Study on Status of Serum Biochemical and Hematological Parameters in COVID-19 Positive Patients Attending a Tertiary Care Hospital

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ABSTRACT

Background

Coronavirus disease 2019 (COVID-19) presents clinically a variety of pathological and clinical organ dysfunctions, ranging in severity from asymptomatic to fatal. The care and monitoring of COVID-19 patients may benefit from the use of biochemical and hematological markers.

Objective

To observe the alteration of serum biochemical and hematological parameters in COVID-19 positive patients, attending a Tertiary Care Hospital.

Method

A descriptive cross-sectional study was conducted on all COVID-19 positive patients attending Nobel Medical College Teaching Hospital, Biratnagar, Nepal from 15th December 2021 to 15th February 2022. The test results of different serum biochemical and hematological parameters done for these patients were recorded in clinical laboratory services and obtained retrospectively for the analysis. The data were entered in MS excel and analyzed by SPSS version 20.

Result

Out of 1537 COVID-11699 declared positive patients, 712 (46.32%) were male and 825 (53.68%) female. Mean age of COVID positive patients was 40.03±20.08 years. The level of serum SGOT, SGPT, ALP and GGT was significantly elevated in 39.9%, 42.8%, 32.3% and 47.2% of COVID positive patients respectively. Blood Urea, creatinine, uric acid and sugar level were significantly elevated in 63%, 56.1%, 33.1% and 47.6% patients respectively. The serum level of LDH, D-dimer, CRP and procalcitonin (PCT) were significantly increased in 52.1%, 75.9%, 71.6% and 61.2% of patients respectively. The serum value of total cholesterol, triglyceride, HDL and LDL were significantly lowered in 52.2%, 43.8%, 70.1% and 60.3% of patients respectively. RBC concentration and level of hemoglobin was reduced in 56.6% and 53.6% of COVID positive patients respectively whereas total leukocyte count was elevated in 80.7% with increase in neutrophil in 87.9% and decrease in lymphocyte in 79.4%.

Conclusion

A portion of COVID-19 positive patients showed drastically altered test results for various serum biochemical and hematological markers, although many of them had normal findings.

KEY WORDS

Biochemical markers, COVID-19, Tertiary hospital

INTRODUCTION

Coronaviruses are enclosed in envelop, non-segmented, positive-sense RNA viruses that are widely present in both humans and other mammals. They are members of the family Coronaviridae and the order Nidovirales.[1] Coronavirus disease 2019 (COVID-19) is an infectious and pandemic illness brought on by coronavirus 2 that causes severe acute respiratory syndrome (SARS-CoV-2).[2,3] The illness is still making its way around the globe. Most SARS-CoV-2 patients exhibit mild sickness and usual symptoms including fever, coughing, and exhaustion and will recover without additional medical attention. However, the likelihood of developing severe illnesses is higher among the elderly and in persons with long-term medical disorders like cancer, diabetes, heart disease, or lung disease.[4,5]

Reports are available on the findings stating alterations of biochemical parameters in COVID-19 positive patients. Several biochemical and hematological parameters like SGOT, SGPT, ALP, Urea, creatinine, CRP, D-dimer, LDH, Procalcitonin, sugar, lipid profile, Hb, RBC, TLC, DLC and platelet are found to be altered in the serum of many COVID-19 positive patients.[6-10] The assessment of changes in the most prevalent biochemical markers that are reported in COVID-19 patients has not yet been fully established, despite the fact that the clinical aspects of COVID-19 have been extensively described.

Therefore, the aim of the present study is to evaluate and analyze the findings of different biochemical and hematological parameters in the sera of COVID-19 positive patients at a tertiary care hospital in the scenario of our present setup.

METHODS

This was a descriptive cross-sectional study carried out at a tertiary care Hospital, Nobel Medical College Teaching Hospital (NMCTH) from 15th December 2021 to 15th February 2022 after getting the approval from institutional review committee, NMCTH. All the patients, who were declared RT-PCR COVID-19 positive from PCR laboratory (NMCTH) and presented themselves at emergency or admitted in the wards, were enrolled in the study. The data for demographics of these patients were obtained from medical record department. The results for different biochemical, serological and hematological parameters from the blood sample of these patients were recorded in the clinical laboratory services, NMCTH and hence acquired. Convenient sampling technique was used to collect the data.

