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Predictability of CRP and D-Dimer levels for in-hospital outcomes and mortality of COVID-19

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ABSTRACT

Background: Systemic inflammation elicited by a cytokine storm is considered a hallmark of coronavirus disease 2019 (COVID-19). This study aims to assess the clinical utility of the C-reactive protein (CRP) and D-Dimer levels for predicting in-hospital outcomes in COVID-19.

Methods: A retrospective cohort study was performed to determine the association of CRP and D-Dimer with the need for invasive mechanical ventilation (IMV), dialysis, upgrade to an intensive care unit (ICU) and mortality. Independent t-test and multivariate logistic regression analysis were performed to calculate mean differences and adjusted odds ratios (aOR) with its 95% confidence interval (CI), respectively.

Results: A total of 176 patients with confirmed COVID-19 diagnosis were included. On presentation, the unadjusted odds for the need of IMV (OR 2.5, 95% CI 1.3–4.8, p = 0.012) and upgrade to ICU (OR 3.2, 95% CI 1.6–6.5, p = 0.002) were significantly higher for patients with CRP (>101 mg/dl). Similarly, the unadjusted odds of in-hospital mortality were significantly higher in patients with high CRP (>101 mg/dl) and high D-Dimer (>501 ng/ml), compared to corresponding low CRP (<100 mg/dl) and low D-Dimer (<500 ng/ml) groups on day-7 (OR 3.5, 95% CI 1.2–10.5, p = 0.03 and OR 10.0, 95% CI 1.2–77.9, p = 0.02), respectively. Both high D-Dimer (>501 ng/ml) and high CRP (>101 mg/dl) were associated with increased need for upgrade to the ICU and higher requirement for IMV on day-7 of hospitalization. A multivariate regression model mirrored the overall unadjusted trends except that adjusted odds for IMV were high in the high CRP group on day 7 (aOR 2.5, 95% CI 1.05–6.0, p = 0.04).

Conclusion: CRP value greater than 100 mg/dL and D-dimer levels higher than 500 ng/ml during hospitalization might predict higher odds of in-hospital mortality. Higher levels at presentation might indicate impending clinical deterioration and the need for IMV.

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KEYWORDS
COVID; d-dimer; CRP

1. Introduction

Currently, the novel coronavirus disease 2019 (COVID-19) has become one of the deadliest pandemics that has ravaged the world and carries a high mortality rate. In the USA (US), as of May 2020, over 100,000 deaths have been reported. A large group of these patients present with a sepsis syndrome and hypoxia, eventually requiring a higher level of care and invasive mechanical ventilation (IMV). Due to a higher volume of patients, it is imperative to look for predictors that can guide us in allocating resources for these patients and be prepared in advance as presently our health systems have been stretched to their limits. In the multitude of blood tests and imaging conducted on these patients, CRP and D-Dimer levels are measured in many health-care settings.

CRP is a protein discovered in the 1930s by Tillett and Francis and is an acute phase reactant. It is a pentameric protein which is synthesized by the liver under the action of cytokine interleukin 6 (IL-6). A very high level of CRP >50 mg/dL is mostly associated with bacterial infections but elevated levels are also seen in injuries, cardiovascular processes and other inflammatory states. Elevated CRP levels not only suggest a pro-inflammatory state but also can be used as a prognostic marker for the underlying disease processes [1].

D-dimers are multiple peptide fragments produced as a result of degradation of crosslinked fibrin, mediated by plasmin [2]. The presence of D-dimers indicates the production and degradation of crosslinked fibrin, reflecting the coagulation and fibrinolysis processes occurring concomitantly. In healthy subjects, it is measurable in small amounts, because 2–3% of fibrinogen is converted to fibrin and enters the fibrinolytic pathway under normal physiological conditions [3]. Any processes that involve production and breakdown of fibrin cause an elevation in D-dimer levels. These include acute

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Supplemental data for this article can be accessed here.

venous thromboembolism (VTE), cancer, pregnancy, acute or chronic inflammatory states, acute infections and surgery. As it lacks specificity its role in the current scenario is mainly limited to rule out acute VTE. D-dimer levels vary among patients with confirmed VTE depending on clot burden, timing of measurement, and initiation of treatment [4].

