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LEVELS OF INTERLEUKIN-6, FERRITIN, C-REACTIVE PROTEIN, LACTATE DEHYDROGENASE, D-DIMER, FIBRINOGEN AND PROCALCITONIN IN BLOOD OF COVID-19 PATIENTS: ITS CORRELATION TO THE DISEASE SEVERITY IN PATIENTS IN A TERTIARY MEDICAL COLLEGE IN EASTERN INDIA

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ABSTRACT The clinical spectrum of SARS CoV 2 infection appears to be wide, encompassing asymptomatic infection, mild upper respiratory tract illness, and severe viral pneumonia with respiratory failure and even death, with many patients being hospitalized with pneumonia This study was a hospital based, cross sectional, observational, non interventional study. This study took place in Medical College and Hospital , Kolkata , study duration was from May 2020 – July 2022 .One-hundred and three patients diagnosed with COVID-19 infection as tested by real-time quantitative PCR (RT-qPCR) test were included. Those presenting with fever and/or respiratory symptoms and chest x-ray findings suggestive of lung infection were diagnosed as having COVID-19 pneumonia (n = 69). Those identified to be positive for RT-qPCR test but did not have any symptoms were considered asymptomatic (n = 34). The results showed that the mean of the serum level of IL6 ,CRP, ferritin, LDH, and D Dimer was higher significantly ($P \leq 0.000$) in COVID19 patients compared to the healthy control group . The mean of theses parameters is significantly increased in patients with severe coronavirus infection and reached (28.63 ± 14.67 pg/ml,471.60 ± 202.92 pg/ml and 443.55 ± 99.38 IU/L) for IL 6, ferritin, and Lactate Dehydrogenase(LDH) respectively, while in patients with simple to moderate infection, the levels of IL6, ferritin, CRP, and LDH is reached (9.56 ± 0.66 pg/ml, 232.14 ± 161.29 g/ml, 25.64 ± 22.53 mg/ml, and 335.80 ± 97.63 IU/L) respectively. We also found that total lymphocyte count was decreased significantly ($P = 0.018$) in patients infected with SARS CoV2 (mean = 13.66 ± 4.29), in contrast, neutrophils count was increased significantly ($P \leq 0.000$) in patients (90.43 ± 12.40) compared with healthy subjects (51.63 ± 5.66). Though for more detailed research a study with much more larger sample size,and study design like prospective cohort should be taken for better understanding of the altered levels of those parameters over the morbidity and mortality of covid 19 positive patients.

KEYWORDS :

INTRODUCTION

Since its first emergence in Wuhan city, China, at the end of 2019, severe acute respiratory syndrome coronavirus 2 (SARSCoV2), a positive sense single stranded enveloped virus which is responsible for the pandemic COVID19 has become a significant health problem all over the world with over 2.1 million cases and 120,000 deaths so far.[1] The clinical spectrum of SARS CoV 2 infection appears to be wide, encompassing asymptomatic infection, mild upper respiratory tract illness, and severe viral pneumonia with respiratory failure and even death, with many patients being hospitalized with pneumonia.[2] Diagnosis of COVID-19 is confirmed by direct detection of SARS-CoV-2 nucleic acids in respiratory tract specimens with a polymerase chain reaction (PCR) . A rapid and accurate diagnosis has wide implications for the patient, healthcare institution, and the public health and administrative personnel. [3]

POTENTIAL ROLE OF BIOMARKERS IN COVID-19

A biomarker is defined as a "characteristic that can be objectively measured and evaluated as an indicator of normal biological and pathological processes, or pharmacological responses to a therapeutic intervention" [4] .Biomarkers in COVID 19 can be useful in the following areas:

(i) Early suspicion of disease
(ii) Confirmation and classification of disease severity
(iii) Framing hospital admission criteria
(iv) Identification of high risk cohort
(v) Framing ICU admission criteria
(vi) Rationalizing therapies
(vii) Assessing response to therapies
(viii) Predicting outcome
(ix) Framing criteria for discharge from the ICU and/or the hospital

A strong working knowledge of the pathophysiology is essential for the initial identification of candidate biomarkers, which is, an understanding of what the virus does to the body and how the body reacts to it.

