Panacea Journal of Medical Sciences 2023;13(2):262–268

Content available at: https://www.ipinnovative.com/open-access-journals

Panacea Journal of Medical Sciences

Journal homepage: http://www.pjms.in/

Original Research Article

Biochemical and Clinical profile of COVID-19 patients and its association with severity of the disease: A study at tertiary care centre

Anita Rani[1,*], **Rohit Kumar**[2], **Omkar Kalidasro Choudhari**[1], **Paarth Bhatia**[3]

[1]*Dept. of Biochemistry, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India*
[2]*Dept. of Respiratory Medicine, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India*
[3]*Himalayan Institute of Medical Sciences, Dehradun, Uttarakhand, India*

ARTICLE INFO

Article history:
Received 25-09-2021
Accepted 18-03-2022
Available online 31-07-2023

Keywords:
COVID-19
Biochemical profile
Clinical profile
Angiotensin converting enzyme (ACE) receptor

ABSTRACT

Background: The Novel Corona Virus pandemic caused significant morbidity and mortality worldwide. The biochemical parameters in affected individuals can differentiate between moderate and severe COVID-19 infection. Early identification will facilitate appropriate care and reduce the mortality.

Objective: In the present study, we are exploring the possibility of association of the data of biochemical investigations done at the time of admission with COVID-19 severity in patients, as timely modulation in medical management could reduce the mortality and shorten hospital stay.

Materials and Methods: A cross sectional study including 452RT-PCR positive, moderate to severe cases of COVID-19 patients admitted to a tertiary care centre, New Delhi were enrolled in the study, in the months of June to October 2020.Biochemical profile of moderate and severe COVID 19 patients was evaluated on admission and correlated with severity of the disease.

Results: Out of 452 patients, 331 patients had moderate disease while 121 had severe disease. Total bilirubin in moderate disease was 0.6mg/dl(0.4-0.9) and 0.6mg/dl(0.4-0.8) in severe disease (p=0.780). AST was 46U/L(31-73.75) and 45 U/L(30-76) in moderate and severe disease respectively (p=0.544), while ALT was 42U/L(25-78.25) and 42U/L(26-72)(p=0.936) respectively in moderate and severe disease. The ALP was 111U/L(86.5-165.5) and 106U/L(77-157) in moderate and severe disease respectively (p=0.828). The serum urea in moderate COVID-19 patients was 32mg/dl(22-61) while 42mg/dl(22-94) in severe disease (p=0.016). The serum creatinine in moderate disease was 0.7mg/dl(0.6-1.1) while 0.8mg/dl(0.6-1.8)(p=0.143) in severe disease. The median (IQR) serum HsCRP in moderate disease was 103.2mg/L(9.7-202) and in severe disease it was 103.76mg/L(19.53-181.26)(p=0.132). The median (IQR) LDH level in moderate COVID-19 patients was 245U/L(137.25-372.25) while in severe disease it was 385U/L(278-598)(p<0.001).

Conclusion: The serum biomarkers Urea and inflammatory marker LDH could serve as potential biomarkers to differentiate between moderate and severe COVID-19 patients.

1. Introduction

The COVID-19 pandemic is caused by positive-sense RNA Corona virus. It is the first documented corona virus pandemic so far with reported mortality of more than 1 million people worldwide and still remains as an evolving condition.[1,2] The presentation varies from asymptomatic to severe respiratory distress syndrome requiring invasive ventilation and prolonged hospital stay. The mortality is predominantly seen in people with comorbid conditions and in aged population; however mortality in young adults without antecedent history is also reported.[3] Though the

* *Corresponding author*.
E-mail address: dr.anitabhatia@gmail.com (A. Rani).

https://doi.org/10.18231/j.pjms.2023.052

majority of COVID-19 patients have mild diseases, the clinical deterioration in the form of development of Acute Respiratory Distress Syndrome (ARDS),septic shock or death is seen in the initial eight to ten days.[4] Hence, it is imperative to understand the probable course of the disease at an early stage to enable the clinician to decide on therapeutic modality and reduce mortality. The biochemical parameters on hospital admission, before commencing treatment and their correlation with disease severity could serve as potential early predictor of mortality in COVID-19 patients.[5]However, there is paucity of literature about the relationship between disease severity and clinical and biochemical feature in COVID-19 patients in Indian population.

