Section A -Research paper
ISSN 2063-5346

Markers in Covid-19 Patients of Vadodara: A Tertiary Care Teaching Hospital

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Abstract:

Background:

Coronavirus disease 2019 (COVID-19) is an infectious virus caused by the virus coronavirus 2 resulting in severe acute respiratory syndrome (SARS-CoV-2), which has had a terrible impact on the world, affecting nearly six million individuals. During the COVID-19 pandemic, a link has been observed between COVID-19 infection and acute cardiac injury, which may be related to abnormal levels of inflammation coagulation biomarkers such as troponin, C-reactive protein (CRP), and D-dimer in serum. However, there is currently no agreement on the incidence of cardiac injury, its prognosis, or its possible causes. Therefore, this article presents a detailed analysis and review of the incidence, comorbidities, outcomes, and potential mechanisms of acute cardiac injury in COVID-19 patients.

Aims and objectives: We aimed to detect the rise of various parameters in covid 19 effected patients

Material and methods: This was a cross-sectional, observational study conducted between 12/11/2020 and to may 2021 in covid-19 positive patients and controls. Participants were either gender and age ≥18; Ability to read, understand text and communicate language; and consent to personal data processing. Lack of access of internet. Inability of complete an online survey. Incomplete data in any section of the questionnaire. A total number of RT-PCR-confirmed COVID-19 patients were ordered for a panel of biochemistry tests such as RBS, Urea, Creatinine, T.bil, D.bil, Liver enzymes, Albumin, total protein, Ferritin, D-dimer, Troponin-I, CBP. A total of 190 COVID-19 patients were included in the study. SARS-CoV-2 infection was confirmed by the RT-PCR assay conducted in accordance with the standard protocol.

Results: COVID-19 patients divide into mild, moderate, and severe. These include shortness of breath, chest pain, tachycardia, and hematological parameters such as WBC and platelet, neutrophil, and lymphocyte and coagulation markers such as D-dimer and troponin-I and liver enzyme abnormalities described to be associated with COVID-19 patients. This study has conducted at a tertiary care hospital with a total number of patients was 132 and 132 controls. All these markers are slightly elevated in patients with COVID-19. Determination of coagulation factors such as D-dimer in hospitalized covid-19 patients evidenced a consistent association during the patient's hospital stay.

Conclusion: Biomarkers will play a crucial role in early suspicion, diagnosis, monitoring, and recognition of complications, management and disposition of patients. Each of these components in turn can have crucial implications on the healthcare system and the administrative machinery, directly impacting patient care.

Keywords: COVID-19, RBS, Urea, Creatinine, T-bil, D-bil, Liver enzymes, complete blood count, Albumin, total protein, Ferritin, D-dimer, Troponin-I, CBP.

Introduction:

Coronavirus (Cov) is an enclosed virus with a huge positive-sense, single-stranded RNA genome belonging to the Coronaviridae family. [1] Human pathogenic CoVs are connected with a varied collection of breathing disorders, containing common colds, pneumonia, and bronchiolitis. [2,3] As of January 28, 2021, confirmed COVID-19 infections number over 104 million individuals worldwide, resulting in over 2.21 million deaths. More than 220 countries have reported laboratory-confirmed cases of COVID-19. [4]

The ongoing pandemic of severe acute respiratory syndrome by coronavirus 2 (SARS-CoV-2) continues to pose several diagnostic and therapeutic challenges. First reported from Wuhan in China in December 2019, the World Health Organization on February 11, 2020 officially named this infection, coronavirus disease 2019 (COVID-19) and the virus as SARS-CoV-2. [5] It was declared as a pandemic on March 11, 2020. As on December 9, 2020, there are more than 67 million cases worldwide with more than 1.5 million deaths. [6]

In adults, though SARS-CoV-2 typically causes pneumonia and acute respiratory distress syndrome (ARDS), it is now being recognized as a multisystem disease. In contrast, most children are asymptomatic or have mild to moderate illness. Severe or critical illness is rare. [7] A novel illness, termed multisystem inflammatory syndrome in children (MIS-C) is being increasingly reported in children. Children with MIS-C are sicker, may have multiorgan dysfunction and often require intensive care. [8]