PATHOGENESIS OF COVID-19

Overview

It is amply evident that COVID-19 is not a localized "respiratory infection" but a "multisystem disease" caused by a diffuse systemic process involving a complex interplay of the immunological, inflammatory and coagulative cascades. Genetic and acquired differences in the host immune system further complicate the host repertoire leading to wide heterogeneity in the clinical picture, course and outcome.

Viral Entry and Replication

Coronaviruses are spheroidal, single-stranded RNA viruses with a diameter of 80–220 nm. Transmission of SARS-CoV-2 occurs either through exposure to micro-droplets from infected individuals or by contact transmission through contaminated fomites. The virus reaches the smaller airways and alveoli, and targets the bronchial and alveolar epithelial cells.

The spike surface glycoprotein S on the virus binds to angiotensin-converting enzyme 2 (ACE-2), a membrane carboxypeptidase present in distal airways and alveoli, especially type 2 pneumocytes which have the highest expression of ACE-2, along with alveolar macrophages and dendritic cells. ACE-2 is also expressed on the vascular endothelium, nasal, oral, nasopharyngeal, and oropharyngeal epithelia, gut epithelia, cardiac pericytes, renal proximal tubular cells and in the skin, reticuloendothelial and the central nervous system [5] . ACE-2 expression depends on age, gender, genetic factors, and presence of comorbid conditions such as obesity, chronic cardiopulmonary disease, cancer, and use of immunosuppressive drugs.

Renin cleaves angiotensinogen to produce angiotensin I which is further cleaved by ACE to produce angiotensin II having a dual role. Action through AT1R (angiotensin II type 1 receptor), facilitates vasoconstriction, fibrotic remodeling, and inflammation, while that through AT2R (angiotensin II type 2 receptor) leads to vasodilation and growth inhibition. Angiotensin II is cleaved by ACE2 to Ang 1–7 which counteracts the harmful effects of the ACE/Ang II/AT1 axis.

Thus ACE2 primarily plays a key role to physiologically counterbalance ACE and regulate angiotensin II. Internalization of the ACE-2 after viral interaction leads to its downregulation, and consequent upregulation of angiotensin II. The latter acting through AT1R, activates the downstream inflammatory pathways, leading to the "cytokine storm" that adversely affects multiple organs [6] .

The alveolar epithelial cells, lymphocytes, and vascular endothelial cells are the primary targets of the virions. The virus inhibits the production of interferons which are part of cellular defense mechanisms. Viral replication releases a large number of virions

leading to infection of neighboring target cells and viremia, which then cause an exaggerated pulmonary and systemic inflammatory response respectively. This explains the clinical presentation of severe COVID-19 which is predominated by ARDS, shock, and coagulopathy.

In line with the aforementioned, this study which was undertaken in a tertiary hospital in Eastern India aimed to estimate serum levels of IL 6, D dimer, ferritin, CRP , procalcitonin, fibrinogen as well as total blood lymphocyte counts in patients with COVID19 disease, in addition, to explore the correlation between the levels of the above parameters and severity of the disease.

MATERIALS & METHODS

Study participants

This study was a hospital based, cross sectional, observational, non interventional study.This study took place in Medical College and Hospital , Kolkata , study duration was from May 2020 – July 2022 . One-hundred and three patients diagnosed with COVID-19 infection as tested by real-time quantitative PCR (RT-qPCR) test were included. Those presenting with fever and/or respiratory symptoms and chest x-ray findings suggestive of lung infection were diagnosed as having COVID-19 pneumonia (n = 69). Those identified to be positive for RT-qPCR test but did not have any symptoms were considered asymptomatic (n = 34). Patients with severe/critical illness were admitted in the intensive care units (ICUs) and those with mild–moderate including asymptomatic patients were managed in a specialized COVID-19 care. We excluded patients with any co-morbid diseases in the present study. Details on the demographic characteristics (age and gender), diagnosis, whether received tocilizumab (IL-6 receptor monoclonal antibody) and, levels of CRP, serum ferritin, D-dimer, serum fibrinogen, serum procalcitonin, serum IL-6, serum lactate dehydrogenase and creatine kinase were collected.