In our study, we aim to see if C-reactive protein and D-Dimer values can be potential predictors of adverse outcomes in the hospital.

2. Methods

2.1. Study design and participants

This is a retrospective study in a single community-based academic hospital designed to look at the relationship between different acute phase reactants/inflammatory markers in patients admitted with COVID 19. All patients had a confirmed diagnosis of COVID-19 between 1 March 2020, and 30 May 2020. The study was approved by the Institutional Review Board (IRB) and the requirement for informed consent was waived by the Research Ethics Committee (REC).

2.2. Data collection

Patients were divided into two groups for each comparison. High D-Dimer (>501 ng/ml) and low D-Dimer (<500 ng/ml) groups were compared both on day-1 and day-7 of hospitalization. Similarly, high CRP (>101 mg/dl) and low CRP (<100 mg/dl) were compared for in-hospital outcomes assessment. Clinical, demographic, laboratory, treatment, and outcome data were extracted from electronic medical records (Sunrise) using a standardized data collection form. Most authors contributed in data retrieval and an independent author adjudicated any difference in interpretation between the data extractors. Laboratory procedures, methods for laboratory confirmation of SARS-CoV-2 infection were standardized. Briefly, SARS-CoV-2 detection in respiratory specimens (throat swabs) by next-generation sequencing or real-time qualitative polymerase chain reaction (RT-qPCR) methods at the Thomas Jefferson University Hospitals, USA was used for all included populations. The criteria for discharge were absence of fever, freedom from symptoms for at least 1 day, substantial clinical or radiological improvement. Routine blood work included coagulation profile, complete blood count, serum biochemical tests (renal function, liver function) lactate dehydrogenase (LDH), myocardial enzymes (troponin T TnT) and serum ferritin.

2.3. Statistical analysis

Continuous variables were presented as mean and standard deviations (SD), categorical variables were reported in percentages and proportions. A chi-square ($\chi 2$) test was used for comparison of categorical data, Fisher exact test was only adopted if the expected count in more than 20% cells was less than 5. To quantify the association between the dichotomous categorical variables, an unadjusted odds ratio (OR) was obtained using a Cochran-Mantel-Haenszel method. To explore the risk factors and gauge the impact of potential effect modifiers (covariates) on our endpoints (in-hospital death, need for an upgrade, ventilators and dialysis) binomial and multinomial logistic regression models were applied. The differences in the baseline comorbidities (DM, HTN, CAD, CKD) and medication use (HCQ, tocilizumab, ramdisivir, anticoagulation and steroids) were accounted for to obtain an adjusted odds ratio (aOR) for all outcomes. For normally and abnormally distributed continuous data, an independent sample t-test and Mann–Whitney U test were used, respectively. A one-way analysis of variance (ANOVA) was used to compare differences in the mean of continuous variables for multiple in-hospital complications. A two-sided α of less than 0.05 was considered statistically significant corroborating inference from a 95% confidence interval (CI). Statistical analyses were performed using the SPSS software (version 25).

3. Results

3.1. Demographics and baseline characteristics

A total of 176 patients with a confirmed diagnosis of COVID-19 were included in our study. Patients were divided into two comparison groups [low D-Dimer (<500 ng/ml) vs. high D-Dimer (>501 ng/ml)] and [low CRP (<100 mg/dl) and high CRP (>100)]. The mean age for CRP patients was (63.6 vs. 61.6) and for D-Dimer groups it was (62.6 vs. 63.7) years, respectively. The baseline comorbidities across all groups were comparable except that higher CRP group (>101 mg/dl) had female predominance. The proportions of underlying comorbidities between low and high CRP groups included DM (83.9% vs. 16.1%), HTN (86.9% vs 13.1%), CAD (93.1% vs 6.1%), CKD (87.1% vs 12.9%), and COPD (91.7% vs 8.3%) respectively. These percentages for low and high D-Dimer groups were; DM (21.1% vs 78.9%), HTN (23.0% vs 80.0%), CAD (19.4% vs 80.6%), CKD (25% vs 75%), and COPD (16.7% vs 83.3%) respectively. Patients in both CRP and D-Dimer groups had similar proportions of medication use (HCQ, tocilizumab, AC, steroids) across both groups (p-value ≤0.05). (Table 1)

Table 1. Baseline characteristics of the included population across comparison groups.

