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ORIGINAL ARTICLE

# Evaluation of clinical laboratory parameters in COVID-19 positive cases admitted in Islamabad.

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**ABSTRACT… Objective:** To assess the variation of laboratory parameters in COVID-19 positive patients with different genders and age groups and to clarify the consequences of COVID-19 infection on different patients. **Study Design:** Prospective study. **Setting:** IHITC (Isolation Hospital & Infectious Treatment Center), Islamabad. **Period:** 20th May, 2021 to 25th July, 2021. **Material & Methods:** Study was conducted With 222 participants among them 119 were COVID positive serve as Case and 103 were COVID negative considered as control. Blood samples were drawn from all participants of study to measure biochemical and hematological laboratory parameters with demographic characteristics. Mean ± standard deviation (SD) of different lab parameters analyzed by using IBM SPSS Statistics 20. **Results:** Total 222 participants were analyzed having 115 (50.7%) male and 107 (49.3%) female having mean age 60±13.8. No significant variation has been seen in ALP, total bilirubin, creatinine and uric acid having mean values with in normal range. In 119 positive patients, ALT (p=0.001) (t=2.031), urea (p=0.001) (t=7.590), Ferritin (p=0.001) (t=7.13), CRP (p=0.001) (t=9.90) and D-dimer (p=0.001) (t=5.962) were elevated and good predictor of poor prognosis of disease. Pathological impacts of COVID-19 were also represented by hematological parameters including WBC count (p=0.001) (t=7.126), Neutrophil to Lymphocyte Ratio (p=0.001) (t=9.042) and Lymphocyte count (p=0.001) (t=-12.707). **Conclusion:** According to this research, males and old age population is more susceptible to SARS-2. Our study suggests that laboratory biomarkers including ALT, Urea, Ferritin, CRP, D-dimer and WBC count are significantly associated with poor prognosis in Covid-19 patients.

**Key words:** Biochemical and Hematological Parameters, COVID-19, Disease Severity, Laboratory Tests.

## INTRODUCTION

A novel coronavirus (COVID-19) is in charge of the outbreak of lungs infection like pneumonia. Which was originated in Wuhan city, Hubei a province in China in December 2019.[1] SARS-CoV-2 evolved directly or indirectly from the sarbecovirus (SARS-like virus) group that commonly infect bats.[2] COVID-19 SARS-CoV-2 was named due to the genetically related SARS-CoV which caused a deadly pandemic in 2002–2003.[3] It is mainly associated with gastrointestinal and respiratory tract infections.[4] Six types of Corona virus have been identified. HCoVHKU1, HCoV-OC43, Middle East Respiratory Syndrome coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) are beta coronavirus and HCoV229E and HCoV-NL63 are the members of alpha coronavirus.[5] In 2003 and 2012, the SARS and MERS pandemics gained global attention and are now recently by COVID-19 outbreaks. SARS- CoV and MERS-CoV spread from bats to palm civets or dromedary camels and eventually to humans.[6] After mutation in spike proteins, COVID-19 spread to 220 countries. According to WHO data, COVID-19 spread worldwide with 424,822,073 cases and 5,890,312 confirmed deaths as of February 20, 2022. In Pakistan, 1,501,680 cases and 30,040 deaths are confirmed till February 20, 2022.[7]

SARS CoV-2 is a 120 nm sized spherical virus that has a special glycoprotein (spike protein) on its surface that is responsible for the recognition and binding to target cells. The glycoprotein helps the

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virus entrance into the host cell by attachment of viral hemagglutinin with cell receptors.-10 Droplets produced by coughing, sneezing, or talking of infected people are the main cause of transmission of COVID-19.[11] Contact of hands with contaminated surfaces or objects and touching of these hands with the month and eyes can also cause infection.[11] Binding of spike proteins and ACE receptors on lungs and other tissue allow the fusion of the virus and cell membrane that help the entry of virus into the cell. The virus can cause injury and damage to host cell by two methods. First way of damage is "Cytokines Storm" that is an excessive immune reaction in the host that is caused by inflammatory response and second method is "MicroCLOTS" (microvascular COVID-19 lung vessels obstructive thromboinflammatory syndrome) that cause lungs injury by inflammatory response and by microvascular pulmonary thrombosis.[12] COVID-19 causes cough, loss of appetite, fatigue, shortness of breath, sputum production and lead to pneumonia, multi-organ failure and death. COVID-19 can cause damage to the gastrointestinal tract, liver, and nervous system.[13] After confirmation of infection by RT-PCR, different laboratory parameters are useful biomarkers for disease management as in Figure-1.