Estimation methods of the evaluated biomarkers -

A) CRP was done by using the automated ERBA EM 200 System from Transasia that uses the immunoturbidimetric technology with the reference range (RR): 0–6 mg/l.
B) Procalcitonin was measured in serum by ECLIA assay using COBAS 6000 with a RR of less than 0.5 pg/ml.
C) Plasma D-dimer were measured by the STAGO Hemostasis System, a fully automated coagulation system, using immunoturbidimetry assay. D-dimer RR is 0.1- 0.5 microgm/ml.
D) Plasma fibrinogen were also measured by the STAGO Hemostasis System, a fully automated coagulation system, using immunoturbidimetry assay. Reference interval
E) IL-6 was measured by CLIA and is considered positive if it is above 4.4 pg/ml. Serum ferritin samples assayed on Seimen's ADVIA Centaur fully automated system. The assay is a two-site sandwich immunoassay using direct chemiluminometric technology, which uses constant amounts of two antiferritin antibodies with RR of 16– 323 µg/l.
F) Serum lactate dehydrogenase and creatine kinase were assayed on COBAS 6000 fully automated system. The assay is RRA reaction using the IFCC standardized method with RR of LDH being 135–225 U/l.

Statistical analysis

Descriptive statistics such as median (range) and mean (standard deviation [SD]) was used for representing the demographic variables. Mann–Whitney U-test was used to assess the statistical significance of biomarker levels between asymptomatic and those who developed pneumonia. Concerning procalcitonin, only those who did not have any secondary bacterial infection (values <2 ng/ml) were compared between pneumonia and asymptomatic patients. Receiver operating characteristics curve was plotted for each of the following biomarkers: serum ferritin, D-dimer, serum fibrinogen and CRP in differentiating COVID-19 pneumonia from asymptomatic individualsand area under the curve (AUC) with 95% CI were estimated. Cut-off values for each of the above biomarkers with the maximum sensitivity and specificity was calculated. Pearson correlation coefficient values were calculated for assessing the association between IL-6 and other biomarkers. All the statistical tests were carried out using SPSS version 26 (Released 2018. IBM SPSS Statistics for Windows, Version 26.0, IBM Corp., NY, USA).

RESULTS

Demographic characteristics of the study participants

The results of the current study, which included (100) patients suffering from SARS CoV2 infection, found, as illustrated in Figure 1, that the percent of COVID19 infection was higher in men (60%) than women (40%).

Table 1: The differences in the serum levels of interleukin-6, ferritin, lactate dehydrogenase, C-reactive protein and D-Dimer in COVID-19 patients and control group

Parameters	Mean±SD		*P*
	Patients	Control	
IL-6 (pg/ml)	26.72±5.05	5.38±0.89	≤0.000
Ferritin (µg/ml)	447.65±10.62	70.71±8.32	≤0.000
CRP (mg/ml)	110.24±11.26	2.73±0.92	≤0.000
LDH (IU/L)	432.78±13.51	137.85±9.88	≤0.000
D-Dimer (µg/ml)	1.83±0.99	0.21±0.06	≤0.041

SD: Standard deviation, CRP: C-reactive protein, LDH: Lactate dehydrogenase

The results of Table 1 are showing that the mean of the serum level of IL6 was higher significantly ($P \leq 0.000$) in COVID19 patients (26.72 ± 5.05 pg/ml) compared to the control group (5.38 ± 0.89 pg/ml). Likewise, the mean of the serum levels of CRP, ferritin, LDH, and D Dimer was also elevated significantly among COVID19 patients compared to the control group.