The clinical presentation of cases of this novel virus varies from mild to severe infection. Predominantly, COVID-19 cases are mild in nature, presented with fever, sore throat or myalgia and rarely require hospitalisation while moderate and severe cases often need admission and oxygen supplementation along with supportive therapy.

The available evidence speculates that binding to Angiotensin Converting enzyme 2(ACE2) receptor serve as the entry point of virus in cellular invasion and hijacks the genomic machinery of the host cell.[6]Though SARS CoV2 has respiratory epithelium tropism, its course of invasion via ACE 2 receptor present in liver and kidney leads to biochemical abnormality.[7] In the course of the infection there is rapid release of pro inflammatory and inflammatory cytokines which are found to directly and indirectly alter the biochemical profile much earlier in the disease.[8] While the virus per se can infect the cells and cause biochemical abnormality, the drugs used in the treatment may exacerbate the liver and kidney injury.

In the present study, we are exploring the possibility of association of the data of biochemical investigations done at the time of admission with COVID-19 severity in patients, as timely modulation in medical management could reduce the mortality and shorten hospital stay.

2. Materials and Methods

A single-centred observational cross-sectional study was carried out in the Department of Clinical Biochemistry and Department of Respiratory Medicine, Safdarjung Hospital, New Delhi. Data was collected from a total of 452 patients enrolled from June 26^{th} 2020 to October 30^{th} 2020 in a tertiary care hospital, a nodal centre for the admission and treatment of COVID-19 patients by random sampling. All the participants were confirmed with COVID-19 infection by RT-PCR from various centres in Delhi and national capital region (NCR) of Delhi. The demographic data, work details, travel history, history of any treatment and personal factors along with number of days of onset of symptoms were collected from patients. Blood sample taken for routine biochemical assessment of the admitted patient was used for the study. Sample size was calculated taking Confidence interval of 95% with margin of error of 5% and estimated to be a minimum of 278 patients. Inclusion criteria comprised moderate and severe COVID-19 patients who gave written consent. Patients not willing to give written consent were excluded. Along with the biochemical parameters, clinical profile of these patients was also recorded.

In the present study we are presenting the data of a onetime assessment of Liver function test, Kidney function test, HsCRP, LDH analysis which was carried out by the investigators at the time of admission. Before the test, written consent of the subjects was taken by investigator. Moderate COVID-19 was defined as adolescent or adult with clinical signs of pneumonia and maintaining $SpO_2 \geq 90\%$ with no concomitant features of severe pneumonia while severe COVID-19 was defined as above mentioned symptoms with respiratory distress along with respiratory rate of $\geq$ 30/min and SpO2 <90% for the purpose of this study.[9]

The serum biochemical analysis of urea, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin (T.Bil), High sensitivity C reactive protein (Hs-CRP) and lactate dehydrogenase (LDH) was processed on a fully automated analyser with strict adherence to laboratory internal and external quality control standards.

2.1. Statistical analysis

All the data was collected in a predesigned proforma and analysed. Parametric data is represented as median and inter quartile range, and categorical data was presented as percentage. The independent sample t test or Mann-Whitney U test was used for continuous variables. A two tailed 'P value' of less than 0.05 was considered significant. All data was analysed by SPSS 16.0 (USA). Logistic regression analysis was used to identify variables independently correlated with severe corona virus disease-19.

2.2. Ethics

The study was approved by the Institutional ethics committee (2020-06/98). All patients gave informed consent to participate in the study according to the Helsinki Declaration of the World Medical Association (WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects, 2013) and personal data processing.

3. Results

The analysis included 452 patients with 331 having moderate COVID-19 disease while 121 participants had severe disease. The mean age in moderate group was 42.76±12.45 years and severe group was 41.68±14.47

years. Among the severe group, 63 patients were on oxygen supplementation, 47 patients were on non-invasive ventilation (NIV) while 24 patients were on invasive mechanical ventilation (IMV) on admission. The baseline characteristic is shown inTable 1.

