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Carcinoembryonic antigen (CEA) and other surrogate inflammatory biomarkers in COVID-19

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It has been two years since the global outbreak of the highly contagious and deadly corona virus disease (COVID-19) caused by SARS-CoV-2 first emerged in China. Since then, various diagnostic, prognostic and treatment strategies undertaken to address the pandemic have been dynamically evolving. Predictive and prognostic role of various biomarkers in COVID-19 has been a subject of intense exploration. We aimed to determine the association of Carcinoembryonic antigen (CEA) and various surrogate inflammatory biomarkers with the severity of COVID-19 disease. This retrospective cohort study was carried out on 98 patients admitted in Jaypee Hospital, Noida with COVID-19 disease. Information regarding demographics, laboratory parameters and clinical history was collected from Hospital Information System. Serum levels of CEA and other biomarkers such as Neutrophil-lymphocyte ratio (NLR), C-reactive protein (CRP), Interleukin-6 (IL-6), Ferritin, and Procalcitonin (PCT) were assessed. Correlation analyses were performed between the parameters and acute respiratory distress syndrome (ARDS) stages. Logistic regression and ROC curve analysis were performed to assess the various parameters for distinguishing COVID-19 patients requiring ICU admission. Mean hospital stay, NLR, CEA, IL-6, CRP, Ferritin (P <0.0001) and PCT (P = 0.01) were significantly higher in ICU patients when compared to general ward patients. NLR, median serum CEA, IL-6, and CRP levels were significantly higher in non-survivor compared to the survivors (P <0.0001, 0.0341 and 0.0092). CEA correlated well with disease severity based upon ARDS classification and was a better marker to differentiate patient according to ARDS stages (ARDS 0 *vs* 2 P = 0.0006; 0 *vs* 3 P <0.0001; ARDS 1 *vs* 2 P = 0.0183; 1 *vs* 3 P = 0.0006). The area under the Receiver operating characteristic (ROC) curve for CEA was 0.7467 (95% CI- 0.64885- 0.84459) which revealed the potential of CEA as a biomarker to distinguish COVID-19 patients requiring ICU admission. CEA can be used to predict the severity of COVID-19 associated ARDS as well as patients requiring ICU admission. Along with routine inflammatory biomarkers (NLR, CRP, IL-6, PCT, and ferritin), CEA should be used for early identification of critical COVID-19 positive patients and for assessing prognosis.

Keywords: Acute respiratory distress syndrome, Biochemical parameters, CEA, Inflammatory markers

Carcinoembryonic antigen (CEA) is a cell adhesion oncofoetal glycoprotein normally expressed by the colonic epithelium during the embryonic phase and the expression is negligible after birth. It has been widely used as a biomarker for diagnosis and assessing prognosis in various malignant tumors, including lung cancer[1,2]. Blood levels of CEA are found to be elevated in benign conditions such as emphysema, biliary obstruction, hypothyroidism, and inflammation such as pancreatitis[3]. In COVID-19 patients, several inflammatory biomarkers such as procalcitonin (PCT), C-reactive protein (CRP), and interleukin-6 (IL-6) were observed to be deranged[4]. In addition to the above-mentioned biomarkers, CEA also has been reported to be crucial in assessing the prognosis in severe COVID-19 patients[1]. Although the diagnostic, prognostic, and predictive role of blood CEA in various malignant conditions (colon, lung cancer, *etc*.) is well established, its role in newly emerged COVID-19 disease and its associated inflammation is still under investigation. Chen *et al*., 2020[5] reported that elevated CEA levels increased the

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Abbreviations: COVID-19, Coronavirus- 2019: CEA, Carcinoembryonic antigen; CRP, C-reactive protein; IL-6, Interlukin-6; PCT, Procalcitonin; ARDS, Acute respiratory distress Syndrome; NLR, Neutrophill Lymphocyte ratio

risk of death from COVID-19 and CEA levels were related to CT scores of the discharged patients positively. Further evidence is needed to establish the role of CEA in COVID-19 disease.

