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ORIGINAL ARTICLE

Retrospective Observational Study of Hematological and Biochemical Parameters of COVID 19 Patients

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Abstract

Background: COVID 19 has a potential to spread exponentially during its incubation period. Early diagnosis and management are therefore key in checking its progression. **Aims and Objectives:** The aim of the present study is to make a retrospective assessment of hematological and biochemical parameters, along with inflammatory biomarkers, in COVID 19 patients to ascertain if they act as independent factors in disease prognosis. **Study Design**: A retrospective observational study was conducted on 120 patients, in the Department of Biochemistry in collaboration with Department of Pathology, Government Medical College, Jammu. **Materials and Methods:** All patients admitted with positive real time reverse transcriptase polymerase chain reaction (RT-PCR) and hospitalized in various COVID 19 wards of GMC Jammu and Patients in the age group of 18 years and above were included for the current analysis. **Results:** There were, 79 (65.83%) males and 41 (34.17%) females. 75.83% patients recovered without any adverse outcome, 9.17% patients were severely/critically ill, 2.5% died. Significantly higher neutrophils (71.34 ± 11.55) were associated with prolonged hospital stay. 46/120 (38.33%) patients had co-morbidities, 13 (10.83%) patients had Diabetes Mellitus and 11 (9.17%) were hyper-tensive. D-dimer, CRP and Ferritin levels were significantly elevated, NLR was seen significantly higher among patients (3.99 ± 1.87) with prolonged stay and severity of disease. **Conclusions:** Hematological parameters and inflammatory biomarkers in COVID 19 patients can potentially act as independent factors and affect the disease prognosis and treatment process.

Keywords

COVID 19 , Hematological Parameters, Biochemical Parameters, Inflammatory Biomarkers

Introduction

SARS-COV-2 is a non-segmented, RNA virus responsible for 2019 coronavirus disease and hence (COVID 19) pandemic.[1] The genome contains four major structural proteins: the spike (S), membrane (M), envelope (E) and the nucleocapsid (N). The primary organs of involvement by COVID 19 infection are lungs, and most of the patients tend to present symptoms of respiratory distress.[2] The outbreak of COVID 19 has brought focus to global health concerns, and the world is still curious to know the transmission dynamics and spectrum of illness. The sudden peaking of COVID 19 wave could be attributed to the late identification of source of infection, while the host, being asymptomatic & continuously shedding the virus around.[3]

Coronavirus disease, in a short period of three months, had rapidly evolved into a global pandemic effecting more than 1 million individuals worldwide.[4] Primarily recognized as a respiratory tract infection, researches have indicated that COVID 19 cause an illness which has a wide variety of clinical features, which may include mild to moderate upper respiratory tract infection, as well as severe systemic diseases which involve gastrointestinal, neurological, cardiovascular, immunological and hematopoietic systems.[5]

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Coagulopathies like disseminated intravascular coagulation, sepsis induced coagulopathy (SIC), local microthrombi, venous thromboembolism (VTE), arterial thromotic complications and thrombo inflammation have been known to be associated with COVID 19 .[6] Therefore, hematological manifestations of the particular virus should be tracked closely. Hematological and inflammatory biomarkers like complete blood count, D-dimer, C-reactive protein, ferritin and coagulation profile can provide a better guide for prompt management of patients, and help in decreasing the disease morbidity and mortality.

There is lack of evidence on the relationship between hematological and biochemical abnormalities associated with COVID 19, therefore the aim of the present study is to make a retrospective assessment of hematological and biochemical parameters, along with inflammatory biomarkers, in COVID 19 patients to ascertain if they act as independent factors in disease prognosis.

Material and Methods

A retrospective observational study was conducted on 120 patients, selected randomly, in the Department of Biochemistry in collaboration with Department of Pathology, Government Medical College, Jammu.

Inclusion Criteria: All patients admitted with positive real time reverse transcriptase polymerase chain reaction (RT-PCR) and hospitalized in various COVID 19 facilities of GMC Jammu. Patients in the age group of 18 years and above, with or without co-morbidities, were selected for the study. Covid positive patients with age above 65 years were also included in the study.