The sample size was calculated as 196 by using the formula $N=Z^2pq/d^2$ [where n= minimum required sample size, Z= 1.96 at 95% Confidence Interval (CI), p= prevalence taken as 50% for maximum sample size, q= 1-p, d= margin of error, 7%]. However we have considered more than 196 COVID positive samples for the analysis of different biochemical and hematological parameters according to the availability of the reports in the records of laboratory.

For the detection of coronavirus, E gene, N gene and ORF1a/b gene were targeted. Template was extracted using automatic extraction method (ZK-96 automatic nucleic acid extraction and purification instrument). The entire extracted template was amplified by Taq Man assay on Quant Studio 5 (Thermofisher) instrument in the PCR laboratory, NMCTH. The tests for all the biochemical parameters were done by the sera of the patients in fully automated analyzer (Labsystems Diagnostics, Nano Lab 200) in clinical laboratory services, NMCTH. Similarly the serological parameters in the sera of these COVID positive patients were assayed in the analyzer Hurricane (HP-083/4-II) based on the principle of nephlometry. Hematological parameters in the whole blood of these COVID positive patients were tested in the analyzer named Accurex (CBC Fully Analyzer 3 parts)

The results for the liver function test (Bilirubin, SGOT, SGPT, ALP, Total protein and Albumin) of 278 COVID-19 positive patients were available in the records of laboratory and therefore we have taken those data for analysis. Similarly, random blood sugar level and renal function test (Urea, Creatinine, electrolytes) done for 451 COVID-19 positive patients were obtained and analyzed. The results of lipid profile (Total Cholesterol, Triglyceride, HDL) performed on 224 positive patients in the laboratory were also analyzed. In the same way, the level of LDH, D-dimer, CRP and Procalcitonin were estimated in 394 COVID-19 positive patients. The data for these study parameters were also analyzed.

The data were entered in MS Excel and analyzed by SPSS 20 version. Point estimation of frequency, percentage, mean and standard deviation was done. Statistical significance was tested by one-sample t test. The data was considered as significant if $p < 0.05$ at 95% confidence interval.

RESULTS

Out of 8748 Samples received at PCR laboratory, NMCTH for RT-PCR COVID-19 test in the study period, 1537 (17.6%) samples were tested positive. Among 1537 COVID-19 positive patients, 712 (46.3%) were male and 825 (53.7%) were female. The mean age of the positive patients was 40.03±20.08 years. The maximum number 576 (37.5 %) of patients were in the age group 15-30 year. The maximum and minimum CT value during RT-PCR among the COVID positive samples were recorded as 33.75 and 11.32 respectively as shown in table 1.

We analyzed the result of liver function test (LFT) among 278 COVID positive cases according to the availability of the data in the clinical laboratory services. It was observed that the mean value of Total (3.6±1.4) and Direct (1.8±0.7)

Table 1. Demographic characteristics of COVID-19 positive patients (n=1537)

Characteristics	Number	Percentage
Male	712	46.3
Female	825	53.7
Mean age (years) ± SD	40.03±20.08	
Age in years		
< 15	68	4.4
15-30	576	37.5
31-50	453	29.5
51-70	267	17.4
> 70	173	11.2
CT value for RT-PCR in positive cases		
Maximum	33.75	
Minimum	11.32	

Bilirubin, SGOT (626.3±421.5), SGPT (739.9±517.4), ALP (389.7±171.6), GGT (132.4±51.7) in the serum of few COVID positive patients was significantly higher than the normal reference range. In the contrary, the mean values of Total protein (4.7±0.5) and Albumin (2.4±0.5) in the serum of few COVID positive patients were significantly decreased than the normal range. Many of COVID positive patients had normal findings in LFT as shown in table 2.

The results of renal function test (RFT) and level of random blood sugar among 451 COVID positive patients were also analyzed. The mean values of random blood sugar (228.7±62.4), urea (107.9±54.9), creatinine (3.4±1.8), Na+ (150.5±3.6), K+ (6.2±0.9), uric acid (8.5±1.2) were significantly increased than normal reference value in some of COVID positive patients, whereas the mean value of serum calcium (7.5±0.4) in few positive patients was significantly decreased. The finding of random blood sugar and RFT was quite normal in many of COVID positive patients as mentioned in table 3.

