DOI: https://doi.org/10.54393/pbmj.v5i1.321

PAKISTAN BIOMEDICAL JOURNAL

https://www.pakistanbmj.com/journal/index.php/pbmj/index

Volume 5, Issue 1 (January 2022)

Original Article

An Assessment of Biochemical Biomarkers Alterations in COVID-19 Patients

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ARTICLE INFO

Key Words:

COVID-19, Biochemical Markers, Parameters, C Reactive Protein, Ferritin, Metabolic Alteration

How to Cite:

Javaid, S. ., ., M., Abbas, K. ., Rehman, H. M., Kousar, S. ., Bashir, F. ., Gul, S. ., & jamil, R. (2022). An Assessment of Biochemical biomarkers alterations in COVID-19 patients: Biochemical Biomarkers Alterations in COVID-19 Patients. Pakistan BioMedical Journal, 5(1), 327-331. https://doi.org/10.54393/pbmj.v5i1.321

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ABSTRACT

Coronavirus disease 2019 (COVID-19) is a sickness as a result of a virulent virus named SARS-CoV-2 and turned into discovered in December 2019 in Wuhan, China. **Objectives:** To evaluate the most common biochemical parameters that are increased in COVID-19 positive patients and ultimately can be used as a diagnostic marker for the evaluation and staging of disease. **Methods:** This study included 200 COVID-positive patients confirmed with PCR. The clinical profile was recorded from various conventional laboratories. Data was analyzed statistically by applying a sample t-test to the data. **Results:** Total 200 patients were included in the study. Increased levels of various biochemical parameters have been found including ferritin, CRP, and d- dimmer. D-Dimer was elevated in 99.5 percent (n = 199) whereas 0.5 percent (n = 1) were normal and ferritin was elevated in 65.5 percent (n = 131) and was normal in 32.5 percent (n = 65). CRP was elevated in 81.5% (n=163) patients. Variations was also seen in Electrolytes like potassium was elevated in 53 % (n=106) and was low value in 8% (n= 16) while it remained normal in normal in 39% (n= 78). Sodium ions were high in 25.5% (n=51), reduced in 37.5% (n = 75) while 375 (n=74) were normal. Chloride was elevated in 32.5% reduced in 26% while it was normal in 41.5%. The metrics that remained normal were: urea (96.5%), creatinine (66.5%), total bilirubin (84%), platelets (86.5%), and TLC (73%). Ferritin, CRP and d-dimmer had a p-value lower than 0.05 showing significant results. **Conclusions**: This study concluded that some parameters particularly D-Dimer, ferritin, and C-reactive protein were considered to be predictive markers for the initial diagnosis of COVID-19.

INTRODUCTION

Coronaviruses are ribonucleic acid (+RNA) viruses of the Coronaviridae family and Nidovirales order. SARS-CoV (Severe acute respiratory syndrome) and MERS-CoV (Middle East Respiratory Syndrome) are the two zoonotic coronaviruses [1]. The SARS-CoV initially surfaced in China in November 2002, causing widespread worry as the epidemic expanded swiftly, with over 8000 cases reported in 26 countries by July 2003. In December of this year, a new coronavirus, SARS-CoV-2, was found [2]. The International Committee on Virus Taxonomy (ICTV) recently categorized 28 distinct virus classes into four genera: alpha, beta, gamma, and delta-CoVs. Gamma and delta CoVs cannot infect mammals, but alpha and beta CoVs may. Coronaviruses are enveloped pleomorphic viruses with crown-shaped peplomers ranging in size from 80 to 160 nM and positive polarity of 27 to 32 kb. Numerous investigations have been conducted to establish the structure of the coronavirus genome. The four fundamental proteins include spike (S), membrane (M), envelope (E), and nucleocapsid (N) [3]. SARS-CoV-2 has spread to 216 nations and territories as of June 12, 2020, with 7.7 million definite cases and over 425,000 fatalities worldwide [4]. The spike (S) glycoprotein on the envelope of these coronaviruses assists in their attachment to the host cell. The S1 subunit of the Coronavirus S glycoprotein is in control of the virus-host cell receptor, whereas the S2 subunit is required for virus-host cell membrane fusion. The receptor-binding domain (RBD) of these viruses' S1 subunit interacts with the claw-like structure of ACE2 [5,6]. Several studies relating diseased and healthy,

DOI: https://doi.org/10.54393/pbmj.v5i1.321

symptomatic and asymptomatic patients during the COVID-19 infection found varied changes in chosen immunological laboratory measurements [7]. WBC count, neutrophil total, lymphocyte count, D-dimer, albumin, and pro-calcitonin were revealed to be risk features for ICU treatment in COVID-19 patients in previous research [8]. COVID-19 may induce pneumonia and metabolic problems, which can progress to ARDS, MODS, and potentially septic shock and death [9,10]. The purpose of these sorts of research investigations was to contrast or distinguish the findings by using unrelated characteristics, age grouping, and a total average of the percentages that were completed in the study to estimate the virulence of illness in a specific population.