In the present study, we aimed to determine changes in the levels of CEA and other inflammatory biomarkers in patients having different stages of acute respiratory distress syndrome (ARDS). We compared levels of CEA and other inflammatory biomarkers in intensive care unit (ICU) and non-ICU COVID-19 patients to determine the association of these analytes with the severity of the COVID-19 disease. After the devastating second wave, although the current daily caseload of COVID-19 in India is under control, the average daily COVID-19 cases are still around 40,000. A total of 3, 62,207 active cases have been registered till September 14, 2021. The data generated from this study will provide an additional important biomarker that will help in planning the management, follow-up, and treatment strategies of active cases of COVID-19 patients.

Materials and Methods

The present study was a retrospective observational study conducted on 98 COVID-19 positive patients at the Department of Biochemistry, Jaypee hospital, Noida. The study was approved by the Institutional Ethics Committee (IEC-6/4/2021). Data from patients with confirmed COVID-19 disease admitted to our centre from June 2020 to October 2020 were extracted from the electronic database system using the convenient sampling method. The posterior (retrospective) strategy was used for data abstraction. The study included patients above the age of 20 admitted with the COVID-19 disease. Information regarding demographics, laboratory parameters, and clinical history was collected. Parameters such as age, gender, co morbidity, ARDS stage, and levels of biochemical parameters (CEA, Interleukin 6 (IL-6), C-Reactive Protein (CRP), Procalcitonin (PCT), ferritin and haematological parameters neutrophil/ lymphocyte ratio (NLR) were tabulated and used for data analysis. Patients with a history of cancer, peptic ulcer, pancreatitis, biliary obstruction, emphysema, and hypothyroidism were excluded from the study. Based upon the severity, ARDS was classified into mild, moderate, and severe using Berlin criteria[6].

Blood samples were collected from all subjects in serum separating tube (SST) and EDTA vials by venepuncture at the time of admission and processed for serum CEA, IL-6, CRP, PCT, ferritin, Neutrophill and Lymphocyte. The tests were performed on VITROS XT-7600 Integrated Analyzer using reagents provided by the manufacturer at the Clinical Biochemistry Laboratory, Jaypee Hospital Noida. CEA, PCT, and Ferritin were analyzed using the chemiluminescence immunoassay technique. The levels of IL-6 were estimated using Cobas e411 electrochemiluminescence immunoassay analyzer using reagents provided by the manufacturer. CRP was estimated using VITROS CRP microslide, which is a multilayered, analytical element coated on a polyester backing and uses an enzymatic heterogeneous, sandwich immunoassay model for estimation. Neutrophill and lymphocyte were estimated in Sysmex XN 1000 analyzer using reagent provided by the manufacturer.

Statistical analysis

Statistics analyses were performed using Graph Pad Prism software. Categorical variables were displayed as frequency and percentage while continuous variables were expressed as mean, standard deviation, median, and percentile. Normality test of continuous variables was done using Kolmogorov-Smirnov test. The comparison of categorical variables between groups was done using the chi-square test. Mann Whitney U test was used for comparisons of continuous variables between different groups. Comparison of biochemical parameters between multiple groups was performed using the Kruskal-Wallis test. Dunn test was used for posthoc analysis. Correlation between individual variables was assessed using Spearman's rank correlation test. Logistic regression analysis was performed to identify variables that can differentiate severe COVID-19 patients (ICU) from non-severe (WARD) patients. The odds ratio was calculated to determine the power of inflammatory biomarkers as a predictor for admission to ICU in COVID-19 patients.Receiver operating characteristic (ROC) curve analysis of these parameters determined the optimal cutoff to be used for distinguishing COVID-19 patients requiring ICU admission. An area under the curve (AUC) value of 0.9-1.0 signified a perfect biomarker with excellent accuracy, 0.8-0.9 as very good, 0.6-0.7 as sufficient, and a value of 0.5 signified it was no better than what would be expected by chance. The optimal cut-off value was the value that had the highest combined sensitivity and specificity. A P-value of < 0.05 was considered statistically significant for all the tests.

