Biochemical Parameters in Confirmed Covid-19 Patients: A Hospital Based Study from Eastern Nepal

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ABSTRACT

Background

COVID-19 has posed a global threat to almost every part of the world. The disease has varied form of presentation and the modern medicine has still not been able to provide definite treatment for the disease.

Objective

To assess the biochemical parameters in confirmed patients of COVID-19 admitted at B.P. Koirala Institute of Health Sciences (BPKIHS), Dharan, Nepal.

Method

This is a retrospective hospital based cross-sectional study conducted in the Department of Biochemistry, B.P. Koirala Institute of Health Sciences, Dharan from October to December, 2020. Convenient sampling technique was used to enroll the data of the patients for whom the biochemical parameters were requested by the clinicians. Routine biochemical tests were performed in Cobas c311 autoanalyzer.

Result

A total of 202 patients with confirmed COVID-19 infections and admitted at COVID Hospital, BPKIHS were enrolled. The findings depict an elevated liver enzyme (alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma glutamyl transpeptidase and cardiac enzymes (creatine kinase-total and creatine kinase- MB) in the study population. Increased serum ferritin (1026.08±220.53), hs CRP (41.52±5.22) and lactate dehydrogenase 360 [303.50-526.75] was found in the patients. Also, majority of the patients (> 50%) had abnormal biochemical findings.

Conclusion

Biomarkers like C-reactive protein, lactate dehydrogenase and ferritin have shown significant clinical implications in effective management, monitoring, and assessment of the severity of disease in COVID- 19 patients. Simple and cost-effective markers like CRP, LDH, HbA1c could be used for monitoring the severity of COVID-19 infection.

KEY WORDS

Biomarkers, COVID-19, Ferritin, hs-CRP, Inflammation

INTRODUCTION

Coronavirus Disease 2019 (COVID-19) is a contagious viral illness caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).[1] It has been reported to be severe than Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV) which has already been introduced to humans in the past.[1-3] Disease encompasses wide range of mild to severe clinical features which comprises of mild symptoms like dry cough, fever, sore throat, nasal congestion, and muscle pain to features of severe pneumonia such as dyspnoea, respiratory frequency ≥ 30 breaths per minute and blood oxygen saturation ≤ 93%.[4-7] Consequently, critical COVID-19 is characterized by respiratory failure, septic shock, and/or multiple organ failure respectively.[8,9]

Evidence suggests the use of numerous inflammatory markers that has been shown to be useful in monitoring the disease in COVID-19. Biomarkers like C-reactive protein (CRP), Lactate Dehydrogenase (LDH), D-dimer, ferritin could possibly be used as the markers of hyperinflammation and cytokine storm which is prevalent in COVID-19 patients.[10-12] The abnormal levels of biomarkers have been implicated in severe COVID-19 signifying severe inflammation and thrombosis that may be associated with the disease. Additionally, these markers are also the predictor for increased risk for admission in the Intensive Care Unit (ICU), invasive ventilatory support, and death.[13]

Here, we report the retrospective analysis of the biochemical parameters of the COVID-19 infected patients admitted in the COVID hospital at B.P. Koirala Institute of Health Sciences, Dharan, Nepal.

METHODS

This is a hospital based retrospective cross-sectional study conducted in the Department of Biochemistry at B.P. Koirala Institute of Health Sciences (BPKIHS) for a period of 3 months (from October, 2020 to December 2020). COVID-19 hospital at BPKIHS is a 100-bedded tertiary care hospital located within the premises of BPKIHS with its own laboratory comprised of biochemistry, hematology and microbiology. The data were retrieved from the record book from Department of Biochemistry after receiving ethical clearance from Institutional Review Committee.

Convenient sampling was used to record all the data of the confirmed COVID-19 patients. Based on a cross-sectional study done in India by Agarwal et al. the proportion of symptomatic patients with COVID-19 was 16.67%.[14]

Taking this in account, the sample size is calculated as:

$n=z^2pq/d^2$

Where, z=1.96

p=16.67

q= (1-p) = 83.33

d (Permissible error) = 10% of p= 1.667

Hence,

$n= 1.96X19.6X16.67X83.33/(1.667)^2$

n= 1920

Based on our laboratory records till date, laboratory investigations of total of 181 patients diagnosed of COVID-19 have been done.