We also found that total lymphocyte count was decreased significantly ($P = 0.018$) in patients infected with SARS CoV2 (mean = 13.66 ± 4.29), in contrast, neutrophils count was increased significantly ($P \leq 0.000$) in patients (90.43 ± 12.40) compared with healthy subjects (51.63 ± 5.66).

Table 2: The total count of lymphocytes and neutrophils in COVID-19 patients and control group

Parameters	Mean±SD		*P*
	Patients	Control	
Lymphocyte (cell/ml)	13.66×103±4.29×103	26.40×103±4.79×103	0.018
Neutrophils (cell/ml)	90.43×103±12.40×103	51.63×103±5.66×103	≤0.000

The results of the current study revealed, as shown in Table 3, that all of IL6,ferritin, LDH, and CRP, except D Dimer, are associated with severity of SARS CoV2 infection. The mean of theses parameters is significantly increased in patients with severe coronavirus infection and reached (28.63 ± 14.67 pg/ml,471.60 ± 202.92 pg/ml and 443.55 ± 99.38 IU/L) for IL 6, ferritin, and Lactate Dehydrogenase(LDH) respectively, while in patients with simple to moderate infection, the levels of IL6, ferritin, CRP, and LDH is reached (9.56 ± 0.66 pg/ml, 232.14 ± 161.29 g/ml, 25.64 ± 22.53 mg/ml, and 335.80 ± 97.63 IU/L) respectively. Furthermore, the D Dimer level was found to decreased non significantly ($P = 060$) in a patient with severe infection (1.68 ± 0.30) compared to a patient with mild to moderate symptoms [Table 3].

Table 3: Differences in the levels of interleukin-6, ferritin, lactate dehydrogenase, C-reactive protein, and D-Dimer in COVID-19 patients according to the severity of infection

Parameters	Mean±SD		*P*
	Simple to moderate	Severe	
IL-6 (pg/ml)	9.56±0.66	28.63±14.67	0.006
Ferritin (µg/mL)	232.14±161.29	471.60±202.92	0.014
CRP (mg/ml)	25.64±22.53	119.98±68.54	0.004
LDH (IU/L)	335.80±97.63	443.55±99.38	0.026
D-Dimer (µg/mL)	0.48±0.61	1.68±0.30	0.60 (NS)

Table 4: Differences in lymphocytes and neutrophils count in COVID-19 pat according to the severity of infection

Parameters	Mean±SD	
	Simple to moderate	Severe
Lymphocyte (cell/ml)	18.14×103±3.29×103	13.16×103±4.12×103
Neutrophils (cell/ml)	77.04×103±12.05×103	91.26×103±12.28×103

In the same context, we found, as shown in the Table 4, that lymphocytes are decreased significantly (P = 0.012) in patients with severe COVID 19 disease, while neutrophils are significantly increased (P = 0.013) in patients with severe symptoms of SARS CoV2 infection.

DISCUSSION

In the present study, 60% of the SARS CoV2 infected patients were women and 40% were men. In agreement with our results, Gebhard et al., found that female's percentage of infection were higher than males and reached (52%) in Switzerland and Belgium, (54%) in Portugal, (53%) in France, and (60%) in South Korea.[7]

Females and males have a variable response to viral infection just such as SARS CoV, Middle East respiratory syndrome (MERS) CoV, SARS CoV2, and other viruses. These differences are the leading of disease severity and incidence between the two genders. Multiple factors contribute to the disparity in sex specific disease outcomes following virus infections. Sex specific steroids and the activity of X linked genes, both of which modulate the innate and adaptive immune response to virus infection, influence the immune response. Furthermore, the differences in the expression of angiotensin converting enzyme (ACE) 2 receptor and the cellular serine protease TMPRSS2, which are necessary for the binding and priming of SARS CoV2, may have an important role.[7,8]

There is a significant increase in the serum levels of IL6, ferritin, CRP, LDH, and D Dimer in COVID 19 patients [Table 1]. In addition, the levels of theses parameters are effectively associated with the diseases severity in the patients as shown in [Table 3].

