Original Article

DOI: 10.7860/JCDR/2023/61458.18170

Gastrointestinal Manifestations and Liver Abnormalities in COVID-19: A Real-World Experience and a Novel COVID-19 Prognostic Index

Internal Medicine Section

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ABSTRACT

Introduction: Gastrointestinal (GI) manifestations and liver function abnormalities have been reported in Coronavirus Disease-2019 (COVID-19). However, data is variable and lacking from the Indian Population. Moreover, the prognostic implication of these manifestations has not been well-defined.

Aim: To determine the impact of COVID-19 on the gastrointestinal tract and Liver Function Test (LFT) and develop a prognostic model for mortality

Materials and Methods: An observational descriptive study was conducted in the Department of Internal Medicine at a temporary dedicated COVID-19 centre in a Tertiary Care Cardiothoracic Centre, Western Maharashtra, India. The hospital records of all the patients admitted from July 2020 to September 2020 were analysed. Clinical details and laboratory details were obtained from 589 Reverse Transcription- Polymerase Chain Reaction (RT-PCR) confirmed patients. The data was analysed and a prognostic scoring system was developed. Patients with positive Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) RT-PCR on nasopharyngeal or oropharyngeal swabs were enrolled. The data was entered in Microsoft Excel 2010 worksheet and t-test or Mann-Whitney test was also applied to compare the mean of variables being studied by separation of living and deceased patients based on the normality of the quantitative data.

Results: The mean age±SD of the study participants was 44.74±19.61 years. The majority {127/589 (21.56 %)} of the patients were in the age group of 51-60 years. A total of 5 (0.84%) out of 589 patients had diarrhoea, and 3 (0.51%) had vomiting at the time of admission. Elevated Aspartate Aminotransferase (AST), Alanine Transaminase (AST), Alkaline Phosphatase (ALP), Gamma-glutamyl Transferase (GGT), Lactate Dehydrogenase (LDH), Creatine Kinase Myocardial Band (CK-MB) was reported in non survivors in 45 (90%), 39 (78%), 15 (30%), 28 (56%), 48 (96%) and 49 (98%) out of 50 cases, respectively. The prognostic scoring system was developed with the following variables: age, Diabetes Mellitus (DM), symptomatic, breathlessness, albumin, AST, ALP, LDH, Prothrombin Time (PT), and D-Dimer. The area under the curve, came out to be 0.91 and a cut-off value of three in the scoring system was able to predict death at a sensitivity of 85.5% and specificity of 79.6%.

Conclusion: GI manifestations and abnormalities in LFTs are important extrapulmonary manifestations of COVID-19. Patients with abnormal liver tests had higher risks of progressing to severe disease. Hence, LFT should be monitored and evaluated frequently during hospitalisation for COVID-19.

Keywords: Aspartate aminotransferase, Coronavirus disease-2019, Lactate dehydrogenase, Liver function tests, Severe acute respiratory syndrome coronavirus 2

INTRODUCTION

India has been one of the worst affected countries with over 41 million cases and 500 thousand deaths due to COVID-19 [1]. Besides the classical symptoms of influenza-like illness and pneumonia, patients can also have GI symptoms like anorexia, diarrhoea, nausea, vomiting, and pain abdomen. The frequency of these GI symptoms like diarrhoea and vomiting in COVID-19 patients, has been reported in upto 50% cases in some studies [2-5]. However, the data from India, shows much lesser frequency [6]. Many studies have shown that deranged LFTs are predictors of severe disease and poor outcomes. Deranged liver function tests are seen in a wide range of patients with severe COVID-19 [7-10]. Few studies have shown that, the derangement of AST, ALT, ALP, GGT, total bilirubin and hypoalbuminaemia may occur in patients with COVID-19, but does not correlate to mortality [11,12].

In COVID-19, early prognostication of the disease needs to be achieved for better preparedness of hospitals in pandemic situations. Some studies have tried to predict mortality using different scoring systems. The majority of the scoring systems have used age, co-morbidities, inflammatory markers like, C-reactive protein, Interleukin-6 (IL-6), procalcitonin, Neutrophil to Lymphocyte Ratio (NLR), liver enzymes, albumin, blood urea, PT, imaging of chest and D-Dimer [13-15]. The problem with existing scores like COVID-19 Scoring System (CSS), COVID-19 laboratory score, Age, Body ache,Body temperature, Contact, Cough, Dyspnoea (ABCD)-mortality score, CORONATION-TR model, Dublin-Boston score is that performing tests like High-Resolution Computed Tomography (HRCT), IL-6 and procalcitonin is tedious and expensive for patients with COVID-19, especially in an Indian setting [13,14,16-18].

