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Original Research

Analysis of Biochemical and Hematological Parameters During the First and Second Wave of SARS-CoV-2 Infection among North-East Indian Cancer Patients

Sawmik Das	Department of Biochemistry, Dr B Borooah Cancer Institute, Gopinath Nagar, Guwahati 781016, Assam, India.
Anupam Sarma	Department of Oncopathology, Dr B Borooah Cancer Institute, Gopinath Nagar, Guwahati 781016, Assam, India.
Biki Chandra Das	DBT Centre for Molecular Biology and Cancer Research, Dr B Barooah Cancer Institute, Gopinath Nagar, Guwahati 781016, India.
Dhruba Jyoti Sarma	DBT Centre for Molecular Biology and Cancer Research, Dr B Barooah Cancer Institute, Gopinath Nagar, Guwahati 781016
Rashmisnata Barman	Department of Microbiology, Dr B Borooah Cancer Institute, Gopinath Nagar, Guwahati 781016, Assam, India.
Mouchumee Bhattacharyya	Department of Radiation Oncology, Dr B Borooah Cancer Institute, Gopinath Nagar, Guwahati 781016, Assam, India.
Amal Chandra Kataki	Department of Gynaecologic Oncology, Dr B Borooah Cancer Institute, Gopinath Nagar, Guwahati 781016, Assam, India.
Avdhesh Kumar Rai	DBT Centre for Molecular Biology and Cancer Research, Dr B Barooah Cancer Institute, Gopinath Nagar, Guwahati 781016, India.

Introduction: SARS-CoV-2 (COVID-19) affects respiratory airways as well as the kidneys, hearts etc. This study aims to demonstrate the impact of COVID-19 infection on biochemical and hematological parameters in cancer patients of North-East India.
Methods: The study includes biochemical parameters for 907 and hematological parameters for 1103 cancer patients who were tested for COVID-19 between 1st June 2020 and 1st June 2021. All the data were analyzed by the statistical software SPSS (ver20).
Results: AST (p = 0.023), GGT (p = 0.026) and Urea (p = 0.004) significantly increased in COVID-19 positive cancer patients compared to negative cancer patients. Eosinophils (p=0.01), eosinophils absolute (p=0.01), monocyte (p=0.04) and MCHC (p=0.01) were significantly decreased in COVID-19 positive cancer patients compared to negative. Various biochemical and haematological parameters analysed in our study were found to be altered between the COVID-19 positive and negative group but their association was not found to be statistically significant.
Conclusion: We conclude that in cancer patients of North-East India, significant alterations of biochemical and hematological parameters AST, GGT, Urea, Eosinophils, eosinophils absolute, monocyte and MCHC were found in COVID-19 positive cancer patients compared to negative cancer patients.

Introduction

The SARS-CoV-2 (COVID-19) pandemic has been spreading around the world from 2019. More than 380 lakh people have been infected by this virus in India and almost 4.88 lakh people have lost

their lives [1,2]. There is an increased risk of hospitalization and mortality for individuals with co-morbidities such as kidney disease, cardiac disease, heart disease and cancer [3]. The World Health Organization (WHO) has identified and reported multiple variants of SARS-CoV-2 including alpha, beta, gamma, delta and omicron. The effects of different variants of COVID-19 vary from individual to individual and organ to organ [4].

Patients diagnosed with COVID-19 showed changes in haematological and biochemical parameters which may lead to other complications [5]. SARS-CoV-2 due to damage to endothelial cells in various organs resulting in lymphocytic endotheliitis and vasoconstriction [6]. Due to SARS-CoV-2 infection, some other complications like pulmonary embolism (PE), deep vein thrombosis (DVT), venous thrombo-embolism, corpulmonale, systemic, pulmonary arterial thrombosis, embolism and myocardial infarction (MI) were also reported [7-9]. Mortality of COVID-19 patients was found to be most commonly associated with pulmonary embolism and deep vein thrombosis is common among the dead [10]. Various cardiac complications as ischemic cardiac injury can occur in patients [11, 12]. COVID-19 also affects the brain as ACE2 receptors are present in the cerebral cortex and brain stem. Neurological manifestations may be the only ones which can be observed or may occur in combination with respiratory or other symptoms [8,13]. It was also reported that skin, gastrointestinal tract, eyes along with mental complications were also adversely affected due to SARS-CoV-2.