Hence, for the finite sample size, calculation is done as follows:

n= Sample Size/ 1+ (Sample size -1)/Population

n= 1920/1 + (1920-1)/200

n= 181.25

During the study period, we took the data of 202 patients infected with COVID-19 and admitted in the COVID hospital- BPKIHS who had undergone the biochemical investigations. All the patients were confirmed cases of COVID-19 diagnosed by RT-PCR and admitted in the COVID hospital, BPKIHS.

Blood samples of the patients sent for various biochemical investigations were recorded for the study. Routine biochemical investigations were performed in Cobas c311 autoanalyzer (Roche Diagnostics) in Department of Biochemistry.

Data were entered in Microsoft Excel™ and statistical analysis was done using Statistical Package for the Social Sciences (SPSS) version 22.0. Descriptive statistics were presented as mean, median and IQR, and percentages for continuous data and categorical data. P value < 0.05 was considered to be statistically significant.

RESULTS

The findings from our study illustrates that the mean age of the patients infected with COVID-19 and admitted at our hospital was 44.84 ± 15.26 years with the majority of the patients being male as depicted in table 1.

Table 1. Demographic Profile of the study population (n=202)

Variables	Values
Age	44.84 ± 15.26
Gender	
Male	127 (n=65%)
Female	75 (n= 35%)

Biochemical parameters revealed elevated liver enzymes (ALT, AST, ALP, GGT) and cardiac enzymes (CK-NAC and CK-MB) in the study population. Also, we also found raised ferritin, LDH, hs-CRP and glycated hemoglobin in these patients respectively as shown in table 2.

Table 2. **Biochemical parameters in the study population**

Parameters	Values
Glucose	119.50 (99.00, 178.50)
Urea	36.50 (23.00, 79.00)
Creatinine	1.00 (0.70, 1.50)
Total Protein	7.36 ± 1.10
Albumin	3.85 ± 0.87
Total Bilirubin	0.60 (0.40, 0.90)
Conjugated Bilirubin	0.20 (0.10, 0.30)
Alanine Aminotransferase	42.00 (24.50, 77.00)
Aspartate Aminotransferase	39.00 (20.50, 73.50)
Alkaline Phosphatase	109.00 (73.00. 145.50)
Gamma Glutamyl Transferase	120.66 ± 36.05
CK-NAC (n=25)	293.40 ± 39.90
CK-MB (n=25)	81.00 (40.25, 122.00)
Qualitative Troponin I (n=14)	
Positive	2
Negative	12
Ferritin (n= 45)	1026.08 ± 220.53
Hs CRP (n=5)	41.52 ± 5.22
Lactate Dehydrogenase (n=165)	360.00 (303.50, 526.75)
Uric Acid	12.60 ± 1.66
Calcium	9.46 ± 0.50
Phosphate	6.42 ± 1.27
Amylase	100.50 (56.50, 165.25)
Lipase	89.00 (29.00, 139.00)
Glycated Hemoglobin (n=20)	8.30 ± 1.73
Sodium	139.68 ± 6.08
Potassium	4.61 ± 1.27

Table 3. **Proportion of patients with abnormal biochemical parameters in the study population**

Variables	No. of Patients	Cut-off value	Proportion of the patients (%)
Glucose	(n=202)	> 200 mg/dl	36
Urea	(n=202)	> 40 mg/dl	47
Creatinine	(n=202)	> 1.5 mg/dl	28
Albumin	(n=202)	< 3.5 mg/dl	27
ALT	(n=202)	> 35 U/L	67
AST	(n=202)	> 37 U/L	63
ALP	(n=202)	> 105 U/L	84
GGT	(n=25)	> 40 U/L	78.2
Ferritin	(n= 65)	M > 400 µg/dl	14
	(n=35)	F > 150 µg/dl	9
CK-NAC	(n=25)	> 200 U/L	25
CK-MB	(n=25)	> 25 U/L	20
LDH	(n=165)	> 250 U/L	20
HbA1C	(n=20)	> 6.5%	25

We further divided the patients with high values of the biochemical parameters in the patients and found that majority of the patients had abnormal biochemical findings prevalent in more than 50% of the study population as represented in table 3.

DISCUSSION

Current scenario of this global pandemic due to COVID-19 is challenging for almost all of the areas majorly affecting the health-care and laboratory professionals.[6] It has not only challenged the competencies of the health care professionals but also widen the area for the laboratory in terms of importance of biomarkers in identification and risk stratification in COVID-19 patients.[15,16] We conducted this study to retrospectively assess the biochemical abnormalities in patients infected with COVID-19 at BPKIHS, the largest tertiary care center of eastern Nepal.

