e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2022; 14(7); 282-289

Original Research Article

Role of Biochemical Markers in the Monitoring of COVID-19 Patients

Jyoti Kumari[1], Dev Kant[2], Anita Suneel[3]

[1]Assistant Professor, Department of Biochemistry, SKMCH, Muzaffarpur, Bihar, India
[2]Assistant Professor, Department of Ophthalmology, SKMCH, Muzaffarpur, Bihar, India
[3]Associate Professor, Department of Biochemistry, SKMCH, Muzaffarpur, Bihar, India

Received: 15-04-2022 / Revised: 20-05-2022 / Accepted: 05-06-2022
Corresponding author: Dr Dev Kant
Conflict of interest: Nil

Abstract

Objectives: This present study was to evaluate the role of biomarkers for diagnosis and management of COVID-19 patients.

Methods: Throat-swab upper respiratory specimens were obtained from 100 patients and real-time PCR (polymerase chain reaction) was used to confirm SARS-CoV-2 infection. Clinical characteristics and blood biochemical tests of COVID-19 patients were examined and recorded. Venous blood (4.5 mL) was obtained. Blood samples were dispensed into a gel tube. All tubes were allowed to stand for 30 minutes at room temperature, followed by centrifugation for 10 minutes at 3500 rpm to get the serum. Liver and kidney function test were performed to all patients.

Results: In this present study, out of 100 COVID-19 patients, they had 20(20%) diabetic, 29(29%) smokers, 04(04%) cancerous and 15(15%) hypertensives. Mean age of COVID-19 patients was 42.4±13.18 years.

Conclusions: Abnormalities in biochemical markers play a pivotal role in the SARS-CoV-2 pandemic, it is not only from a diagnostic point of view but also in terms of the management and prognosis of COVID-19 patients. It helps for clinical decision making in order to adjust the therapy to the biological changes experienced by the subjects. Changes in the biochemical markers indicate abnormalities in various tissues and organs, indicating the development of COVID-19. Urea, CK, and LDH show the most predictive parameters of severe COVID-19 patients. LDH as an important biomarker is associated with poor outcomes in COVID-19 patients.

Keywords: COVID-19 patients, Biochemical markers, Age

Background

COVID-19 is an infectious disease caused by the SARS CoV-2 virus, which has given rise to a global sanitary emergency. In December 2019, the city of Wuhan in China became the epicenter of unexplainable cases of pneumonia, which in January 2020 were identified as a new coronavirus, turning rapidly into a major problem of public health worldwide [1]. This pathogen, corresponding to a beta coronavirus, is made up of single chains of positive RNA belonging to the large Coronaviridae subfamily and has the

ability to infect mammals and other animals [2]. Coronavirus disease (COVID-19) causes the severe acute respiratory syndrome (SARS-CoV-2) [3], which spread rapidly all over the world and was declared by the World Health Organization (WHO) as a pandemic on 11 March 2020 [4].

The disease reported in a cluster of atypical pneumonia cases and primarily transmitted through respiratory and body contact [5]. Patients with coronavirus disease demonstrated a series of clinical symptoms, including raised body temperature, cough, headache, nausea, vomiting, anorexia, diarrhoea, dyspnoea, multiple organ dysfunctions [6]. A large proportion of infected patients reported mild symptoms of the disease and recover [7]. Some patients progressively develop serious complications, including sepsis, acute respiratory failure, metabolic acidosis, heart failure, kidney injury, hypoxic encephalopathy, and eventually die of the illness.3 A recent report reported a few new symptoms, including anosmia and ageusia [8]. Considering high transmission and infectivity patterns, World Health Organisation announces it as an emergency of public health concern on March 31, 2020 [9]. In the initial phase of the disease outbreak, the mortality ranges from 2 to 5%, much higher in the elderly [6]. The mortality in coronavirus cases admitted in Wuhan city reached 7% in the outbreak's initial days [10].