Diagnosis of COVID-19 is confirmed by direct detection of SARS-CoV-2 nucleic acids in respiratory tract specimens with a polymerase chain reaction (PCR). [9] A rapid and accurate diagnosis has wide implications for the patient, healthcare institution, and the public health and administrative personnel. In the current pandemic, healthcare systems are struggling to meet the increasing demands of the rapidly rising infected population. Effective utilization of available resources is paramount to saving the maximum number of lives. Clinical assessment is indispensable, but laboratory markers, or biomarkers, can provide additional, objective information which can significantly impact many components of patient care. [10]
Despite the burgeoning COVID-19 literature database, the treating clinician needs to be effectively updated to offer the best care at the bedside. This article attempts to provide updated and practical information to clinicians on the role of biomarkers in COVID-19.

Aim of the study:
The study aimed to observe the various parameters such as RBS, Urea, Creatinine, T.bil, D.bil, Liver enzymes, Albumin, total protein, Ferritin, D-dimer, Troponin-I, and CBC. In covid-19 affected individuals.

Material and methods: This was a cross-sectional, observational study conducted between 12/11/2020 and to may 2021 in covid-19 positive patients and controls.
Inclusion criteria: Participants were either gender and age ≥18; Ability to read, understand text and communicate language; and consent to personal data processing.

Exclusion criteria: Lack of access of internet. Inability of complete an online survey. Incomplete data in any section of the questionnaire.

A total number of RT-PCR-confirmed COVID-19 patients were ordered for a panel of biochemistry tests such as RBS, Urea, Creatinine, T.bil, D.bil, Liver enzymes, Albumin, total protein, Ferritin, D-dimer, Troponin-I, CBP.

A total of 132 COVID-19 patients were included in the study. SARS-CoV-2 infection was confirmed by the RT-PCR assay conducted in accordance with the standard protocol. All the COVID-19 patients were severe with SpO_2 <90% on room air at sea level and respiratory rate >30/min. Patients with cancer; with pre-existing musculoskeletal disease; with chronic diseases of liver, kidney, and heart; with bacterial and non-covid viral infections; and on immunosuppressive drugs for another disease and pregnant and lactating women were excluded.

Samples
In plain vacutainer, 5 ml of venous blood was collected and allowed to clot for 30 min at room temperature and then centrifuged at 2400×g for 10 min to separate serum. The analysis of inflammatory markers (CRP, LDH, ferritin), SpO_2, liver markers (AST, ALT, ALP), markers of kidney function (electrolytes, urea, creatinine), and random blood sugar (RBS) was performed.

Methods
Tests for biochemical parameters were performed on the Integrated Systems according to the manufacturer's instructions. CRP was determined based on the principle of the latex agglutination. LDH was determined based on the principle of the enzymatic coupling reaction. LDH catalyzes the conversion of pyruvate and NADH to lactate and NAD^+. Oxidation of NADH was monitored by reflectance spectrophotometry, which is used to measure the LDH activity. The ferritin was measured using the principle of immuno-turbidimetry. Agglutination formed due to the reaction between latex-bound ferritin antibodies and the antigen in the sample to form an antigen/antibody complex was measured turbidometrically.

Statistical Analysis:
Data obtained on RBS, Blood Urea, Creatinine, T. Bil, and D. Bil, levels were expressed as mean ± standard deviation

(SD) OT, PT, ALP, Tp, Alb, Ferritin, D-Dimer, Troponin-I, CRP, HB, TC. Differences in the levels of Urea, CRP, WBC, LYM, NEU, Albumin, AST, ALT, and LDH between the RT-PCR positive and negative patients were assessed using student's t-test**.**

Result:
COVID-19 patients divide into mild, moderate, and severe. These include shortness of breath, chest pain, tachycardia, and hematological parameters such as WBC and platelet, neutrophil, and lymphocyte and coagulation markers such as D-dimer and troponin-I and liver enzyme abnormalities described to be associated with COVID-19 patients. This study has conducted at a tertiary care hospital with a total number of patients was 132 and 132 controls. All these markers are slightly elevated in patients with COVID-19.