In this study, the serum biochemical markers including Total Bilirubin, AST, ALT, ALP, Hs-CRP, LDH were assessed and their median (IQR) were compared which showed significant differences in Urea and LDH among moderate and severe COVID-19 patients.(Table 2)

Out of 452 patients, 331 patients had moderate disease while 121 had severe disease. Total bilirubin in moderate disease was 0.6mg/dl(0.4-0.9) and 0.6(0.4-0.8)mg/dl in severe disease (p=0.780). AST was 46U/L(31-73.75) and 45U/L(30-76) in moderate and severe disease respectively(p=0.544), while ALT was 42U/L(25-78.25) and 42U/L(26-72) respectively(p=0.936). The ALP was 111U/L(86.5-165.5) and 106U/L(77-157) in moderate and severe disease respectively (p=0.828). The serum urea in moderate COVID-19 patients was 32mg/dl(22-61) while 42mg/dl(22-94) in severe disease(p=0.016). The serum creatinine in moderate disease was 0.7mg/dl(0.6-1.1) while 0.8mg/dl(0.6-1.8) (p=0.143) in severe disease. The serum HsCRP in moderate disease was 103.2mg/L(9.7-202) and in severe disease it was 103.76mg/L(19.53-181.26) (p=0.132) while LDH level in moderate COVID-19 patients was 245U/L(137.25-372.25) while in severe disease it was 385U/L(278-598)(p<0.001).

The association of independent variables with severity of COVID-19 using univariate and multivariate analysis shown in Table 3. In the univariate analysis, urea, LDH were associated with the severity of COVID-19 while in multivariate analysis, urea, LDH could serve as independent risk factor for the severity of COVID-19.

4. Discussion

The COVID-19 pandemic caused significant morbidity and mortality and put enormous burden on the healthcare infrastructure. Though the clinical signs of presentation of the disease are mild in most cases, but in the backdrop of abnormalities of critical biochemical parameters at the time of admission, apart from the clinical criteria, these parameters may help in early recognition of severity and initiate the treatment accordingly. Our study is a comprehensive conglomeration of clinical and biochemical data comprising 452 patients of moderate and severe COVID-19. In our study, the median (IQR) levels of serum Urea, LDH significantly differed in the moderate and severe group.

The hypothesis of biochemical abnormalities in COVID-19 are attributed to the infection of hepatocytes by virus per se or through cholangiocytes via ACE 2 receptor. Another possible way is via the cytokine storm which mediates the immune medicated hepatocyte injury.[10,11] Numerous inflammatory cytokines such as IL6, TNFα, INFγ are released by the immune cells. Among these cytokines IL6 has a direct action on the liver as it is a ligand for the receptor of membrane bound IL6 receptor (mIL6r). IL6 induces the production of acute phase reactants. There is a cascade effect of increase in the levels of liver enzymes along with the acute phase reactants.[12]

In our study, the median level of AST was 46U/L(31-73.75) in moderate COVID-19 disease patients while the median level in severe COVID-19 patient was 45U/L(30-76) which was statistically insignificant (p=0.544). The minimum value of AST with moderate disease was 10 U/Land the highest value for AST was 823 U/L, whereas in severe COVID-19 the minimum value was 12 U/L and the

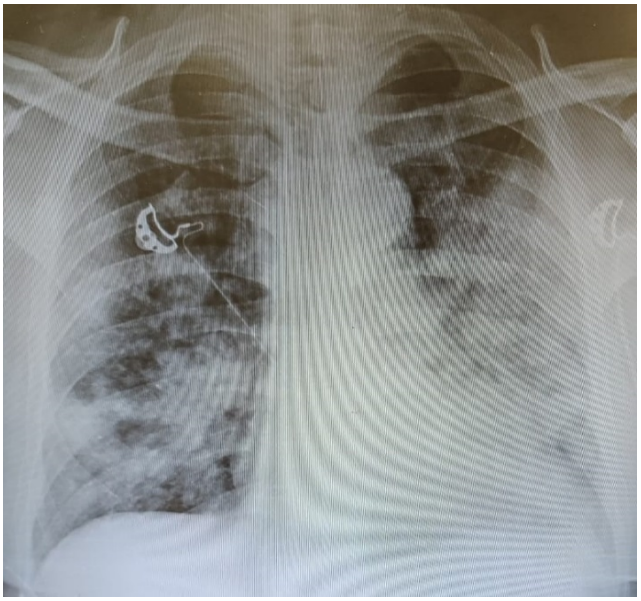

Fig. 1: Bilateral mid zone and lower zone opacities in severe COVID-19 patient.