		CRP <100	CRP>101	Sig	D-Dimer <500	D-Dimer>501	Sig
Age		63.6 years	61.6 years	p = 0.71	62.6 years	63.7 years	p = 0.65
Sex	**Male**	66 (80.50%)	16 (19.50%)	p = 0.167	23 (27.70%)	60 (72.30%)	p = 0.04
	Female	75 (88.20%)	10 (11.80%)		13 (14.90%)	74 (85.10%)	
DM	**No**	92 (85.20%)	16 (14.80%)	p = 0.716	23 (21.10%)	86 (78.90%)	p = 0.974
	Yes	49 (83.10%)	10 (16.90%)		13 (21.30%)	48 (78.70%)	
HTN	**No**	48 (80.00%)	12 (20.00%)	p = 0.237	14 (23.30%)	46 (76.70%)	p = 0.611
	Yes	93 (86.90%)	14 (13.10%)		22 (20.00%)	88 (80.00%)	
CAD	**No**	114 (82.60%)	24 (17.40%)	p = 0.16	30 (21.60%)	109 (78.40%)	p = 0.784
	Yes	27 (93.10%)	2 (6.90%)		6 (19.40%)	25 (80.60%)	
CKD	**No**	114 (83.80%)	22 (16.20%)	p = 0.65	28 (20.30%)	110 (79.70%)	p = 0.557
	Yes	27 (87.10%)	4 (12.90%)		8 (25.00%)	24 (75.00%)	
COPD	**No**	119 (83.20%)	24 (16.80%)	p = 0.29	32 (21.90%)	114 (78.10%)	p = 0.56
	Yes	22 (91.70%)	2 (8.30%)		4 (16.70%)	20 (83.30%)	
HCQ	**No**	27 (87.10%)	4 (12.90%)	p = 0.65	8 (27.60%)	21 (72.40%)	p = 0.354
	Yes	114 (83.80%)	22 (16.20%)		28 (19.90%)	113 (80.10%)	
TM	**No**	117 (84.80%)	21 (15.20%)	p = 0.78	28 (20.30%)	110 (79.70%)	p = 0.557
	Yes	24 (82.80%)	5 (17.20%)		8 (25.00%)	24 (75.00%)	
SD	**No**	115 (83.30%)	23 (16.70%)	p = 0.39	32 (22.90%)	108 (77.10%)	p = 0.247
	Yes	26 (89.70%)	3 (10.30%)		4 (13.30%)	26 (86.70%)	
AC	**No**	115 (85.80%)	19 (14.20%)	p = 0.318	25 (18.40%)	111 (81.60%)	p = 0.075
	Yes	26 (78.80%)	7 (21.20%)		11 (32.40%)	23 (67.60%)	

3.2. Mean differences in CRP and D-Dimer

3.2.1. In interventions

The mean difference in the levels of CRP and D-Dimers between patients on definitive COVID-19 therapy compared to those not receiving therapy were mostly identical across its respective groups with few exceptions. On day-1 of presentation, the mean CRP for patients receiving HCQ vs. no HCQ were (130.3 ± 91 vs 130.2 ± 100.0, p = 0.99), tocilizumab vs. no tocilizumab (130.6 ± 69.5 vs 130.2 ± 97.0, p = 0.98), AC vs. no AC (158.3 ± 114.7 vs. 123.3 ± 88.0, p = 0.045) and steroids vs no steroids (151.3 ± 105.8 vs 125.8 ± 88.9, p = 0.17) respectively. Similarly, there was no significant difference in the post-treatment (day 7) mean values of CRP in patients who received HCQ vs. no HCQ (126.5 ± 110.4 vs 99.4 ± 133.5, p = 0.53), AC vs. no AC (170.6 ± 154.7 vs. 112.9 ± 93.7, p = 0.06), and steroids vs no steroids (116.72 ± 151.1 vs 113.9 ± 95.8, p = 0.083), respectively. The mean CRP for patients on Tocilizumab was significantly lower compared to the no Tocilizumab group (65.5 ± 88.9 vs 141.1 + 111.6, p = 0.001), respectively (Figure 1).