METHODS

This research study was carried out at the University Institute of Medical Laboratory Technology, The University of Lahore, Pakistan. The study encompasses 200 COVID-19 positive patients and alterations in the metabolic markers were noticed. The data for the whole study was collected from various institutes and conventional laboratories. In this quantitative study, 122 males and 78 females which were aged between17 to 56 were selected for the study. 19 parameters were shortlisted for the current study which are mentioned as hemoglobin, mean cell volume, total leukocyte count, platelets, urea, sodium ions, calcium, Bilirubin, ALT, AST, ALP, total protein, C-reactive protein, D-Dimmer, LDH, and Ferritin. These were considered for the purpose of diagnosing COVID-19 infection earlier. A COVID-19 patient's sample was collected via oropharyngeal swab, nasopharyngeal swab, and bronchoalveolar lavage by various protocols. Molecular testing (PCR) were performed for the confirmation of COVID-19 and biochemical parameters were tested. In the statistical analysis, a single-sample t-test was performed. The data mean, standard deviation, p-value, high, low, and normal percentages were computed to provide the findings.

RESULTS

Overall 200 subjects were comprised in the study including 122 (61%) Males and 78 (39%) Females. The mean ± SD of age was 31.6± 9.8. The patients were categorized into three age sets. Group 1: 17-30 years old, group 2: 31-43 years old, and group 3: 44-56years old. The mean ± SD of group 1, group 2, and group 3 was 23.7 ± 3.0, 36.3± 3.9, and 49.5±3.6 respectively as shown in (Table 1).

Groups	Age groups	Mean ± SD
Group 1	17-30 years	23.7 ± 3.0
Group 2	31-43 years	36.3± 3.9
Group 3	44-56 years	49.5±3.6

Table 1: Distribution of age groups

The parameters like Hb, MCV, TLC, Platelets were studied. The mean ±SD of Hb was 13.0 ± 2.0 and it was high in 2 % (n=4), low in 14.5% (n=29) and normal in 83.5% (n=167) individuals. The mean± SD of MCV was 83.2 ± 10.0 and it was high in 22% (n=44), low in 28.5% (n=57) and normal in 49.5% (n=99) individuals. Similarly the mean ±SD was TLC was 8.7 ± 4.0 and it was high in 21% (n=42), low in 6% (n=12) and normal in 73% (n=146) subjects. Likewise the mean ±SD of platelets was 247.5 ± 90.1 and it was high in 2% (n=4), low in 11.5% (n=23) and normal in 86.5% (n=173) studied subjects. All of these parameters were statistically non-significant (Table 2).

Parameters	High % (n=)	Low % (n=)	Normal % (n=)	Mean ± SD	P-value
HB	2 % (n=4)	14.5% (n=29)	83.5% (n=167)	13.0 ±2.0	0.6
MCV	22% (n=44)	28.5% (n=57)	49.5% (n=99)	83.2 ±10.0	0.9
TLC	21% (n=42)	6% (n=12)	73% (n=146)	8.7 ± 4.0	0.8
Platelets	2% (n=4)	11.5% (n=23)	86.5% (n=173)	247.5 ± 90.1	0.9

Table 2: Mean ± SD, p-value Vs HB, MCV, TLC, and platelets
P-value < 0.05= statistically significant

The mean ±SD of urea was 28.6 ± 15.2 and it was high in 3.5% (n=7) and normal in 96.5% (n=193) individuals and statistically it was non-significant with p- value 0.9. The mean ±SD of creatinine was 1.67 ± 2.31and it was high in 33.5% (n=67) and normal in 66.5% (n=133) individuals with p-value 0.6 indicating non-significant results. The mean ±SD of sodium was 139.8 ± 16.7and it was high in 25.5% (n=51), low in 37.5% (n=75) and normal in 37% (n=74) subjects having p value 0.9 showing non-significant results. The mean ±SD of potassium was 5.7 ± 1.9 and it was high in 53% (n=106), low in 8% (n=16) and normal in 39% (n=78) subjects and it was statistically non-significant with p value 0.6. The mean ±SD of chloride was 102.2 ± 13.1 and it was high in 32.5% (n=65), low in 26% (n=52) and normal in 41.5% (n=83) subjects and it was statistically non-significant with p-value 0.9 (Table 3).

