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Santosh Kumar Sidhwani, Talat Mirza, Ambrina Khatoon, Fouzia Shaikh, Rizma Khan, Omer Ahmed Shaikh, Abdulqadir J. Nashwan

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Inflammatory Markers and COVID-19 Disease Progression

1. **Dr. Santosh Kumar Sidhwani**
Associate Professor
Department of Pathology
Ziauddin University
santosh.kumar@zu.edu.pk

2. **Dr. Talat Mirza**
Meritorious Professor
Executive Director
Department of Research
Ziauddin University
deanresearch@zu.edu.pk

3. **Dr. Ambrina Khatoon**
Assistant Professor
Department of Research
Ziauddin University
ambrina.khatoon@zu.edu.pk

4. **Dr. Fouzia Shaikh**
Professor and Head
Department of Pathology
Ziauddin University
fouzia.shaikh@zu.edu.pk

5. **Dr. Rizma Khan**
Assistant Professor
Department of Molecular Genetics
Ziauddin University
rizma.khan@zu.edu.pk

6. **Dr. Omer Ahmed Shaikh**
MBBS
Department of Medicine
Ziauddin University
omerahmedshaikh@gmail.com

7. **Abdulqadir J. Nashwan *(Corresponding Author)**
Director of Nursing for Education
Hamad Medical Corporation, Doha, Qatar
Email: anashwan@hamad.qa
ORCID: https://orcid.org/0000-0003-4845-4119

***Corresponding Authors:**

1. Abdulqadir J. Nashwan, Hamad Medical Corporation, Doha, P.O. Box 3050, Qatar. Email: anashwan@hamad.qa; ORCID: https://orcid.org/0000-0003-4845-4119

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Conflict of interest

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Ethics approval

Ethical approval was taken from the institutional approval from Ethical review committee dated November 5th, 2020. (Reference code: 2650920SKPAT).

Author's contribution

Dr. Santosh Kumar and Dr. Talat Mirza conceived the idea, designed the project. Dr. Ambrina Khatoon did the bioinformatics analysis and bench work along with Dr. Rizma Khan and Dr. Fouzia Shaikh supervised the project. Dr. Santosh Kumar and Dr. Omer Ahmed Shaikh wrote the manuscript and done the statistics. Abdulqadir Nashwan reviewed critically and edited the manuscript.

Abstract

Background: The COVID-19 pandemic has resulted in a global humanitarian crisis. Despite ongoing research, transmission risks and many disease characteristics remain unclear. Most patients have displayed elevated levels of certain inflammatory markers, which we sought to investigate further in relation to disease severity. The aim of this study was to examine the correlation between inflammatory markers and the severity of COVID-19 among patients.

Methods: We conducted a cross-sectional study from April to September 2020, involving 143 COVID-19 PCR-positive patients from Ziauddin Hospital. Electronic patient records provided data on demographics, clinical status, and laboratory results.

Results: The majority of PCR-positive patients were elderly males with comorbidities such as diabetes and hypertension. Almost all patients exhibited increased levels of various inflammatory markers, with procalcitonin (97.2%) being the most common. Statistically significant differences were observed in the levels of TLC (p=0.005), CRP (p=0.001), LDH (p=0.001), Ferritin (p=0.001), D-dimer (p=0.001), and procalcitonin (p=0.028), in relation to COVID-19 severity.

Conclusions: The data suggest a significant association between levels of inflammatory markers and COVID-19 severity. All markers, except procalcitonin, demonstrated a significant correlation with disease severity. These results could enhance our understanding of COVID-19 pathogenesis and help predict and manage severe cases.

