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Original Article

Association of Clinical, Biochemical Markers of Cardiac Injury and Inflammation, and Treatment Strategies with Mortality in Hospitalized COVID-19 Patients

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ABSTRACT

Objective: To evaluate the association of clinical, biochemical markers of inflammation and cardiac injury and treatment strategies with adverse outcome in COVID-19 in-patients

Study Design: Retrospective longitudinal study

Place and Duration of Study: Pak Emirates Military Hospital (PEMH), Rawalpindi, Pakistan, from Dec 2020 to Mar 2021.

Methodology: This study involved medical records of laboratory confirmed COVID-19 patients over a period of 03 months at a 1000 bedded facility marked for such patients. All patients were categorized according to cardiac injury; demographic details, presenting features, diagnostic workup, treatment instituted and outcome recorded and analyzed.

Results: *A t*otal of 393 patients were included in the final analysis. Median age of patients was 56 years. Ninety-eight out of 393 patients (24.9%) were female. One hundred and nineteen (30.28%) had cardiac injury, and 54(13.7%) died. Patients with cardiac injury revealed higher median inflammatory markers (Interleukin-6, C-reactive protein, Procalcitonin, Ferritin and Lactate Dehydrogenase) as well as markers of cardiac injury including Brain Natriuretic Peptide-1, Troponin-I, Creatine Kinase-MB and Creatine Kinase. Survival was significantly better in those not having cardiac injury (p<0.001). Cardiac injury, male gender, IL-6 and cough were found to be significantly associated with mortality (p< 0.05).

Conclusion: Hospitalized COVID-19 patients revealed abnormally high inflammatory and cardiac biomarkers in those suffering from cardiac injury. Such patients harbor pronounced clinical course, require more support and had increased mortality. Male gender, cardiac injury, high IL-6 and cough lead to poor outcome.

Keywords: Cardiovascular Diseases, COVID-19, C-Reactive Protein , Interleukin-6, Procalcitonin, Troponin I.

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INTRODUCTION

Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV2), commonly called COVID-19 originated at Wuhan China in December 2019.[1] is a rapidly spreading zoonotic disease that changed the shape of global travel, tourism, business, social fabric and public healthcare altogether.[2] As of 2024, 704,753,890 cases have been reported worldwide.[3] In Pakistan, 1,581,936 cases and 30,664 have been reported up till April 2024.[4] Healthcare infrastructure collapsed completely, especially in developing world leading to catastrophic humanitarian and health crisis.[4]

Although considered a serious communicable disease, most people affected suffer mild to moderate symptoms (fever, fatigue and cough), which usually settle within a week or so.[5] However, life-threatening complications that vary in degree between different individuals may develop rapidly without prediction; these include severe pneumonia, wide spread thrombosis, inappropriate immune storm, cardiac injury, multi-organ dysfunction and death.[5] Though the respiratory tract is primarily affected, there is mounting evidence that cardiac injury underpins survival in COVID-19 patients.[10] Mortality among critical patients is very high (ranging from 26% to 61.5%) especially those suffering from cardiac injury. The postulated mechanisms involve, myocarditis, which ma trigger cardiac arrhythmia and heart failure, in addition to heart destruction affecting almost 40% of non-survivors6. High C-reactive protein (CRP), advanced age, comorbidities especially Diabetes Mellitus, hypertension and Chronic Obstructive Pulmonary Disease increase mortality.[7] However, this association still necessitates further clarification so that appropriate cardiovascular risk stratification may be instituted to avert morbidity as well as mortality.[10] Laboratory biomarkers are less expensive, faster,

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easier to obtain, repeatable and preferred via media to gauge the disease and predict its outcomes and prognosis.[8] Our study therefore retrospectively analyzed data from one of the largest treatment centers from Pakistan to delineate potential correlation between cardiac injury and mortality based upon inflammatory and cardiac biomarkers among COVID-19 patients.

METHODOLOGY

This retrospective longitudinal study was conducted at Pak Emirates Military Hospital (PEMH), Rawalpindi, Pakistan, over a period of 03 months from December 2020 to March 2021 after approval of Ethical Review Board (vide letter no. #A/28/EC/303/2021).

Inclusion Criteria: Medical records of patients admitted to Pak Emirates Military Hospital with laboratory-confirmed COVID-19 (positive real-time polymerase chain reaction and High-resolution computed tomography) chest were included.