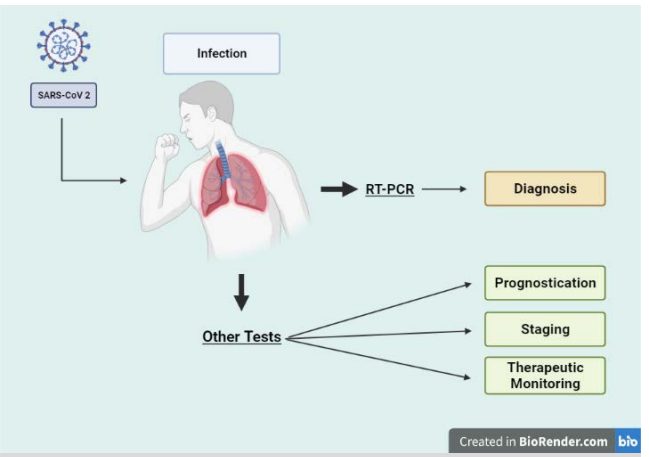


**Figure-1. Significance of laboratory tests in Covid-19 infection.**

Many patients have been observed with a higher level of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and lactate dehydrogenase (LDH), in the MERS outbreak of 2012.[14] Laboratory data identified that patients infected with SARS-1 had elevated level of C-reactive protein (CRP), aminotransferase, LDH and creatine kinase, lymphopenia and leukopenia.[15] Few studies have reported the change in different diagnostic parameters in COVID-19 patients. These changes are due to the damage of different tissues like Lungs, Heart or Kidney by COVID-19.[16,18] This study is aimed to analyze and correlate different laboratory parameters of COVID-19 positive patients isolated in tertiary care hospital Islamabad. We also aimed to assess the impact of Covid-19 infection on different laboratory parameters and to determine the significance of abnormal laboratory findings in the diagnosis and prognosis of COVID-19.

This prospective cross-sectional study was conducted in IHITC (Isolation Hospital & Infectious Treatment Center) in Islamabad. A total of 222 people were screened for COVID-19, of which 119 were positive and 103 were negative. Positive patients were considered as case, while negative patients were served as control. From May 20, 2021 to July 25, 2021, blood samples were drawn from all participants and their biochemical and hematology laboratory parameters were analyzed. The study protocol was approved by the Institutional Review Board, National Institute of Health, Islamabad (FI-5/RAPID/2018-19).

The demographic characteristics of all the studied participants were analyzed. Laboratory parameters including alanine transaminase (ALT), alkaline Phosphatase (ALP), total bilirubin (TBIL), creatinine (Cr), uric acid (UA), urea, ferritin, C-reactive protein (CRP), D-Dimer and complete blood count (CBC) were measured. Data for ALT, Urea, Ferritin, CRP, D-dimer, WBC and NLR levels were presented as mean and (±) standard deviation (SD). Differences in the levels of ALT, Urea, Ferritin, CRP, D-dimer, WBC and NLR between the COVID-19 positive and negative patients were assessed using t-test analysis.

## MATERIAL & METHODS

Two hundred and twenty-two study participants were analyzed with mean age of 60.06±13.8 (range 17-100) with 50.7% males while rest of the 49.3% were females. 119 (52.4%) were COVID-19

positive and 103 (48.6%) were tested negative shown in Table-I & II.

| Variable | Categories | Frequency (%) |
|---|---|---|
| Gender | Male | 115 (50.7%) |
| | Female | 107 (49.3%) |
| COVID Results | Positive | 119 (52.4%) |
| | Not-Detected | 103 (48.6%) |

**Table-I. Demographic analysis of study participants (%) (n=222).**

| | N | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|---|
| Age of Covid-19 Patients | 222 | 17.00 | 100.00 | 60.06 | 13.81 |

**Table-II. Age analysis of participants.**

## Descriptive Analysis

The descriptive analysis of various parameters in Table-III showed that ALP, Total Bilirubin, Creatinine and Uric Acid were recorded above normal in some of COVID-19 positive individuals but remained between normal range in most of the cases. The Remaining analyzed parameters had significant abnormality in most of the cases. Therefore, they are subjected to the independent t-test.