The present study was aimed to describe the incidence of GI manifestations of COVID-19; describe the laboratory parameters, which predicted the poor outcome and build a scoring system based on age, co-morbid illness and laboratory parameters, including those pertaining to the liver for prognostic significance.

MATERIALS AND METHODS

An observational descriptive study was conducted in the Department of Internal Medicine at a temporary dedicated COVID-19 centre in a Tertiary Care Cardiothoracic Centre, Western Maharashtra, India. The hospital take records of all the patients admitted from July 2020 to September 2020 were analysed. The study was approved by the Institutional Ethical Committee (IEC/2020/85). The records and patients' case notes written by the treating team were retrieved from the hospital's electronic database.

Inclusion criteria: Patients with positive SARS-CoV-2 RT-PCR on nasopharyngeal or oropharyngeal swabs and aged above 16 years were included in the study.

Exclusion criteria: Clinically severe acute respiratory illness with negative SARS-nCoV-2 RT-PCR and record files in which all study variables were missing, excluded from the study.

Study Procedure

The patients' medical records were analysed by a team comprising of a general physician, pulmonologist, and gastroenterologist for the demographic profile like age, gender, duration of hospitalisation, symptoms at admission and co-morbid conditions. The severity of COVID-19 was classified as follows [19]: mild: respiratory rate <24/minute, SpO_2 >94% at room air), moderate: respiratory rate: 24-30/minute, SpO_2 90-94% at room air) and severe: respiratory rate >30/minute SpO_2 <90%), Acute Respiratory Distress Syndrome (ARDS) and septic shock. The following laboratory parameters were studied at admission: haemoglobin, Total Leucocyte Count (TLC), neutrophil percentage, lymphocyte percentage, platelet count, blood urea, serum creatinine, sodium, potassium, ALT, AST, LDH, GGT, ALP, Creatine Phosphokinase (CPK), CK-MB, PT, activated Partial Thromboplastin Time (aPTT), total bilirubin, total protein, albumin, and D-Dimer levels.

STATISTICAL ANALYSIS

All the data was entered in a password-protected Microsoft Excel 2010 worksheet. The normality of the data was based on the results attained from the Kolmogorov-Smirnov test. Furthermore, the present study, utilised median and Interquartile Range (IQR) to describe quantitative data and also, frequency and percentage to describe qualitative data. The t-test or Mann-Whitney test, was also applied to compare the mean of variables being studied by separation of living and deceased patients based on the normality of the quantitative data. The Chi-square test or Fisher's-exact test was applied to compare the qualitative data between the two groups. The cut-off value for the quantitative variables was based on the maximum optimal cut-point value of sensitivity and specificity.

In order to initiate the modelling process and select the best variables to enter the multivariable model, the step-wise selection method with conditional forward approaches, along with Akaike's Information Criterion (AIC) was done using the Jamovi package version 2.3. Univariate and multivariable logistic regression models were also employed to evaluate the variables being studied and to further construct a prediction model. Variables with a p-value <0.1 in multivariate analysis were used for the development of the score. In addition, to assess the overall performance of the model, the AIC criterion, Nagelkerke's R-squared and co-linearity statistics (variable inflation factor) were used and also, the Area Under Curve (AUC), Receiver Operating Characteristic (ROC) curve was utilised to measure discrimination capability. Cut-off point was set and calculations of discrete rating data were performed using the JROCFIT java program. Similarly, validity indices such as Negative Predictive Value (NPV), Positive Predictive Value (PPV), accuracy, sensitivity and specificity were applied to evaluate the validity of the final model. All statistical analysis in the present was performed using Jamovi software version 2.3.4. Also, all calculations were done at a significance level of p-value <0.05 with a 95% confidence interval. Univariate analysis was done for clinical and biochemical parameters to predict mortality. For modelling, all variables with a p-value <0.1 were taken for the conditional step forward approach in multivariable logistic regression [20-24].