The critical role of laboratory medicine in this pandemic extends far more than the etiological diagnosis of COVID19. In spite of the broadly defined clinical characteristics of COVID-19, we still lack the understanding of the abnormalities in the laboratory findings in COVID-19 patients. Since laboratory medicine plays an important role in the early detection, diagnosis, prognosis as well as management of the disease we can use this tool for a better understanding of this novel coronavirus disease [11]. Also, the lack of specific treatment towards this disease [12], early diagnosis becomes a very important factor. Biochemical monitoring of COVID-19 patients through testing is critical for assessing disease severity and progression, as well as monitoring of therapeutic intervention [13]. In addition to more common laboratory tests like Liver Function Test (LFT), Kidney Function Test (KFT), Blood Gas, etc., evidence suggests that patients with severe COVID-19 could be at risk of cytokine storm syndrome [14, 15]. Cytokine tests, particularly IL-6, should be used to assess patients exhibiting severe illness and those suspected of hyper-inflammation [16]. Such patients with features of systemic hyper-inflammation are categorized display macrophage activation syndrome (MAS) or cytokine storm [11]. Few studies have been published globally to investigate the role of biochemical markers & immunoassay markers in COVID 19 patients [17]. The essential role of Biochemistry, Immunology, and routine pathology laboratory is well known in the modern healthcare system. These Laboratory biomarkers play an essential role in the patient admission protocol, assessment of staging of disease according to severity, prognostication, patient monitoring, and therapeutic guide [18]. Objective of our present study was to evaluate the role of biomarkers in monitoring of COVID-19 patients.

Materials and Methods

This present study was conducted in Department of Biochemistry with the collaboration of Department of Medicine, SKMCH, Muzaffarpur, Bihar India during a period from April 2021 to January 2022. Entire patients signed an informed consent approved by institutional ethical committee of Shri Krishna Medical College and Hospital (SKMCH), Muzaffarpur, Bihar, India was sought.

Methods

Throat-swab upper respiratory specimens were obtained from 100 patients and real-

time PCR (polymerase chain reaction) was used to confirm SARS-CoV-2 infection. Clinical characteristics and blood biochemical tests of COVID-19 patients were examined and recorded. Gender, age, and clinical characteristics such as diabetes mellitus, hypertension, and smoking had been investigated.

Sample Collection: Venous blood (4.5 mL) was obtained. Blood samples were dispensed into a gel tube. All tubes were allowed to stand for 30 minutes at room temperature, followed by centrifugation for 10 minutes at 3500 rpm to get the serum.

Liver and kidney function tests: Alanine transaminase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin, creatinine, and blood urea were measured. Uric acid, triglyceride, total cholesterol, high-density lipoprotein (HDL), calcium (Ca+2), sodium (Na+), potassium (K+), chloride (Cl−), magnesium (Mg+2), and phosphorus (P) were also measured using Gesan Chem-200 platform (Gesan Production SRL, Italy) according to the manufacturing protocols.

Statistical Analysis

Data was analysed by using latest version of SPSS software. Mean± S.D were observed. P-value was taken less than or equal to 0.05 ($p \leq 0.05$) for significant differences.

Observations

A total of 100 COVID-19 patients were enrolled in this study. Among them, 52(52%) were males and 48(48%) were females.

Table 1: Gender wise distribution of COVID-19 patients

Gender	No. of cases
Male	52(52%)
Female	48(48%)
Total	100(100%)

In this present study, out of 100 COVID-19 patients, there were 20(20%) diabetic, 29(29%) smokers, 04(04%) cancerous and 15(15%) hypertensives. Mean age of COVID-19 patients was 42.4±13.18 years.

Table 2: Clinical Status of COVID -19 patients

Clinical status	No. of cases
Diabetic	20(20%)
Non-diabetic	80(80%)
Smokers	29(29%)
Non-smoker	71(71%)
Cancerous	04(4%)
Non- cancerous	96(96%)
Hypertension	15(15%)
Non-hypertension	85(85%)

Table 3: Biochemical parameters of COVID-19 patients.