Cytokine release syndrome (CRS) is an over-exaggerated immune response involving an overwhelming release of pro-inflammatory mediators. This mechanism underlies several pathological processes including acute respiratory distress syndrome (ARDS) [9]. Studies investigating the role of cytokines in SARS and MERS have had also found a link between CRS and disease severity [10]. Understanding their role in COVID-19 disease may help facilitate the design of novel immunotherapies. Studies have revealed that levels of IL-6, the most common type of cytokine released by activated macrophages, rise sharply in severe manifestations of COVID-19 [11]. However, since most studies to date have been observational, it is difficult to extrapolate if the rise is significant enough to cause the manifestations seen in severe forms.

Zhu et al., 2020[12] reported that IL 6 is elevated in COVID 19 patients and reached to (24.11 pg/ml) and its level was significantly correlated with the severity of the symptoms in COVID 19 patients. Similarly, Huang et al., in 2020[13] found that IL 6 is increased in patients with SARS CoV2 infection and its high level was closely associated with the level of virus RNA in the blood and disease progression. It is stated that during viral infection, IL 6 together with transforming growth factor beta induces the differentiation of naïve CD4 into Th17 cells, which are important for the defense against viruses and other pathogens at mucosal sites. In addition, there is synergic interaction between IL 6 and IL 7 and IL 15 to induce the differentiation and catalytic ability of CD8 T cells which is important in the response against viral infections.[14]

Serum ferritin is a spherical protein structure, made-up of 24 Hand L-subunits that is expressed in several tissues and cell types and is also present in body fluids like blood plasma and serum [15]. Iron status can change with inflammation while ferritin levels are increased and can act as a marker [16]. During this pandemic time, studies have found that elevation of serum ferritin levels were associated withCOVID-19 infection and mortality[17].

The ferritin level in COVID19 patients, as shown in Table 1, was significantly increased and reached to (447.65 ± 210.62 µg/mL). Likewise, the serum level of CRP was also elevated significantly in patients when compared with the healthy group. The elevation of ferritin and CRP was correlated with the disease progression [Table 3].Several publications have shown that elevated ferritin levels have been associated with worse outcomes, along with several other pro inflammatory markers, involving CRP and IL6, and may even help predict these outcomes.[18-20] Elevated ferritin levels due to secondary hemophagocytic lymphohistiocytosis and cytokine storm syndrome have been reported in severe COVID19 patients. It has been proposed that COVID19 could be part of the broader spectrum of hyperinflammatory syndromes such as the secondary hemophagocytic lymphohistiocytosis.[21] Hyperferritinemia is a cardinal characteristic of these syndromes. COVID 19 severity and worse prognosis mean that mortality could be due to virally induced hyper inflammation which is substantially associated with high ferritin level. However, the circulating levels of ferritin can not only represent a strong phase response but play an important role in inflammation.[22]
CRP is a plasma protein produced by the liver and induced by various inflammatory mediators such as IL-6. Despite being non-specific, this acute phase reactant is used clinically as a biomarker for various inflammatory conditions; a rise in CRP levels are associated with an increase in disease severity [23]. The application of CRP in COVID-19 has been highlighted by a retrospective single-centre study in Wuhan, China, where the majority of patients in the severe cohort showed significantly higher levels compared to the non-severe cohort (57.9 mg/L vs 33.2 mg/L, P<0.001) [24]. A second retrospective cohort study found the likelihood of progressing to severe COVID-19 disease increased in patients with CRP levels>41.8 mg/L [25]. Both studies suggest CRP levels are a strong indicator to reflect the presence and severity of COVID-19 infection.