Exclusion Criteria: Cases with incomplete clinical, radiological and biochemical data were excluded.

A total of 1122 cases were initially selected from the database. Out of these, 326(29.1%) cases were not confirmed, 214(19.1%) cases were duplicate medical records and 189(16.8%) patients did not have core laboratory parameters. Hence, a total of 729(65.0%) cases were excluded. A final number of 393 cases was finally included for analysis. This process has been illustrated in Figure-1.

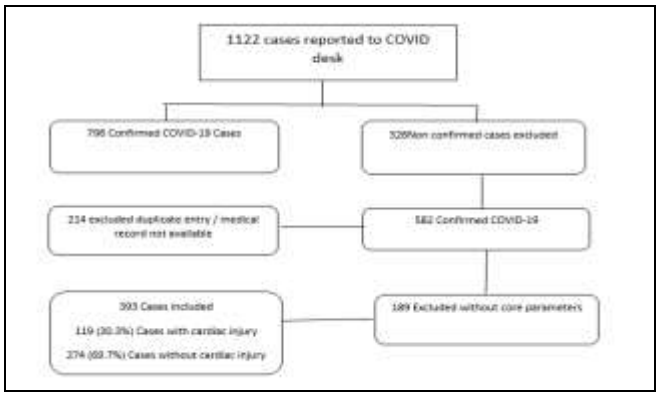

Figure-1: Overview of patient recruitment

Demographic details (age, gender, socioeconomic status, Body Mass Index), clinical parameters (admission severity, symptoms, comorbidities), radiology (CT severity index), laboratory biomarkers (inflammatory, cardiac), treatments and outcome (alive or died) for participants were collected by 02 investigators and independently reviewed and entered into SPSS by 02 analysts. Patients were categorized according to cardiac injury which was defined as levels of cardiac biomarkers including Troponin I (Trop I), Brain natriuretic peptide-1 (BNP-1), Creatinine Kinase- Myocardial Band (CKMB), Creatinine Kinase (CK) above 99th percentile upper reference limit. The clinical outcome (mortality, hospital stay) was noted till 20th March 2021.

Data was analyzed using Statistical Package for the Social Sciences version 25.0. Frequency and percentages were determined for categorical variables and compared by Chi-square test while mean (SD) or median (interquartile range) were used for continuous data, which was analyzed by independent sample T test or Mann-Whitney U test as appropriate. A binary logistic regression analysis was conducted in order to establish a risk model for relating the predictor variables with the occurrence of mortality. Odds ratios with 95% Confidence Intervals (CI) were calculated. A *p*-value of less than 0.05 was considered significant.

RESULTS

Out of these 393 cases, 119 (30.28%) had cardiac injury. The median age of patients was 56 years, and 98 (24.9%) patients were female. Majority 145(36.9%) belonged to middle class. Thirty-seven-point-nine percent presented with severe disease, with median BMI being 26. Fever was the most common presenting feature, observed in 291 (74%) patients, followed by fatigue 232(59%), shortness of breath 229(58.3%), poor appetite 226(57.5%), and cough 208(52.9%). Diarrhea, headache, sore throat and rhinorrhea were rare findings in 46 (11.6%), 77(19.6%), 48(12.2%) and 70(17.8%) patients, respectively. Diabetes (n=192, 48.9%), hypertension (n=185, 47.1%) and cardiovascular disease (n=73, 18.6%) were the most common comorbid conditions, while chronic obstructive pulmonary disease 33(8.4%), cancer 17(4.3%), chronic kidney disease 12(3.1%) and chronic liver disease 11(2.1%) were found sparingly.

Compared with patients without cardiac injury, those having cardiac injury were older (65 versus 54 years, $p<0.001$), having higher BMI (27 vs 26, $p<0.001$), severe disease at admission (87 vs 62, $p<0.001$) and more symptomatic (fever, fatigue, shortness of breath, cough, poor appetite, muscle aches and headache; all $p<0.001$). Moreover, coexisting conditions including diabetes (97 vs 95), hypertension (109 vs 76), cardiovascular disease (58 vs 15), COPD (20 vs 13), CLD (08vs 03) and CKD (07 vs 05) were all present

more often among those having cardiac injury (all p<0.001). This can be seen in Table-I.