Results

A total of ninety-eight confirmed COVID-19 patients hospitalized at our centre were included in the study. Of the 98 patients, 27 (27.6%) were female and 71 (72.4%) were male. The number of patients with one or more pre-existing comorbidities was 65 (66.3%). The demographic and clinical characteristics of all those 98 patients were presented in (Table 1). The study subjects were divided based upon their admission to the ward or ICU. A total of 52 patients were admitted to ICU and 46 patients were admitted in general wards. The median hospital stay for the patients was 12 days and 30.6% of patients were in stage-3 of ARDS. Out of 98 patients, 21 patients succumbed to death.

Table 1 — Baseline demographic and clinical characteristics of study population

Characteristics	Number (N)	Percent/Range
Gender		
Male	27	27.6%
Female	71	72.4%
Age (years) (Median& range)	57	22-92
Hypertension (N, %)	51	52%
Diabetes mellitus (N, %)	64	65.3%
Hypothyroidism (N, %)	15	15.3%
Ward	46	46.9%
ICU	52	53.1%
ARDS Stage		
0	27	27.6%
1	26	26.5%
2	15	15.3%
3	30	30.6%
Survivors	21	21.4%
Non-survivors	77	78.6%
Hospital Stay (Days) (Median& range)	12	3-120

Abbreviation: ARDS- Acute Respiratory Distress Syndrome

Table 2 depicts the gender-wise comparison of biochemical parameters. Median serum CRP levels were significantly higher in male COVID-19 patients when compared to female patients (P <0.0001). However, no significant difference was observed between the genders for other biochemical parameters (CEA, IL-6, PCT, NLR and Ferritin) (Table 2).

The median hospital stay, NLR, levels of CEA, IL-6, CRP, Ferritin (P <0.0001), and PCT (P = 0.01) were significantly higher in patients admitted to the ICU compared to patients admitted to the general wards. Also, mean O_2 saturation was significantly lower in ICU patients (P <0.0001) (Table 3).

On comparison of demographic and biochemical markers between survivors and non-survivors, non-survivor COVID-19 patients showed a significantly lower mean O_2 saturation (P = 0.0034) and a significantly higher median serum CEA, IL-6, and CRP levels. (P <0.0001, 0.0341 and 0.0092, respectively). Median NLR in non-survivors was double of its value in survivors (P = 0.007) (Table 4).

Analysis of NLR, CEA, IL-6, CRP, PCT, and Ferritin inpatients in different ARDS stages

Multi-group analysis showed that NLR, CEA, IL-6, and CRP correlated well with disease severity based upon ARDS classification and were able to differentiate patients better according to ARDS stages. Value of NLR was significantly higher in ARDS stage 2 and 3 patients compared to stage 0 and stage 1 (P <0.001).

The level of CEA in ARDS stage 2 and 3 were significantly higher when compared to patients with ARDS stage 0 and 1 (ARDS 0 *vs* 2 P = 0.0006; 0 *vs* 3 P <0.0001; ARDS 1 *vs* 2 P = 0.0183; 1 *vs* 3 P = 0.0006). Similarly, the levels of IL-6 were significantly higher in ARDS stage 3 patients compared to the stage 0 (P = 0.0313) and stage 1 ARDS patients (P = 0.005).

Table 2 — Gender-wise Baseline data on CEA and inflammatory biomarkers in COVID-19 patients

Parameters	Normal Range	Female (N=27)			Male (N=71)			*P* Value
		Median	25th Percentile	75th Percentile	Median	25th Percentile	75th Percentile	
CEA(ng/mL)	(0.0-3.0)	2.2	1.26	9.6	3.56	1.54	6.49	0.9588
Il-6 (pg/mL)	(0.0-7.0)	44.17	28.39	600.8	41.29	15.38	126	0.4228
CRP (mg/dL)	(<1)	13.69	4.2	19.28	5.4	2	14.55	0.0293*
PCT (ng/mL)	(0.03-0.5)	8.18	0.1	0.86	0.13	0.1	0.26	0.3621
Neutrophil- Lymphocyte Ratio (NLR)	1-3	7.87	3.65	13.29	8.07	3.21	12.54	0.8379
Ferritin(ng/mL)	(20-250 Male) (10-120 Female)	184	74	616	397	176	789	0.1434

The levels of IL-6 in ARDS stage 2 patients were also higher compared to stage 1 ARDS patients ($P = 0.0324$). Further, in ARDS stage-3 patients, CRP levels were significantly higher compared to the patients with ARDS stage 0 ($P = 0.0001$), 1 ($P < 0.0001$), and 2 ($P = 0.0427$). Paradoxically, serum procalcitonin and ferritin levels were not associated with the ARDS stage classification in COVID-19 patients (Table 5).