Parameters	High % (n=)	Low % (n=)	Normal % (n=)	Mean ± SD	P-value
Urea	3.5% (n=7)	-	96.5% (n=193)	28.6 ± 15.2	0.9
Creatinine	33.5% (n=67)	-	66.5% (n=133)	1.67 ± 2.31	0.6
Sodium	25.5% (n=51)	37.5% (n=75)	37% (n=74)	139.8 ± 16.7	0.9
Potassium	53% (n=106)	8% (n=16)	39% (n=78)	5.7 ± 1.9	0.6
Chloride	32.5% (n=65)	26% (n=52)	41.5% (n=83)	102.2 ± 13.1	0.9

Table 3: Mean ± SD, P-value vs. urea, creatinine. Sodium, Potassium, and chloride
P-value < 0.05 = statistically significant

The mean ±SD of total bilirubin was 0.78 ± 0.68 and it was high in 16% (n=32) and normal in 84% (n=168) individuals and it was statistically non-significant with p-value 0.07. The

DOI: https://doi.org/10.54393/pbmj.v5i1.321

mean ±SD of ALT was 44.6 ± 51.4 and it was high in 43% (n=86) and normal in 57% (n=114) individuals and it was statistically non-significant with a p-value of 0.9. The mean ±SD of AST was 50.8 ± 59.7 and it was high in 40% (n=80) and normal in 60% (n=120) individuals and it was statistically non-significant with a p-value of 0.9. The mean ±SD of ALP was 104 ± 62.2 and it was high in 2% (n=4), low in 47% (n=94) and normal in 51% (n=102) subjects and it was also statistically non-significant with a p-value of 0.8. The mean ±SD of total protein was 6.3 ± 1.0 and it was low in 41.5% (n=83) and normal in 58.5% (n=117) subjects and it was also statistically non-significant with a p-value of 0.4 (Table 4).

Parameters	High % (n=)	Low % (n=)	Normal % (n=)	Mean ± SD	P-value
Total bilirubin	16% (n=32)	-	84% (n=168)	0.78 ± 0.68	0.07
ALT	43% (n=86)	-	57% (n=114)	44.6 ± 51.4	0.9
AST	40% (n=80)	-	60% (n=120)	50.8 ± 59.7	0.9
ALP	2% (n=4)	47% (n=94)	51% (n=102)	104 ± 62.2	0.8
Total Protein	-	41.5% (n=83)	58.5%(n=117)	6.3 ± 1.0	0.4

Table 4: Mean ± SD, p-value vs. Total bilirubin, ALT, AST, ALP, and Total Protein
P-value < 0.05 was considered statistically significant

The mean ±SD of CRP was 18.5 ± 23.9 and it was high in 67.5% (n=135) and normal in 32.5% (n=65) individuals. The mean ±SD of D-dimer was 241 ± 103 and it was high in 60% (n=120) and normal in 40% (n=80) of studied subjects. The mean ±SD of ferritin was 491 ± 283 and it was high in 71.5% (n=143) and normal in 28.5% (n=57) individuals. The mean ±SD of LDH was 470 ± 308 and it was high in 68% (n=136) and normal in 32% (n=64) individuals. These four parameters are also statistically significant (Table 5).

Param eters	High % (n=)	Low % (n=)	Normal % (n=)	Mean ± SD	P-value
CRP	67.5% (n=135)	-	32.5% (n=65)	18.5 ± 23.9	0.02
D-dimer	60% (n=120)	-	40% (n=80)	241 ± 103	0.04
Ferritin	71.5% (n=143)	-	28.5% (n=57)	491 ± 283	0.04
LDH	68% (n=136)	-	32% (n=64)	470 ± 308	0.03

Table 5: Mean ± SD, p-value vs. CRP, D-Dimer, Ferritin, and LDH
P-value < 0.05 was considered statistically significant