Determination of coagulation factors such as D-dimer in hospitalized covid-19 patients evidenced a consistent association during the patient's hospital stay. Data retrieved from the patients diagnosed with Covid-19 positive patients between 2020-21 Data from 133 patients were analyzed RBS was elevated in most patients. RBS, BLOOD UREA, CREATININE, T.BIL, D.BIL, OT, PT, ALP, TP, ALB, FERRITIN, D-DIMER, TROPONIN-I, CRP, HB, TC.

Table 1: Baseline characteristics of the patient population Mean and SD of various parameters:

PARAMETER	MEAN ± SD	REFERENCE RANGE
RANDOM BLOOD SUGAR	199.3 ± 53.06	79-140 mg/dL
BLOOD UREA	29.75 ± 13.42	10-40 mg/dL
SERUM CREATININE	1.05 ± 0.60	0.7–1.4 mg/dl
TOTAL BILIRUBIN	0.62 ± 0.18	0.2–1 mg/dl
DIRECT BILIRUBIN	0.25 ± 0.10	0.1-0.4 mg/dl
ALKALINE PHOSPHATASE	59.16 ± 29.54	40–125 IU/L
TOTAL PROTEIN	7.22 ± 0.47	6–8 g/dl
ALBUMIN	3.85 ± 0.68	6–8 g/dl
FERRITIN	219.28 ± 148.58	24-336 µg/L
D-DIMER	3.89 ±21.91	≤ 0.50ng/mL
TROPONIN-I	0.21 ± 0.43	1–10 µg/L
C-REACTIVE PROTEIN	24.74 ± 17.21	≤ 10 mg/L
HEMOGLOBIN	9.32 ± 1.28	12-14 g/dl
TOTAL COUNT	6474.24 ± 2645.30	3.93 - 5.69 million cells/ cubic mm
SGOT	27.66 ± 13.86	8-45 units/ liter
SGPT	24.26 ± 9.03	7 - 56 units / litre
PLATELET	4.40 ± 6.79	1.5 to 4.5Lakhs/µL of blood
NEUTROPHIL	61.5 ± 13.4	1,500 to 8,000 /µL
EOSINOPHIL	5.55 ± 1.49	0 to 500 cells/microL
MONOCYTE	3.87 ±1.31	200-800 cells/microL
LYMPHOCYTE	32.53±7.05	1,000 - 4,800 microliter
BASOPHIL	0 ± 0	0 ± 0

Table 2: Baseline characteristics of the control population Mean and SD of various parameters

PARAMETER	MEAN ± SD	REFERENCE RANGE
RANDOM BLOOD SUGAR	199.30 ± 53.06	79-140 mg/dL
BLOOD UREA	24.47 ± 4.71	10-40 mg/dL
SERUM CREATININE	0.92 ± 0.48	0.7–1.4 mg/dl
TOTAL BILIRUBIN	0.51 ± 0.47	0.2–1 mg/dl
DIRECT BILIRUBIN	0.24 ± 0.98	0.1-0.4 mg/dl
ALKALINE PHOSPHATASE	56.82 ± 29.70	40–125 IU/L
TOTAL PROTEIN	7.32 ± 0.32	6–8 g/dl
ALBUMIN	3.93 ± 0.63	6–8 g/dl
FERRITIN	193.22 ± 66.65	24-336 µg/L
D-DIMER	3.89 ± 29.81	<0.50
TROPONIN-I	0.13 ± 0.19	1–10 µg/L
C-REACTIVE PROTEIN	18.49 ± 5.57	≤ 10 mg/L
HEMOGLOBIN	13.31 ± 8.89	12-14 g/dl
TOTAL COUNT	6056.81 ± 1992.93	3.93 - 5.69 million cells/ cubic mm

SGOT	26.93 ± 13.45	8-45 units/ liter
SGPT	23.42 ± 18.90	7 - 56 units / litre
PLATELET	2.88 ± 0.97	1.5 to 4.5Lakhs/μL of blood
NEUTROPHIL	66.27 ± 8.28	1,500 to 8,000 /μL
EOSINOPHIL	2.81 ± 1.03	0 to 500 cells/microL
MONOCYTE	3.98 ± 1.35	200-800 cells/microL
LYMPHOCYTE	32.53±7.05	1,000 - 4,800 microliter
BASOPHIL	0 ± 0	0 ± 0