Key Words: COVID-19, CRP, LDH, Inflammatory, Markers, Pandemic

Introduction:

When numerous cases of a deadly respiratory disease were discovered in Wuhan City, Hubei Province, China, at the end of 2019, it signaled the beginning of a new humanitarian crisis. (1) The problem's scope quickly grew to become a pandemic. More than 213 nations throughout the world have been affected, and it has been estimated that over 6 billion deaths have been reported to date, affecting about 15 million people. (2) The unique 2019 coronavirus illness (COVID-19) spread quickly in China before affecting 213 nations in Europe, America, Australia, and Asia, including Pakistan. (3) It became a global public health emergency. Although the numbers are already declining internationally, more than 2,470,772 deaths and 111,419,939 confirmed cases have been affected. (4)

The novel coronavirus's pathogenicity is highlighted by the entry of the virus through Angiotensin converting enzyme 2 (ACE2) receptors, cleavage of the complex, and activation of the S-protein by TMPRSS 2. (5) ACE2 is broadly distributed throughout the human body. It is expressed in the kidney, testis, intestine, lung, retina, cardiovascular system, adipose tissue, and central nervous system. (6) The human ACE2 gene maps to chromosome Xp22 and contains 18 exons. The ACE2 protein, which has a full length of 805 amino acids, exhibits an extracellular N-terminal claw-like protease domain (PD) and a C-terminal collectrin-like domain (CLD) with a cytosolic tail. (7) By 2003, ACE2 was identified as a functional receptor for severe acute

respiratory syndrome coronavirus (SARS-CoV), which mediated the process of infection and transmission. The efficacy of the infection was 10-fold increased when the SARS-CoV was applied onto the apical surface of cells that expressed ACE2. (8) According to structural analyses, spike protein of SARS-CoV (SARS-S) contacted the apex of subunit I of the ACE2 catalytic domain but did not influence the subunit II nor occlude the active site of peptidase. (9) Once attached to ACE2 by SARS-CoV, the ectodomain of ACE2 is cleaved, accompanied by endocytosis of transmembrane domain into the cell. Sometimes ACE2 can be internalized as an intact molecule. The internalization and virus particle–host cell fusion are essential for virus entry. (10)

(11) The danger of COVID-19 transmission of virus is yet not fully understood and is being looked. However, as the epidemic expanded, close contact between people was accepted, especially when respiratory droplets from coughing and sneezing were involved. (12) Some virus-infected individuals don't exhibit any symptoms. (13) The 2019 coronavirus illness (COVID-19) signs and symptoms may appear two to fourteen days after exposure. The interval between exposure and the start of symptoms is known as the incubation period. (14)

Radiological abnormalities such as lung opacities, a ground glass appearance, and bilateral infiltrates are significant findings linked to serious illness. (15) Additionally, the majority of patients have altered levels of inflammatory indicators like elevated cell counts, D-dimers, C-Reactive protein (CRP), ferroprotein, erythrocyte sedimentation rate (ESR), Lactate Dehydrogenase (LDH), and others (Urea, Creatinine). (16) The National Health Commission of China has developed a severe and critical diagnosis and treatment program for "New corona virus infected Pneumonia" based on the clinical symptoms of patients with coronavirus infection. Their prognostic importance in COVID-19, however, is unknown. (17) In current study, we aimed to analyze the inflammatory markers of COVID-19 and severity of the disease.

Material and methods:

Patient's recruitment:

This cross-sectional study was completed after seeking approval from the ethics review committees of Ziauddin University (reference code 2650920SKPAT). According to the laws, regulations, and institutional policies, the study was carried out. From April 2020 to September 2020, 143 COVID-19 PCR positive patients visited the OPD, wards, and ICU at the Ziauddin Hospital locations in Clifton, KDLB, and North Nazimabad using the non-probability consecutive sampling technique. Every patient admitted in hospital and encountered in OPDs during the study period were included. The trial's participants gave written informed consent, as did each participant under the age of 18 and their parent or legal guardian. Patients under the age of 14, those with mental illnesses, people who had received chemotherapy or radiation treatment, people who had cancer of any kind, and anyone who hadn't provided their consent were excluded.