Exclusion Criteria: Age less than 18 year; Pregnant Women, patients whose either bio-markers or CBC count were not analyzed were excluded from the study. Laboratory tests done at later stages after admission were excluded. Patients with incomplete record or who were transferred to other level of care, before recovery, were excluded from the study. Patients discharged within 2 days of admission.

Medical records and patient files, as sourced from COVID 19 facilities, were reviewed to collect the information pertaining to patients' demographics, clinical manifestations and presence and absence of any co-morbidity. Symptomatology and treatment protocol of patients were recorded. Indian guidelines of COVID 19 management were followed for each patient included in the study, according to which, RTPCR for COVID 19 was done every third day till the report is negative and thereupon, it was repeated after 24 hours for confirmation. Patients were considered 'recovered' from COVID 19 when they became asymptomatic and had rRT-PCR negative, 24 hours apart.[7] Patients can, however, experience lingering symptoms for weeks to months following COVID-19 and can also easily improve with time. Patients having shown considerable improvement in symptoms and clinical manifestations and discharged within 2 to 14 days were taken as early recovery. All such cases of prolonged or severity of symptoms and clinical manifestations, beyond 10 days of admission, except very severe/ critical illness or death, were taken as prolonged hospital stay. Severe or Critical outcomes of COVID-19 could be defined as: admission to the intensive care unit (ICU), need of intubation or mechanical ventilation, or death.[8] The present study was conceived as a one-point data-based study, the dynamic data collection or follow-up of all such patients was not part of the study design.

Complete blood count was performed on automatic hematology analyzer and other biochemical investigations on ABOTT architect fully automated analyzer. Data of investigation reports, including that of CBC count, was gathered from electronic patient record as well as registers corresponding to hematology analyzer from Postgraduate Department of Pathology and biochemical investigations and other biomarkers from fully automatic analyzer and registers maintained in the main lab, Department of Biochemistry, GMC Jammu.

Ethical approval to the study was conveyed by the Institutional Ethics Committee, GMC Jammu, [vide no: IEC/GMC/2022/1120, under Cat-B/C-12 dated 29.8.2022. The previous studies on similar Hematological parameters in COVID 19 patients, particular to biomarkers involved had shown median values of biomarkers like D-Dimer higher to the cut-off marks/ range values, therefore by taking the power of study at 80%, margin of error: 5%, minimum sample size came out to be: 108, which was taken as 120 for the betterment of the study.

Statistical Analysis: was done using MS Excel 2010 software. Results of continuous variables were expressed as mean ± SD, and percentage values. Independent t-test was applied to analyze variables between groups and p-value <0.05 was considered significant.

Results

120 confirmed cases of SARS-CoV-2 infection were enrolled in the study. The median age of all patients enrolled was 38.50 years. There were, in total, 79 (65.83%) males and 41 (34.17%) females. (*Table 1*) 75.83% patients recovered without any adverse outcome, while 9.17% patients were severely/critically ill, out of which 2.5% died. (*Fig* 1)

Young age was a major factor behind early recovery. Patients who were hospitalized for long showed

significantly higher neutrophils (71.34 ± 11.55), but lower lymphocytes (21.68 ± 10.67). NLR ratio was also found critical and significant. Platelet Count, AST, ALT and Blood Urea (mg/dl) also showed significant variation between the two. (*Table 1*)

In total 46 patients suffered from one or the other co-morbidity. 7 patients presented with two or more co-morbidities, while 13 (10.83%) patients had Diabetes Mellitus as the primary co-morbidity. (*Fig 2*)

Discussion

In the December of 2019, several of patients, in Wuhan, China, presented with an unidentified form of viral pneumonia and respiratory syndrome. Most of them had a common history of having visited the Huanan seafood market. The virus was isolated from biological samples and identified as genus betacoronavirus, which was peculiar to pathogenetic, epidemiological and clinical features of Severe Acute respiratory syndrome (SARS) and Middle East Respiratory Syndrome. [9] On the basis of phylogenetic analysis of coronaviruses, it was designated as severe acute respiratory syndrome coronavirus (SARS-COV-2) by the coronavirus study group (CSG) of International Committee on Taxonomy of Viruses.[10]

It has been observed that patients with clinical symptoms quite frequently progress to pneumonia, with radiological evidence of parenchymal disease, with 80.9% presenting with mild disease, 13.8% with severe and 4.7% with critical disease.[11] Patients admitted to intensive care units manifest high plasma levels of proinflammatory cytokines including interleukins and tumour necrosis factor, which suggests that individuals with severe disease may develop cytokine storm effect.[12] This way, a patient may develop acute respiratory distress syndrome immediately after onset of disease. This makes it important to diagnose COVID 19 at the very onset and determine the disease severity as early as possible. Generally detected by nasopharyngeal /oropharyngeal swab of suspected cases, it can also be isolated from saliva, blood, gastrointestinal tract, and urine, but these require further investigation and study.