RESULTS

A total of 589 patients with confirmed COVID-19 by RT-PCR were admitted from July 2020 to September 2020. The mean age±SD of the patients was 44.74±19.61 years. The majority {127/589 (21.56 %)} of the patients were in the age group of 51-60 years. Males constituted 474/589 (80.47%) of the study population [Table/Fig-1].

Clinical and laboratory profile of the study population in various clinical categories of COVID-19: Out of the total 589 patients, majority 481 (81.66%) had a mild illness, rest had moderate to severe illness. In patients above 60 years, 58/135 (42.96%) had moderate to severe disease (p<0.001). The age-wise distribution of patients in the three clinical categories of COVID-19 is given in [Table/Fig-1]. GI manifestations were seen in 8 (1.35%) patients, 5 (0.84%) patients had diarrhoea and 3 (0.51%) had vomiting at the

Parameters		Clinical severity of COVID-19			Total	p-value
		Mild n=481 (%)	Moderate n=50 (%)	Severe n=58 (%)	N=589	
Age groups (in years)	≤30	113 (23.5)	1 (2.0)	0	114 (19.4)	**<0.001**
	31-40	112 (23.3)	3 (6.0)	7 (12.1)	122 (20.7)	
	41-50	80 (16.6)	9 (18.0)	2 (3.4)	91 (15.4)	
	51-60	99 (20.6)	6 (12.0)	22 (37.9)	127 (21.6)	
	61-70	59 (12.3)	18 (36.0)	20 (34.5)	97 (16.5)	
	>70	18 (3.7)	13 (26.0)	7 (12.1)	38 (6.5)	
Gender	Male	392 (81.5)	38 (76.0)	44 (75.9)	474 (80.50	0.429
	Female	89 (18.5)	12 (24.0)	14 (24.1)	115 (19.5)	
Co-morbidities	DM	69 (14.3)	9 (18.0)	25 (43.1)	103 (17.5)	**<0.001**
	HTN	70 (14.5)	16 (32.0)	14 (24.1)	100 (17.0)	**0.003**
	CAD	10 (2.1)	3 (6.0)	3 (5.1)	16 (2.7)	0.113
	Respiratory illness	8 (1.6)	2 (4.0)	2 (3.4)	12 (2.0)	0.364
	Malignancy	3 (0.6)	1 (2.0)	0	4 (0.7)	0.341
	Neurological	9 (1.8)	2 (4.0)	1 (1.7)	12 (2.0)	0.762
	Miscellaneous	15 (3.1)	1 (2.0)	2 (3.4)	18 (3.1)	0.922

Abnormal laboratory parameters	Urea (mg/dL)	84 (17.4)	30 (60)	44 (75.8)	158 (27.1)	**<0.001**
	Creatinine (mg/dL)	59 (12.2)	13 (26)	26 (44.8)	98 (16.8)	**<0.001**
	Uric acid (mg/dL)	116 (24.1)	10 (20)	13 (22.4)	139 (23.9)	0.791
	Total bilirubin (mg/dL)	48 (9.9)	7 (14)	14 (24.1)	69 (11.8)	**0.007**
	Albumin (gm/dL)	231 (48.0)	43 (86)	56 (96.5)	330 (56.8)	**<0.001**
	AST (IU/L)	272 (56.5)	39 (78)	52 (89.6)	363 (62.4)	**<0.001**
	ALT (IU/L)	303 (62.9)	41 (82)	43 (74.1)	387 (66.6)	**0.009**
	ALP (IU/L)	43 (8.9)	5 (10)	14 (24.1)	62 (10.6)	**0.003**
	GGT (IU/L)	205 (42.6)	36 (72)	33 (56.9)	274 (47.1)	**<0.001**
	LDH (IU/L)	266 (55.3)	47 (94)	56 (96.5)	369 (63.5)	**<0.001**
	CPK (IU/L)	171 (35.5)	23 (46)	28 (48.2)	222 (38.2)	0.089
	CK-MB (IU/L)	115 (23.9)	8 (16)	2 (3.45)	125 (21.5)	**<0.001**
	Na (>145) (mEq/L)	22 (4.5)	4 (8)	21 (36.2)	47 (8.0)	**<0.001**
	K (>5.5) (mEq/L)	28 (5.8)	7 (14)	8 (13.7)	43 (7.4)	**0.018**
	Hb (<13) (gm/dL)	155 (32.2)	26 (52)	34 (58.6)	215 (37.0)	**<0.001**
	TLC (>11000) (per cumm)	24 (4.9)	10 (20)	22 (37.9)	56 (9.6)	**<0.001**
	Platelets (<1.5 lac) (per cumm)	107 (22.2)	7 (14)	18 (31.0)	132 (22.7)	**0.007**
	D-dimer (>0.5)	134 (27.8)	18 (36)	12 (20.6)	164 (28.2)	**<0.001**
	Prothrombin time (seconds)	66 (13.7)	6 (12)	0	72 (12.3)	0.067
	APTT (seconds)	158 (32.8)	14 (28)	15 (25.8)	187 (32.1)	**0.04**