		S.CREATININE	**TB**	**DB**	**TP**	**ALB**	**FERRITIN**	**D - DIMER**	**TROPONIN - I**	**HB**	**PLT**	**RBS**	**B. UREA**	**OT**	**PT**	**ALP**	**CRP**
S. CREATININE	Pearson's r-	-	-	-	-												
TB	Pearson's r-	0.071	-	-	-												
DB	Pearson's r-	0.067	0.080	-	-												
TP	Pearson's r-	-0.037	-0.021	0.050	-												
ALB	Pearson's r-	-0.031	-0.007	-0.121	0.000-	-											
FERRITIN	Pearson's r-	-0.029	0.082	-0.121	0.014	0.012	-										
D-DIMER	Pearson's r-	-0.054	0.026	0.039	0.067	0.155	0.229	-	-								
TROPONIN-I	Pearson's r-	-0.067	0.061	-0.105	-0.034	0.065	0.150	0.122	-	-							
HB	Pearson's r-	-0.060	-0.000	0.026	0.040	0.040	-0.019	-0.016	-0.053	-	-						
PLT	Pearson's r-	0.039	0.038	0.077	0.040-	0.040	-0.044	0.059	0.045	-0.047	-						
RBS	Pearson's r-	0.065	0.037	-0.001	-0.024	0.002	-0.010	0.035	-0.068	0.068	-0.051	-					
B. UREA	Pearson's r-	0.427	0.074	0.082	-0.08	-0.014	-0.017	0.026	-0.115	-0.040	0.056	-0.014	-				

					3												
OT	Pearson's r-	0.037	0.056	-0.159	0.004	0.076	-0.060	-0.073	0.030	-0.065	-0.029	-0.009	0.085	-			
PT	Pearson's r-	0.027	-0.057	-0.198	-0.029	0.033	-0.065	-0.018	-0.194	-0.061	-0.004	0.068	0.050	0.165	-		
ALP	Pearson's r-	-0.020	0.083	0.040	0.207	-0.017	0.199	0.269 -	0.009	0.012	0.113	-0.033	-0.025	-0.131	-0.027	-	
CRP	Pearson's r-	0.091	0.076	0.026	0.105	-0.080	0.111	0.036	0.202	-0.061	-0.036	-0.038	0.064	-0.039	-0.001	-0.033	-
N	Pearson's r-	0.001 -	0.057	-0.054	0.089	0.067	-0.168	0.055	-0.204	0.034	-0.191	0.092	-0.073	-0.045	0.136	-0.007	-0.087
L	Pearson's r-	0.064	0.114	-0.090	-0.015	0.000	-0.053	-0.058	-0.016	-0.120	0.022	-0.181	0.050	0.035	0.058	0.058	0.019
E	Pearson's r-	0.094	0.285	0.070	-0.083	-0.028	0.059	0.076	0.208	-0.188	0.054	-0.061	0.205	0.017	0.007	0.011	0.137
M	Pearson's r-	0.021	0.056	0.070	-0.012	0.035	-0.093	-0.088	-0.055	0.108	-0.111	-0.007	-0.016	-0.057	0.023	-0.054	0.048

DISCUSSION:

Based on the findings of this study ALT, CRP, NEU, LDH, and Urea have very good accuracy in predicting cases with positive RT-PCR for COVID-19. Our study aimed at exploring various parameters such as LFT, TROPONIN, and D-DIMER CBC in COVID-19 patients, large portion of patients had increased levels of Higher levels of troponin I, white blood cells (WBCs), D-dimer, and CRP levels are seen in individuals who died of covid-19. Elevated NLR and PLR levels are common in COVID-19 hospitalized patients and, with elevated D-dimer, and prolonged prothrombin time.

CRP levels and serum albumin levels had a strong negative correlation with ESR. In patients with severe COVID- 19, serum albumin had a strong negative correlation with both ESR and CRP levels. In patients with COVID-19, fever, leucocytosis, and an elevated CRP were associated with severe outcomes. Elevation of CRP and blood leukocytes may be used as an indicator of the severity of COVID- 19. The serum levels of CRP along with WBC can effectively assess disease severity and predict outcomes in patients with COVID-19.