In addition, a significant positive correlation was observed between parameters such as CRP & IL-6 with duration of hospital stay (IL-6: r- 0.25; $P = 0.0130$ & CRP: r- 0.22; $P = 0.0284$). No significant correlation ($P > 0.05$) could be observed between CEA (r- 0.07; $P = 0.4406$), PCT (r- 0.04; $P = 0.6679$) and Ferritin (r- 0.10; $P = 0.3000$) with the duration of hospital stay.

Linear regression analysis of CEA with other inflammatory biomarkers and NLR showed that CRP had significant positive correlation with CEA (r- 0.31; $P = 0.0001$) (Fig. 1).

Table 3 — Comparison of CEA and inflammatory biomarkers in COVID-19 patients in ICU and ward

Parameters	Normal Range	Ward (N=45)			ICU (N=52)			*P* Value
		Median	25th Percentile	75th Percentile	Median	25th Percentile	75th Percentile	
Gender (Male/ Female)	----		36/9			35/17		0.159
Age(years) (Mean±SD)			57.88±15.48			56.63±10.65		0.6396
Hypertension (%)			42.22%			61.53 %		0.057
Diabetes Mellitus (%)			40%			71.15 %		0.248
Hospital stay (Days) (Mean±SD)			10.4±2.83			18.42±21.99		0.0073
O2 Saturation (Mean±SD)			84.1±8.56			92.4±5.44		<0.0001
Neutrophil- Lymphocyte Ratio (NLR)	(1-3)	4.73	2.6	8.4	10	7.72	15.68	0.0001
CEA (ng/mL)	(0.0-3.0)	1.83	1.24	3.75	5.19	1.95	9.78	<0.0001
IL-6 (pg/mL)	(0.0-7.0)	24.76	8.98	62.37	57.24	33.66	246.8	0.0010
CRP (mg/dL)	(<1)	4.55	1.65	10.55	12.89	4.65	19.28	0.0003
PCT (ng/mL)	(0.03-0.5)	0.11	0.1	0.18	0.19	0.11	184	0.0107
Ferritin (ng/mL)	(20-250 M) (10-120 Female)	259	96.2	530	412.5	184	1127	0.0276

Table 4 — Comparison of CEA and inflammatory biomarkers in survivors and non-survivors COVID-19 patients

Parameters	Normal Range	Survivor (N=77)			Non-survivor (N=21)			*P* Value
		Median	25th Percentile	75th Percentile	Median	25th Percentile	75th Percentile	
Gender (Male/ Female)	----		55/22			16/5		0.665
Age (years) (Mean±SD)			56.14±14.21			56.63±10.65		0.6396
Hypertension (%)			48.68 %			66.67%		0.144
Diabetes Mellitus (%)			64.47 %			71.42%		0.552
Hospital stay (Days) (Median-IQR)			12 (8-14)			10 (8-16)		0.4343
O2 Saturation (Mean±SD)			89.41±7.57			82.85±9.18		0.0034***
Neutrophil- Lymphocyte Ratio (NLR)	(1-3)	6.50	3.14	12.22	12.02	8.062	17.17	0.0007
CEA (ng/mL)	(0.0-3.0)	2.2	1.26	4.73	8.76	4.98	11.8	<0.0001***
IL-6 (pg/mL)	(0.0-7.0)	39.4	13.01	115.1	74.95	37.96	234.9	0.0341*
CRP (mg/dL)	(<1)	5.9	2	14.55	13.96	5.1	19.28	0.0092**
PCT (ng/mL)	(0.03-0.5)	0.13	0.1	0.32	0.19	0.1	0.86	0.4019
Ferritin (ng/mL)	(20-250 M) (10-120 Female)	345.0	129.0	770.0	432.0	184.0	616.0	0.2046