[Table/Fig-1]: Comparison of baseline demographic and laboratory parameters in different categories of COVID-19 pneumonia.
AST: Aspartate transaminase; ALT: Alanine transaminase; ALP: Alkaline phosphatase; APTT: Activated partial thromboplastin time; GGT: Gamma glutamyl transferase; LDH: Lactate dehydrogenase; CK-MB: Creatine kinase; Bold p-value: Statistically significant

time of admission. The most common symptom at presentation was cough, which was seen in 236 (40.06%) of the patients, while fever was seen in 226 (38.37%) patients. In the present study, 387 (65.70%) patients did not have any co-morbid condition. DM followed by hypertension was the most common co-morbid illness in the study. A total of 83 out of 589 individuals had multiple co-morbidities. The co-morbid illnesses other than DM did not have a statistically significant association with the clinical severity of COVID-19.

An abnormal blood urea, serum creatinine, low albumin, raised total bilirubin and raised AST, ALT, ALP, GGT, LDH, CK-MB, low haemoglobin, hypernatremia, hyperkalaemia, raised TLC, raised D-Dimer, and abnormal aPTT was associated with moderate to severe disease, as compared to mild disease and the difference was statistically significant. The median values and IQR of the different laboratory parameters in the three clinical categories of COVID-19 are given in [Table/Fig-2].