Similarly, we have analyzed the results of other biochemical parameters also according the data available in the records of laboratory. The mean level of LDH (1240.5±468.4) in the sera of few COVID patients was significantly higher than the normal reference range. The level of CRP (148.9±94.8), Pro-calcitonin (3.5±2.3) and D-dimer (5.8±3.3) were also found to be elevated significantly in some of COVID positive patients when compared with reference value as shown in table 4.

The mean values of total cholesterol (80.1±18.6), Triglyceride (90.3±11.3), HDL (24.9±6.7) and LDL (45.3±9.6) in the sera of some of COVID positive patients were significantly lower than the normal refrence range. Many of COVID positive had normal finding in lipid profile as shown in table 5.

Table 2. The findings of liver function test of COVID-19 positive patients (n=278)

Parameters	Normal finding		Abnormal Finding			
	N (%)	Mean	N (%)	Mean	Range	p-value
Total Bilirubin (mg/dl)	174 (62.5)	0.6±0.2	104 (37.4)	3.6±1.4	1.5-5.5	0.001
Direct Bilirubin (mg/dl)	183 (65.8)	0.2±0.08	95 (34.1)	1.8±0.7	0.7-3.2	0.001
SGOT (IU/L)	167 (60.0)	22.1±10.3	111 (39.9)	626.3±421.5	78-1575	<0.001
SGPT (IU/L)	159 (57.2)	27.1±6.6	119 (42.8)	739.9±517.4	89-1854	<0.001
ALP (IU/L)	188 (67.6)	168.3±112.7	90 (32.3)	389.7±171.6	312-756	0.002
Total Protein (g/dl)	156 (56.1)	7.1±0.7	122 (43.8)	4.7±0.5	4.0-5.5	0.001
Albumin (g/dl)	143 (51.4)	4.6±0.7	135 (48.6)	2.4±0.5	1.9-3.3	0.001
GGT (IU/L)	147 (52.8)	36.4±7.1	131 (47.2)	132.4±51.7	67-223	0.001

Table 3. The results of random blood sugar level and renal function test of COVID-19 positive patients (n=451)

Parameters	Normal finding		Abnormal Finding			
	N (%)	Mean	N (%)	Mean	Range	p-value
RBS (mg/dl)	237 (52.5)	93.8+17.4	214 (47.6)	228.7±62.4	112-327	<0.001
Urea (mg/dl)	167 (37.0)	29.0±13.1	284 (63.0)	107.9±54.9	52-207	0.002
Creatinine (mg/dl)	198 (43.9)	0.8±0.2	253 (56.1)	3.4±1.8	1.5-6.6	<0.001
Na (mmol/l)	221 (49.0)	137.9±4.2	230 (51.0)	150.5±3.6	146-157	0.003
K(mmol/l)	205 (45.6)	3.9±0.6	246 (54.5)	6.2±0.9	5.1-7.7	0.001
Uric acid (mg/dl)	302 (66.9)	5.01±1.07	149 (33.1)	8.5±1.2	7.2-9.8	0.02
Calcium	196 (43.4)	9.8±0.7	255 (56.6)	7.5±0.4	7.0-7.9	0.04

Table 4. The level of different proteins in sera of COVID-19 positive patients (n=394)

Parameters	Normal finding		Abnormal Finding			
	N (%)	Mean	N (%)	Mean	Range	p-value
LDH (IU/L)	189 (47.9)	265.3±94.6	205 (52.1)	1240.5±468.4	543-1938	<0.001
D-Dimer (µg/ml)	95 (24.1)	0.05±0.01	299 (75.9)	5.8±3.3	1.4-14.45	<0.001
CRP (mg/dl)	112 (28.4)	1.9±1.7	282 (71.6)	148.9±94.8	7.5-307	<0.001
Procalcitonin (ng/ml)	153 (38.8)	0.06±0.02	241 (61.2)	3.5±2.3	0.8-10.6	<0.001

Table 5. The findings of lipid profile of COVID-19 positive patients (n=224)

Parameters	Normal finding		Abnormal Finding			
	N (%)	Mean	N (%)	Mean	Range	p-value
Total Cholesterol (mg/dl)	107 (47.8)	183.1±19.4	117 (52.2)	80.1±18.6	49-105	0.001
Triglyceride (mg/dl)	126 (56.2)	108.6±30.3	98 (43.8)	90.3±11.3	72-107	0.004
HDL (mg/dl)	67 (29.9)	46.6±5.9	157 (70.1)	24.9±6.7	14-34	0.048
LDL (mg/dl)	89 (39.7)	105.0±14.7	135 (60.3)	45.3±9.6	30-62	0.002