## RESULTS

T and P values of biochemical parameters of cases and controls represented in Table-IV. It was found that the ALT value of Covid-19 positive cases were slightly increased with M=52.90, S.D= 76.7, while for COVID negative patients, M=37.5, S.D 11.0, with $t(220)=2.031$, $p<0.005$. A significant increase in Urea (M=55.04, S.D±35.06) and for COVID negative patients M=27.7, S.D 10.6, with $t(220)=7.59$, $p<0.005$. Ferritin in COVID positive patients was (M=703.8041, S.D =625.82) and in Control participants M=244.2, S.D=23.3 with $t(220)=7.13$, $p<0.005$. CRP in COVID positive patients was (M = 46.0621, S.D =33.25693) and in control participants was M= 11.7, S.D=12.2 with $t(220)=9.90$, $p<0.005$. D-dimer in COVID positive cases was (M = 1210, S.D 1646.32) and in control participant M=230, S.D 112.2 with $t(220)=5.962$, $p<0.005$.

Particulars of Hematological parameters are enlisted in Table-V. The results of the current study also presented a remarkable increase in WBC count (M=13.6840, S.D=5.83243) and in control cases, M=6.78, S.D=2.31 with $t(89)=7.126$, $p<0.005$. Neutrophil to Lymphocyte Ratio in covid positive patients was (M=13.9196, S.D=8.30984) and in control participant M=2.7, S.D 1.59, $t(95)= 9.042$, $p<0.005$. The Differential Leukocyte Count showed a relative decrease in the Lymphocyte count (M = 8.5800 S. D=5.70) and control participants M=28.5,S.D=9.37, with $t(95)=-12.70$, $p<0.005$. The negative sign shows negative hypothesis between lymphocytes and COVID PCR. As we have significant p value thus we reject null hypothesis.

Gender base variation in mean values of ALT, Urea, Ferritin, CRP, D-dimer, Lymphocytes and Neutrophils represented in Figure-2. Ferritin, D-dimer and neutrophil mean values were significantly differing among males and females.

| Descriptive | N | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|---|
| ALT | 222 | 10 | 800 | 45.71 | 57.07 |
| ALP | 222 | 17.00 | 338.00 | 87.03 | 42.25 |
| Total Bilirubin | 222 | .06 | 4.50 | .81 | .68 |
| Creatinine | 222 | .06 | 9.90 | 1.01 | 1.02 |
| Uric Acid | 222 | 1.50 | 32.00 | 4.12 | 2.73 |
| Urea | 222 | 3.21 | 207.00 | 42.40 | 29.91 |
| Ferritin | 221 | 17.00 | 4221.00 | 489.60 | 528.87 |
| CRP | 220 | 0.00 | 164.00 | 29.98 | 30.83 |
| D-Dimer | 222 | 0.00 | 8167.00 | 755.40 | 1313.27 |
| White Blood Count | 91 | 1.80 | 30.90 | 10.57 | 5.73 |
| Neutrophils | 97 | 49.00 | 96.00 | 76.16 | 12.18 |
| Lymphocyte | 97 | 2.00 | 46.00 | 18.22 | 12.59 |
| White Blood Count | 91 | 1.80 | 30.90 | 10.57 | 5.73 |

**Table-III. Descriptive analysis of scales parameters with mean values, maximum and minimum limits among study participants.**

ALT: alanine transaminase, ALP: alkaline phosphatase, CRP: C-reactive protein, N: number of patients.