	Median (Interquartile range)					
Laboratory parameters	Mild	Moderate	Severe	Dead	Survivors	Reference range
Urea (mg/dL)	25 (20- 33)	44 (33.5-62.3)	56.5 (43-102.8)	79.5 (47-129.8)	26 (20-37)	10-50
Creatinine (mg/dL)	0.9 (0.8-1.1)	0.9 (0.8-1.3)	1.1 (0.8-2.0)	1.3 (0.8-2.3)	0.9 (0.8-1.1)	0.7-1.3
Uric acid (mg/dL)	5.5 (4.1-7.0)	4.9 (3.1-6.5)	5.0 (3.3-6.8)	5.8 (3.3-7.7)	5.4 (4.0-6.9)	3.5-7.2
Total bilirubin (mg/dL)	0.6 (0.4-0.8)	0.6 (0.5-0.9)	0.7 (0.5-1.0)	0.8 (0.5-1.2)	0.6 (0.4-0.8)	0.2-1.0
Albumin (mg/dL)	3.5 (3.0-3.8)	2.7 (2.4-3.2)	2.3 (2.0-2.7)	2.2 (1.9-2.6)	3.4 (2.9-3.8)	3.5-5.0
AST (IU/L)	45 (31-75)	60.5 (45.8-85.3)	67.0 (50.3-133.8	78.5 (57.5-153.3)	47 (31-76.5)	15-40
ALT (IU/L)	49.0 (34.0-76.0)	64 (46-92.8)	63.0 (41.0-88.3)	66.5 (46.5-94.3)	51 (35-77.5)	16-60
ALP (IU/L)	79.0 (65.0-97.0)	76.0 (63.5-95.3)	92.0 (69.3-119.0)	104.5 (77.8-129.0)	78 (65-96)	46-120
GGT (IU/L)	45 (31.0-72.0)	71.5 (49.3-149.0)	60.0 (48.4-94.3)	59 (39.3-109.3)	47 (32-78.5)	<90
LDH (IU/L)	239 (190-335)	388 (294.3-572.5)	585 (399-853)	684 (471-990)	255 (194-354)	85-225
CPK (IU/L)	140 (89.5-222)	156 (99-331)	163 (92-418)	201 (107-469)	140.5 (89.8-234)	0-170
CK-MB (IU/L)	35 (26-52)	56 (39-74)	68 (39-110)	68 (42-116)	37 (26-57)	0-25
Sodium (mEq/L)	140 (136-142)	138 (135-142)	142.5 (138-149)	143.5 (138-150.5)	140 (136-142)	136-145
Potassium (mEq/L)	4.5 (4.1-4.9)	4.7 (4.2-5.1)	4.6 (4.0-5.2)	4.7 (4.0-5.3)	4.5 (4.1-4.9)	3.5-5.1
Hb (g/dL)	13.8 (12.4-14.9)	12.8 (11.7-14.5)	12.2 (10.7-14.0)	12.2 (10.3-13.9)	13.8 (12.3-14.9)	13-15.5
TLC (per cumm)	5700 (4600-7200)	7100 (4800-9100)	9650 (7100-15125)	10400 (7100-16900)	5800 (4600-7400)	4000-11000
Neutrophils (%)	56 (48-67.5)	78 (65.8-88)	90 (82.3-93.0)	91 (86-94)	57 (50-71)	40-75%
Lymphocytes (%)	34 (23-41)	13 (7-26)	6 (3-10)	5 (3-7)	32 (20-40)	20-45%
Platelets ($x10^3$) (per cumm)	197 (152-263)	218 (169-277)	194 (120-280)	191 (122-259)	200 (153-267)	$15-400\times10^3$
PT (seconds)	14.4 (13.3-16.2)	13.8 (13.3-14.7)	16.2 (14.7-19.1)	17.3 (15.4-19.3)	14.3 (13.3-16.0)	10-14
APTT (seconds)	33.9 (30.8-38.0)	35.6 (29.9-39.5)	45 (32.8-52.3)	38.2 (31.6-51.6)	34.0 (30.8-38.2)	30-35
D-Dimer (ng/dL)	0.4 (0.3-0.7)	1.0 (0.4-1.6)	1.3 (0.6-5.2)	1.5 (0.7-15.7)	0.4 (0.3-0.8)	<500

[Table/Fig-2]: Comparison of median laboratory parameters values in the three clinical categories of COVID-19 and in patients with different outcomes (N=589).

Distribution of baseline demographic and abnormal laboratory parameters in survivors and patients with poor outcome: In the present study, 50 (8.48%) patients died due to COVID-19 illness in the hospital. The median (IQR) age of the patients, who died was 60.5 (55.0-62.0) years, as compared to 45.0 (32.0-57.0) years in the survivors. Among LFTs, abnormal AST, ALT, ALP, GGT, LDH, and CK-MB among the patients with poor outcome was seen in 45 (90%), 39 (78%), 15 (30%), 28 (56%), 48 (96%), and 49 (98%), respectively. On univariate analysis, parameters age >60 years, co-morbidity- DM, symptomatic, breathlessness, hypoalbuminemia, elevated ALP, elevated LDH, and reduced PT were found to be significantly associated with outcome as death [Table/Fig-3]. Further, a scoring system COVID-19 Prognostic Index (COPI) was formed including age, DM, symptomatic, breathlessness, albumin, AST, ALP, LDH, PT, and D-Dimer using binomial multivariable logistic regression [Table/Fig-3-5]. The ROC