There is a multi-factorial association of hematogical abnormalities in severe COVID 19 cases. Hematological abnormalities in COVID 19 are related with disease progression, severity, and mortality. Lymphopenia, thrombocytopenia, abnormal coagulation profile and sepsis are also well documented in patients of Covid-19.[13] Platelet count is simple and an effortlessly available hematological parameter, which is independently associated with disease severity and risk of mortality in the intensive care unit (ICU).[14]

The study reported that males were more affected from the disease than females. A study conducted by Jin JM, *et al.*[15] reported that according to the clinical classification of severity, men had more severe disease than women.

Our study demonstrated that leucocytosis, neutrophilia and increased neutophil to lymphocyte ratio, which might

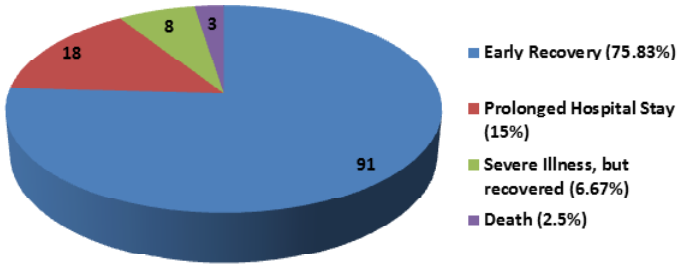

Fig 1: Clinical Profile and Clinical Outcome of COVID 19 ***patients***

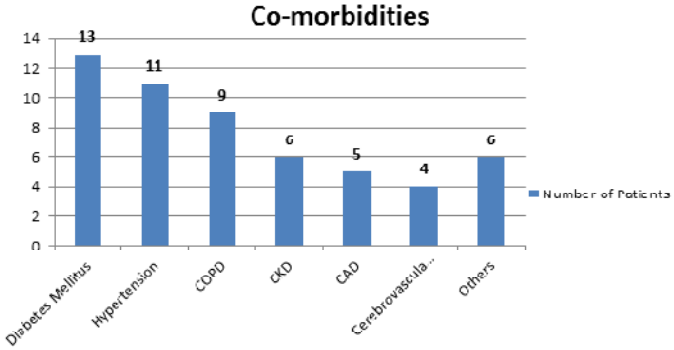

Fig 2: Patients with Co-morbidities

Table 1: Comparison of Hematological / Biochemical Parameters Among* COVID-*19 patients

Sr No	Variables	Mean Values (Mean ± SD)		p-value
		Early Recovery (n=91)	Others	
1	Age (in years)	36.42 ± 12.33	49.92 ± 16.22	<0.001*
2	Gender:			
	Male	61	18	---
	Female	30	11	
3	Hb (gm/dl)	12.21 ± 2.92	11.74 ± 3.06	0.403
4	TLC (/mm^3)	7005.3 ± 1662.2	8590.6 ± 3781.9	0.037*
5	Neutrophil (%)	63.18 ± 7.70	71.34 ± 11.55	0.008*
6	Lymphocytes (%)	27.08 ± 9.14	21.68 ± 10.67	0.044*
7	NLR	2.43 ± 1.04	3.99 ± 1.87	<0.001*
8	Platelet Count (lacs/µl)	2.37 ± 0.44	1.65 ± 0.61	0.002*
9	FBS (mg/dl)	94.18 ± 17.75	111.34 ± 45.56	0.036
10	Serum Bilirubin (mg/dl)	0.98 ± 0.65	0.88 ± 0.32	0.044
11	AST (U/l)	29.98 ± 19.14	63.86 ± 49.73	<0.001*
12	ALT (U/l)	39.33 ± 34.51	68.46 ± 50.06	<0.001*
13	Blood Urea (mg/dl)	29.93 ± 21.89	36.60 ± 19.23	0.008*
14	Serum Creatinine (mg/dl)	1.31 ± 0.87	1.25 ± 0.54	0.311
15	Serum LDH (U/l)	408.47 ± 133.58	558.67 ± 246.37	0.012*
16	D Dimer (ng/ml)	513.63 ± 203.34	3813.91 ± 1102.08	<0.001*
17	CRP (mg/L)	48.69 ± 36.05	208.78 ± 186.24	<0.001*
18	Ferritin (mg/L)	770.18 ± 489.30	1908.53 ± 1286.39	<0.001*
19	Hospital Stay, including ICU stay (Days)	5.90 ± 1.87	8.64 ± 2.45	0.003*