Globally, cancer ranks among the top 10 causes of death. As per the National Cancer Registry Program,

13.9 lakh cancer cases were reported in 2020. Further, in North-East India, the number of cancer patients is increasing throughout the year. The National Centre for Disease Informatics and Research (NCDIR) and the Indian Council of Medical Research suggested in their report that the number of new cancer cases in North East India will rise to 57131 by 2025. Due to the alterations in biochemical and hematological parameters that SARS- CoV-2 causes, a cancer patient's ability to combat the virus is greatly compromised, which increases mortality. In India, the mortality rate of COVID-19 patients is higher in 2021 than in 2020 because of the emergence of various COVID-19 variants. With this study, we intend to compare the biochemical and hematological parameters of various cancer patients infected with COVID-19 in 2020 and 2021. The study was conducted at a comprehensive tertiary cancer treatment centre, Dr B Borooah Cancer Institute (Dr BBCI) Guwahati. Due to the ongoing COVID-19 pandemic, the COVID-19 testing centre and COVID ward facility are available at the Institute. All the prescribed rules and regulations by State and Central governments regarding COVID-19 were followed. Before admission to the Institute, all new patients must undergo RT-PCR tests for SARS-CoV-2. The objective of the study is to determine the effect of SARS-CoV-2 on the haematological and biochemical parameters of cancer

patients by using their mean values.

Materials and Methods

It was a retrospective and cross-sectional analytic study of biochemical parameters of 907 cancer patients and haematological parameters of 1103 cancer patients tested for COVID-19 by using Real-Time Polymerase Chain Reaction (RT-PCR). Biochemistry and haematological parameters for the blood samples of cancer patients were determined by using the fully automated biochemistry analyzer OCD 6500 (Orthoclinical Diagnostics Vitros 6500) and fully automated haematology analyzer (Sysmex XN-1000) respectively at the Biochemistry Laboratory of our Institute. The RT-PCR test for SARS-CoV-2 virus detection; the nasopharyngeal and oropharyngeal swab samples of cancer patients were collected and the samples were processed for the RT-PCR test within 6 hours from the collection of samples. All the biochemical and haematological parameters were collected for those cancer patients tested for COVID-19 by RT-PCR test from 1st June 2020 to 1st June 2021. Biochemical and haematological parameters of COVID-19 positive and COVID-19 negative cancer

patients were statistically analyzed by calculating the mean, standard deviation and P-value for all the parameters. We prepared the comparative statistical analysis of COVID-19 impacts on biochemical and haematological parameters separately by comparing the data with the normal value as standardized by our Institute.

Results

Association of biochemical parameters with COVID-19 infection: A total of 907 SARS-CoV-2 tested cancer patients were enrolled for the study of COVID-19 effects on biochemical parameters of cancer patients. Out of 907 (male (n=530) female (n=377)) cancer patients, 26.75% (n=241) patients were tested COVID-19 positive and the remaining 73.42% (n=666 patients) were COVID-19 negative. The mean age for the negative group was 48.15 and for the positive group was 47.79. The age range for the positive group was 1-85 years and for the negative group was 2-88 years.

In Table1, the mean value of the biochemical parameters are being compared with the normal range.