COVID-19 in vitro diagnostic test:

SARS-CoV-2 RNA positivity was determined using qualitative RT-PCR with in vitro diagnostic kits, (Roche, USA) following the manufacturer's recommendations. The assay included positive control template and RNA internal extraction control. USFDA approved Triple target genes (Sarbecovirus E gene, SARS-CoV-2 N gene, and SARS-CoV-2 RNA-dependent RNA polymerase) were used, along with Seegene kit (#RP10244Y Allplex™ 2019-nCoV Assay, Seegene South Korea) based RT-PCR. SARS-CoV-2 positive patients had at least one positive RT-PCR test result, while SARS-CoV-2 negative patients had solely negative RT-PCR test findings.

Clinico-pathological parameters of study participants:

Demographic information, clinical details, and outcomes were provided through the electronic patient records. Each patient's age, sex, medical history, initial symptoms (fever, cough, and dyspnea), and prognosis were all noted. The following definition of severity was used by the Center of Disease Control and Prevention (CDC): "Asymptomatic" refers to the absence of any signs or symptoms; "mild" refers to patients, whether inpatients or outpatients, who do not exhibit any signs of dyspnea but do not require oxygen; "moderate" refers to hospitalized patients who exhibit these signs but do not require high flow oxygen; and "critical" refers to all patients who require mechanical ventilation, all COVID-19-related deaths that take place during the hospital stay, or both.

Statistical Evaluation:

SPSS version 21 was used for all statistical analysis. All dependent variables in COVID-19 had their frequencies and percentages calculated. We used the Chi-Square test was used to analyze the relationship between all dependent variables and clinicopathological features. For statistical difference of mean of different inflammatory markers in COVID-19 severity group Krusk al-Wallis test was applied. All estimations were considered significant if the P-value was less than 0.05.

Results:

Demographic and clinical characteristics of the patients:

Among the all-PCR positive patients majority were severe (45: 31.5%) followed by critical (32: 22.3%). Males were predominant (80; 55.9%) with the age of presentation of more than 50 years (106: 74.1%). Most of the patients included had the diabetes mellitus (71: 49.4%) and hypertension (83: 58%). Few of them also had other known diseases of other system like cardiovascular (22: 15.4%), respiratory (7: 4.9%) and many more as described in Table: 1. Fever (90: 62.9) was the most frequent symptom encountered in all patients with the dyspnea (87: 60.8%) being the second common symptom. Almost all inflammatory markers were raised in every patient, procalcitonin (139: 97.2%) being the most frequently raised marker.

Table: 1 Demographic and clinical characteristics of patients.

Characteristic	Frequency (%)
Severity	
Asymptomatic	20 (14%)
Mild	11 (7.7%)
Moderate	35 (24.5%)
Severe	45 (31.5%)
Critical	32 (22.3%)
Age (Years)	
<=50	37 (25.9%)
>50	106 (74.1%)
Gender	
Male	80 (55.9%)
Female	63 (44.1%)
Medical History	
DM	71 (49.7%)
HTN	83 (58%)
Cardiovascular	22 (15.4%)
Respiratory	7 (4.9%)
Urinary Tract	7 (4.6%)
Gastrointestinal	4 (2.8%)
Endocrine	4 (2.8%)
Neurological	3 (2.1%)
Musculoskeletal	3 (2.1%)
Presentation	
Fever	90 (62.9)
Cough	58 (40.6%)
Dyspnea	87 (60.8%)
Bodyache	18 (12.6%)
Loss of Taste	4(2.8%)
Loss of Smell	6 (4.2%)
Generalized Weakness	31 (21.7%)
Others	67 (46.9%)
Raised Inflammatory Markers	
TLC	120 (83.9%)
Ferritin	100 (69.9%)
LDH	127 (88.8%)
Procalcitonin	139 (97.2%)
De-Dimer	105 (73.4%)
CRP	92(64.3%)
Outcome	
Discharged	110 (76.9%)
Deaths	33 (23.1%)

[a]Cardiovascular includes the ischemic heart disease, coronary artery disease and valvular disease, it does not include the arterial diseases and hypertension. [b]Endocrine diseases do not include the diabetes mellitus. DM; Diabetes mellitus (Both Type 1 and 2: Years not included), CRP; C-

reactive protein, HTN; Hypertension (number of years not included), LDH; Lactate dehydrogenase, TLC; Total leukocyte count.