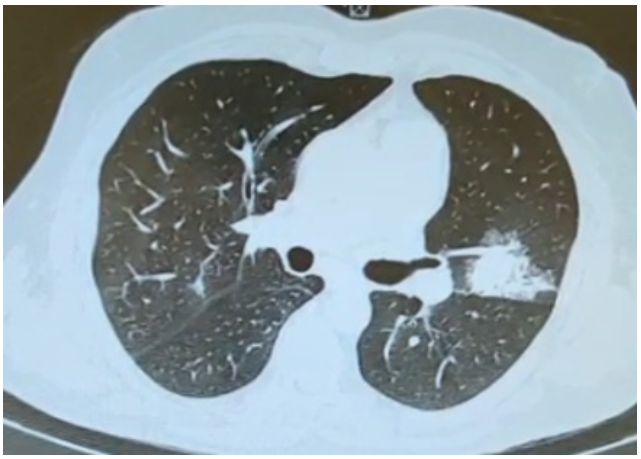

Fig. 2: Left sided consolidation in the Severe COVID-19 patient.

Table 1: Baseline and Clinical profile of patients infected with COVID-19 (Data are mentioned as median(IQR) or N(%).

Parameters	Moderate disease (n=331)N(%)	Severe Disease (n=121)N(%)	P value
Age	42.76±12.45	41.68±14.47	0.106
Male	182(54.98%)	56(49.55%)	0.111
Female	149(45.01%)	65(57.52%)	
Smokers	47(14.19%)	29(25.66%)	0.404
Alcohol intake	65(19.17%)	38(33.63%)	0.001
History of Comorbidities			
Hypertension	61(18.42%)	16 (14.15%)	0.207
Diabetes Mellitus	68(20.06%)	92 (81.41%)	<0.001
Coronary Artery Disease	26 (7.85%)	7(6.19%)	0.544
SYMPTOMS			
Fever	331(100%)	121(100%)	
Cough/ expectoration	331(100%)	121(100%)	
Diarrhoea	46 (13.89%)	14 (12.38%)	0.639
Malaise	123 (37.16%)	27 (23.89%)	0.003
Sore Throat	168 (20.54%)	83 (73.35%)	0.001
Anosmia	16 (4.83%)	5 (4.43%)	1.000

Table 2: Onset of symptoms in number of days from the time of admission (%)

Symptoms on presentation	1-2 days	3-4 days	5-6 days
Fever	13%	47%	40%
Cough/ expectoration	45%	34%	21%
Diarrhoea	2%	78%	20%
Malaise	77%	15%	08%
Sore Throat	31%	57%	18%
Anosmia	34%	61%	05%

Table 3: Biochemical profile of moderate and severe COVID-19 patients.[Median(IQR)]

	Moderate disease N=331	Severe Disease N=121	P value	Normal range	Univariate regression analysis OR (95%CI)	Multivariate Regression analysis OR (95%CI)
Liver function tests						
T.Bil mg/dl	0.6(0.4-0.9)	0.6(0.4-0.8)	0.780	0.8-1.2	1.02 (0.88-1.18)	
AST U/L	46(31-73.75)	45(30-76)	0.544	0-40	1.0001 (0.9997-1.0005)	
ALT U/L	42(26-78.25)	42(26-72)	0.936	0-40	0.9999 (0.9992-1.0006)	
ALP U/L	111(86.5-165.5)	106(77-157)	0.828	53-128	1.0002 (0.9979-1.0025)	
Kidney function tests						
Urea mg/dl	32(22-61)	42(22-94)	0.016	17-43	1.0030 (1.0004-1.0055)	1.0041 (1.0014 – 1.0067)
Creatinine mg/dl	0.7(0.6-1.1)	0.8(0.6-1.8)	0.143	0.9-1.3	1.05 (0.98 – 1.12)	
Inflammatory markers						
LDH mg/L	245(137.25-372.25)	385(278-598)	<0.001	140-280	1.0015 (1.0008-1.0022)	1.0015 (1.0008-1.0022)
HSCRP U/L	103.2(9.7-202)	103.76(19.53-181.26)	0.132	< 1	0.9990 (0.9977-1.0003)	