Table 6. The findings of Hematological parameters of COVID-19 positive patients (n=263)

Parameters	Normal finding		Lower Finding		Higher Finding	
	N (%)	Mean	N (%)	Mean	N (%)	Mean
Hb (g/dl)	103 (39.1)	13.1±1.7	149 (56.6)	8.4±1.8	11(4.3)	17.8±1.4
RBC (millions cells/µl)	113 (43.0)	6.4±0.87	141 (53.6)	3.9±0.68	9 (3.4)	7.7±1.2
Platelet (cells/µl)	182 (69.3)	2,87,000±69000	53 (20.1)	95000±23000	28 (10.6)	4,96,000±34000
MCV (fL)	104 (39.5)	88.7±8.1	151(57.4)	76.4±7.9	8 (3.1)	107±5.2
MCH (pg/cell)	106 (40.3)	29.7±2.8	148 (56.3)	25.7±2.6	9 (3.4)	35.3±2.4
MCHC (g/dl)	115 (43.7)	34.3±2.2	143 (54.4)	29.9±3.4	5 (1.9)	39.7±2.8
TLC (cells/µl)	44 (16.7)	8300±1900	7 (2.6)	2750±876	212 (80.7)	19600±8779
Neutrophil (%)	32 (12.1)	57.3±14.5	0	-	231(87.9)	87.6±14.7
Lymphocyte (%)	54 (20.6)	33.6±6.2	209 (79.4)	14.3±5.4	0	-
Monocyte (%)	65 (24.7)	4.7±1.2	194 (73.8)	2.3±0.7	4 (1.5)	13.3±1.4
Eosinophil (%)	74 (28.1)	2.9±1.0	186 (70.8)	1.7±0.6	3 (1.1)	10.4±1.6
Basophil (%)	112 (42.6)	1.0±0.0	150 (57.1)	0.4±0.5	1 (0.3)	1

The value of hematological parameters was also found to be differed in many of COVID positive patients. The mean value of Hb (8.4±1.8), RBC (3.9±0.68), Platelet (95000±23000), MCV (76.4±7.9), MCH (25.7±2.6) and MCHC (29.9±3.4) was reduced than the normal reference range in many COVID positive patients, whereas the mean value of TLC (19600±8779) was observed to be higher many positive patients. Similarly, differential leukocyte count were also found to be altered, however remaining of the patients had normal findings too. The results of all the hematological parameters are depicted in table 6.

DISCUSSION

The total number of sample received in PCR laboratory NMCTH for RT-PCR COVID 19 test in the study period was 8748. Out of that, 1537 (17.6%) were declared positive. Among 1537 COVID positive patients, 712 (46.32%) were male and 825 (53.68%) were female. Mean age of COVID positive patients was 40.03±20.08 years. We had extended our study by analyzing the number of COVID positive patients in the different age groups and it was observed that the maximum number of positive patients were 576 which belonged to the age group 15-30. A study conducted on 200 COVID positive patients in the period of three months (May-July 2020) in the neighboring country India (Lucknow) reported that among those positive patients, 73.5% were male and 26.5% were female and the maximum number (60%) of patients were in the age group 36-50.[10] The findings of the study conducted in Lucknow is quite different from the current study in terms of number of male, female and maximum number in the age groups of COVID positive patients. Another study carried out in BPKIHS (Dharan, Nepal) in 202 COVID-19 positive patients, showed 65% disease occupancy by male and 35% by female with mean age of patient's 44.84±15.26 years.[11] Based on the data released by the Ministry of Health and Population, Government of Nepal, Dhimal et al. reported in a study that the total number of COVID-19 positive patients between January to November 2020 in Nepal was 233452

with 65.6% male and 34.4% female and the maximum number of positive patients in the age group 25-29.[12]

While analyzing the different biochemical parameters in the sera of these COVID positive patients, we noticed remarkable and significant alterations in their values, however many of them had normal findings also. We analyzed LFT, blood sugar, RFT, lipid profile and other biomarkers. Analyzing LFT in 278 COVID patients, we revealed that total and direct bilirubin were significantly higher in 37.4% and 34.1% respectively of these patients. Similarly, the level of serum SGOT, SGPT, ALP and GGT was significantly elevated in 39.9%, 42.8%, 32.3% and 47.2% respectively of COVID positive patients. The level of serum total protein and albumin were significantly decreased in 43.8% and 48.6% respectively of the COVID positive patients. Similar finding was reported in a study conducted in Egypt, which concluded that 40% of COVID-19 positive patients had LFT abnormalities.[13] A study conducted in china reported that among COVID-19 positive patients, 76.3% had abnormal LFT finding with SGPT, SGOT, Total Bilirubin and GGT elevated significantly in 23.4%, 14.8%, 11.5% and 24.4% of patients respectively.[14]