Majority of the patients presented with moderate CT severity index (CTSI) (n=159, 40.5%), and statistically significant difference in CTSI was found between those having cardiac injury and those without (64.7% vs11.3%, p value <0.001). Patients with cardiac injury revealed higher median inflammatory markers (IL-6, C-reactive protein, Procalcitonin, Ferritin and LDH,) as well as cardiac injury markers (BNP-1, Troponin-I, CKMB and CK), with having a p-value <0.001, as can be seen in Table-I.

All patients received protocol driven antiviral as well as antibiotic therapy while steroids. Actemra® and plasma exchange therapy was administered to 279(71%), 93(23.7%) and 74 (18.8%) patients, respectively. Supplemental oxygen was required in 181(46.1%) patients, non-invasive ventilation (NIV) in 92(23.4%) and ventilatory support in 63(16%) patients. Those with cardiac injury were more likely to require oxygen / ventilatory support, steroids and plasma exchange therapy (all p<0.001) while there was no difference between 2 groups with regard to Actemra® (p=0.077). Survival was significantly better in those not having cardiac injury (96.7% vs 62.2% p<0.001). Data analysis in respect of survival revealed that non-survivors were older (p<0.001), had higher BMI (p<0.001), severe disease at admission (p<0.001), severe CTSI (p<0.001), higher Charlson Comorbidity Index (CCI) (p<0.001), more symptomatic (p<0.001), more likelihood of having oxygen saturation less than 93% at admission (p<0.001), longer hospital stay (p<0.001), significant raised inflammatory as well as cardiac biomarkers and higher incidence of cardiac injury (p<0.001, Table II).

We further analyzed the potential factors related to the clinical outcome. The variables considered were cardiac injury, gender, IL-6 levels, cough and the presence of fever. The model had a Nagelkerke R square value of 0.566, making it a moderately strong model. This suggests that the model significantly

Table-I Baseline Characteristics and Clinical Markers Patients with COVID-19 as per Cardiac Injury Status (n=393)

Characteristic		Cardiac Injury		Total n(%)	*p*-value
		Yes n (%)	No n (%)		
Age* Median (IQR)		65 (17)	54 (20)	56 (21)	< 0.001
Gender	Male	86 (72.27%)	209 (76.28%)	295 (75.06%)	
	Female	33 (27.73%)	65 (23.72%)	98 (24.94%)	0.399
BMI* Median (IQR)		27 (5)	26 (3)	26 (4)	< 0.001
Severity at Admission	Mild	4 (3.36%)	114 (41.61%)	118 (30.03%)	
	Moderate	28 (23.53%)	98 (35.77%)	126 (32.06%)	
	Severe	87 (73.11%)	62 (22.63%)	149 (37.91%)	<0.001
Socioeconomic Status	Upper	26 (21.85%)	96 (35.04%)	122 (31.04%)	
	Middle	47 (39.50%)	98 (35.77%)	145 (36.90%)	0.026
	Lower	46 (38.66%)	80 (29.20%)	126 (32.06%)	
CT Severity Index	Mild	4 (3.36%)	122 (44.53%)	126 (32.06%)	
	Moderate	38 (31.93%)	121 (44.16%)	159 (40.46%)	
	Severe	77 (64.71%)	31 (11.31%)	109 (27.74%)	< 0.001
Charlson Comorbidity Index CCI	None	1 (0.84%)	42 (15.33%)	43 (10.94%)	
	Mild	4 (3.36%)	169 (61.68%)	173 (44.02%)	
	Moderate	28 (23.53%)	40 (14.60%)	68 (17.30%)	< 0.001
	Severe	86 (72.27%)	23 (8.39%)	109 (27.74%)	
Patient Admission Status	Ward	4 (3.36%)	114 (41.61%)	118 (30.03%)	
	AMU	28 (23.53%)	98 (35.77%)	126 (32.06%)	
	HDU	26 (21.85%)	23 (8.39%)	49 (12.47%)	
	ITC	61 (51.26%)	39 (14.23%)	100 (25.45%)	< 0.001
Comorbidities	CVS Disease	58 (48.74%)	15 (5.47%)	73 (18.58%)	< 0.001
	Hypertension	109 (91.60%)	76 (27.74%)	185 (47.07%)	< 0.001
	Diabetes	97 (81.51%)	95 (34.67%)	192 (48.85%)	< 0.001
	Cancer	7 (5.88%)	10 (3.65%)	17 (4.33%)	0.317
	CKD	7 (5.88%)	5 (1.82%)	12 (3.05%)	0.050
	CLD	8 (6.72%)	3 (1.09%)	11 (2.80%)	0.004
	COPD	20 (16.81%)	13 (4.74%)	33 (8.40%)	< 0.001
Fever		112 (94.12%)	179 (65.33%)	291 (74.05%)	< 0.001
Cough		92 (77.31%)	116 (42.34%)	208 (52.93%)	< 0.001
Shortness of Breath		117 (98.32%)	112 (40.88%)	229 (58.27%)	< 0.001
Oxygen Saturation	>93%	0 (0%)	130 (47.45%)	130 (33.08%)	
	85-92%	39 (32.77%)	129 (47.08%)	168 (42.75%)	< 0.001
	< 85%	80 (67.23%)	15 (5.47%)	95 (24.17%)	