DISCUSSION

Clinical parameters which could be raised in infected patients were studied. Male gender is more frequently infected gender as compared to female gender. Studies revealed that the male gender is more likely infected gender as compared to the female gender [11-14]. Various studies conducted especially in China and India revealed that the young age group is mostly affected by coronavirus [12,15,16]. These findings are similar to our study in which the mean age which is frequently affected by COVID-19 is 32 years. On the other hand, studies published in the UK and the USA highlighted older age groups e.g., >65 years [13,14,17]. Hematological abnormalities are archived in COVID-19 patients and have prognostic and restorative importance [18]. Raised d-dimers are accounted for in patients with moderate to extreme sickness [19,20]. However various studies have shown that raised ferritin levels have been related to more lethal outcomes, alongside a few other supportive of inflammatory markers, including CRP may even assist the severity of disease [21,22]. In our study serum ferritin is significantly high in COVID-19 infected patients. In COVID-19 patients CRP is frequently raised depending upon the severity of infection. In our study, 67.5% of the level of CRP is elevated in COVID-19 infected patients which indicates that CRP could be considered a prognostic marker in initial diagnosis for infected patients. It concluded from our results that LDH could also be considered as predictive marker in COVID-19 infection. In COVID-19 positive individuals, 68 percent of LDH is increased, according to our statistical study. Pyruvate is converted into lactate with the help of an enzyme LDH (Lactate Dehydrogenase) using NAD+ as a hydrogen acceptor, in cells from practically all organ systems [23]. D-Dimer elevation was shown to be common in COVID-19 patients at admission, and it was connected to higher disease cruelty and in-hospital death. D-dimers are one of the pieces generated when plasmin cleaves fibrin to break down clots. Plasma D-Dimer levels are raised by any pathologic or non-pathologic event that stimulates fibrin formation or breakdown [24]. D-Dimer is also raised to a substantial degree in our research, which is not to be overlooked. According to our findings, 60% of COVID-19 positive individuals had high D-dimer levels, which might be a useful diagnostic in the identification of COVID-19 infection. D-Dimer levels have been linked to the severity of pneumonia and medical outcome in many studies [25,26]. According to the interim guideline, there was an association between D-Dimer levels and disease rigorousness, which was graded by the extent of damaged lungs on chest CT, the oxygenation index, and clinical staging. In addition, the new study discovered a higher proportion of D-Dimer elevation than previously reported. Different researches have also shown a link between dysfunctional liver and COVID-19 infection in certain ways. Our research discovered a greater frequency of irregular liver tests than formerly reported, and only a minor percentage of patients had an underlying liver illness, suggesting that liver damage in individuals with coronavirus infection may be caused by a viral infection of liver cells [27]. ACE2 was shown to be the primary receptor for SARS-CoV-2 cell entrance in two recent studies [28,29].

DOI: https://doi.org/10.54393/pbmj.v5i1.321

It was predominantly discovered in the heart, kidney, and testes, but it was also identified in a range of other tissues, including the colon and lung, at low levels. According to recent research, SARS-CoV-2 may directly attach to ACE2-positive cholangiocytes and induce liver damage [30]. In contrast to earlier research, we found that the overall leukocyte count was not significantly affected in our investigation. For example, several types of researches have indicated that total leukocyte count is altered, with one study concluding that Lymphopenia is the most often encountered irregularity in 35–83 percent of patients and is linked to the severity of illness [20,31]. However, according to our findings, only 21% of the total leukocyte count was aberrant, and the remainder of the sample population had no influence on TLC and had a normal range of TLC even when infected with COVID-19. TLC cannot be used as a prognostic sign in the evaluation of COVID-19 infection, it is also stated. According to our findings, 83.5 percent of COVID-19 infected individuals had normal hemoglobin levels, whereas only 2% of infected patients have high levels and 14.5 percent had low levels. This is a relatively small proportion of aberrant hemoglobin values, hence it cannot be regarded as substantial enough to show a relationship between abnormal hemoglobin values and covid-19 infection. However, whereas our study found higher levels of creatinine (33.5%) and urea (3.5%) in Coronavirus patients, the research led by Xiucui Han and Qing Ye found higher levels of creatinine (27%) [32]. Another study headed by Rajab et al. found findings for urea that were similar to ours [33].

CONCLUSION

It is concluded that some parameters are slightly raised in COVID-19 infection while others the most prominent parameters which are ferritin, D-Dimer, CRP, and LDH are significantly increased in COVID-19, and we can consider them as predictive markers in the initial diagnosis of COVID-19 infection. TLC and Hb were non-significant in COVID-19 infection and can be raised in other clinical conditions thus these parameters cannot be suggested as confirmatory parameters in COVID-19 infection.

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