S. No.	Variables	Crude odds ratio	95% CI	p-value
1.	Age group	4.08	2.24-7.42	0.048
2.	Sex	1.74	0.902-3.36	0.125
3.	Co-morbidity: DM	4.15	2.25-7.66	**<0.001**
4.	Co-morbidity: HTN	1.65	0.828-3.29	0.151
5.	Co-morbidity: CAD	1.59	0.35-7.19	0.546
6.	Co-morbidity: Respiratory illness	2.24	0.476-10.5	0.295
7.	Co-morbidity: Malignancy	1.20[a]	0.0634-22.5	0.544
8.	Co-morbidity: Neurological disorder	0.994	0.126-7.87	0.996
9.	Co-morbidity: Miscellaneous	1.38	0.309-6.20	0.670
10.	Asymptomatic	0.024[a]	0.0147-0.390	**<0.001**
11.	Breathlessness	10.10	5.27-19.5	**<0.001**
12.	Cough	1.14	0.629-2.06	0.670
13.	Fever	1.47	0.819-2.65	0.193
14.	Sore throat	0.777	0.269-2.24	0.641
15.	Vomiting	5.56	0.495-62.5	0.118
16.	Weakness/bodyache	0.162	0.022-1.20	0.102
17.	Loose motion/diarrhoea	0.976[a]	0.053-17.9	0.497
18.	Urea	1.62	0.617-2.98	0.204
19.	Creatinine	11.1	0.686-181	0.303
20.	Uric acid	1.00	0.496-2.02	0.996
21.	Albumin	0.441	0.232-0.838	**0.011**
22.	Globulin	1.26	0.696-2.26	0.449
23.	AST	0.701	0.476-0.903	0.098
24.	ALT	1.42	0.79-2.57	0.237
25.	ALP	4.70	2.38-9.26	**<0.001**
26.	GGT	1.46	0.81-2.62	0.207
27.	LDH	15.7	3.78-65.5	**<0.001**
28.	CPK	1.79	0.97-3.22	0.104
29.	CK-MB	1.32	0.694-2.50	0.399
30.	Sodium	0.931	0.403-2.51	0.836
31.	Potassium	0.441	0.123-1.58	0.197
32.	Haemoglobin	3.88	2.04-7.39	**<0.001**
33.	PT	0.361	0.198-0.655	**<0.001**
34.	aPTT	0.764	0.395-1.48	0.423
35.	D-Dimer	1.225	0.975-1.45	0.093
36.	Bilirubin	0.143	0.019-1.06	0.067
37.	NLR	0.852	0.401-1.81	0.676

[Table/Fig-3]: Univariate analysis to predict mortality in study population.
CI: Confidence interval; NLR: Neutrophil to lymphocyte ratio; Bold p-value: Statistically significant

Variables	Cut-off	Score
Age (in years)	>60	1
	≤60	0
Symptomatic	Symptomatic	1
	Asymptomatic	0
Breathlessness	Present	1
	Absent	0
Diabetes mellitus	Present	1
	Absent	0
Haemoglobin (gm/dL)	<13	1
	>13	0
AST (IU/L)	40	1
	≤40	0
ALP (IU/L)	>120	1
	≤120	0
LDH (IU/L)	>225	1
	≤225	0
Serum albumin (gm/dL)	<3.5	1
	≥ 3.5	0
Prothrombin time (seconds)	>15	1
	<15	0
D-Dimer (mg/L)	>0.5	1
	≤0.5	0

[Table/Fig-4]: Variables of the COVID-19 Prognostic Index (COPI) and their weightage.

analysis for the index at a cut-off value of three had a sensitivity of 85.5% and specificity of 79.6% to predict mortality and the AUC was 0.91 [Table/Fig-6].