Parameters	Mean ± S. D
Age (Years)	42.4±13.18
Na (mmol/L	152.32 ± 3.01
Ca (mmol/L	2.45 ± 0.23
K (mmol/L	4.23 ± 0.24
Cl (mmol/L	100.12 ± 1.63
Mg (mg/dL	1.98 ± 0.4

P (mg/dL)	3.12 ± 0.51
Urea (mg/dL)	33.34 ± 6.8
Creatinine (mg/Dl)	1.01 ± 0.44
Uric acid (mg/dL)	4.92 ± 0.91
Cholesterol (mg/dL)	175.28 ± 25.71
Triglyceride (mg/dL)	185.86 ± 38.42
HDL (mg/dL)	42.12 ± 5.96
GOT (U/L)	33.34 ± 13.01
GPT (U/L)	37 ± 14.61
TSB (mg/dL)	0.51 ± 0.31
ALK (U/L)	193.81 ± 89.62

Mean abnormalities of biochemical markers of COVID-19 patients had (Na) 152.32 ± 3.01 mmol/L, (Ca) 2.45 ± 0.23 mmol/L, (K) 4.23 ± 0.24 mmol/L, (Cl) 100.12 ± 1.63 mmol/L, (Mg) 1.98 ± 0.4 mg/dL, (P) 3.12 ± 0.51 mg/dL, (urea) 33.34 ± 6.8 mg/dL, (creatinine) 1.01 ± 0.44 mg/dL, (uric acid) 4.92 ± 0.91 mg/dL, (cholesterol) 175.28 ± 25.71 mg/dL, (triglyceride) 185.86 ± 38.42 mg/dL, (HDL) 42.12 ± 5.96 mg/dL, (GOT) 33.34 ± 13.01 U/L, (GPT) 37 ± 14.61 U/L, (TSB) 0.51 ± 0.31 mg/dL and (ALK) 193.81 ± 89.62 U/L.

Discussions

Clinical laboratories play an essential role in the detection of the virus as well as to the follow-up of patients (monitoring their evolution) and epidemiological surveillance via the determination of serological markers in their systems [19]. Laboratory tests validated for SARS-CoV-2 are crucial for the timely management of COVID-19 because they support the clinical decision-making process for controlling infections and detecting asymptomatic cases. This expedites speedy isolation, adequate treatment and consequently reduces contagion rates [20].

Many laboratory parameters make it possible to assess the severity of the disease and predict the risk of it evolving toward more serious afflictions such as acute respiratory distress syndrome (ARDS), disseminated intravascular coagulation (DIC) and multiple organ failure (MOF) [21]. Some parameters for which an unfavourable course of the disease has been described are absolute neutrophilia, thrombocytopenia, hypoalbuminemia, the elevation of liver enzymes, creatinine and nonspecific inflammatory markers such as C-reactive protein (CRP) and Interleukin 6 (IL-6) [22]. Huang *et al*. [23] established that the plasma concentrations of IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1A, and TNF-α were higher in Intensive Care Unit (ICU) patients in comparison with non-ICU patients. In turn, Qin *et al*. [24] reported that a majority of severe cases showed an elevation of biomarkers related to infection (procalcitonin, serum ferritin and CRP) and inflammatory cytokines (IL-2R, IL-6, IL-8, IL-10 and TNF-α). C-reactive protein is a plasma protein that is synthesized by the liver and induced by different inflammatory mediators such as IL-6. Despite being nonspecific, it is used clinically as a biomarker for different inflammatory complaints, and an increase in its levels is associated with greater severity of the disease [25]. This protein can activate the complement through the classic route and has the ability to modulate the function of phagocytic cells, properties that suggest it would play a role in the opsonization of infectious agents and damaged cells [26].