Data are mentioned as Median(IQR)
Multivariate regression model includes urea and LDH

maximum value was 5149U/L. This shows multi factorial causation behind the elevation in liver enzymes. It includes genetic susceptibility including up regulation and down regulation of ACE 2 receptors for binding of the virus or an exaggerated immune response to the activation of cytokines and their mediated hepatic tissue injury apart from the other sources of AST, which are also seen to be involved in the pathogenesis of COVID-19 like myocardium.[7–9,13,14] Pulmonary embolism is seen in 24% of COVID-19 patients may also contribute to the rise of AST.[15] Since our study is a one-time assessment of the biochemical parameters at admission, the possibility of rise of AST due to pulmonary embolism is scarce though, the possibility of micro-thrombi at the time of admission cannot be ruled out.[16] Our findings are inconsistent with other study, revealing increased risks of propagation of the disease into severe form based on the elevated AST, which in our study did not differ significantly in moderate and severe disease.[17]

In any hepatocellular injury, the cytosolic ALT present in hepatocytes get released into the circulation and higher values can be seen. ALT has diurnal variation and is specific to Liver aetiology.[18] In our study, its median level in moderate cases were 42U/L(25-78.25) while in severe cases it was 42U/L(26-72)(p=0.936). The minimum value of ALT for moderate disease was 12 U/L while maximum ALT value documented in severe COVID19 was 5149 U/L; similar findings were also seen in other study indicating mild elevated in the level of ALT.[19]

In our study, the median level of ALP and total Bilirubin in moderate cases did not differ in moderate and severe cases (p=0.828) and (p=0.780) respectively. The gastro-intestinal manifestation of COVID-19 includes diarrhoea, vomiting.[20] Hence, the contribution of intestinal alkaline phosphatase may be responsible for the elevation of ALP in some cases. In our study, though we have revealed no statistical significance between moderate and severe disease ALP levels, they remained within the higher limits in both the groups. Even other studies did not reveal association of serum ALP levels with COVID-19 severity or association was observed in few patients with the severity of the disease.[19,21]

The main attributing factor in the co- existence of kidney function abnormalities in COVID-19 is suggested also by the ACE 2 receptor tropism of virus.[7] The kidney has abundant amount of these receptors and these receptors are down-regulated with increased age; hence the probability of KFT abnormalities increases with the age, as seen in COVID-19 cases. ACE 2 receptor is mainly expressed in proximal tubules and glomerulus.[22] When the virus attaches to the ACE 2 receptor present in the kidney, it brings about conformational changes in the glomerulus and starts manifesting as proteinuria. Rapid deterioration was seen COVID-19 leading to biochemical parameters abnormalities and high values of KFT corresponds to the severe disease. Our study findings are contrary to other studies which showed high creatinine levels in COVID-19 patients however in our study we have analysed serum urea found to be associated with the severity of the COVID-19.[23]

Apart from the presence of ACE 2 receptor on the various body organs and their subsequent manifestation in COVID-19,there is gender wise difference in the down regulation and decreased expression of the ACE 2 receptor in males than females, probably that is the reason, why females have less severe disease than males as the ACE 2 has protective role and presence of estrogen up regulates ACE 2 expression.[24,25] The reason behind the more expression of ACE 2 receptor in females is postulated in some of the studies as X chromosome inactivation. The ACE 2 gene is located on small arm of 22nd X chromosome. Since females have 2 X chromosomes and ACE 2 receptor by unknown mechanism escapes the inactivation of another X chromosome and results in the high expression of ACE 2 receptors which have protective roles in COVID-19.[24]

C-reactive Protein (CRP) is an acute phase reactant mainly synthesized by liver. It is marker of systemic inflammation with raised values seen from infections, autoimmune disorders to neoplastic diseases.[26] Its high sensitivity assay can even detect low level of inflammation. High sensitivity C reactive Protein (hs-CRP) is one of the early markers of inflammation. It is from long time used as marker for cardio vascular risk apart from use in sepsis and prognosis marker in admitted patients.[27] The available literature also showed that same properties of Hs-CRP can be used in COVID-19 patients. In our study, Hs-CRP levels did not significantly differed in moderate and severe cases. However, A study by Li Q also demonstrated the role of Hs-CRP in COVID-19 patient and their use for early triage but, this study was combined with Eosinophil (Eo), leucocyte count and Hs-CRP together forming nearly 67% of sensitivity and 78.2% specificity in suggesting the severity of the infection.[28] Another study by Chen W et al described higher odds ratio in Severe disease when compared to the moderate disease in patients with high levels of hsCRP.[29]