The mean D-Dimer values closely followed the overall trend of mean CRP ratios. The mean D-Dimer in HCQ vs. no HCQ were (2293.30 ± 8171.39 vs 3891.29 ± 14,074.41, p = 0.43), tocilizumab vs. no tocilizumab (2304.37 ± 8700.43 vs 2579.0 ± 9377.55, p = 0.88), AC vs. no AC (7931.61 ± 18,845.18 vs 1262.83 ± 3067.02, p = 0.67) and steroids vs no steroids (1437.03 ± 2587.24 vs 2767.67 ± 10,118.28, p = 0.47) respectively. On day-7, the mean D-Dimer for the patients on tocilizumab was significantly higher than those not on tocilizumab (9889.32 ± 13,679.72 vs 2631.49 ± 5264.85, p = 0.007) and AC vs no AC (10,868.13 ± 14,097.24 vs 2418.93 ± 4695.69, p = 0.003). The mean D-Dimer for patients on HCQ vs. no HCQ (4,470.67 ± 8,701.19 vs 894.50 ± 1,263.14, p = 0.318), steroids vs no steroids (6824.79 ± 10,379.90 vs 3725.50 ± 7914.01, p = 0.132), respectively, were not significantly different.

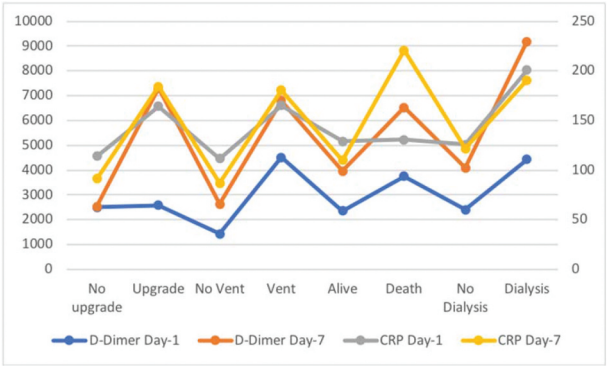

Figure 1. The mean values of CRP and d-dimer levels on day-1 and day-7 of hospitalization across different outcomes.

3.2.2. Outcomes

The mean differences in CRP and D-Dimer for hard clinical outcomes such as in-hospital mortality and resources allocation were also calculated. The mean CRP differences on day-1 of admission were significantly higher for patients requiring an upgrade (164.1 ± 93.9 vs. 114.2 ± 87.4, p = <0.001), IMV (165.2 ± 96.1 vs. 111.4 ± 84.8, p = <0.001) and dialysis (200.7 ± 85.1 vs. 125.9 ± 91.2, p = 0.01) compared to corresponding patients not requiring these supports. The mean CRP difference on day 1 was not significant for patients surviving compared to dead patients (129.1 ± 91.3 vs 130.8 ± 101.6, p = 0.66). On day-7, a higher mean CRP was associated with a higher requirement for upgrade to

a higher level of care (184.0 ± 141.7 vs 91.3 ± 70.6, p = <0.001), IMV (180.5 ± 140.7 vs. 86.8 ± 61.9, p = <0.001) and increased mortality (220.6 ± 140.2 vs. 109.8 ± 98.4, p = 0.003). A higher mean D-Dimer on day 7 was associated with a higher need for an upgrade (7305.36 ± 10,651.83 vs. 2527.91 ± 6420.57, p = 0.005) and IMV (6790.8 ± 9218.44 vs. 2636.31 ± 7660.64, p = 0.007). There was no significant difference in the mean D-Dimer levels for surviving vs. dead patients both on day-1 and day-7.

3.2.3. In complications

In terms of in-hospital complications, patients with deep venous thrombosis and pulmonary embolism had significantly higher mean D-Dimer levels (69,000 and 16.907, p = <0.001), respectively. There was no significant difference in the mean CRP and D-Dimer levels for other in-hospital complications as shown in supplementary tables.