In our present study, total of 100 COVID-19 patients were enrolled. Mean age of Covid-19 patients had 42.4±13.18 years. 52(52%) were males and 48(48%) were females. Most cases experienced influenza-like symptoms such as fever,

cough, and mild myalgia during their time at the hospital. All patients were discharged following recovery of clinical symptoms. Diabetes mellitus was presented in 20(20%). Most common comorbidity, followed by hypertension was presented in 15(15%) patients. In the hypertensive group, triglycerides, alanine aminotransferase (GPT), and alkaline phosphatase (ALP) were the most common biochemical laboratory abnormalities identified in table.3. However, no significant association was found between elevated blood pressure and normal blood pressure in all biochemical laboratory parameters. Among the biochemical parameters, cholesterol and triglycerides had a significant difference between the diabetic and nondiabetic COVID 19-infected patients. Furthermore, in a few patients, creatinine, alanine aminotransferase (GPT), alkaline phosphatase (ALP), and aspartate aminotransferase (GOT) levels were shown to be higher than the normal range. However, when comparing them according to diabetic and nondiabetic classification, none of these variations were statistically significant. Some biochemical measures such as creatinine, triglycerides, alkaline phosphatase and GOT, were found to have increased levels. However, when comparing these biomarkers between males and females, no evidence of significant differences was found. Smoking has been shown to increase serum lipid profiles including triglycerides [27]. We, therefore, analyse whether smoking habits may influence the balance of serum biochemistry in patients with COVID-19. Low serum concentrations of magnesium, phosphorus, and calcium, have been seen in certain patients. Further analysis revealed high serum levels of creatinine, GPT, ALP, GOT, and urea in just a few other patients whereas only potassium concentrations were significantly differences when comparing smokers with non-smoker patients. A strong relationship between lipid profiles and hypertension has been reported in [28, 29]. Higher triglycerides values were found in patients with elevated blood pressure which are consistent with these reports.

We found that triglycerides, GPT, and GOT were elevated although there was no significant difference between COVID-19 patients with elevated and normal blood pressure suggesting that COVID-19 infection may alter these biochemical laboratory markers regardless of hypertension. Furthermore, the higher triglyceride levels in certain patients might be due to body fat and distribution, a condition not investigated in this study. These findings seem to be consistent with other studies which found that high levels of triglyceride were more positively correlated with body fat than with changes in blood pressure [30, 32].

We found a marked increase in levels of cholesterol and triglycerides in diabetic and nondiabetic COVID-19-infected patients. Creatinine, GPT, ALP, and GOT values were shown to be higher than the normal range in some COVID-19- infected patients. &e most notable comorbidities with COVID-19 in our study were diabetes (23%) and hypertension (14%). Coronaviruses bind to their target cells via angiotensin converting enzyme 2 (ACE2), which is widely expressed in the kidney, intestine, and epithelial cells of the lung [33]. It has also been demonstrated that the expression of ACE2 is markedly upregulated in patients with diabetes which would promote the infection with COVID-19 [33, 34].

The entry of SARS CoV2 into the cell is mediated by the spike protein through the cell receptors binding, followed by the fusion of the membrane [35]. SARS-Cov-2 spike protein binds itself to angiotensin-converting enzyme 2 (ACE2) receptor. The host cell consists of type 2 transmembrane serine protease (TMPRSS2) that promotes viral uptake by cleaving ACE2 and activates the SARS-

CoV-2 S protein. This process mediates the entry of coronavirus into alveolar epithelial type II pneumocytes. Alveolar epithelial type II cells show the expression of ACE2 and TMPRSS2. Multiplication of viral copy occurs inside the host cells. The infected cells and alveolar macrophage release inflammatory signal. Pulmonary edema with hyaline membrane formation leads to ARDS (acute respiratory distress syndrome) [36].