Lactate dehydrogenase (LDH) is a marker of tissue injury. It is distributed in all the tissues and required in many metabolic reactions of the body. LDH is present in 5 isoforms namely LDH-1 to LDH-5.The conversion of pyruvate to lactate and regeneration of NAD+ from Nicotinamide Adenine Dinucleotide (NADH) require LDH.[30] High levels are seen in Megaloblastic anaemia, haemolytic anaemia, infections, liver diseases, autoimmune disorders, Human Immune Deficiency Virus (HIV).[31] Its use in patients admitted in critical care unit is also well correlated with severity. Though LDH sources could be multifactorial, its use in ICU and emergency admitted patients can predict the severity and as well serve as prognostic marker. In our study, COVID-19 patients also

showed raised LDH in correlation with the severity of the disease. In our findings significant difference was observed among LDH values in moderate and severe patients. Our findings are consistent with another study by Wu M et al which also showed usefulness of LDH in in evaluating clinical severity and therapeutic monitoring purpose.[32] Another study by Poggiali E. et al related both Hs-CRP and LDH with respiratory failure which is the main consequence of acute respiratory distress syndrome (ARDS) in causing death among COVID-19 patients.[33]

The role of cytokine mediated storm and subsequent multi organ failure is mainly mediated by IL-6 along with IL-1β, TNF-α.[34] This cytokine storm is mediated by NF-kβ which brings the increased capillary permeability, capillary leakage, development of ARDS along with septic shock, hypotension ultimately leading to multi organ failure and death.

In our study, 77 patients were hypertensive with twenty-seven being on ACE inhibitors and Angiotensin Receptor Blockers (ARB), their baseline liver enzymes, urea and creatinine would have been higher and hence could be the confounding bias in our study. Moreover 160 participants were known Diabetic and on medical management. Anti-diabetic medication also causes increase in liver enzymes. Out of participants, 33 patients were of Coronary artery disease and on anti-platelets and lipid lowering drugs like statins. Since the participants were already on treatment on the day of admission, they could act as possible confounding bias in our study. Since LDH measured do not distinguish the source, the source specific values are unknown. The Hs-CRP is a systemic marker of inflammation. The role of inflammation in atherosclerosis formation is well known phenomenon. Our patient may have underlining atherosclerosis and high Hs-CRP values pertaining to it, which may have higher baseline Hs-CRP levels and same is with LDH, which is commonly seen in Megaloblastic anaemia with high prevalence in India. Hence the LDH values would be high from baseline. Apart from the above mentioned confounding bias alcohol intake and smoking in the subjects may give high liver enzymes values. Since patients RT PCR results are from different diagnostic centres on admission, the cycle threshold (CT) values of RT PCR were not known and could not be compared with the clinical severity in our study. The strength of our study is since the investigations were done on admission, we can use them markers of severity, segregate patients for appropriate management and judicious use of hospital resources.

5. Conclusion

1. The serum biomarkers i.e. Urea and LDH could serve as a potential biomarkers to differentiate between moderate and severe COVID-19 infection.
2. Increase in the serum Urea and LDH might be able to give us an outlook on ongoing or impending cytokine storm which may lead to COVID-19 patients having a poor outcome.
3. The early segregation into moderate and severe disease may not only reduce the mortality but also shorten the hospital stay. To conclude, the variation in the Biochemical parameters (Serum Urea and LDH) is associated with the severity of COVID-19 infection.

6. Conflicts of Interests

The authors have no financial interests or conflicts of interests.

7. Source of Funding

None.

8. Acknowledgement

Dr. Charanjeet Kaur, Head of Department of Biochemistry, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi for her guidance during the project work.