| Variables | COV Positive n=119 | | COV Not Detected n=103 | | t | p |
|---|---|---|---|---|---|---|
| | M | S.D | M | S.D | | |
| ALT | 52.91 | 76.69 | 37.42 | 11.06 | 2.031 | 0.001 |
| Urea | 55.04 | 35.08 | 27.79 | 10.63 | 7.590 | 0.001 |
| Ferritin | 703.80 | 652.82 | 244.19 | 23.39 | 7.13 | 0.001 |
| CRP | 46.06 | 33.26 | 11.72 | 12.23 | 9.90 | 0.001 |
| D-dimer | 1210.03 | 1664.33 | 230.15 | 112.17 | 5.962 | 0.001 |

**Table-IV. Comparison of lab parameters between Covid-19 positive and negative participants. COV: Covid-19, ALT: alanine transaminase, ALP: alkaline phosphatase, CRP: C-reactive protein, n: number of patients, M=Mean, S.D=standard deviation.**

| Variables | COV Positive n=50 | | COV Not Detected n=41 | | | |
|---|---|---|---|---|---|---|
| | M | S.D | M | S.D | t | p |
| White Blood Count | 13.68 | 5.83 | 6.78 | 2.32 | 7.126 | 0.001 |
| Lymphocyte | 8.58 | 5.70 | 28.47 | 9.38 | -12.707 | 0.001 |
| Neutrophil to Lymphocyte Ratio (NLR) | 13.92 | 8.31 | 2.77 | 1.60 | 9.042 | 0.001 |

**Table-V. T test analysis of hematological parameters between case and control groups.**

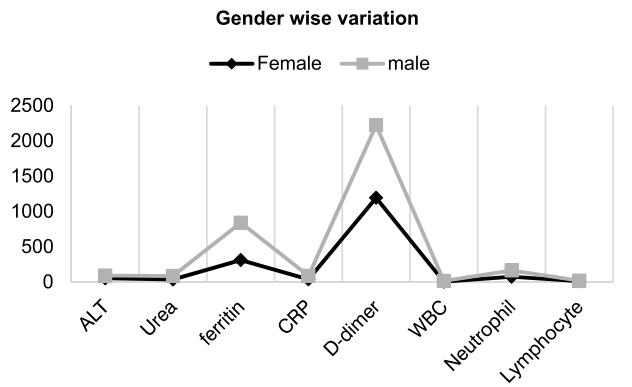


**Figure-2. Mean values variation among male and female participants.**

## DISCUSSION

According to this study, males were found more susceptible (50.7%) to COVID-19 infection than females (49.3%). Another study reported similar findings that men were more susceptible to COVID-19 infection.[19] A research report supported these findings by highlighting lower participation of women in workforce in Pakistan due to cultural, social and religious barriers, which indirectly restrict the females going to populated areas.[20] This factor may reduce the chances of female exposure to COVID-19. The other factor that influence the low susceptibility of females to viral infection is the sex hormones (estrogen) related immune response. High estrogen level in females can be helpful in the clearance of viruses from the body.[21] The average age of total participants showed a striking fact that most of reported case of COVID-19 were above 60 years. An international study compares the age distribution of cases in China and South Korea with similar findings.[22] Another study also indicate that most affected population was from old age.[23] Mostly old age persons i.e. more than 50 years, suffer from other comorbidities increasing the severity of COVID-19 disease.[24] Adults over 65 years of age represent 80% of hospitalizations and have a 23 times more mortality rate than those under 65.[25] Gradual decrease in immune functions with age is major cause of disease severity among elderly people. Moreover, individuals with comorbidities such as cardiovascular disease, diabetes, obesity and COPD, are at greater risk for COVID-19 fatality.[26]

This study showed no significant changes in parameters such as bilirubin, ALP, creatinine and uric acid. Significant elevation in the levels of serum ALT, Urea, Ferritin, CRP and D-dimer in correlation with positive RT-PCR confirm the active disease. T-tests analysis of these parameters represents the variation among positive and negative participant's groups. Serum ALT and Urea levels are important parameters to diagnose and evaluate the liver and kidney damage due to any infection and disease like COVID-19 infection.

In our study, mean values of ALT and Urea among positive case group is higher than mean value in negative control group with significant p=0.001, which means that positive patients were more likely to suffer from liver and kidney impairment due to COVID-19. International studies have shown and supported our results that the liver and kidney dysfunction is most likely a secondary damage[27,28] caused by several factors, importantly the systemic inflammatory response observed in this COVID-19 and toxicity of drug used. There is no evidence of direct action of corona virus on liver and kidney.