On comparing the demographic and clinical characteristics with the severity of the COVID-19 disease we found the significant statistical association of age (p value, 0.016), gender ((p value, 0.022). fever (p value, 0.001), cough (p value, 0.001), dyspnea (p value, 0.001), loss of taste (p value, 0.001), de-dimer (p value, 0.001), LDH (p value, 0.001), ferritnin (p value, 0.001), and CRP (p value, 0.001). Patients having the age more than 50 years are at more risk to acquire the severe or critical diseases and may need oxygen at the time of presentation. We also found that males are more prone to have the COVID infection with more severity. Fever, cough and dyspnea are the symptoms that were frequently present in every severity from mild to critical while the loss of taste and smell were more related to mild and moderate diseases. Table: 2

Table: 2 Association of demographic and clinical characteristics with the severity of the diseases

Characteristics	n=143	Severity					p value[a]
		Asymptomatic	**Mild**	**Moderate**	**Severe**	**Critical**	
		20 (14%)	**11 (7.7%)**	**35 (24.5%)**	**45 (31.5%)**	**32 (22.3%)**	
Age (Years)							
<=50	37 (25.9%)	11 (7.7%)	3 (2.1%)	5 (3.5%)	12 (8.4%)	6 (4.2%)	0.016*
>50	106 (74.1%)	9 (6.3%)	8 (5.6%)	30 (21%)	33 (23.1%)	26 (18.2%)	
Gender							
Male	80 (55.9%)	11 (7.7%)	3 (2.1%)	22 (15.4%)	20 (14%)	24 (16.8%)	
Female	63 (44.1%)	9 (6.3%)	8 (5.6%)	13 (9.1%)	25 (17.5%)	8 (5.6%)	0.022*
Hypertension							
Yes	83 (58%)	10 (7%)	8 (5.6%)	19 (13.3%)	31 (21.4%)	15 (10.5%)	0.238
No	60 (42%)	10 (7%)	6 (2.1%)	16 (11.2%)	14 (9.8%)	17 (11.9%)	
Diabetes Mellitus							
Yes	71 (49.7%)	8 (5.6%)	6 (4.2%)	15 (10.5%)	24 (16.8%)	18 (12.6%)	0.689
No	72 (50.3%)	12 (8.4%)	5 (3.5%)	20 (14%)	21 (14.7%)	14 (9.8%)	
Fever							
Yes	90 (62.9%)	0 (0%)	4 (2.8%)	27 (18.9%)	35 (24.5%)	24 (16.8%)	0.001*
No	53 (37.1%)	20 (14%)	7 (4.9%)	8 (5.6%)	10 (7%)	8 (5.6%)	
Cough							
Yes	58 (40.6%)	0 (0%)	4 (2.8%)	14 (9.8%)	28 (19.6%)	12 (8.4%)	0.001*
No	85 (59.4%)	20 (14%)	7 (4.9%)	21 (14.7%)	17 (11.9%)	20 (14%)	
Dyspnea							
Yes	87 (60.8%)	0 (0%)	3 (2.1%)	20 (14%)	38 (26.6%)	26 (18.2%)	0.001*
No	56 (39.2%)	20 (14%)	8 (5.6%)	15 (10.5%)	7 (4.9%)	6 (4.2%)	
Bodyache							
Yes	(18 (12.6%)	0 (0%)	4 (2.8%)	5 (3.5%)	6 (4.2%)	3 (2.1%)	0.062
No	125 (87.4%)	20 (14%)	7 (4.9%)	30 (21%)	39 (27.3%)	29 (20.3%)	
Loss of Taste							
Yes	4 (2.8%)	0 (0%)	2 (1.4%)	2 (1.4%)	0 (0%)	0(0%)	0.009*
No	139 (97.2%)	20 (14%)	9 (6.3%)	33 (23.1%)	45 (31.5%)	32 (22.3%)	

