4 ± 38.9 IU/L, C-Reactive protein (CRP) 84.8 ± 7.7 mg/L, lactate dehydrogenase (LDH) 644.6 ± 175.1 U/L, Ferritin 828.3 ± 195.4 μ g/L, D-Dimer [2680.9 (1899.0 - 5475.7 ng/ml)] were elevated in severe cases than mild group. In contrast, serum total proteins (6.3 ± 0.7 g%) and globulin (2.8 ± 0.5 g%) levels were significantly decreased in severe cases than mild/moderate cases. Study may conclude that presence of co-morbidities, abnormalities in biochemical and hematological parameters, should be regularly monitored, especially in severe / critical COVID-19 patients.

Keywords: biochemical; Covid-19; D-dimer; Ferritin; hematological parameters; Liver function tests; renal function tests.

Coronavirus, designated as Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2), was first identified in Wuhan, China¹.

SARS-CoV-2 primarily acts on lungs. Most of these patients present with typical respiratory symptoms and signs. SARS-CoV-2 is detected

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by nasopharyngeal/oropharyngeal swab(s) of suspected subjects, but it has also been isolated from blood, GIT, saliva and urine. Yet, these routes of potential transmission further need to be investigated².

SARS - CoV-2, so infectious disease, even asymptomatic patients may become potential source of infection. COVID-19 patients present with a great number of clinical manifestations like pharyngalgia, fever, cough, headache, nausea, and acute respiratory distress syndrome (ARDS) etc³.

Early identification of risk factors among critical patients could be helpful for appropriate care and to reduce mortality⁴. The rapid spread of this virus has prompted the conduct and reporting of numerous research studies in order to explore the clinical, biochemical, radiological, and genetic predictors for progression of the disease. Therefore, identification of these predictors / risk factors, will help in stratifying the risk and planning further intervention, to target the patients at risk of worsening and/or progression to death. Demographic factors like advanced age, male gender, comorbidities, ARDS, and radiological predictors have been reported^{5,6}.

Wang *et al.*, conducted a study on 138 Covid-19 cases and reported changes in neutrophil, lymphocyte and D-dimer levels⁷. In COVID-19 patients, elevated inflammatory markers such as ESR, IL-6 and CRP have been reported⁸. However, Biochemical and Hematological predictors, which represent the changes at elementary/molecular level, are yet to be adequately reported in Indian patients. This study conducted to evaluate the alterations in biochemical and hematological parameters in COVID-19 patients in a tertiary care hospital.

MATERIALS AND METHODS

This observational study was conducted in the Department of Biochemistry, in association with Department of General Medicine, at a tertiary care hospital, Coastal Karnataka, India. after obtaining the approval from the Institutional Ethics Committee (YEC No:1/2020/085) and written informed consent from all study subjects. Confirmation of COVID-19 was done by reverse-transcriptase polymerase chain reaction (RT-PCR) assay using nasopharyngeal swabs. In this study,

124 COVID-19 patients were involved and were grouped into two categories: Mild / Moderate (n=76) and Severe / Critical (n=48). Mild/Moderate patients were categorized as per WHO criteria and Severe/ Critical cases were defined as those admitted to ICU, with any of following symptoms: respiratory rate >30 breaths/min, oxygen saturation <93% at room air, ARDS or requirement of mechanical ventilation⁹.

Venous blood samples were collected from all the cases, following universal precautions, and used for analysis of Biochemical parameters such as RBS, HbA1c, renal profile, liver function tests, LDH, Ferritin, D-Dimer and Hematological parameters such as Hemoglobin (Hb), platelets, MCV, MCH, MCHC, PCV, RBC count and ESR, by using commercially available autoanalyzer kits. Demographic, physical and clinical details too were collected.

Statistical analysis

Results were presented as Mean±SD. Non-normally distributed variables represented as median (inter-quartile range). Categorical variables were represented as percentages. Data Analyses was performed by using SPSS version 22.0 (IBM SPSS), and P <0.05 was considered as significant.

RESULTS

In this study, males were 87 (70.1%) and females were 37 (29.8%). Comorbidities, such as hypertension was observed in 98 (79%), diabetes in 91 (73.3%), cardiovascular disease in 20 (16.1%), chronic kidney disease in 4 (3.2%) and liver disease in 2 (1.6%) cases. Hypertension and diabetes were more common among these. Symptoms such as fever was found in 109(87.9%), dry cough in 102 (82.2%), fatigue in 89 (71.7%), chest tightness in 79 (63.7%), myalgia in 67 (54%) and mild shortness of breath in 46 (37%) cases as represented in table 1 & figure 1.