Muscle Aches		97 (81.51%)	71 (25.91%)	168 (42.75%)	< 0.001
Appetite		17 (14.29%)	150 (54.74%)	167 (42.49%)	< 0.001
Diarrhoea		12 (10.08%)	34 (12.41%)	46 (11.70%)	0.510
Sore Throat		13 (10.92%)	35 (12.77%)	48 (12.21%)	0.607
Headache		38 (31.93%)	39 (14.23%)	77 (19.59%)	< 0.001
Fatigue		49 (41.18%)	183 (66.79%)	232 (59.03%)	< 0.001
Rhinorrhea		20 (16.81%)	50 (18.25%)	70 (17.81%)	0.731
Hospital Stay	< 7 Days	32 (26.89%)	2 (0.73%)	34 (8.65%)	
	8 – 15 Days	9 (7.56%)	211 (77.01%)	220 (55.98%)	< 0.001
	16 – 21 Days	6 (5.04%)	37 (13.50%)	43 (10.94%)	
	<22 Days	72 (60.50%)	24 (8.76%)	96 (24.43%)	
IL-6*		243 (557.5)	18.8 (39.8)	30.1 (62.7)	< 0.001
C-Reactive Protein*		200.9 (273)	46.6 (65.7)	65.5 (115.7)	< 0.001
Procalcitonin*		0.35 (0.86)	0.05 (0.13)	0.09 (0.24)	< 0.001
Ferritin*		934 (1269)	377 (412)	504 (586)	< 0.001
LDH*		681 (506)	353 (251)	420 (327)	< 0.001
BNP-1*		768 (418.4)	106.6 (249.3)	224.1 (515)	< 0.001
Troponin I*		0.25 (0.24)	0.10 (0.01)	0.1 (0.1)	< 0.001
CKMB Activity*		56 (33)	19 (10)	23 (29)	< 0.001
Creatinine Kinase*		298 (115)	110 (89)	156 (170)	< 0.001
Supplemental Oxygen		115 (96.64%)	66 (24.09%)	181 (46.06%)	< 0.001
NIV		41 (34.45%)	51 (18.61%)	92 (23.41%)	0.001
Mechanical Ventilation		50 (42.02%)	13 (4.74%)	63 (16.03%)	< 0.001
Antiviral Therapy		119 (100%)	274 (100%)	393 (100%)	---
Steroids		119 (100%)	160 (58.40%)	279 (70.99%)	< 0.001
Antibiotics Therapy		119 (100%)	274 (100%)	393 (100%)	---
Actemra®		35 (29.41%)	58 (21.17%)	93 (23.66%)	0.077
Plasma Exchange Therapy		65 (54.62%)	9 (3.28%)	74 (18.83%)	< 0.001
Survival		74 (62.18%)	265 (96.72%)	339 (86.26%)	< 0.001

*AMU: Acute Medical Unit, HDU: High Dependency Unit, ITC: Intensive Care Unit, CLD: Chronic Liver Disease, CKD: Chronic Kidney Disease, COPD: Chronic Obstructive Pulmonary Disease, CVS: Cardiovascular System, CKMB: Creatine-Kinase Myocardial Band, LDH: Lactate Dehydrogenase, BNP: Brain Natriuretic Peptide, IL-6: Interleukin-6. *: Median (IQR)*

predicts 56.6% of the variation in the occurrence of mortality. The odds of mortality significantly increased by 3.969 with the presence of cardiac injury in patients. The odds of mortality decreased by 0.327 for female patients as compared to males. For every unit increase in IL-6 levels, the odds of mortality increased by 1.005. Mortality increased significantly by odds of 5.012 for patients having a cough. There was no significant association between fever and mortality (Table-III).