Usefulness of Elevated Troponin to Predict Death in Patients With COVID-19 and Myocardial Injury Levels of D-dimer, CRP, TROPONIN and viral load was higher in patients who died of covid and in survivors, WBC count was very high. There was a positive correlation between troponin and myocardial injury and mortality of covid-19 patients. Peripheral blood leukocyte and lymphocyte counts are normal or slightly reduced. Following viremia, SARS-CoV-2 primarily affects the tissues expressing high levels of ACE2 including the lungs, heart, and gastrointestinal tract.

Both CRP and leucocyte count elevated during covid 19 is common among hospitalized patients. Consistent elevation of D-dimer and Hemoglobin observed and D dimer elevation and decreased platelet count associated with disease worsening. Lymphopenia and neutrophilia were observed. Levels of Troponin, D-dimer, CRP, and WBCs were significantly higher in patients who died of COVID-19 than in COVID-19 survivors.

Elevated levels of serum ferritin were an independent predictor in COVID-19 patients. Albumin levels in patients with covid 19 are associated with the severity of the infection and the risk of death. Covid-19 is associated with elevated liver transaminases especially AST predominantly associated. The degree of inflammation in covid 19 patients is represented by high ferritin levels and independent predictive hospital death.

This study provided the baseline laboratory characteristics of severe COVID-19 patients. Twenty-five percent of the severe cases were Control. While there was an increase in the levels of inflammatory markers in all severe COVID-19 patients, they were significantly higher in Control Group compared to Normal Group. Several studies have been conducted to ascertain the relationship between inflammatory markers and the overall outcome of patients with COVID-19 disease. Alroomi showed that ferritin independently predicts in-hospital mortality in Kuwaiti population [12].

A retrospective study of Huang using a large sample size of 1751 Chinese patients showed that LDH associated with higher mortality risk [13]. In contrast, the meta-analysis of Martha concluded that LDH was associated with poor prognosis in COVID-19 patients [14]. Ahmeidi showed that elevation in serum inflammatory marker CRP may be indicative of COVID-19 infection severity and mortality and suggested that these parameters may predict COVID-19 severity [15]. However, their study was limited by inadequate sample size and study design. Yet in another study, El-Shabrawy showed that CRP/albumin ratio predicted 30-day mortality in COVID-19 patients [16].

This study showed that COVID-19 male patients had significantly higher values of ferritin, urea, and creatinine compared to female counterparts. Previously, Gandini showed that higher ferritin levels in males could predict worse outcome in male patients [17]. This is contradictory to the study of Chen, where female COVID-19 patients had significantly higher ferritin levels than male counterparts [18]. Further, a retrospective analysis of 12,413 COVID-19 patients showed that serum creatinine and blood urea nitrogen (BUN) levels are higher in males than females [19].

In the current study, SpO_2 was reduced in COVID-19 patients and showed a negative correlation with LDH and ferritin. Though no previous studies reported the correlation of ferritin with SpO_2, Poggiali *et al*. revealed by retrospective observation study that CRP (r = 0.55, *p-value* < 0.0001) and LDH (r = 0.62, *p-value* < 0.0001) showed strong inverse correlation with the respiratory performance (PaO2/FiO2) [20]. Significant elevation of potassium, urea, and creatinine levels in severe COVID-19 nonsurvivors compared to survivors who had normal levels of urea and creatinine, positive correlation of LDH and ferritin with urea and creatinine levels, and positive correlation of LDH with serum potassium levels are indicative of inflammation-mediated renal failure among nonsurvivors. This is in line with the study of Ng *et al*. among hospitalized COVID-19 patients, which showed higher rate of mortality among patients with end-stage kidney disease than those without this disease [21].

CONCLUSION:
COVID-19 infection is accompanied by vigorous immune and inflammatory response that causes severe lung damage to limit the entry of oxygen to the bloodstream, resulting in long-term breathlessness and severe complications including renal failure. Inflammatory markers (ferritin/LDH) could be useful as a predictor for COVID-19 mortality and respiratory failure and could help the physicians to discern at-risk COVID-19 patients to facilitate early treatment. Elevated LDH increases the odds of severe COVID-19 disease and mortality among ICU-admitted patients.

Conflicts of Interest: Nil

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