In COVID19 patients, CRP levels were increased and it was shown that survivors had a mean CRP of approximately 25 mg/L, while nonsurvivors had a mean CRP of (120 mg/L), suggesting a good association with the severity and prognosis of the disease .[5]

In addition to IL 6, ferritin, and CRP, our results also found a significant elevation in the level of LDH as well as D Dimer in COVID 19 patients. However, the increases in both D Dimer and LDH were effectively correlated with disease severity as shown in Table 3.

D-dimer originate from the lysis of cross-linked fibrin with rising levels indicating the activation of coagulation and fibrinolysis [26]. Early studies have associated COVID-19 with haemostatic abnormalities with one study observing elevated levels of D-dimer, the measure of coagulation, in non-survivors compared to survivors [27]. A retrospective cohort study composed of 191 patients found that Ddimer levels>1.0 µg/mL(p=0.0033) were associated with increased mortality among COVID-19 patients. Furthermore, they found that levels of 2.0 µg/mL or more on admission was the optimum cut-off to predict in-hospital mortality for COVID-19 [28]. Studies have reported that nearly 90% of inpatients with pneumonia had increased coagulation activity marked rising D-dimer levels [29]. Furthermore, Huang et al. found that levels of D-dimer on admission could be used to triage patients into critical care [30]. The researchers found that median D-dimer levels were higher in ICU patients compared to non-ICU patients (2.4 mg/L vs. 0.5 mg/L; p=0.0042). This, along with the previous study, suggests that D-dimer levels can be used as a prognostic marker and help clinicians monitor those who are likely to deteriorate earlier.

D Dimer is a commonly used fibrin degradation test used to diagnose thrombotic diseases at an early level. [31] Prior studies have shown that D Dimer level is higher in extreme cases of community acquired pneumonia and chronic obstructive pulmonary disease and can be used as a significant biomarker and that D Dimer >1 µg/mL is one of the mortality risks factors in adults with COVID 19 who receive the medication for their pneumonia in a group acquired environment.[32,33] It was also stated that D Dimer at admission more than 2.0 µg/mL (fourfold increase) could effectively be correlated with disease severity and mortality in COVID 19 patients, as shown in Table 3 in this review. These results indicated that D Dimer could be an early and helpful marker to improve the management of COVID 19 patients.[31,34,35]

In glucose metabolism, the enzyme LDH converts pyruvate to lactate. LDH secretion is triggered by necrosis of the cell membrane, hinting to viral infection or lung damage, such as the pneumonia induced by SARS-CoV-2 [36]. There is convincing evidence linking LDH levels to the development of COVID-19 disease [37]. A study found significantly higher levels of LDH in ICU patients than non-ICU patients (248 U/L vs 151 U/L, p=0.002). Since high levels of LDH continued in the ICU patients number of days post-admission (160 U/L vs 218 U/L, p=0.002), LDH may be a predictive biomarker of severe disease. However, the one centre study may be prone to selection bias which could potentially reduce its validity [38]. A multi-centre study involving 1099 patients reported supporting evidence correlating extent of tissue damage and inflammation with increasing levels of LDH [39]. Furthermore, when LDH levels were correlated with CT

scans, significantly higher levels reflected the severity of pneumonia [40].

LDH is a glycolytic cytoplasmic enzyme present in virtually every tissue. In general, its elevation suggests tissue injury. In patients infected with MERS CoV, increased LDH was a typical finding in.[41,42] Independent mortality factors have been identified for patients with the extreme acute respiratory syndrome[43] and H1N1 infection.[44] Possible subclinical tissue damage was indicated by our observation of increased LDH in the early stage of extreme COVID 19 cases. Although the virus binds to the human ACE2 receptor in the lungs,[45,46] which explains why the lungs are the first affected organs, different cytokine abnormalities and multiple organ dysfunction can be observed in serious patients as the disease progresses, suggesting systemic organ damage caused by excessive immune system activation.[47,48]

Results of Table 2 showed that COVID 19 patients have significantly decreased lymphocyte count (P = 0.018) and significantly increased neutrophils count (P ≤ 0.000). The decreased and elevated lymphocyte and neutrophils count was significantly correlated to the disease severity as shown in the Table 4.