Conclusions

This present study concluded that the abnormalities in biochemical markers play a pivotal role in the SARS-CoV-2 pandemic, not only from a diagnostic point of view but also in terms of the management and prognosis of COVID-19 patients. It helps for clinical decision making in order to adjust the therapy to the biological changes experienced by the subjects. Changes in the biochemical markers indicate abnormalities in various tissues and organs, indicating the development of COVID-19. Urea, CK, and LDH show the most predictive parameters of severe COVID-19 patients. LDH as an important biomarker is associated with poor outcomes in these patients.

References

1. Abuelgasim E, Saw LJ, Shirke M, Zeinah M, Harky A. COVID-19: Unique public health issues facing Black, Asian and minority ethnic communities. Mosby Inc 2020; 1–10.
2. Gorbalenya AE, Baker SC, Baric RS, de Groot RJ, Drosten C, Gulyaeva AA, *et al*. The species severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. Nature Microbiology 2020; 5(4): 536–44.
3. Lai CC, Shih TP, Ko WC, Tang HJ, Hsueh PR. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. Elsevier B.V. 2020: 105924.
4. Estevão A. Artículo de opinión: COVID-19. Acta Radioló - gica Portuguesa 2020; 32(1): 1–5.
5. Sheng L, Wang X, Tang N, *et al*. Clinical characteristics of moderate and severe cases with COVID-19 in Wuhan, China: a retrospective study. Clinical and Experimental Medicine. 2020.
6. Kumar R, Singh V, Mohanty A, Bahurupi Y, Gupta PK. Corona health-care warriors in India: knowledge, attitude, and practices during COVID-19 outbreak. J Educ Health Promot. 2021;10(44):1–8.
7. Wang D, Hu B, Hu C, *et al*. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in wuhan, China. JAMA. 2020;323: 1061–1069.
8. Gautier J-F, Ravussin Y. A new symptom of COVID-19: loss of taste and smell. Obesity. 2020: 848.
9. World Health Organization World Health Organization. Statement on the second meeting of the international health regulations (2005). Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV); 2020.
10. Lu J, Hu S, Fan R, *et al*. ACP risk grade: a simple mortality index for patients with confirmed or suspected severe acute respiratory syndrome coronavirus 2 disease (COVID-19) during the early stage of outbreak in Wuhan. Med Rxiv China; 2020; 20025510.
11. Plebani M, Laposata M, Lippi G. A manifesto for the future of laboratory medicine professionals. Clin Chim Acta. 2019; 489:49–52.
12. Gao Y, Li T, Han M, Li X, Dong W, Yuanhong X, *et al*. Diagnostic utility of clinical laboratory data determinations for patients with the severe COVID-19. J Med Virol. 2020;92(7):791–6.
13. Lippi G, Plebani M. Laboratory abnormalities in patients with COVID-