DISCUSSION

Our Median cohort age was 56 years (IQR 21), aligning with prior studies.12 Niraula et al. reported a mean age of 55 years, while Wuhan data showed median 64 years.11,13 A US study reported mean age 57.5±16.8, close to ours.[14,15]

Most patients presented with severe disease 149(37.9%); 145(36.9%) were from the middle socioeconomic group. Diabetes, hypertension, and heart disease were the most common comorbidities,

Table-II Baseline Characteristics and Clinical Markers of 393 Patients with COVID-19 as per Survival Status (n=393)

Characteristic		Survival		Total	*p* value
		Yes n(%)	No n(%)		
Age*		55 (20)	70 (13)	56 (21)	< 0.001
Gender	Male	264 (77.9%)	31 (57.4%)	295 (75.1%)	0.001
	Female	75 (22.1%)	23 (42.6%)	98 (24.9%)	
BMI*		26 (3)	28 (5)	26 (4)	< 0.001
Severity at Admission	Mild	118 (34.8%)	0 (0%)	118 (30%)	< 0.001
	Moderate	120 (35.4%)	6 (11.1%)	126 (32.1%)	
	Severe	101 (29.8%)	48 (88.9%)	149 (37.9%)	
Socioeconomic Status	Upper	102 (30.1%)	20 (37%)	122 (31%)	0.072
	Middle	121 (35.7%)	24 (44.4%)	145 (36.9%)	
	Lower	116 (34.2%)	10 (18.5%)	126 (32.1%)	
CT Severity Index	Mild	126 (37.2%)	0 (0%)	126 (32.1%)	< 0.001
	Moderate	150 (44.2%)	9 (16.7%)	159 (40.5%)	
	Severe	63 (18.6%)	45 (83.3%)	108 (27.5%)	