References

1. Liu Y, Kuo R, Shih S. COVID-19: The first documented coronavirus pandemic in history. *Biomed J*. 2020;43(4):328–33.
2. WHO Coronavirus Disease (COVID-19) Dashboard. [Accessed 10 OCT 2020]. Available from: https://covid19.who.int/?gclid=Cj0KCQjwvb75BRD1ARIsAP6Lcqt0BnJkM3a4_1KG_gsEJHw9PGnawXYM-EAp4wocI855fRt6lIP_QwaAvyNEALw_wcB.2020.
3. Polat V, Bostanci GI. Sudden death due to acute pulmonary embolism in a young women with COVID-19. *J Thromb Thrombolysis*;2020:1–3.
4. Ronco C, Navalesip, Vincent J. Coronavirus epidemic: preparing for extracorporeal organ support in intensive care. *Lancet Respir Med*. 2020;8(3):240–1. doi:10.1016/S2213-2600(20)30060-6.
5. Kermali M, Khalsa RK, Pillai K, Ismail Z, Harky A. The role of biomarkers in diagnosis of COVID-19 - A systematic review. *Life Sci*. 2020;254:117788. doi:10.1016/j.lfs.2020.117788.
6. Albini A, Guardo GD, Noonan DM, Lombardo M. The SARS-CoV-2 receptor, ACE-2, is expressed on many different cell types: implications for ACE-inhibitor- and angiotensin II receptor blocker-based cardiovascular therapies. *Intern Emerg Med*. 2020;15(5):759–66.
7. Li M, Li L, Zhang Y, Wang X. Expression of the SARS-CoV-2 cell receptor gene ACE2 in a wide variety of human tissues. *Infect Dis Poverty*. 2020;9(1):45. doi:10.1186/s40249-020-00662-x.
8. Tang Y, Liu J, Zhang D, Xu Z, Ji J, Wen C, et al. Cytokine Storm in COVID-19: The Current Evidence and Treatment Strategies. *Front Immunol*. 2020;11:1708. doi:10.3389/fimmu.2020.01708.
9. Clinical Management Of COVID-19. World health organization. [Accessed 11 August 2020]. Available from: https://www.who.int/publications/i/item/clinical-management-of-covid-19>2020.
10. Kumar P, Sharma M, Kulkarni A, Rao PN. Pathogenesis of Liver Injury in Coronavirus Disease. *J Clin Exp Hepatol*. 2020;10(6):641–2. doi:10.1016/j.jceh.2020.05.006.
11. Alqahtani SA, Schattenbergjm. Liver injury in COVID-19: The current evidence. United. *United European Gastroenterol J*. 2020;8(5):509–19. doi:10.1177/2050640620924157.
12. Kerner A, Avizohar O, Sella R, Bartha P, Zinder O, Markiewicz W, et al. Association Between Elevated Liver Enzymes and C-Reactive Protein: Possible Hepatic Contribution to Systemic