Loss of Smell							
Yes	6 (4.2%)	0 (0%)	2 (1.4%)	2 (1.4%)	2 (1.4%)	0(0%)	0.098
No	137 (95.8%)	20 (14%)	9 (6.3%)	33 (23.1%)	43 (30.1%)	32 (22.3%)	
TLC							
Raised	120 (83.9%)	17 (11.9%)	9 (6.3%)	32 (22.4%)	37 (25.9%)	25 (17.5%)	
Normal	21 (14.7%)	2 (1.4%)	1 (0.7%)	3 (2.1%)	8 (5.6%)	7 (4.9%)	0.185
Below Normal	2 (1.4%)	1 (0.7%)	1 (0.7%)	0 (0%)	0 (0%)	0 (0%)	
De-Dimer							
Raised	105 (73.4%)	5 (3.5%)	8 (5.6%)	26 (18.2%)	38 (26.6%)	28 (19.6%)	0.001*
Normal	38 (26.6%)	15 (10.5%)	3 (2.1%)	9 (6.3%)	7 (4.9%)	4 (2.8%)	
Ferritin							
Raised	100 (69.9%)	8 (5.6%)	7 (4.9%)	29 (20.3%)	30 (21%)	26 (18.2%)	0.008*
Normal	43 (30.1%)	12 (8.4%)	4 (2.8%)	6 (4.2%)	15 (10.5%)	6 (4.2%)	
LDH							
Raised	127 (88.8%)	9 (6.3%)	10 (7%)	32 (22.4%)	44 (30.8%)	32 (22.3%)	0.001*
Normal	16 (11.2%)	11 (7.7%)	1 (0.7%)	3 (2.1%)	1 (0.7%)	0 (0%)	
CRP							
Raised	92 (64.3%)	4 (2.8%)	3 (2.1%)	23 (16.1%)	39 (25.2%)	26 (18.2%)	0.001*
Normal	51 (35.7%)	16 (11.2%)	8 (5.6%)	12 (8.4%)	9 (6.3%)	6 (4.2%)	
Procalcitonin							
Raised	139 (97.2%)	20 (14%)	10 (7%)	35 (24.5%)	43 (30.1%)	31 (21.7%)	0.456
Normal	4 (2.8%)	0 (0%)	1 (0.7%)	0 (0%)	2 (1.4%)	1 (0.7%)	

*significant p value ($P < 0.05$), [a]Chi square test, CRP; C-reactive protein, LDH; Lactate dehydrogenase, TLC; Total leukocyte count.

We also sought out to find the association of the severity with the age and inflammatory markers of the infection in current survey. We found the significant statistical link between these variables as shown in table: 3 and figure: 1