Table 5 — Comparison of CEA and inflammatory biomarkers in COVID-19 patients based on ARDS stage

ARDS Group	N	Neutrophil-Lymphocyte Ratio	CEA (ng/mL)	Il-6 (pg/mL)	CRP (mg/dL)	PCT (ng/mL)	Ferritin (ng/mL)
				Median (IQR)			
0	26	5.18 (2.60-8.48)	1.59 (1.15-3.56)	46.55 (16.5565.24)	4.7 (2-7.8)	0.13 (0.1-0.29)	358 (160-1280)
1	26	4.80 (3.02-8.46)	2.36 (1.42-4.88)	25.07 (6.08-41.29)	3.5 (1.4-6.9)	0.11 (0.1-0.21)	246.5 (129-526)
2	16	13.07 (7.72-17.26)	5.12 (2.31-7.23)	48.77 (11.37-349.2)	13.16 (1.9-13.96)	0.11 (0.1-0.18)	357 (73.7-770)
3	30	10 (6.79-14.46)	7.54 (3.13-10.9)	76.77 (37.96-258.7)	15.77 (5.4-19.28)	0.19 (0.1-0.51)	412 (184-974)
P value		0.0097[&]	0.0006[&]	0.0324[$]	0.0001[#]	0.0464[~]	0.0442[^]
		0.0040[#]	<0.0001[#]	0.0005[^]	<0.0001[^]		
		0.0037[$]	0.0183[$]		0.0427[~]		
		0.0012[^]	0.0006[^]				

*symbol represents the comparison of the group of 0 ARDS score *vs.* 1 ARDS score
&symbol represents the comparison of the group of 0 ARDS score *vs*. 2 ARDS score
#symbol represents the comparison of the group of 0 ARDS score *vs*. 3 ARDS score
$ symbol represents the comparison of the group of 1 ARDS score *vs*.2 ARDS score
^ symbol represents the comparison of the group of 1 ARDS score *vs*. 3 ARDS score
~ symbol represents the comparison of the group of 2 ARDS score *vs*. 3 ARDS score

Table 6 — Prediction of need for ICU admission of COVID-19 patients based upon value of biochemical markers

Parameters	OR (95% CI)	z	Pvalue
CEA	1.18 (1.01-1.38)	2.16	0.031*
IL6	1.00 (0.99-1.00)	0.79	0.431
CRP	1.07 (0.99-1.16)	1.91	0.056
PCT	0.95 (0.85-1.07)	-0.70	0.482
Ferritin	1.00 (0.99-1.00)	1.87	0.062

Abbreviations: OR- Odds Ratio, CI- Confidence Interval
* *P* <0.05, ** - *P* <0.01, *** *P* <0.001

Logistic regression analysis odd ratio and ROC curve analysis

We performed a multivariate logistic regression analysis of various biomarkers to assess the efficacy of biomarkers to distinguish COVID-19 patients requiring ICU admission from those who do not. The results showed that only CEA was an independent predictor for progression to severe COVID-19 disease (Table 6). Using the cut-off point of 2.68 ng/mL (sensitivity 73.08% and specificity 62.22%) of serum CEA, the odds ratio for ICU admission was 1.18 (95% CI-1.01-1.38; *P* = 0.031). The area under the ROC curve for CEA was 0.7467 (95% CI- 0.64885- 0.84459) revealing the better prognostic ability of CEA in COVID-19 patients. Although serum IL-6, CRP, PCT, and Ferritin levels were significantly higher in ICU patients, no reasonable cut-offs could differentiate patients requiring ICU admission from those who do not (Table 7 and Fig. 2).