COVID-19 is an inflammatory disease that has a potential to damage human organs by cytokines storm and by micro-CLOTS.[12] Ferritin is an important parameter for identifying and diagnosing the inflammatory response to COVID-19.[29] According to our study, the case group had significantly higher ferritin levels with a mean of 703.8±653.8. These results show the severity of inflammatory response among COVID-19 positive patients. Another international study showed a direct correlation between ferritin levels and disease severity. The ferritin level was significantly increased in severe patients compared with non-severe patients.[30] The elevation of ferritin level indicates the inflammatory response produce by corona virus that is main cause of lung injury. Ferritin is associated with poor prognosis and can predict exacerbation in COVID-19 patients. CRP is an acute plasma protein that is elevated in any inflammatory response and is a good predictor of infection and inflammatory disease.

In our results, CRP has significant variation among COVID-19 positive group with t=9.90 and p=0.001, which strongly prove the hypothesis of severe inflammation in COVID-19. This inflammatory response may be due to cytokine release syndrome, the main pathological mechanism of COVID-19 (12). Higher CRP is associated with a higher inflammatory response and can contribute to disease severity, an abnormality that helps to assess COVID-19 prognosis.[31] D-dimer is an important coagulatory parameter, that predict the formation of thrombus/clots in body.[32] Corona virus can cause coagulopathy by producing lung vessels obstructive thrombo-inflammatory syndrome, results in micro-clots formation in lungs.[33] D-dimer is a risk factor for death in hospitalized adults with COVID-19.[34] In our study, D-dimer present significantly higher values among positive case group with mean value of 1210.03±1664.32 {(t=5.962) (p=0.001)}. Its level correlates with disease severity and is a reliable prognostic indicator of mortality in patients admitted in hospital with active COVID-19 infection.[35]

This study also summarized the variation in hematological parameters during active COVID-19 infection. Abnormalities in hematologic parameters due to COVID-19 infection are associated with disease progression, severity, and mortality. Leukocytosis was found in study population who were tested positive for COVID-19 by RT-PCR with mean value of 13.68±5.83 (t=7.126), which indicate bacterial infection or superinfection, either neutrophilia, lymphocytosis, or a combination of the two (36). Available data suggest that neutrophilia, a manifestation of cytokine storm and a hyperinflammatory state, has an important pathogenic role in COVID-19 and related infections such as SARS-I.[37] Lymphopenia is a common manifestation in patients infected with COVID-19 and is thought to represent a defective immune response against virus.[36]

A recent meta-analysis stated that 35%-75% of patients have lymphopenia, which is a more common feature of patients who died of the disease.[38] ACE receptor is expressed in two types of circulating mononuclear cells, monocytes and T lymphocytes, but at different levels. T lymphocytes contain the highest number of ACE receptors, about 28 times more than monocytes which can increase viral attachment to the cell and subsequent lysis.[39] Neutrophil to lymphocyte ratio (NLR) has been identified as an independent risk factor for critical illness in patients with COVID-19 infection. It is found that NLR is an early predictor of the possible development of critical illness in COVID-19 infected persons. Old aged patients showing greater NLR ratio had poor prognosis of disease as reported in an international study.[40]

## CONCLUSION

According to this study, males (old age) were found more frequently infected. It also concludes that the abnormal levels of laboratory parameters like, ALT, Urea, Ferritin, CRP, D-dimer and differential leukocyte count (DLC) are significantly associated with poor prognosis, disease staging and therapeutic monitoring in COVID-19 patients. These biomarkers can be helpful in formulating prevention policies and in responding to significant disease development.



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| 2 | Muhammad Usman | Supervision, study designing, facilitation in lab, review and final approval of mansucript. |  |
| 3 | Sheikh Ishaque Aamir | Data and sample collection and questionnaire design. |  |
| 4 | Hamza Irshad | Statistical analysis and data compiling. |  |
| 5 | Muhammad Akram | Data and sample collection and transport. |  |