In the present study, hemoglobin (9.4±1.7 %) and platelets (240.1±89.7) were decreased significantly and ESR (50.7±15.7) showed significant increase in severe/critical cases. In this study, the mean ± SD values of RBS was 245.6±126.9 mg/dl, HbA1c 7.9±2.8%, Blood Urea 82.8±25.2 mg/dl, Serum Creatinine 3.2±1.5 mg/dl, Uric acid 6.8±1.5 mg/dl, Total Bilirubin 1.2±0.6 mg/dl, ALP 135.4±38.9 IU/L, CRP 84.8±7.7 mg/L,

LDH 644.6±175.1 U/L, Ferritin 828.3±195.4 µg/L, D-Dimer [2680.9 (1899.0-5475.7 ng/ml)] levels were elevated in severe cases than mild group. In contrast, Serum Total Proteins (6.3±0.7g%)

and Globulin (2.8±0.5 g%) levels significantly decreased in severe/critical cases than mild/moderate cases as indicated in table 2.

Table 1. Demographic and Baseline details of two groups of Covid-19 patients

	Total (N=124)	Mild/Moderate (N=76)	Severe/Critical (N=48)
Age (years)	58.3±15.5	57.0±15.3	60.3±15.7
Male	87 (70.1%)	21 (27.6%)	31 (64.5%)
Female	37 (29.8%)	55 (72.3%)	17 (35.4%)
Co-morbidities			
Hypertension	98 (79.0%)	59 (77.6%)	39 (81.2%)
Diabetes Mellitus	91 (73.3%)	54 (71.0%)	37 (77.0%)
Cardiovascular disease	20 (16.1%)	12 (15.7%)	8 (16.6%)
Chronic kidney disease	4 (3.2%)	7 (9.2%)	1 (2.0%)
Liver disease	2 (1.6%)	2 (2.6%)	0
Symptoms and Signs			
Fever	109 (87.9%)	69 (90.7%)	40 (83.3%)
Fatigue	89 (71.7)	52 (68.4%)	36 (75%)
Dry cough	102 (82.2%)	60 (78.9%)	42 (87.5%)
Chest tightness	79 (63.7%)	44 (57.8%)	34 (70.8%)
Myalgia	67 (54.0%)	38 (50%)	29 (60.4%)
Mild shortness of breath	46 (37.0%)	25 (32.8%)	21 (43.7%)
Chill	42 (33.8%)	27 (35.5%)	15 (31.2%)
Dyspnea	41 (33.0%)	22 (28.9%)	19 (39.5%)
Diarrhea	23 (18.5%)	16 (21.0%)	7 (14.5%)
Nausea or vomiting	25 (20.1%)	18 (23.6%)	7 (14.5%)
Headache	9 (7.2%)	3 (3.9%)	6 (12.5%)

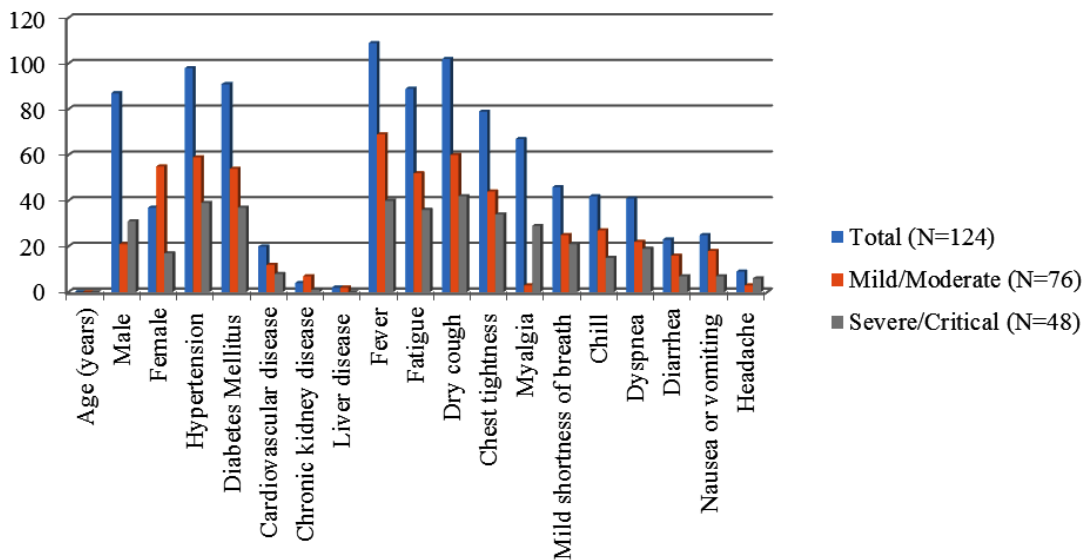


Fig. 1. Demographic and Baseline details of two groups of Covid-19 patients

Table 2. Comparison of Biochemical and Hematological parameters between mild/moderate Vs severe/critical COVID-19 patients