Biochemistry Parameters	Normal Range	Negative (n=666)	Positive (n=241)	p-value
		Mean	Mean	
Age (Years)		48.15	46.79	0.596
RBG (mg/dL)	80.0-130.0	118.83	116.06	0.93
Sodium (meq/l)	130.0-140.0	136.17	135.68	0.232
Potassium (meq/l)	3.5-5.0	4.12	4.12	0.832
Chlorides (mmol/i)	95.0-106.0	100.23	99.49	0.366
Protein (g/dl)	5.7-8.0	7.33	7.15	0.008
Albumin (g/dl)	3.5-5.0	3.84	3.74	0.106
Globulin (g/dl)	2.6-3.5	3.49	3.4	0.03
Alkaline Phosphatase (IU/l)	96.0-297.0	155.63	158.31	0.271
Total Bilirubin (mg/dl)	0.3-1.2	1.14	0.96	0.495
Direct Bilirubin (mg/dl)	0.1-0.4	0.65	0.48	0.664
Indirect Bilirubin (mg/dl)	0.2-0.6	0.5	0.48	0.763
AST (IU/l)	5.0-35.0	46.46	49.27	0.023
ALT (IU/l)	4.0-35.0	40.61	37.29	0.26
Calcium (meq/l)	8.8-10.8	9.25	9	0.098
GGT (IU/l)	0.0-30.0	69.59	77.55	0.026
Urea (mg/dl)	10.0-50.0	27.7	32.63	0.004
Uric Acid (mg/dl)	2.6-6.0	4.38	4.44	0.942
Creatinine (mg/dl)	0.5-1.0	0.72	0.73	0.217

Table 1. Association of Biochemical Parameters between COVID-19 Positive and Negative Cancer Patients.

We observed that protein (p = 0.008) and globulin (p = 0.030) were significantly decreased in COVID-19 positive cancer patients compared to negative patients. AST (p = 0.023) and GGT (p = 0.026) were also significantly increased in COVID-19 positive cancer patients. There was also a further increase from the normal range post-infection. Urea was also (p = 0.004) significantly increased in COVID-19-positive cancer patients but remain within the normal range. Direct bilirubin and ALT were also decreased after COVID-19 infection. Alkaline phosphatase, uric acid and creatinine were in the normal range for both positive and negative cancer patients. RBG, sodium, chlorides, albumin, total bilirubin, indirect bilirubin, potassium, and calcium had not shown any significant difference between COVID-19 positive and negative cancer patients (Table 1).

Association of haematological parameters with COVID-19 infection: Analysis of haematological parameters of COVID-19 tested cancer patients (n=1101) was done. COVID-19 positive cancer patients constitute 26.16 % (n=288) and 73.84% (n=813) were COVID-19 negative. Male cancer patients were higher in number (n=644) as compared to female patients (n=457).

We found that eosinophils (p=0.01), eosinophils absolute (p=0.01), monocyte (p=0.04) and MCHC (p=0.01) were significantly decreased in COVID-19 positive cancer patients. The mean age for COVID-19 positive cancer patients was 45.67 years and 47.08 years for COVID-19 negative cancer patients. Basophil, HCT and lymphocytes were lower than the normal range in the COVID-19 positive and negative group of cancer patients.

TLC and neutrophils absolute were in the normal range in cancer patients before COVID-19 infection but they exceeded the normal range post-COVID-19 infection. Neutrophil, basophil absolute, Hb, lymphocyte absolute, MCH, MCV, PCT, PDW and RBC were in the normal range and they have not shown any statistically significant difference between COVID-19 positive and negative groups (Table 2).