2019 infection. Clin Chem Lab Med (CCLM). 2020;58(7):1131–4.
14. TanuSinghal A. Review of coronavirus disease-2019 (COVID19). Indian J Pediatr. 2020;87(4):281–6.
15. Tobacco use and COVID-19. 11 May 2020 Statement. Geneva: World Health Organization.
16. Samsudin I, Vasikaran SD. Clinical utility and measurement of procalcitonin. Clin Biochem Rev. 2017;38(2):59–68.
17. Lippi G, Simundic A-M, Plebani M. Potential preanalytical and analytical vulnerabilities in the laboratory diagnosis of coronavirus disease 2019 (COVID-19). Clin Chem Lab Med. 2020;58(7):1070–6.
18. COVID-19 Coronavirus Real-Time PCR Kit. https://www.who. int/diagnostics_laboratory/eual/eul_05 15_202_00_covid19_coronavirus_real _time_pcr_kit_ifu.pdf?ua=1. Assessed 15th August 2020.
19. Giuseppe L, Mario P. Laboratory abnormalities in patients with COVID-2019 infection. In: Clinical Chemistry and Laboratory Medicine (CCLM). De Gruyter. 2020; 1-4.
20. Kubina R, Dziedzić A. Molecular and serological tests for COVID-19: A comparative review of SARS-CoV-2 corona virus laboratory and point-of-care diagnostics. Diagnostics. 2020;10(6):1-18.
21. Lippi G, Plebani M. The critical role of laboratory medicine during coronavirus disease 2019 (COVID-19) and other viral outbreaks. Clin Chem Lab Med. 2020;58(7):1063-1069.
22. Ramírez-Truque M, Herrera-Morice M. Rol del laboratorio clínica antela epidemia del COVID-19: Revisión de los métodos diagnósticos disponibles y sus limitaciones. Revista médica de Costa Rica. 2020;85(629):73-80.
23. Gong J, Dong H, Xia Q, Huang Z, Wang D, Zhao Y, *et al*. In: Correlation analysis between disease severity and inflammation-related parameters in patients with COVID-19 pneumonia. Cold Spring Harbor Laboratory. 2020.
24. Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, *et al*. Kidney disease is associated with in-hospital death of patients with COVID-19. Kidney Int. 2020;97(5):829- 838.
25. Li Z, Wu M, Yao J, Guo J, Liao X, Song S, *et al*. In: Caution on kidney dysfunctions of COVID-19 patients. Cold Spring Harbor Laboratory. 2020.
26. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 2020;46(5):846-848.
27. M. Koda, I. Kitamura, T. Okura, R. Otsuka, F. Ando, and H. Shimokata, "&e associations between smoking habits and serum triglyceride or hemoglobin A1c levels differ according to visceral fat accumulation," Journal of Epidemiology, 2016; 26(4):208–215.
28. G. Ghooshchi, M. S. Yazdi, and M. P. Ramezan, Evaluation of the Lipid Profile of Hypertensive Patients Compared to Nonhypertensive Individuals, Mashhad University of Medical Sciences, Mashhad, Iran, 2014.
29. A. Gebrie, N. Gnanasekaran, M. Menon, M. Sisay, and A. Zegeye, "Evaluation of lipid profiles and hematological parameters in hypertensive patients: laboratory-based crosssectional study," SAGE Open Medicine 2018; 6: 2050312118756663.
30. M. Royo-Bordonada, C. Garces, L. Gorgojo *et al*., "Saturated ´ fat in the diet of Spanish children: relationship with anthropometric, alimentary, nutritional and lipid profiles," Public Health Nutrition 2006; 9(4): 429–435.
31. R. O. Halperin, H. D. Sesso, J. Ma, J. E. Buring, M. J. Stampfer, and J. Michael Gaziano, "Dyslipidemia and the risk of incident hypertension in

men," Hypertension 2006; 47(1): 45–50.
32. Y. Wan, J. Shang, R. Graham, R. S. Baric, and F. Li, "Receptor recognition by the novel coronavirus from wuhan: an analysis based on decade-long structural studies of SARS coronavirus," Journal of Virology 2020; 94: 7.
33. Z. Liu, X. Xiao, X. Wei *et al*., "Composition and divergence of coronavirus spike proteins and host ACE2 receptors predict potential intermediate hosts of SARS-CoV-2," Journal of Medical Virology 2020; 92(6): 595–601.
34. X. C. Li, J. Zhang, and J. L. Zhuo, "& vasoprotective axes of the renin-angiotensin system: physiological relevance and therapeutic implications in cardiovascular, hypertensive and kidney diseases," Pharmacological Research, 2017; 125: 21– 38.
35. W.-j. Guan, Z.-y. Ni, Y. Hu *et al*., "Clinical characteristics of coronavirus disease 2019 in China," New England Journal of Medicine 2020; 382(18):1708–1720.
36. J. M. Leung, C. X. Yang, A. Tam *et al*., ACE-2 expression in the small airway epithelia of smokers and COPD patients: implications for COVID-19, European Respiratory Journal, 2020; 55: 5.