Our study findings report the mean age of the patients with COVID-19 admitted in our hospital was 44.84±15.26 years with the majority of the patients being males (65%). This was similar to the study reported by Singh et al. from India.[13] In contrast, our age group was slightly younger compared to the Chinese study published by Chen et al. who had reported the mean age of 55.5±13.1 year with the majority of patients being males (68%) and study reported from Belgium by Khourssaji et al. (mean age = 59.5) respectively.[7,17] There has been variability in age distribution in COVID-19 across the countries and geographical regions. Our study reports the similar mean age group in patients infected with COVID-19 to that of India but younger than the other countries.[13] It has been reported that severe COVID-19 is more prevalent in older age groups due to number of factors such as presence of co-morbidities like Diabetes Mellitus, Hypertension and other cardiovascular diseases.[6,18] Also, studies have reported significantly higher mortality in older patients.[18,19]

We observed that there was changes in baseline biochemical parameters which includes the glucose, urea, creatinine, electrolytes which was in accordance with the study reported by Singh et al., Khourssaji et al. and Kantri et al. respectively.[13,17,20] We also evaluated the liver enzymes i.e. ALT, AST, GGT and ALP in the patients and found that more than 60% of the patients had raised ALT and AST. Similarly, approximately 80% of the patients had abnormal ALP and GGT values. This clearly indicates the liver injury ongoing in patients with COVID-19. Evidence suggests that the biomarkers used for the assessment of liver function could be used as a prognostic marker in patients with COVID-19.[4,21,22]

The most commonly used marker which is also considered a specific marker of liver disease is LDH which has been considered as an indicator of lung injury as well.[22] Our study finding depicts increased LDH levels in patients with COVID-19 similar to the findings reported by Chen et al.

and Khourssaji et al.[7,17] Scientists suggest that a raised LDH level illustrates two consecutive events, i.e., direct lung damage and a more widespread tissue injury.[22,23]

Another important finding from our study was increased ferritin level in the study patients similar to the reports published from various part of the world.[17,20,24,25] Though, we did not have more data for serum ferritin, but the values from available data suggest that there is an increased ferritin level in patients with COVID-19 in our population as well. Researchers have delineated that raised ferritin level can be seen in bacterial and/or viral infections, hemochromatosis, and long-term transfusion. Also, an increased ferritin during infection has been postulated to the release of iron in the reticuloendothelial system, the decrease of the ability of transporting ferritin in the liver and spleen, and increased synthesis and release of intracellular ferritin.[25,26] Though, an increased ferritin level is commonly seen in bacterial than viral infection, but in COVID-19 raised ferritin levels might indicate severe secondary bacterial infection and thus, used as a marker for poor prognosis. Furthermore, higher serum ferritin level is associated with ARDS, mortality, and severe COVID-19. This may lead to the concept of the presence of secondary hemophagocytic lymphohistiocytosis (sHLH) in COVID-19.[25,26] We also report increased levels of hs-CRP in patients with COVID-19. Though, the number of hs-CRP values were few in number, but the values are significantly higher in these patients (> 40 ng/ml). CRP is an acute phase reactant synthesized by hepatocytes in response to inflammation.[27-29] Increased levels of CRP are seen in bacterial infections compared to viral infections. An elevated CRP level has been reported in COVID-19 patients with higher values seen in severe patients compared to non- severe ones. CRP can be used as biomarker for disease progression and severity in COVID-19 patients.[27-29] A recent study has depicted that CRP is significantly associated with disease progression, ROC analysis and a KM curve confirmed that CRP is a valuable predictor of disease progression in non- severe COVID-19 patients.[27] In addition, the literature suggests that COVID-19 patients with high levels of CRP should be adequately monitored and treated even though their respiratory function indicators do not meet the criteria for severe cases.[27]

CONCLUSION

This retrospective analysis of the biochemical parameters in patients infected with COVID-19 depicts that there is a marked alteration in biochemical markers in patients with COVID-19 in Nepalese population. The panel of biochemical markers could be effectively used as a predictor of disease prognosis and monitoring of the severity in hospitalized and critically ill patients. Also, the effective use of other laboratory parameters including hematological and serological parameters could be more beneficial for the clinicians on duty for the segregation of critically ill and non-critical patients infected with COVID-19 for the treatment.

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