Charlson Comorbidity Index CCI	None	43 (12.7%)	0 (0%)	43 (10.9%)	
	Mild	173 (51%)	0 (0%)	173 (44%)	
	Moderate	60 (17.7%)	8 (14.8%)	68 (17.3%)	< 0.001
	Severe	63 (18.6%)	46 (85.2%)	109 (27.7%)	
Patient Admission Status	Ward	118 (34.8%)	0 (0%)	118 (30%)	
	AMU	120 (35.4%)	6 (11.1%)	126 (32.1%)	
	HDU	43 (12.7%)	6 (11.1%)	49 (12.5%)	
	ITC	58 (17.1%)	42 (77.8%)	100 (25.4%)	< 0.001
Comorbidities	CVS Disease	40 (11.8%)	33 (61.1%)	73 (18.6%)	< 0.001
	Hypertension	135 (39.8%)	50 (92.6%)	185 (47.1%)	< 0.001
	Diabetes	147 (43.4%)	45 (83.3%)	192 (48.9%)	< 0.001
	Cancer	15 (4.4%)	2 (3.7%)	17 (4.3%)	1.000
	CKD	11 (3.2%)	1 (1.9%)	12 (3.1%)	1.000
	CLD	5 (1.5%)	6 (11.1%)	11 (2.8%)	0.001
	COPD	20 (5.9%)	13 (24.1%)	33 (8.4%)	< 0.001
Fever		243 (71.7%)	48 (88.9%)	291 (74%)	0.007
Cough		163 (48.1%)	45 (83.3%)	208 (52.9%)	< 0.001
Shortness of Breath		175 (51.6%)	54 (100%)	229 (58.3%)	< 0.001
Oxygen Saturation	>93%	130 (38.3%)	0 (0%)	130 (33.1%)	
	85-92%	160 (47.2%)	8 (14.8%)	168 (42.7%)	< 0.001
	< 85%	49 (14.5%)	46 (85.2%)	95 (24.2%)	
Muscle Aches		116 (34.2%)	52 (96.3%)	168 (42.7%)	< 0.001
Appetite		164 (48.4%)	3 (5.6%)	167 (42.5%)	< 0.001
Diarrhoea		38 (11.2%)	8 (14.8%)	46 (11.7%)	0.444
Sore Throat		40 (11.8%)	8 (14.8%)	48 (12.2%)	0.530
Headache		58 (17.1%)	19 (35.2%)	77 (19.6%)	0.002
Fatigue		191 (56.3%)	41 (75.9%)	232 (59%)	0.007
Rhinorrhea		57 (16.8%)	13 (24.1%)	70 (17.8%)	0.731
Hospital Stay	< 7 Days	22 (6.5%)	12 (22.2%)	34 (8.7%)	
	8 – 15 Days	213 (62.8%)	7 (13%)	220 (56%)	
	16 – 21 Days	34 (10%)	9 (16.7%)	43 (10.9%)	< 0.001
	<22 Days	70 (20.6%)	26 (48.1%)	96 (24.4%)	
IL-6*		21.6 (45.5)	560 (751.7)	30.1 (62.7)	< 0.001
C-Reactive Protein*		53.5 (69.2)	276.8 (310)	65.5 (115.7)	< 0.001
Procalcitonin*		0.07 (0.18)	0.44 (1.60)	0.09 (0.24)	< 0.001
Ferritin*		448 (538)	906 (986)	504 (586)	< 0.001
LDH*		390 (292)	765 (398)	420 (327)	< 0.001
BNP-1*		155.2 (398.4)	875.5 (480)	224.1 (515)	< 0.001
Troponin I*		0.10 (0.04)	0.33 (1.13)	0.1 (0.1)	< 0.001
CKMB Activity*		21 (24)	62 (50)	23 (29)	< 0.001
Creatinine Kinase*		145 (146)	299.5 (117)	156 (170)	< 0.001
Supplemental Oxygen		127 (37.5%)	54 (100%)	181 (46.1%)	< 0.001
NIV		86 (25.4%)	6 (11.1%)	92 (23.4%)	0.022
Mechanical Ventilation		17 (5%)	46 (85.2%)	63 (16%)	< 0.001
Antiviral Therapy		339 (100%)	54 (100%)	393 (100%)	---
Steroids		225 (66.4%)	54 (100%)	279 (71%)	< 0.001
Antibiotics Therapy		339 (100%)	54 (100%)	393 (100%)	---
Actemra®		77 (22.7%)	16 (29.6%)	93 (23.7%)	0.267
Plasma Exchange Therapy		35 (10.3%)	39 (72.2%)	74 (18.8%)	< 0.001
Cardiac Injury		74 (21.8%)	45 (83.3%)	119 (30.3%)	< 0.001

*AMU: Acute Medical Unit, HDU: High Dependency Unit, ITC: Intensive Care Unit, CLD: Chronic Liver Disease, CKD: Chronic Kidney Disease, COPD: Chronic Obstructive Pulmonary Disease, CVS: Cardiovascular System, CKMB: Creatine-Kinase Myocardial Band, LDH: Lactate Dehydrogenase, BNP: Brain Natriuretic Peptide, IL-6: Interleukin-6, BMI: Body Mass Indes, NIV: Non-Invasive Ventilation. *: Median (IQR)*

which is similar to other Asian.[13,14] Fever was the predominant symptom, followed by dyspnea, cough, and myalgia, comparable with other reports, though Suleyman *et al.* found cough most common.[14,15] Direct

Table-III Logistic Regression Model of Predictor Variables for the Occurrence of Mortality

Factor	Study Parameter		Univariate Logistic Regression			Multivariate Logistic Regression		
	Yes	No	*p* Value	Unadjusted OR (UOR)	95% CI for UOR	*p* Value	Adjusted OR	95% CI for AOR
Cardiac Injury	45(37.8%)	9(3.3%)	< 0.001	17.905	8.368-38.212	0.010	3.969	1.969-11.292
Gender	Male 31 (10.5%)	Female 23 (23.5%)	0.002	0.383	0.211- 0.696	0.011	0.327	0.138- 0.776
IL-6*	--	--	< 0.001	1.006	1.005-1.007	< 0.001	1.005	1.003- 1.007
Cough	45(21.6%)	9(4.9%)	< 0.001	5.399	2.559-11.392	0.003	5.012	1.760-14.272
Fever	48(16.5%)	6(5.9%)	0.010	3.160	1.310-7.267	0.141	0.407	0.123-1.346
Constant	--	--	< 0.001	0.063	--	< 0.001	0.033	--