Hematological Parameters	Normal range	Negative (n=813)	Positive (n=288)	p value
		Mean	Mean	
Eosinophils (%)	1.0-6.0	3.21	2.5	0.01
Neutrophil (%)	40.0-80.0	73.81	74.99	0.105
Basophils (%)	1.0-2.0	0.21	0.19	0.107
Basophils abs (10e9/L)	0.02-0.1	0.02	0.02	0.947
Eosinophils abs (10e9/L)	0.02-0.1	0.23	0.17	0.019
HB (g/dl)	12.0-15.0	10.55	10.66	0.734
HCT (%)	36.0-46.0	32.45	33.03	0.214
Lymphocyte (%)	20.0-40.0	18.85	18.62	0.235
Lymphocyte abs (10e9/L)	1.0-3.0	1.24	1.31	0.968
Monocyte (%)	2.0-10.0	3.86	3.6	0.042
Monocyte abs (10e9/L)	0.2-1.0	0.32	0.41	0.356
MCH (pg)	27.0-32.0	27.46	27.49	0.666
MCHC(g/Dl)	31.5-34.5	32.35	32.18	0.013
MCV (fL)	83.0-101.0	85.04	85.46	0.809
MPV (fL)	7.5-10.5	11.74	11.93	0.051
Neutrophils abs (10e9/L)	2.0-7.0	6.41	7.33	0.164
PCT(%)	0.12-0.36	0.33	0.32	0.899
PDW(%)	25.0-65.0	15.18	15.25	0.949
PLATELETS (10e9/L)	150-400	249.15	235.86	0.09
RBC (10e9/L)	3.8-4.8	3.86	3.89	0.65
RDW(% CV)	11.6-14.0	17.02	17.24	0.069
TLC (10e9/L)	4.0-10.0	8.93	10.12	0.137

Table 2. Association of Haematological Parameters between COVID-19 Positive and Negative Cancer Patients.

We observed that in COVID-19-positive cancer patients mean value for all biochemical parameters except urea has decreased in the second wave compared to the first wave of COVID-19 positive cancer patients. Urea level was significantly increased in COVID-19 positive cancer patients of first wave only. Though biochemical parameters have shown alterations in first and second wave COVID-19-positive cancer patients but these differences failed to achieve the statistical significance. (Table 3).

			1st wave of COVID			2nd wave of COVID	
Biochemistry Parameters	Normal Range	Positive	Negative	P value	Positive	Negative	P value
		Mean	Mean		Mean	Mean	
Alkaline Phosphatase (IU/l)	96.0-297.0	159.24	137.87	0.112	158.31	182.53	0.126
Total Bilirubin (mg/dl)	0.3-1.2	1.16	1.27	0.18	0.96	1.12	0.085
Direct Bilirubin (mg/dl)	0.1-0.4	0.69	0.77	0.16	0.48	0.59	0.096
AST (IU/l)	5.0-35.0	51.42	47.1	0.06	49.27	44.81	0.258
ALT (IU/l)	4.0-35.0	40.2	42.5	0.361	37.29	38.55	0.24
GGT (IU/l)	0.0-30.0	106	72.42	0.062	77.55	48.15	0.19
Urea (mg/dl)	10.0-50.0	30.2	23.83	0.002	32.63	27.43	0.074

Table 3. Association of Biochemical Parameters in Cancer Patients During 1st and 2nd wave of COVID-19 Infection.

Eosinophils ($p^{1st\ wave}$ -0.023, $p^{2nd\ wave}$ -0.041) and eosinophils absolute ($p^{1st\ wave}$ -0.039, p 2nd ^{wave}-0.044) had shown significant differences between COVID-19 positive and negative cancer patients in first and second wave of COVID-19 infection. Whereas, MPV ($p^{1st\ wave}$ - 0.001) and neutrophils absolute ($p^{1st\ wave}$ - 0.014) has shown significant difference between positive and negative cancer patients in the first wave but not in the second wave. Even though there were alterations in the other hematological parameters but they were not statically significant. (Table 4).