3.3. Odds ratios of outcomes

The unadjusted odds for CRP served as reliable predictors for primary endpoints at presentation. A high CRP (>101 mg/dl) was associated with a significantly higher odds of ventilator requirement (OR 2.5, 95% CI 1.3–4.8, p = 0.012) and upgrade to ICU (OR 3.2, 95% CI 1.6–6.5, p = 0.002). It, however, was not significant for mortality (OR 0.94, 95% CI 0.37–2.4, p = 0.89) and requirement for dialysis (OR 7.6, 95% CI 0.-94–61.8, p = 0.06). On day 7 of hospitalization, the unadjusted odds of being upgraded to the ICU (OR 2.4, 95% CI 1.1–4.9, p = 0.02) and mortality (OR 3.5, 95% CI 1.2–10.5, p = 0.03) was significant. Furthermore, the odds of being on IMV (OR 2.8, 95% CI 0.9–3.6, p = 0.12), and receiving hemodialysis (OR 1.4, 95% CI 0.3–6.8, p = 0.92) were not statistically significant (Table 2, Figure 2).

By contrast, on presentation, the unadjusted odds ratio for in-hospital mortality (OR 2.4, 95% CI 0.89–6.68, p = 0.13), need for upgrade to ICU (OR 1.42, 95% CI 0.7–2.7, p = 0.38), requirement for IMV (OR 2.30, 95% CI 1.2–4.4, p = 0.15) and dialysis (OR 2.3, 95% CI 0.57–9.2, p = 2.5) were not significantly different between patients with a higher D-Dimer (>501 ng/ml) as compared to a low D-Dimer (<500 ng/ml). However, on day-7 of hospitalization, a high D-Dimer (>501 ng/ml) was associated with higher odds of in-hospital mortality (OR 10.0, 95% CI 1.2–77.9, p = 0.02), increased need for upgrade to the ICU (OR 7.8, 95% CI 2.8–21.6, p = <0.001) and higher requirement for IMV (OR 8.2, 95% CI 3.1–21.6, p = <0.001). (Table 3, Figure 3)

A multivariate regression model was used to adjust the observed odds ratios for baseline comorbidities and medications including DM, HTN, CKD, CAD, use of AC at home, HCQ, tocilizumab, steroids and therapeutic anticoagulation during hospital stay. The adjusted odds values were mostly consistent with unadjusted odds ratios indicating no influence of

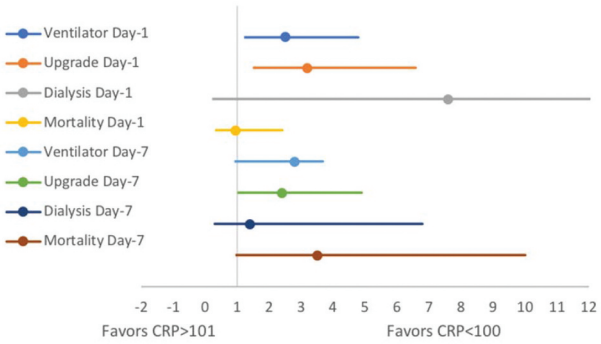

Figure 2. Forest plot for in-hospital outcomes in high and low CRP groups.

Table 2. The unadjusted and adjusted odds ratio of CRP across in-hospital outcomes.

Outcomes	total	CRP <100 mg/dl	CRP >101 mg/dl	Odds (p = value) Day-1	Adjusted odds ratio (p value) Day-1	Odds (p = value) Day-7	Adjusted odds ratio (p value) Day-7
Vent	60	18 (30%)	42 (70%)	OR 2.5 (1.3–4.8, p = 0.012)	aOR 2.5 (1.3–5.3, p = 0.015)	OR 2.8 (0.92–3.67, p = 0.12)	aOR 2.5 (1.05–6.0, p = 0.04)
No Vent	111	57 (51)	54 (49%)				
Upgrade	55	14 (26%)	41 (74%)	OR 3.24 (1.60–6.59, p = 0.002)	aOR 3.2 (1.6–9.9, p = 0.003)	OR 2.4 (1.1–4.9, p = 0.02)	aOR 4.5 (1.7–11.7, p = 0.002)
No Upgrade	116	61 (52.6%)	55 (47.4%)				
Dialysis	10	1 (10%)	9 (90%)	OR 7.6 (0.94–61.8 p = 0.06)	aOR 7.4 (0.86–63, p = 0.07)	OR 1.4 (0.3–6.8, p = 0.92)	aOR 1.1 (0.15–9.6, p = 0.86)
No Dialysis	161	74 (46%)	87 (54%)				
Died	20	9 (45%)	11 (55%)	OR 0.94 (0.37–2.4, p = 0.89)	aOR 0.9 (0.35–2.6, p = 0.95)	OR 3.5 (1.2–10.5, p = 0.03)	aOR 3.7 (1.1–12.5, p = 0.03)
Alive	151	66 (44%)	85 (56%)				

Table 3. The unadjusted and adjusted odds ratio of d-dimer values across in-hospital outcomes.