Hematologic variations were established as supporting evidence of infection with COVID 19 and as potential signs of serious illness. Numerous clinical guidelines define that potential SARS CoV2 infection, especially in severe cases, exhibits irregularities in hemocytometry. The U. S. Centers for Disease Control and Prevention have issued guidelines emphasizing that the most common laboratory abnormalities recorded in hospitalized COVID 19 patients with pneumonia were leukopenia (92%–5%), leukocytosis (24%–30%), and lymphopenia (63%).[49] Lymphopenia was also a clear finding and experiments using flow cytometry showed that these improvements were correlated with lower counts of CD4+ and CD8+ T lymphocytes[50,51] In the same context, Song et al. 2020[52] have revealed that the most consistent abnormal hemocytometric findings in COVID 19 patients are lymphopenia and increased neutrophils, and these changes can also increase throughout the disease, especially in those with serious illness. In pregnant women with COVID 19, lymphopenia was also reported; however, this finding is even less significant in infected children.[53]

Procalcitonin is a 116 amino acid peptide that has an approximate MW of 14.5 kDa and belongs to the Calcitonin (CT) super family of peptides. Calcitonin is a hormone released from C-cells of the thyroid gland with the function of regulating the body's calcium metabolism and during infection, procalcitonin levels are elevated [54]. Our data shows a significantly higher procalcitonin levels in elder patients when compared to young and middle-aged patients (p<0.0001), similar findings were noted by Guo et al. [55], Kim et al. [54]. However few studies were noted no significant age-related association of procalcitonin [56]. The levels may be secondary to more severe disease with longer ICU stay and thereby increased risk of secondary infections.

CONCLUSION

In this observational, hospital based, cross sectional and non interventional study undertaken in a tertiary care hospital over two year and three months (May 2020 – July 2022)., One-hundred and three (RT-qPCR) positive COVID-19 were included. Severely affected COVID 19 patients meant those presenting with fever and/or respiratory symptoms and chest x-ray findings suggestive of lung infection (n = 69). And Those positive for RT-qPCR test but asymptomatic or with mild symptoms considered mild / moderate affected(n = 34). The results showed that the mean of the serum level of IL6 ,CRP, ferritin, LDH, and D Dimer was higher significantly (P ≤ 0.000) in COVID19 patients compared to the healthy control group . The mean of theses parameters is significantly increased in patients with severe coronavirus infection and reached (28.63 ± 14.67 pg/ml,471.60 ± 202.92 pg/ml and 443.55 ± 99.38 IU/L) for IL 6, ferritin, and Lactate Dehydrogenase(LDH) respectively, while in patients with simple to moderate infection, the levels of IL6, ferritin, CRP, and LDH is reached (9.56 ± 0.66 pg/ml, 232.14 ± 161.29 g/ml, 25.64 ± 22.53 mg/ml, and 335.80 ± 97.63 IU/L) respectively. We also found that total lymphocyte count was decreased significantly (P = 0.018) in patients infected with SARS CoV2 (mean = 13.66 ± 4.29), in contrast, neutrophils count was increased significantly (P ≤ 0.000) in patients (90.43 ± 12.40) compared with healthy subjects (51.63 ± 5.66). This result is in harmony with findings of F. Liu et al, L. Zhang et al and N. Tang et al [25], [26], [27].

Though for more detailed research a study with much more larger sample size,and study design like prospective cohort should be taken for better understanding of the altered levels of those parameters over the morbidity and mortality of covid 19 positive patients.

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