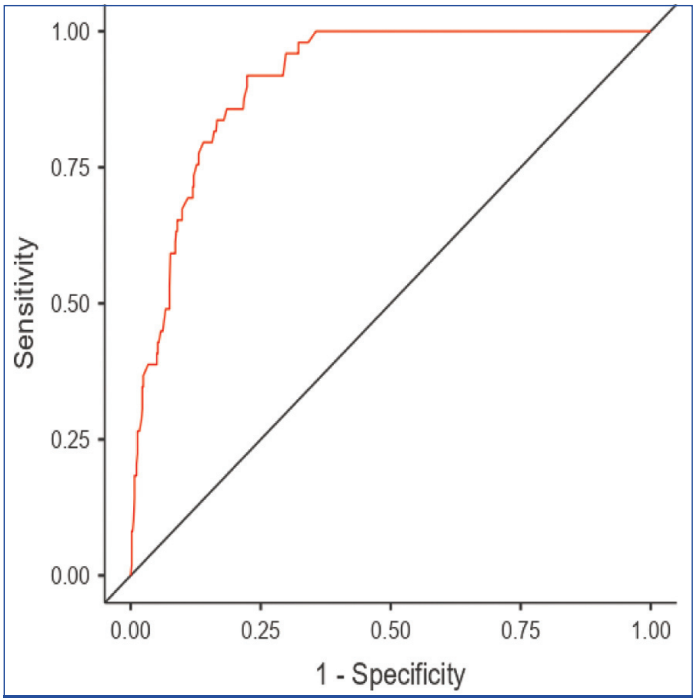
DISCUSSION

The present study is among the first comprehensive study of the pattern of LFT and its association with outcomes in COVID-19 patients in the Indian population. In patients with COVID-19 3 (0.51%) patients vomiting and diarrhoea 5 (0.84%) at presentation. The frequency of diarrhoea reported was (2%-49.5%) and vomiting (1%-29.4%) of the patients, from the rest of the world [2,3,25,26]. However, in a recent publication in India, frequency of diarrhoea occurred in 1.6% and vomiting occurred in 1.1% of the patients with COVID-19 [6]. The analysis of LFT revealed hyperbilirubinaemia in 69 (11.71%), hypoalbuminaemia in 330 (56.0%), and elevated PT in 118 (20.0%) patients in the present study. Other studies have shown hyperbilirubinaemia in (6%-16.7%) [3,25,27-29], hypoalbuminaemia in (55.5%-60%) [28,30] and elevated Indian Rupee (INR) in (9.7-18%) [3,18,20,22,28,30] cases of COVID-19. The results of the present study were similar to published reports [31].

Elevated liver enzymes were AST 363 (61.6%), ALT 387 (65.70%), ALP 63 (10.6%), and GGT 274 (46.51%) in the present cases. Other studies have reported elevated AST: 15-25.3%, AST: 15-25.4%, ALP: 4.6-9.6% and GGT in 21.1-24.4% cases [3,25-30,32]. The laboratory parameters like leucocytosis, lymphopaenia, NLR, d-Dimer, ferritin, procalcitonin, and IL-6 are proven to have prognostic significance in COVID-19 [33,34]. The higher prevalence of deranged LFTs in the present study, is likely due to the higher severity of cases in the study population and varied demography. The comparison of LFTs in COVID-19 with previous studies has been described in [Table/Fig-7] [3,25,28,30,35]. In the present study, a novel scoring system was devised to predict a model for mortality. The novel COPI utilises age, DM, symptomatic, breathlessness, low albumin, elevated AST, ALP, LDH, PT and

Variables						95% Confidence interval	
Predictor	Estimate	SE (standard coefficient of error)	Z (estimate/SE)	p-value	Odds ratio	Lower	Upper
Intercept	-5.24227	0.861	-6.0891	<0.001	0.00529	9.78e-4	0.0286
Age (in years)							
1-0	0.44959	0.377	1.1915	0.233	1.56767	0.7483	3.2842
Co-morbidity: DM							
1-0	0.91493	0.376	2.4343	0.015	2.49661	1.1951	5.2153
Asymptomatic							
1-0	-15.90699	769.904	-0.0207	0.984	1.24e-7	0.0000	Infinity
Breathlessness							
1-0	1.53654	0.372	4.1254	<0.001	4.64848	2.2401	9.6461
Albumin							
1-0	-0.12960	0.399	-0.3252	0.745	0.87845	0.4023	1.9184
AST							
1-0	-0.00706	0.397	-0.0178	0.986	0.99297	0.4565	2.1600
ALP							
1-0	1.43233	0.433	3.3104	<0.001	4.18843	1.7937	9.7802
LDH							
1-0	2.00597	0.765	2.6210	0.009	7.43327	1.6585	33.3147
Haemoglobin							
1-0	0.74161	0.388	1.9131	0.056	2.09932	0.9820	4.4879
PT							
1-0	-0.06887	0.430	-0.1601	0.873	0.93345	0.4018	2.1684
D-Dimer							
1-0	-0.86064	0.491	-1.7532	0.080	0.42289	0.1616	1.1069
Bilirubin							
1-0	-2.13631	1.060	-2.0153	0.044	0.11809	0.0148	0.9430

[Table/Fig-5]: Binomial multivariable logistic regression for mortality prediction.
Note. Estimates represent the log odds of "Outcome=1" vs "Outcome=0"; SE: Standard error



[Table/Fig-6]: ROC curve was plotted for the new scoring system to find out how well it can predict an adverse outcome. Area under the curve came out to be 0.91 and a cut-off value of three in the scoring system was able to predict death at a sensitivity of 85.6% and specificity of 79.6%.