Biochemistry Parameters			1st wave of COVID			2nd wave of COVID	
	Normal Range	Positive	Negative	P value	Positive	Negative	P value
		Mean	Mean		Mean	Mean	
Eosinophils (%)	1.0-6.0	3.2	2.51	0.023	3.27	2.46	0.041
Basophils (%)	1.0-2.0	0.21	0.18	0.076	0.2	0.21	0.37
Eosinophils abs (10e9/L)	0.02-0.1	0.22	0.17	0.039	0.3	0.18	0.044
Lymphocyte (%)	20.0-40.0	18.85	18.35	0.332	18.88	19.2	0.432
Monocyte abs (10e9/L)	0.2-1.0	0.33	0.47	0.189	0.25	0.27	0.224
MPV (fL)	7.5-10.5	11.68	12	0.001	12.11	11.79	0.065
Neutrophils abs (10e9/L)	2.0-7.0	6.34	7.52	0.014	6.84	6.95	0.434
PLATELETS (10e9/L)	150-400	251.06	235.83	0.089	236.94	234.28	0.439
RDW (% CV)	11.6-14.0	16.93	17.05	0.313	17.6	17.67	0.445
TLC (10e9/L)	4.0-10.0	8.72	9.67	0.179	10.25	11.13	0.294

Table 4. Association of Haematological Parameters in Cancer Patients During 1st and 2nd Wave of COVID-19 Infection.

Discussion

It has been demonstrated in various studies that several biochemical and haematological factors

can predict COVID-19 related severity of symptoms and associated mortality. In our study we found that AST, GGT, Urea were significantly higher whereas protein, globulin, direct bilirubin, ALT were decreased in COVID-19 positive cancer patients.

The results of the previous meta-analysis revealed that severe COVID-19 cases displayed higher ALT, AST and total bilirubin levels as compared to non-severe patients. Whereas the value of albumin was significantly lower in severe cases. It was also reported that albumin was significantly lower in a progression group than in the improvement or stabilization group of COVID-19 patients [14]. Huang et al. introduced decreased albumin along with increased LDH, ALT and total bilirubin levels as appropriate biomarkers with the ability to discriminate between severe and non-severe groups of COVID-19 patients [15].

COVID-19-related liver damage could be traced back to the early report in Wuhan, China. It was reported that 28% of patients had abnormally elevated ALT and 35% of COVID-19 patients had abnormally elevated AST in which patients had severe liver damage [16]. Another Chinese study reported 22.2% and 21.3% of patients had abnormally elevated AST, and ALT [17]. It was also reported that overall survival among the severe COVID-19 patients may be predicted by very high level of AST [16]. Higher levels of bilirubin, AST and GGT were predominantly observed in COVID-19 related mortality [16]. It was reported that related bio-markers such as LDH [18, 19], AST and ALT [18, 19] bilirubin [19] and creatinine [20] were also found to be COVID-19 severity

predictors.

We found that eosinophils, eosinophils absolute, monocyte and MCHC were significantly decreased in COVID-19 positive cancer patients. Neutrophil, basophil absolute, Hb, lymphocyte absolute, MCH, MCV, PCT, PDW and RBC were in the normal range and they have not shown any statistically significant difference between COVID-19 positive and negative groups. Previous studies reported that eosinophils, basophils and platelets were decreased whereas lymphocytes counts, neutrophils, monocytes were variable or remain unchanged after COVID-19 infection [21-29].

We had also compared the biochemical and hematological parameter differences between the COVID-19 positive and negative cancer patients during the first and second wave of COVID-19 infection. Only Eosinophils and eosinophils absolute had shown significant differences between COVID-19 positive and negative cancer patients in both first and second wave of COVID-19 infection.

Cancer patients are more prone to infect with COVID-19. After the COVID-19 infection, changes in the parameters adversely affect normal body function and changes may lead to the mortality rate among various cancer patients.

In conclusion, in cancer patients of North-East India, we found significant alteration of AST, GGT, Urea, Eosinophils, eosinophils absolute, monocyte and MCHC in COVID-19 positive cancer patients as compared to negative cancer patients. Comparing the first and second wave of COVID-19 infections (driven by different variants of SARS-CoV-2) impact in cancer patients of North-East India we observed that patterns of alterations in haematological and biochemical parameters were more or less similar. Future studies with a larger cohort of cancer patients will be required to validate our current observations.

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Conflicts of interest

There are no conflicts of interest. This study has not received any financial support.

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