In the present study, we observed altered findings in renal function test in few of COVID positive patients. Urea, creatinine and uric acid level were significantly elevated in 63%, 56.1% and 33.1% of positive patients respectively with also significant higher level of electrolytes. Blood sugar was significantly increased in 47.6% of positive patients. Similar finding was observed in a study from UAE, which reported as 45.3% of COVID-19 patients had mild-severe renal impairment.[15] A study conducted in china concluded that serum creatinine and urea were generally elevated during the course of COVID-19.[16] Wu et. al. reported that elevation of blood glucose level in COVID-19 infected patients was associated with worse outcome.[17] A study from Rajsthan, India reported that out of 300 COVID-19 positive patients, 21.3% of them had higher blood urea nitrogen and serum creatinine.[18] In the present study, 56.6% of COVID positive patients had significantly lower level of calcium. A report from china revealed that hypocalcemia mostly observed in severe COVID-19 patients and also associated with poor outcome.[19]

We noticed that the serum level of LDH, D-dimer, CRP and procalcitonin (PCT) were significantly increased in 52.1%, 75.9%, 71.6% and 61.2% of COVID positive patients respectively. Liu et. al. reported that 62.6% COVID positive patients had higher level of CRP and PCT.[19] It has been reported that mean serum procalcitonin (PCT) levels were over four times higher in severe patients compared to moderate patients and over eight times higher in critical patients compared to moderate patients.[20] Report from china stated that D-dimer is commonly elevated with the patients suffering from COVID-19 infection.[21,22] Gustian et al. from Indonesia reported that D-dimer value increases with the severity of COVID-19 infection.[23] A study conducted in USA concluded that elevated LDH values were associated with 6-fold increased odds of severe COVID-19 disease.[24] Another study from Mexico reported that LDH and CRP levels above normal are linked to a greater risk of in-hospital death in Mexican patients admitted with COVID-19.[25]

We observed the altered findings in the parameters of lipid profile in the sera of few of COVID positive patients. It has been noted that the serum value of total cholesterol, triglyceride, HDL and LDL were significantly lowered in 52.2%, 43.8%, 70.1% and 60.3% of COVID-19 positive patients. Many studies had reported that the parameters in the lipid profile are significantly decreased in COVID positive patients.[26-28] Hematological parameters were also found to be altered in many of COVID positive patients in the present study. Lower hemoglobin and RBC concentration was seen in 56.6% and 53.6% of COVID positive patients respectively. Similarly, it has been noted that 20.1% of these positive patients suffered with thrombocytopenia and 10.6% with thrombocytosis. Total leukocyte count was found to be elevated in 80.7% of COVID positive patients. Neutrophil was elevated in 87.9% whereas lymphocyte was found to be lowered in 79.4% of COVID positive patients. The level of Monocyte, Eosinophil and Basophil was reduced in majority of these positive patients. The reports from different research has shown that Hb, RBC, MCV, MCH, MCHC, lymphocyte, Monocyte, Eosinophil and Basophil concentration was greatly reduced whereas TLC and Neutrophil was highly elevated with altered platelet level in majority of COVID positive patients.[10,29-32]

The current study does have a few limitations. A single study center has included the biochemical parameters of patients who tested positive for COVID-19. If more samples that tested positive for COVID had been enlisted from various centers in Nepal, the results may have been interpreted more reasonably.

CONCLUSION

The present study revealed that among COVID-19 positive patients, female were more sufferers than male with predominant number of patients in age group 15-30. The biochemical parameters of LFT, RFT, Lipid profile, were significantly altered in many COVID positive patients. The blood level of sugar, LDH, D-dimer, CRP and PCL were significantly elevated in many COVID positive patients. Similarly, hematological parameters like Hb, RBC, TLC, DLC and platelet count were differed in many positive patients whereas the biochemical and hematological parameters were within normal reference range in few COVID positive patients.

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