Parameters	Total (N=124), No (%)	Mild/Moderate (N=76)	Severe/Critical (N=48)	P-value
RBS (mg/dl)	211.5±112.5	189.9±97.3	245.6±126.9	0.014*
HbA1c (%)	7.0±2.1	6.7±1.0	7.9±2.8	0.001*
Urea (mg/dl)	70.4±25.8	62.5±20.5	82.8±25.2	0.002*
Creatinine (mg/dl)	2.1±1.12	1.5±0.8	3.2±1.5	<0.001*
Uric acid (mg/dl)	5.9±1.3	5.4±0.8	6.8±1.5	<0.001*
Total Bilirubin (mg/dl)	1.0±0.63	0.95±0.58	1.2±0.6	0.017*
Direct Bilirubin (mg/dl)	0.38±0.30	0.37±0.27	0.4±0.3	0.969
Indirect Bilirubin (mg/dl)	0.66±0.50	0.58±0.41	0.7±0.6	0.047
AST(IU/L)	66.6±24.1	58.3±26.8	79.8±22.2	0.098
ALT (IU/L)	46.8±23.7	39.1±21.1	59.1±23.9	0.809
ALP (IU/L)	117.6±36.7	106.4±30.5	135.4±38.9	<0.001*
Total proteins (g%)	6.4±0.89	6.5±0.98	6.3±0.7	0.022*
Albumin (g/dl)	3.3±0.57	3.3±0.64	3.4±0.4	0.775
Globulins (g/dl)	3.0±0.60	3.1±0.61	2.8±0.5	0.001*
A/G ratio	1.15±0.30	1.0±0.27	1.2±0.3	0.003*
CRP (mg/L)	71.8±14.6	63.7±11.8	84.8±7.7	<0.001*
Sodium (mmol/L)	139.2±25.9	138.6±24.1	140.0±28.9	0.089
Potassium (mmol/L)	5.6±2.1	6.2±1.5	4.7±0.8	0.183
Chloride (mmol/L)	98.4±9.7	98.1±10.6	98.9±8.1	0.568
LDH (U/L)	504.5±181.6	415.9±120.1	644.6±175.1	<0.001*
Ferritin (µg/L)	589.8±276.6	439.2±205.3	828.3±195.4	<0.001*
D-Dimer (ng/ml)	1837.5±2054.4	706.1 (576.7-788.9)	2680.9(1899.0-5475.7)	<0.001*
Hb (%)	10.8±2.6	11.0±3.0	9.4±1.7	<0.001*
Platelets (lakhs)	246.0±116.1	245.2±130.6	240.1±89.7	<0.001*
MCV (fl)	84.8±9.8	84.6±9.0	84.7±10.4	0.060
MCH (Pg)	28.1±3.6	28.0±4.1	28.1±2.6	0.070
MCHC (gm/dl)	32.7±3.3	32.8±3.9	32.6±2.2	0.341
PCV (%)	35.8±8.4	36.3±9.2	35.0±6.9	0.400
RBC (millions /cubic mmm)	4.0±0.92	3.9±0.9	4.1±0.8	0.809
ESR (mm/1hr)	44.5±15.5	40.5±14.1	50.7±15.7	<0.001*

RBS - Random blood sugar; HbA1c - Glycated hemoglobin; AST – Aspartate transaminase; ALT – Alanine transaminase; ALP – Alkaline phosphatase; CRP – C-reactive protein; LDH – Lactate dehydrogenase; Hb – hemoglobin; MCV – Mean corpuscular volume; MCH - mean corpuscular hemoglobin; MCHC - mean corpuscular hemoglobin concentration; PCV – Packed cell volume; RBC – Rec blood cell; ESR – Erythrocyte sedimentation rate; * indicates statistical significance

DISCUSSION

Globally, SARS-CoV-2 has spread very rapidly and has exhibited a wide spectrum of severity. Most of the COVID-19 patients have mild to moderate symptoms, up to 5-10% can have severe illness^{10,11}. However, we still need to know a lot about the biochemical/hematological alterations in patients with COVID 19. Therefore, this study, we have tried to summarize the hematological and biochemical parameters of 124 COVID-19 patients.

Patients were divided into mild/moderate vs severe/critical COVID-19 patients. This comparison may be beneficial in the clinical setting to support clinical decision making. The older population tends to have a greater number of comorbidities, reduced organ function and lung capacity, low immune system which may result in severe complications. Hence, clinicians should treat them with more attention^{12,13}.