*Data expressed as Numbers or Mean ± Standard Deviation (SD). *p<0.05 considered significant*

Hb: Hemoglobin; TLC: Total Lucocytes count; NLR: Neutrophil- Lymphocytes Ratio; FBS: Fasting Blood Sugar; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; LDH: lactate dehydrogenase; CRP: C-reactive protein. Early Recovery: Patients discharged within 2 to 14 days; Others: All such cases of prolonged or severity of symptoms and clinical manifestations, except Early Recovery

be due to inflammatory response, have a significant association with disease severity. Neutrophil to lymphocyte ratio was highest in patients with critical disease . Liao , *et al.*[16] also found elevated neutophil to lymphocyte as a useful predictor for severity and mortality of SARS-Cov-2 infection.

The present study was aimed at investigating the relationship between hematological parameters and disease progression in COVID 19 patients and the results revealed that D-dimer, CRP and Ferritin levels were significantly elevated among those with severity or prolonged disease symptoms/ hospital stay. Similar to this, a study by Yuan, *et al.*,[2] on severe and critically ill patients, showed elevated levels of D-dimer and FDP. It may be due to the fact that COVID 19 patients are in hypercoagulable state and plasma D-dimer and FDP levels can help guide the treatment of such patients.

Isolation, extensive tracking of contacts and early testing can help in breaking the chain of transmission of COVID 19 , and help control this pandemic. Here, asymptomatic patients, which are often larger in percentage, can play spoil sport and can cause difficulties in COVID 19 prevention and control.

In our study, 46/120 (38.33%) patients suffered from one or the other co-morbidity. 7 patients presented with two or more co-morbidities, while 13 (10.83%) patients had Diabetes Mellitus as the main co-morbidity and 11 (9.17%) were hyper-tensive. Aggarwal *et al.*[17] has also shown that 17.65% patients were having co-morbidities, most common being diabetes mellitus, followed by

hypertension. Similarly Richardson *et al*[18] had also found hypertension, obesity and diabetes as the most common co-morbidities among COVID 19 patients. Our study showed a higher percentage with co-morbidities because of the fact that we had enrolled only those patients who were hospitalized owing to COVID 19 symptoms/ test. Guan et al observed that 18.2% patients with non-severe disease and 39.4% patients with severe disease had elevated AST level, similarly, ALT levels were observed in 28.1% of patients with severe disease.[19] Our study similarly found statistically significant elevated levels of AST and ALT. NLR was seen significantly higher among patients (3.99 ± 1.87), especially those having prolonged stay and severity of disease. This could mean that NLR may also have prognostic value in determining severity of disease. Similar findings were made by other studies too.[20]

Our current understanding of the spectrum and natural history of SARS-CoV-2 infection is limited, but this study is unique in the sense that it compared hematological and biochemical parameters in a study group involving hospitalized patients of COVID 19 , and provides and better assessment of the disease course and its clinical manifestations. Our study, however, also had a few limitations due to the retrospective design. The present study remained a one-point data-based study, the dynamic data collection of all such patients was not possible or comprehensible. Therefore, we had kept the study of changes in hematological parameters over the duration of hospital stay beyond the scope of this study.

Conclusion

Hematological parameters and inflammatory biomarkers in COVID 19 patients can potentially act as independent factors and affect the disease prognosis and treatment process.

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Conflicts of Interest

There are no conflicts of interest.

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