Outcomes	total	D-Dimer <500 ng/ml	D-Dimer >501 ng/ml	Odds (p = value) Day-1	Adjusted odds ratio (p value) Day-1	Odds (p = value) Day-7	Adjusted odds ratio (p value) Day-7
Vent	59	21 (36%)	38 (64%)	OR 2.30 (1.2–4.4, p = 0.02)	aOR 2.2 (1.1–4.8, p = 0.03)	OR 9.3 (3.30–25.8, p = <0.001)	aOR 15.9 (4.1–60.9, p = <0.0001)
No Vent	106	59 (56%)	47 (44%)				
Upgrade	54	23 (43%)	31 (57%)	OR 1.42 (0.7–2.7, p = 0.38)	aOR 1.4 (0.7–2.9, p = 0.40)	OR 7.8 (2.8–21.6, p = <0.001)	aOR 11.8 (3.1–43.8, p = <0.001)
No Upgrade	111	57 (51%)	54 (49%)				
Dialysis	10	3 (30%)	7 (70%)	OR 2.30 (0.57–9.2, p = 0.38)	aOR 2.1 (0.46–9.9, p = 0.34)	OR – (–, p = 0.20)	aOR – (p = 0.99)
No Dialysis	155	77 (50%)	78 (50%)				
Died	20	6 (30%)	14 (70%)	OR 2.4 (0.89–6.68, p = 0.13)	aOR 2.6 (0.87–7.8, p = 0.08)	OR 10.0 (1.2–77.9, p = 0.02)	aOR 11.9 (1.2–109.9, p = 0.03)
Alive	145	74 (51%)	71 (49%)				

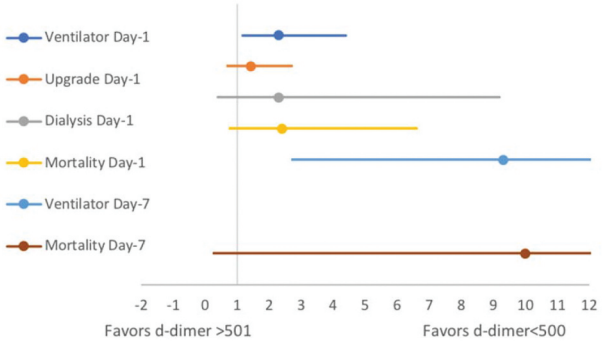

Figure 3. Forest plot for in-hospital outcomes in high and low d-dimer groups.

covariates with one exception. In contrast to unadjusted OR, the adjusted odds ratio for the need of IMV with a high CRP (>101 mg/dl) on day 7 was significant (aOR 2.5, 95% CI 1.05–6.0, p = 0.04).

4. Discussion

Our study reveals that higher D-Dimer levels (>501 ng/ml) on admission might indicate a higher need for invasive mechanical ventilation (IMV). Compared to D-Dimers, a high C-reactive protein (CRP) (>101 mg/dl) on admission predicts not only a greater need for IMV but also for an upgrade to a higher level of care. After completion of therapy for COVID-19, both a high CRP (>101 mg/dl) and elevated D-Dimer levels (>501 ng/ml) were associated with higher odds of in-hospital mortality, need for IMV and upgrade to ICU. When adjusted for baseline comorbidities and medications, patients with CRP level (>101 mg/dl) on presentation have two-fold higher odds of requiring IMV and 3 times higher odds to be upgraded to the intensive care units (ICU). During hospitalization with a consistently higher CRP (>101 mg/dl) on day-7, the odds of requiring IMV and upgrade to ICU increases to 3 and 4 fold compared to patients having lower CRP (<100 mg/dl). Similarly, high CRP (>101 mg/dl) levels were found to confer a 4 times higher rate of in-hospital all-cause mortality when controlled for major confounders.