Inflammation in the Metabolic Syndrome. *ATVB*. 2005;25(1):193–7. doi:10.1161/01.ATV.0000148324.63685.6a.
13. Panteghini M. Aspartate aminotransferase isoenzymes. *Clin Biochem*. 1990;23(4):311–19.
14. Babapoor-Farrokhran S, Gill D, Walker J, Rasekhi R, Bozorgnia B, Amanullah A, et al. Myocardial injury and COVID-19: Possible mechanisms. *Life Sci*. 2020;253:117723. doi:10.1016/j.lfs.2020.117723.
15. Bompard F, Monnier H, Saab I, Tordjman M, Abdoul H, Fournier L, et al. Pulmonary embolism in patients with Covid-19 pneumonia. *Eur Respir J*. 2020;56(1):2001365. doi:10.1183/13993003.01365-2020.
16. Mcfadyen J, Stevens H, Peter K. The Emerging Threat of (Micro)Thrombosis in COVID-19 and Its Therapeutic Implications. *Circ Res*. 2020;127(4):571–87. doi:10.1161/CIRCRESAHA.120.317447.
17. Wang Q, Zhao H, Liu L, Wang Y, Zhang T, Li M, et al. Pattern of liver injury in adult patients with COVID-19: a retrospective analysis of 105 patients. *Military Med Res*. 2020;7(1):28. doi:10.1186/s40779-020-00256-6.
18. Ruhl CE, Everhart JE. Diurnal variation in serum alanine aminotransferase activity in the US population. *J Clin Gastroenterol*. 2013;47(2):165–73.
19. Fan Z, Chen L, Li J, Cheng X, Yang J, Tian C, et al. Clinical Features of COVID-19-related Liver Functional Abnormality. *Clin Gastroenterol Hepatol*. 2020;18(7):1561–66.
20. Cha MH, Regueiro M, Sandhu DS. Gastrointestinal and hepatic manifestations of COVID-19: A comprehensive review. *World J Gastroenterol*. 2019;26(19):2323–32. doi:10.3748/wjg.v26.i19.2323.
21. Qian ZP, Mei X, Zhang YY, Zou Y, Zhang ZG, Zhu H, et al. Analysis of baseline liver biochemical parameters in 324 cases with novel coronavirus pneumonia in Shanghai area. *Zhonghua Gan Zang Bing Za Zhi*. 2020;28(3):229–33. doi:10.3760/cma.j.cn501113-20200229-00076.
22. Tikellis C, Johnston CI, Forbes JM, Burns WC, Burrell LM, Risvanis J, et al. Characterization of renal angiotensin-converting enzyme 2 in diabetic nephropathy. *Hypertension*. 2003;41(3):392–7.
23. Pei G, Zhang Z, Peng J, Liu L, Zhang C, Yu C, et al. Renal Involvement and Early Prognosis in Patients with COVID-19 Pneumonia. *J Am Soc Nephrol*. 2020;31(6):1157–65.
24. Gagliardi MC, Tieri P, Ortona E, Ruggieri A. ACE2 expression and sex disparity in COVID-19. *Cell Death Discov*. 2020;6:37. doi:10.1038/s41420-020-0276-1.
25. Bukowska A, Spiller L, Wolke C, Lendeckel U, Weinert S, Hoffmann J, et al. Protective regulation of the ACE2/ACE gene expression by estrogen in human atrial tissue from elderly men. *Exp Biol Med*. 2017;242(14):1412–23.
26. Nehring SM, Goyal A, Bansal P. C Reactive Protein. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020. Available from: StatPearls[Internet].TreasureIsland(FL): StatPearlsPublishing.
27. Wang HE, Shapiro NI, Safford MM, Griffin R, Judd S, Rodgers J, et al. High-sensitivity C-reactive protein and risk of sepsis. *PLoS One*. 2013;8(7):69232. doi:10.1371/journal.pone.0069232.
28. Li Q, Ding X, Xia G, Chen H, Chen F, Geng Z, et al. Eosinopenia and elevated C-reactive protein facilitate triage of COVID-19 patients in fever clinic: A retrospective case-control study. *EClinicalMedicine*. 2020;23:100375. doi:10.1016/j.eclinm.2020.100375.
29. Chen W, Zheng K, Liu S, Yan Z, Xu C, Qiao Z, et al. Plasma CRP level is positively associated with the severity of COVID-19. *Ann Clin Microbiol Antimicrob*. 2020;19(1):18. doi:10.1186/s12941-020-00362-2.
30. Fan J, Hitosugi T, Chung TW, Xie J, Ge Q, Gu T, et al. Tyrosine phosphorylation of lactate dehydrogenase A is important for NADH/NAD(+) redox homeostasis in cancer cells. *Mol Cell Biol*. 2011;31(24):4938–50.
31. Farhana A, Lappin SL. Biochemistry, Lactate Dehydrogenase. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020. [Updated 2020 May 17]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557536/.
32. Wu M, Yao L, Wang Y, Zhu X, Wangx, Tang P, et al. Clinical evaluation of potential usefulness of serum lactate dehydrogenase (LDH) in 2019 novel coronavirus (COVID-19) pneumonia. *Respir Res*. 2020;21(1):171. doi:10.1186/s12931-020-01427-8.
33. Poggiali E, Zaino D, Immovilli P, Rovero L, Losi G, Dacrema A, et al. Lactate dehydrogenase and C-reactive protein as predictors of respiratory failure in CoVID-19 patients. *Clin Chim Acta*. 2020;509:135–8. doi:10.1016/j.cca.2020.06.012.
34. Ragab D, Eldin HS, Taeimah M, Khattab R, Salem R. The COVID-19 Cytokine Storm; What We Know So Far. *Front Immunol*. 2020;11:1446. doi:10.3389/fimmu.2020.01446.

Author biography

Anita Rani, Director Professor https://orcid.org/0000-0002-8059-3998

Rohit Kumar, Assistant Professor

Omkar Kalidasro Choudhari, Senior Resident

Paarth Bhatia, Student

Cite this article: Rani A, Kumar R, Choudhari OK, Bhatia P. Biochemical and Clinical profile of COVID-19 patients and its association with severity of the disease: A study at tertiary care centre. *Panacea J Med Sci* 2023;13(2):262-268.