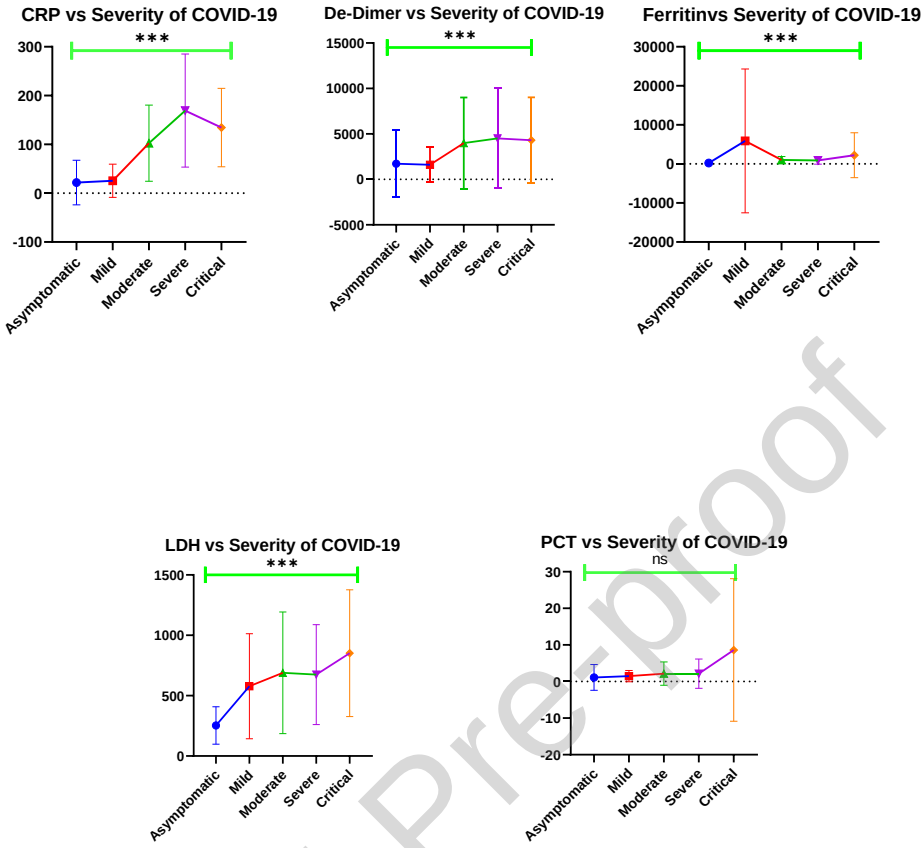
Table: 3 Statistical associations of age and inflammatory markers with the severity of diseases

Parameter		Median (Range)	P-Value
Age (Years)			
	Asymptomatic	47 (25 to 73)	
	Mild	65 (29 to 85)	0.014[a]
	Moderate	63 (25 to 81)	
	Severe	60 (28 to 82)	
	Critical	62 (22 to 82	
Total leukocyte count (10X10E9/L)			
	Asymptomatic	7.15 (6.4 to 20.7)	
	Mild	9.1 (5.3 to 14.2)	0.005[a]
	Moderate	11.8 (1.3 to 17.8)	
	Severe	11.3 (3.8 to 46)	
	Critical	11.45 (2.8 to 31.9)	
D-Dimer (ng/ml, FEU)			
	Asymptomatic	171.5 (98 to 6097)	

	Mild	900 (85 to 6195)	0.001[a]
	Moderate	1507 (100 to 9480)	
	Severe	1310 (100 to 10535)	
	Critical	2036 (100 to 12211)	
Ferritin (ng/ml)			
	Asymptomatic	134.5 (12 to 545)	
	Mild	370 (14 to 61400)	0.001[a]
	Moderate	619 (81 to 4258)	
	Severe	530 (70 to 4681)	
	Critical	1019.5 (17 to 33150)	
LDH (U/L)			
	Asymptomatic	211.5 (94 to 736)	
	Mild	483 (177 to 1708)	0.001[a]
	Moderate	263 (101 to 2414)	
	Severe	612 (213 to 2898)	
	Critical	710.5 (286 to 2787)	
CRP (mg/L)			
	Asymptomatic	0.7 (0.1 to 142.4)	
	Mild	9.64 (0.4 to 85.87)	0.001[a]
	Moderate	97.1 (0.7 to 289.7)	
	Severe	175.3(4.2 to 415.4)	
	Critical	121.6 (4.9 to 271.4)	
Procalcitonin (ng/ml)			
	Asymptomatic	0.19 (0.01 to 16)	
	Mild	1 (0.001 to 4)	0.028[a]
	Moderate	0.68 (0.01 to 14)	
	Severe	1 (0.002 to 25)	
	Critical	1.5 (0.001 to 80)	

[a]Krusk al-Wallis test, *significant p value ($P < 0.05$),

Figure: 1. Significance of inflammatory markers with COVID-19 severity (CRP; C-reactive protein, LDH; Lactate dehydrogenase, PCT; Procalcitonin)