*(OR = Odds Ratio, CI = Confidence Intervals; * = Quantitative Variable)*

ICU/HDU admissions formed the majority (37.9%), which was consistent with regional and local studies.[13,15]

Compared to those without cardiac injury, affected patients were older, had higher BMI, more comorbidities (higher CCI), more severe disease, and longer hospital stay, consistent with prior work.[16-18] Cardiac injury patients showed significantly elevated inflammatory markers and cardiac markers (p<0.001), consistent with earlier reports.[19,20] They also had higher CTSI, greater need for ventilation and ICU care, as noted by Shi *et al*.[21]

Mechanisms of cardiac injury remain unclear but likely involve direct myocardial damage, ACE-2, cytokine storm, and immune mechanisms.[23] Our data showed elevated inflammatory markers is consistent with injury, which is in line with various international studies.[11,12,14,24] Li *et al*. also confirmed correlation between inflammatory and cardiac markers, reinforcing cytokine-mediated injury and its link to mortality.[20]

We noted that cardiac injury patients more often required oxygen (invasive and non-invasive), glucocorticoids, plasma exchange, antibiotics, and IVIG. This is consistent with numerous studies.[11,15,18,19] Mortality was 13.7% overall, but significantly higher with cardiac injury [45 (37.8%) vs 9 (3.3%), p<0.001]. Logistic regression showed cardiac injury, IL-6, and cough as significant mortality predictors, consistent with different studies.[23,24]

Non-survivors were older, more often male, had higher BMI, severe disease, higher CTSI, more symptoms, elevated inflammatory/cardiac markers, and greater need for intensive support and steroids. These findings mirror global data.[13,15]

LIMITATION OF STUDY

This study has several limitations: it is a single-center, retrospective, descriptive study without a control arm, subject to bias from comorbidities, superimposed infections, and multiorgan failure. We also had in-patient data only, and did not follow the patients up for a longer period to check outcomes. In addition, dynamic changes in biomarkers over time were not assessed.

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CONCLUSION

Hospitalized COVID-19 patients in our study frequently exhibited significant cardiac injury with elevated inflammatory and cardiac biomarkers. Male gender, cardiac injury, high IL-6 and cough lead to poor outcome.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

QUAM & MTS: Data acquisition, data analysis, critical review, approval of the final version to be published.

AH & BA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

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Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Coronavirus disease (COVID-2019) situation reports 2021. World Health Organization (Internet). Accessed June 7 2021. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/ situation-reports. World Health Organization, Geneva.
2. Coronavirus disease 2019 (COVID-19). Centers for Disease Control and Prevention (Internet). Accessed June 7, 2021. https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/cases-in-us.html
3. COVID-19 map. John Hopkins Coronavirus Resource Center (Internet). Published 2020. Accessed June 7, 2021. https://coronavirus.jhu.edu/map.html