Compared to CRP, elevated D-Dimer levels (>501 ng/ml) during hospitalization can serve as a more sensitive marker for the severity of COVID-19 infection. Our study showed that patients on the seventh day of admission with D-dimer levels more than 500 ng/mL are 10 times more likely to die than patients with D-dimer levels less than 500 ng/mL. By contrast, the odds of mortality in the higher CRP (>101 mg/dl) were 3 times compared to patients with lower CRP (<100 mg/dl). Even at presentation, elevated D-Dimer (>501 ng/ml) and raised CRP levels (>101 mg/dl) were associated with higher odds of mortality; however, these values did not reach the level of statistical significance. These results contrast the recent findings of a study from Wuhan, China reporting a four-fold increase in in-hospital mortality with a higher D-Dimer level [5]. Previous studies have shown that in medically ill patients, D-dimer levels twice the upper limit of normal were found to have a high risk of developing VTE [6–10]. Our findings also showed a significantly higher mean d-dimer levels for patients developing pulmonary embolism and deep VTE.

Our data on CRP are also in line with literature seen on ICU admissions and mortality pertaining to sepsis syndromes, where a higher CRP was associated with longer length of stays and worse prognosis in terms of mortality [11,12]. To our best knowledge, this is the first study looking at CRP levels and its impact on the need for a higher level of care along with the need for IMV in COVID-19 patients. We believe

that CRP at presentation could serve as a reliable early predictor for in-hospital complications in terms of both the need for IMV and upgrade to ICU, while elevated D-Dimer (>501 ng/ml) could predict only the need for IMV. Nonetheless, both high CRP and raised D-Dimer are useful prognostic markers for overall in-hospital mortality risk, need for IMV and upgrade to ICU. This indicates that both elevated CRP (>101 mg/dl) and D-dimer levels serve as a marker of disease severity at any point during the hospital stay. This is consistent with a smaller retrospective study from Suzhou, China which showed elevated D-Dimer levels in severe COVID-19 patients on day 1, 7 and 14 of hospitalization when compared to mild/moderate COVID-19 patients during the same time period [13].

Previous studies have also shown that patients being admitted to the hospital for COVID 19 can suffer from acute kidney injury and proteinuria that is associated with a higher mortality [14]. Our study, however, demonstrated no significant association of CRP and D-Dimer levels with the in-hospital need for hemodialysis (HD) despite the fact that patients on HD had a higher mean CRP at admission on day-7 of admission.

Briefly, our study advocates for the use of CRP and D-Dimer levels at admission and during hospitalization as the severity and prognostic markers. Patients with rising levels of the markers might need higher levels of care and more vigilant monitoring. Our study highlights the higher risk of adverse outcomes in this patient population allowing physicians to not only anticipate and prognosticate these unfortunate outcomes but also to inform decisions about resource allocation.

5. Limitations

The findings of our study should be interpreted in light of its limitations. Due to the retrospective non-randomized nature of the study, a causal relationship could not be ascertained. Although the overall findings were adjusted for covariates, including baseline comorbidities and medications, the impact of unmeasured confounders such as initiation of several complementary therapies at the treating physician's discretion, could not be determined. Based on our clinical experience, the average duration of any therapy for COVID-19 was less than seven days; therefore, we chose to use day-1 and day-7 laboratory values. However, given the variable frequency of laboratory specimen collection, it is not possible for us to ascertain if these truly represented pre- and post-treatment values accurately in all cases. Moreover, by excluding patients still in the hospital, the case fatality ratio in our study cannot reflect the true mortality of COVID-19. Lastly, the interpretation of our findings might be limited by the sample size. However, by adjusting the adult patients with confirmed disease, we believe our population is the best representative of the real-world cohort.

6. Conclusion

A high CRP (>101 mg/dl) at presentation appears to predict an increased need for IMV and intensive care. A high CRP (>101 mg/dl) and elevated D-Dimer (>501 ng/ml), after COVID-19 therapy, predict higher odds of mortality; however, large scale and longer-term studies are needed to validate our findings.

Disclosure statement

No potential conflict of interest was reported by the authors.

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