D-Dimer. The ROC curve at a cut-off value of three was able to predict death at a sensitivity of 85.5% and specificity of 79.6%. LFT like bilirubin AST, ALT, GGT, INR, and albumin have been shown to have prognostic significance in COVID-19 [35-37]. In the present study, the LFT which were found statistically significant

S. No.	Present study	Cai Q et al., [35]	Mao R et al., [25]	Kulkarni AV et al., [28]	Zarifian A et al., [3]	Kumar A et al., [30]
Number of patients	589	417	6686	20476	13251	4676
Hyperbilirubinaemia (%)	11.71	23.19	6	13.4	7.8	9
INR (%)	20	NA	NA	9.7	18	7
Hypoalbuminaemia (%)	56	NA	NA	55.5	39.8	60
Elevated AST (%)	61.6	18.33	21	22.5	22.8	25
Elevated ALT (%)	65.7	12.9	18	20.1	20.6	23
Elevated ALP (%)	10.6	4.82	NA	6.1	4.6	NA
Elevated GGT (%)	46.51	16.11	NA	21.1	NA	NA

[Table/Fig-7]: Comparison of liver function tests in present study and previous studies [3,25,28,30,35].
NA: Not available

with respect to mortality were elevated PT, hypoalbuminemia, and elevated AST, ALP, and GGT. In a recent study, consisting of 708 COVID-19 positive cases from a single centre in northern India, elevated AST and hypoalbuminaemia were identified independent risk factor for mortality.

The advantage of the scoring system is to classify patients into high and low risk groups for timely intervention. Previously, Shang Y et al., devised a CSS consisting of age, coronary heart disease, lymphocyte %, procalcitonin and D-dimer [13]. It demonstrated good predictive performance, it underestimated mortality of low risk patients, but overestimated mortality of high risk patients. The COVID-19 laboratory score ranged from 0 to 30 points, based only on laboratory parameters including IL-6 and procalcitonin [14]. Though, it is a dynamic score, it is extensive and does not include

clinical characteristics. The Dublin-Boston score is simple score however, it utilises IL6:IL10, which are expensive and not readily available [16]. The CORONATION-TR model of scoring system is a complicated prognostic system consisting for prediction of mortality requires Computed Tomography (CT) chest scans [18]. Some of these tests like IL-6, IL-10, procalcitonin and CT are costly and tedious in COVID-19 pandemic times, especially in the Indian context. The present study's score adequately utilises routine parameters for clinical severity and prognosis.

The authors utilised major laboratory and clinical parameters, routinely performed in all hospitalised COVID-19 cases. However, the present score was based on retrospective data from a single centre and may not apply to the world population. In the study population, certain laboratory parameters such as IL-6, and ferritin were not used in a scoring system due to unavailability. These may be independent risk factors for mortality; however, the present score had a good performance to predict clinical outcomes.

Limitation(s)

The present study was a single-centre study from Western India and the results may not represent the general population. Only LFTs were done. Tests to rule out an underlying liver disease like Hepatitis B surface Antigen (HBsAg), anti-Hepatitis C Virus (HCV), and the autoimmune panel were not done. Moreover, a correlation with abdominal imaging and liver biopsy was not done. The effect of human behaviour such as unhealthy eating, alcohol consumption, and impaired access to healthcare services was not taken into consideration. Another major limitation is patients with underlying cirrhosis and pre-existing liver disease were not adequate in the study population. However, the study had a large study population, and the results effectively reflect the effect of SARS-COV-2 on the GI system especially the liver. Moreover, the study correlated results with the severity of illness and mortality.

CONCLUSION(S)

Gastrointestinal manifestations, particularly abnormal LFT, is common in patients with COVID-19, they may be used to prognosticate disease severity and mortality in patients. In addition, the novel, COPI based on basic parameters is sensitive, it will require further studies for validation.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Nov 19, 2022
- Manual Googling: Jan 11, 2023
- iThenticate Software: Mar 14, 2023 (9%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Nov 17, 2022**
Date of Peer Review: **Dec 26, 2022**
Date of Acceptance: **Mar 22, 2023**
Date of Publishing: **Jul 01, 2023**