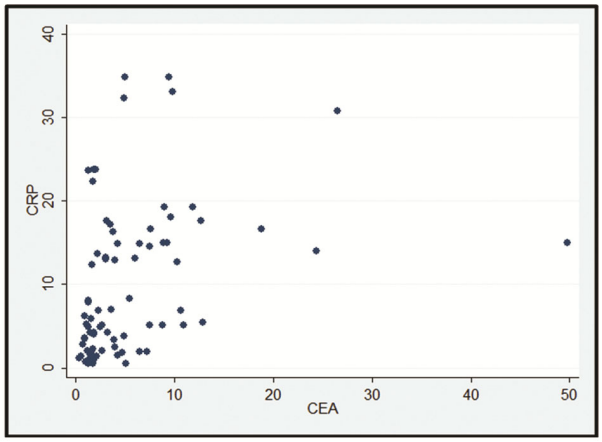

Fig. 1 — Scatterplot between CEA and CRP

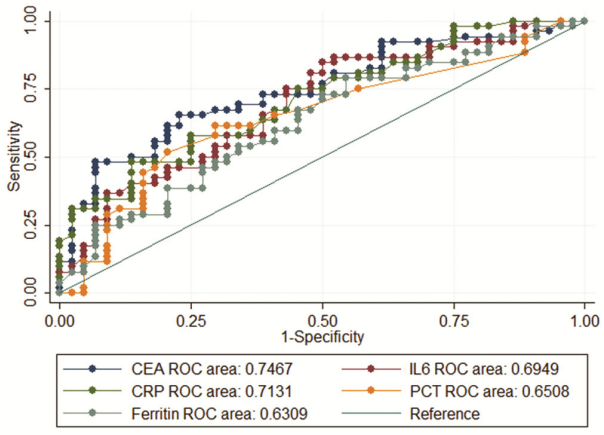

Fig. 2 — The ROC curves for serum CEA, IL-6, CRP, PCT, and Ferritin

Table 7 — ROC curve analysis of serum biomarkers for prediction of need for ICU admission of COVID-19 patients

Parameters	Cut off	Area under the curve	Sensitivity	95% CI	Specificity	*P* value
CEA(ng/mL)	2.68	0.7467	73.08%	0.64885 to 0.84459	62.22%	0.0499*
IL66 (pg/mL)	41.28	0.6949	65.38%	0.58905 to 0.80081	61.36%	0.0540
CRP(mg/dL)	5.4	0.7131	67.31%	0.61158 to 0.81456	59.09%	0.0518
PCT(ng/mL)	0.13	0.6508	65.38%	0.53941 to 0.76217	59.09%	0.0568
Ferritin(ng/mL)	273	0.6309	67.31%	0.51877 to 0.74304	53.33%	0.0572

Abbreviations: CI-Confidence Interval; * P <0.05, ** - P <0.01, *** P <0.001

Discussion

COVID-19 infection, a worldwide menace caused by SARS-CoV-2 has become a significant cause of deaths worldwide. The major complications which are developed in infected patients are acute inflammation, coagulation dysfunction, multiorgan failure, septic shock, and acute respiratory distress syndrome. The patients may succumb to death rapidly if timely treatment measures are not under taken[7,8]. Biochemical and haematological markers play a very significant role in assessing the prognosis of the COVID-19 disease. Diagnosis is mainly based upon epidemiological history, chest computed tomography imaging, and RT-PCR[9]. The levels of certain inflammatory biomarkers, such as NLR, CRP, IL-6, PCT, Ferritin, D-dimer have been routinely used to assess disease progression[7]. In the present study, we explored the prognostic value of these biomarkers along with another less studied biomarker, CEA.

On comparison of inflammatory biomarkers between ICU and non-ICU patients, we found that mean hospital stays, NLR, levels of CEA, IL-6, CRP, Ferritin and PCT were significantly higher in ICU patients. Also, NLR, serum CEA, IL-6, and CRP levels were significantly higher in non-survivor COVID-19 patients when compared to the survivors. NLR, CEA, IL-6, and CRP correlated well with disease severity based upon ARDS classification and were found to be a better marker to differentiate patients according to ARDS stages. Upon linear regression analysis, only CRP showed good correlation with CEA.

NLR is extensively studied parameter since the onset of COVID-19 pandemic. Our study findings were similar with other studies which showed higher NLR at hospital admission and its association with hyper inflammation in COVID-19 pathogenesis with more severe outcomes(Ciccullo A *et al*., 2020, Qin C *et al*., 2020)[10,11].