4. . COVID-19 to slash global economic output by $8.5 trillion over next two years. United Nations department of economic and social affairs (Internet). Accessed June 7, 2021. Available from: https://www.un.org/en/desa/covid-19-slash-global-economic-output-85-trillion-over-next-two-years
5. Boban M. Novel coronavirus disease (COVID-19) update on epidemiology, pathogenicity, clinical course and treatments.Int J Clin Pract 2021; 75(4): e13868. https://doi.org/10.1111/ijcp.13868
6. Beyerstedt S, Casaro EB, Rangel ÉB. COVID-19: angiotensin-converting enzyme 2 (ACE2) expression and tissue susceptibility to SARS-CoV-2 infection.Eur J Clin Microbiol Infect Dis 2021; 40(5): 905-919. https://doi.org/10.1007/s10096-020-04138-6
7. Liu F, Li L, Xu M. Prognostic value of interleukin-6, C-reactive protein, and procalcitonin in patients with COVID-19. J Clin Virol 2020; 127: 104370. https://doi.org/10.1016/j.jcv.2020.104370
8. Yu JS, Pan NN, Chen RD, Zeng LC, Yang HK, Li H. Cardiac Biomarker Levels and Their Prognostic Values in COVID-19 Patients with or Without Concomitant Cardiac Disease. Front Cardiovasc Med 2021; 7(1): 599096. https://doi.org/10.3389/fcvm.2020.599096
9. Salzberger B, Buder F, Lampl B, Ehrenstein B, Hitzenbichler F, Holzmann T, et al. Epidemiology of SARS-CoV-2.Infection 2021; 49(2): 233-239. https://doi.org/10.1007/s15010-020-01531-3
10. Ma L, Song K, Huang Y. Coronavirus Disease-2019 (COVID-19) and Cardiovascular Complications. J Cardiothorac Vasc Anesth 2021; 35(6): 1860-1865. https://doi.org/10.1053/j.jvca.2020.04.041
11. Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. JAMA Cardiol 2020; 5 (7): 802–810. https://doi.org/10.1001/jamacardio.2020.0950
12. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study [published correction appears in Lancet. 2020 Mar 28;395(10229):1038].Lancet. 2020; 395(10229): 1054-1062. https://doi.org/10.1016/S0140-6736(20)30566-3
13. Niraula A, Baral N, Lamsal M, Bataju M, Thapa S. Potential role of biochemical markers in the prognosis of COVID-19 patients. SAGE Open Med 2022; 10: 20503121221108613. https://doi.org/10.1177/20503121221108613
14. Quin JJ, Cheng X, Zhou F, Lie F, Akolkar G, Cai J, et al. Redefining Cardiac Biomarkers in Predicting Mortality of Inpatients With COVID-19. Hypertension 2020; 76(4): 1104–1112. https://doi.org/10.1161/hypertensionaha.120.15528
15. Suleyman G, Fadel RA, Malette KM, Hammond C, Abdulla H, Entz A, et al. Clinical Characteristics and Morbidity Associated With Coronavirus Disease 2019 in a Series of Patients in Metropolitan Detroit. JAMA Netw Open. 2020; 3(6): e2012270. https://doi.org/10.1001/jamanetworkopen.2020.12270
16. Clerkin KJ, Fried JA, Raikhelkar J, Sayer G, Griffin JM, Masoumi A, et al. COVID-19 and Cardiovascular Disease. Circulation 2020; 141(20): 1648-1655. https://doi.org/10.1161/CIRCULATIONAHA.120.046941
17. Azevedo RB, Botelho BG, Hollanda JVG, Ferreira LVL, Junqueira LZ, Oei SSML, et al. Covid-19 and the cardiovascular system: a comprehensive review. J Hum Hypertens 2021; 35(1): 4-11. https://doi.org/10.1038/s41371-020-0387-4
18. Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). JAMA Cardiol 2020; 5(7): 811-818. https://doi.org/10.1001/jamacardio.2020.1017
19. García L, Morell-García D, Rodríguez-Fraga O, Morales-Indiano C, María A, Gutiérrez JI,et al. Cardiac troponin and COVID-19 severity: Results from BIOCOVID study. Eur J Clin Invest 2021 ; 51(6): e13532. https://doi.org/10.1111/eci.13532
20. Li C, Jiang J, Wang F, Zhou N, Veronese G, Moslehi JJ, et al. Longitudinal correlation of biomarkers of cardiac injury, inflammation, and coagulation to outcome in hospitalized COVID-19 patients. J Mol Cell Cardiol 2020; 147: 74-87. https://doi.org/10.1016/j.yjmcc.2020.08.008
21. Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. Lancet Infect Dis 2020; 20(4): 425-434. https://doi.org/10.1016/S1473-3099(20)30086-4
22. Singh SP, Pritam M, Pandey B, Yadav TP. Microstructure, pathophysiology, and potential therapeutics of COVID-19: A comprehensive review. J Med Virol 2021; 93(1): 275-299. https://doi.org/10.1002/jmv.26254
23. Gordon JS, Drazner MH. Biomarkers of Cardiac Stress and Cytokine Release Syndrome in COVID-19: A Review.Curr Heart Fail Rep 2021; 18(3): 163-168. https://doi.org/10.1007/s11897-021-00505-2
24. Marin BG, Aghagoli G, Lavine K, Yang L, Siff EJ, Chiang SS, et al. Predictors of COVID-19 severity: A literature review.Rev Med Virol 2021; 31(1): 1-10. https://doi.org/10.1002/rmv.2146
25. Talasaz AH, Kakavand H, Van Tassell B, Aghakouchakzadeh M, Sadeghipour P, Dunn S,et al. Cardiovascular Complications of COVID-19: Pharmacotherapy Perspective.Cardiovasc Drugs Ther 2021; 35(2): 249-259. https://doi.org/10.1007/s10557-020-07037-2

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