In this study, blood sugar and renal parameters were significantly increased in

severe cases compared to mild cases. In a study, Mahmoudi *et al.*, have reported that 35% of COVID-19 patients had elevated levels of urea and creatinine, suggesting impaired renal function in these patients. It has been reported that COVID-19 particles were observed in urine of these patients indicating that these particles may have been present in kidney, filtered in glomerulus and passed in urine¹⁴. Other studies have reported COVID-19 patients with pneumonia showed significantly elevated urea and creatinine levels, indicating acute kidney injury^{15,16}.

In COVID-19, liver injury has been reported¹⁷. However, its long-term impact on hepatic function is not clear. In this study, total and direct bilirubin levels were significantly elevated in severe cases. Liver enzymes such as AST, ALT and ALP were elevated; amongst which, ALP showed significance difference between the groups. Serum Total Protein and Globulins levels were reduced. Serum bilirubin levels insignificant. A study by An *et al.*, reported increased ALT, GGT and ALP levels along with low levels of albumin in COVID-19 survivors for a period of 14 days after discharge, but there was gradual normalization of these parameters within 2 months¹⁸. Another study by Fan *et al.* demonstrated the disruption of hepatic function in COVID-19 cases and reported reversible mild to moderate increase of liver enzymes (AST & ALT) without any changes in total bilirubin¹⁹.

In the current study, serum LDH levels were significantly elevated in severe cases compared to mild cases. It has been shown that elevated LDH levels were associated with high risk of ARDS, ICU support and mortality²⁰. Furthermore, elevation of LDH used as a marker of lung tissue damage, one of the most common biochemical abnormality in COVID-19 cases²¹. Nakanishi *et al.*, reported an elevated levels of ferritin and LDH in COVID-19 patients²². A meta-analysis reported increased levels of ferritin and LDH in COVID-19 cases suggesting serum ferritin role to monitor prognosis²³. Many studies have reported that patients with mild infection have LDH values within the normal ranges, while significantly elevated levels were observed in critical condition²⁴⁻²⁷. Therefore, monitoring liver function tests is important during the course of

COVID-19, especially in patients with severe illness.

In the current study, CRP levels were significantly elevated in severe cases than the mild cases. The elevated CRP indicates the extent of systemic inflammation in severe cases, which is followed by massive release of cytokines creating a “cytokine storm” results in acute tissue damage and subsequent systemic failure²³.

In this study, ferritin and D-Dimer levels were elevated in severe cases. These findings were similar to study conducted by Qin *et al.*, conducted on 166 non-severe and 286 severe covid-19 patients to evaluate the characteristics of hemogram and lymphocyte subpopulations. They reported that severe cases had elevated neutrophil/lymphocyte ratio (NLR) and elevated levels of inflammatory markers such as CRP, ferritin, IL-6, IL-8, and IL-10. In addition, there was an imbalance in the lymphocyte immune response in severe cases, who had high CD4 lymphopenia, elevated CD4-naïve cells and CD4 suppressor T cells, and few CD4 memory cells and regulatory T cells than the non-severe patients²⁸. A study conducted by Rodriguez *et al.* reported that COVID-19 may affect the lymphocytes, especially T cells, possibly decreasing CD4 and CD8²⁹.

Viral particles spread through the respiratory mucosa, first using ACE2 receptor at ciliated bronchial epithelial cells and then infecting other cells. This causes a cytokine storm in body and generates immune responses, which cause changes in peripheral WBCs and immune cells such as lymphocytes³⁰. In a study conducted by Sibtain *et al.*, on 336 covid -19 patients, reported that ferritin levels were significantly different based on severity and mortality, suggested that serum ferritin levels are promising predictor of mortality in Covid-19³¹. Increased D-dimer level causes of coagulopathy with thromboembolic complications. In a study conducted by Hussein *et al.*, reported that serum ferritin and D-dimer levels were 65% higher in covid-19 patients³².

Similar to our study, Mukesh *et al.*, also reported significantly increased procalcitonin, CRP, AST, potassium, neutrophils count, white blood cell count, prothrombin time and suggested that these indicators might support clinical decision to identify high fatality cases and also poor diagnosis in the initial admission phase¹¹.

CONCLUSION

Based on the interpretation of results of the present study, we conclude that presence of co-morbidities, abnormalities in Biochemical and Hematological parameters, should be regularly monitored, especially in Severe/Critical COVID-19 cases. Early intervention and periodic monitoring of these parameters may help in planning further intervention as well as overall outcome, in terms of morbidity and/or mortality of such patients.

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Conflict(s) of interest

The authors declare no conflict of interest.

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Authors' Contribution

Dr. Nagalakshmi CS, Dr. Shaheen Shaikh were involved in the study conception and design, data collection, Dr. Rajeev Gandham, Dr. Santhosh NU were involved in the analysis and interpretation of results, manuscript preparation along with all authors where all equally contributed.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author.

Ethics Approval Statement

The study has been approved by the Institutional Ethics Committee (YEC-1/2020/085)

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