Higher levels of inflammatory parameters in ICU patients on admission, as well as in deceased patients signifies the need for cautious and regular monitoring of these biomarkers which helps in evaluating the disease progression and timely clinical intervention which would be useful in averting progression to severe disease. The baseline values of these parameters on admission will help to evaluate the severity status of the disease which will help the clinicians to decide treatment strategies. Continuous monitoring of these parameters in all patients will help to determine the dynamics of immune responses and the progression of the disease to a more severe condition.

The SARS-CoV-2 virus invades the airways by attaching to ACE-2 cell receptors and multiplies there. As an immediate body response to infection or infection-mediated tissue damage, the levels of various acute-phase proteins (CRP, Ferritin, PCT, and IL-6) level increased, further causing the activation of cell-mediated immunity and complement system[12,13].

In our study, out of all parameters assessed, we found that only CEA was an independent predictor for progression to severe COVID-19 disease and was able to distinguish COVID-19 positive patients who required ICU admission. Further, a significant positive correlation was observed between CEA and CRP. The study conducted by Yu *et al.* (2021) identified CEA, CRP, PCT, and Ferritin along with other biomarkers as independent prognostic factors. The hazard ratio and 95% confidence interval (CI) of the variables were as follows: Ferritin> 907.4 ng/mL; IL-6 > 10.21 pg/mL; PCT > 0.795 ng/mL; CRP > 102.8 mg/L, and CEA > 33.45 ng/mL[4]. Another study done by Chen *et al*. (2020) observed that COVID-19 patients in the non-survivors had significantly higher CEA levels (ng/mL) than the survivors (14.80 ± 14.20 ng/mL *vs*. 3.80 ± 2.43 ng/mL, P <0.001). The risk of death in COVID-19 increased 1.317 times for every increase in 1.0 ng/mL CEA level (OR = 1.317, 95% CI: 1.099–1.579)[14].

CEA which was initially considered as an oncofoetal antigen is a glycoprotein expressed only by the epithelial cell of the gastrointestinal epithelium. It is also expressed by lung mucosal epithelial cells[15]. Previously, over expression of CEA has been observed in various types of cancers such as adenocarcinoma in the respiratory system or digestive system[16]. Its diagnostic and prognostic role has been established for other non-neoplastic lung diseases like HIV-related pneumocystis carinii pneumonia (PCP) and associated ARDS, pulmonary fibrosis, and allergic bronchopulmonary aspergillosis[17]. In the aforementioned diseases, the increased CEA expression by bronchiolar cells and type II pneumocytes were associated with inflammation induced by mucus plug or unusual epithelial proliferation in pulmonary fibrosis[16,18].

In COVID-19, the lung bronchiolar cells and type II pneumocytes are the major targets of the virus due to the presence of ACE-2 receptors. Based upon previous autopsy and other studies, Chen *et al*. (2020) have hypothesized that SARS-CoV-2 infection may have induced enormous alveolar epithelial cell death which may lead to atypical regeneration of type II pneumocytes for repair along with the CEA production. Besides this, unusual epithelial proliferation, fibrosis and mucus plug may also cause an increase in CEA production and secretion[11]. In our study we have provided the cut-off value of CEA (2.68 ng/mL) to distinguish critically ill COVID-19 patients from non-critical patients.

In conclusion, our study demonstrates that serum CEA can be used to predict the severity of COVID-19 associated ARDS and overall disease severity. Along with routine inflammatory biomarkers such as CRP, IL-6, PCT and ferritin, CEA should be used for prognosis and early identification of critical COVID-19 positive patients. Further, regular monitoring of these biomarkers can help to decide treatment regimens and to reduce its associated mortality.

Conclusion

Our study is based on Indian patients with relatively smaller sample size; therefore, further verification is needed in populations in other geographical regions. Although CEA in COVID-19 has been evaluated in a few scientific reports, further studies in larger cohorts of COVID-19 patients are required.

Conflict of interest

All authors declare no conflict of interest.

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