Furthermore, for the multiple comparisons between the groups we applied the post hoc analysis to evaluate the association of every significant parameter with each group of severity that revealed the significant statistical link of age between the asymptomatic-severe groups (p-value 0.48), asymptomatic-critical groups (p-value 0.025) and asymptomatic-moderate groups (p-value 0.015). For TLC, we found the significant statistical association between the asymptomatic-critical groups (p-value 0.016) and asymptomatic-severe group (p-value 0.006). We also assessed the association of individual inflammatory marker between the groups in which D-dimer showed the significance among the asymptomatic-moderate groups (p-value 0.019), asymptomatic-severe groups (p-value 0.003) and asymptomatic-critical groups (p-value 0.001). Ferritin levels were also significantly associated among the asymptomatic-moderate groups (p-value 0.001), asymptomatic-severe groups (p-value 0.003) and asymptomatic-critical groups (p-value 0.001). LDH and CRP levels were too associated between the asymptomatic-moderate groups (p-value 0.001), asymptomatic-severe groups (p-value 0.001) and asymptomatic-critical groups (p-value 0.001) while the procalcitonin only showed the significant link between the asymptomatic-severe groups (p-value 0.014).

Patients having the raised inflammatory markers were mostly discharged and few were died. While comparing the raised inflammatory markers with the outcome of the patient and hospital stay in number of days, only LDH and CRP had the significant statistical association with outcome and LDH and ferritin with the hospital stay. (Table: 4)

Table: 4 Association of inflammatory markers with the outcome and hospital stay (days). *significant p value ($P < 0.05$), Chi square test, CRP; C-reactive protein, LDH; Lactate dehydrogenase, TLC; Total leukocyte count.

Characteristics	n=143	Outcome			Hospital Stay (Days)		
		Discharged	**Death**		**≤10 Days**	**>10 Days**	
		110 (76.9%)	**33 (23.1%)**	**P-Value**	**88 (61.5%)**	**55 (38.5%)**	P-Value
TLC							
Raised	120 (83.9%)	95 (66.4%)	25 (17.5%)	0.165	75 (52.4%)	45 (31.5%)	
Normal	21 (14.7%)	13 (9.1%)	8 (5.9%)		11 (7.7%)	10 (7%)	0.360
Below Normal	2 (1.4%)	2 (1.4%)	0 (0%)		2 (1.4%)	0 (0%)	
De-Dimer							
Raised	105 (73.4%)	77 (53.8%)	28 (19.6%)	0.067	61 (42.7%)	44 (30.8%)	0.112
Normal	38 (26.6%)	33 (23.1%)	5 (3.5%)		27 (18.9%)	11 (7.7%)	
Ferritin							
Raised	100 (69.9%)	73 (51%)	27 (18.9%)	0.066	54 (37.8%)	46 (32.2%)	0.004*
Normal	43 (30.1%)	37 (25.9%)	6 (4.2%)		34 (23.8%)	9 (6.3%)	
LDH							
Raised	127 (88.8%)	94 (65.7%)	33 (23.1%)	0.011*	74 (51.7%)	53 (37.1%)	0.019*
Normal	16 (11.2%)	16 (11.2%)	0 (0%)		14 (9.8%)	2 (1.4%)	
CRP							
Raised	92 (64.3%)	66 (46.2%)	26 (18.2%)	0.036*	56 (39.2%)	36 (25.2%)	0.485
Normal	51 (35.7%)	44 (30.8%)	7 (4.9%)		32 (22.4%)	19 (13.3%)	
Procalcitonin							
Raised	139 (97.2%)	108 (75.5%)	31 (21.7%)	0.228	86 (60.1%)	53 (37.1%)	0.499
Normal	4 (2.8%)	2 (1.4%)	2 (1.4%)		2 (1.4%)	2 (1.4%)	

Discussion:

SARS and Middle East Respiratory Syndrome (MERS) are two examples of the many viruses in the huge family of coronaviruses that can cause anything from a common cold to potentially fatal pneumonia. On COVID-19 prognostic factors, there isn't a lot of published data, though. (18) During the course of our investigation, we discovered a male predominance of COVID-19, which is explicable given the ACE2 gene's X-chromosomal position and the role of the TMPRSS2 gene in prostate cancer. (19) It is believed that males are more likely than females to have COVID-19. In a recent case-control study of a Chinese population, there was no correlation between ACE2 expression levels and estrogen levels, indicating that estrogen is responsible for the down-regulation of ACE2 expression. (20) When compared to males, this may serve as a protective factor for females who have COVID-19 infection. (21) We discovered in our investigation that the majority of patients who had severity were over 50 years old, which is consistent with the fact that COVID-19 is more severe in older age groups. The number of ACE2 receptors distributed throughout the body in elderly people, who are more prone to serious illnesses, is not yet known. (22) People are at a greater risk of contracting COVID-19 infection because the immune system deteriorates with age and comorbid illnesses including diabetes, hypertension, and others have a significant impact on immune system degeneration. (23) ACE

inhibitors and ARBs are used in the treatment of hypertension, which causes uncontrolled ACE2. (24) These findings suggest that ACE2 expression is elevated in diabetes and that ACE inhibitor and ARB therapy reduces this expression. A COVID-19 infection would be made easier by increased ACE2 expression. Particularly in Asian populations, ACE2 polymorphisms have been linked to diabetes, cerebral stroke, and hypertension. Therapy and the ACE2 polymorphism together may have an impact on a person's sensitivity. (25)

Studies have also evaluated the disease's inflammatory markers, including LDH, ferritin levels, CRP, procalcitonin, D-dimer, and acute phase response proteins. (26) The severity of COVID-19 and its associated risk factors are correlated with an increase in the levels of inflammatory markers. However, there is ongoing debate regarding the function of inflammatory markers in assessing the severity of COVID-19. (27) According to the disease's progression and associated risk factors, our investigation revealed variable levels of all inflammatory markers. It is possible to employ CRP as an indicator of inflammation since it is a highly sensitive systemic acute-phase response marker for infection, tissue injury, and inflammation. (28) As the disease progresses, CRP levels rise, making it a reliable predictor of COVID-19 according to many studies. This is in line with our analysis. (29)

In current study it is found that raised patients who had discharged had raised markers but CRP and LDH had significance with the outcome that has been established that adult CRP readings can predict the severity and outcome of an illness. (30, 31) Usually, a cytokine storm brought on by the immune system's reaction to the SARS-CoV-2 infection is to blame. Particularly in older people, this enormous release of pro-inflammatory cytokines has the potential to result in severe lung injury and a poor prognosis. (32) LDH implication requires further studies to indicate how relevant this marker is in assessing the severity of COVID-19 disease, as sometimes data on this biomarker ended up being contradictory. (33, 34) Previously literature also highlighted that the inflammatory markers are mostly raised in the young adults and children who had the stronger and more developed immune system. Current study only included the acute phase inflammatory markers that are raised during the active disease.

Extreme COVID-19 has caused a spike in inflammatory markers that is similar to elevations in related indicators during infection with other diseases. For instance, during a bacterial infection, procalcitonin (PCT) and ferritin are released into the bloodstream, and elevated levels in peripheral blood are correlated with the severity of the infection. (35) The idea that PCT and ferritin are inflammatory mediators is supported by the sequence similarities between PCT and ferritin and other human cytokines, such as the TNF family of cytokines, IL-6, etc. (36) Additionally, patients with severe COVID-19 disease and those hospitalized to the ICU had higher serum ferritin levels. The D-dimer concentration was elevated in the majority of instances, especially in patients with severe illnesses. (37) This suggests secondary hyperfibrinolysis and a hypercoagulable condition. (38) Additional work is required to associate the inflammatory markers to comorbidities and other medical conditions/risk factors provided as these factors were not included into the current investigation. In additionally, follow-up research employing serial or daily blood inflammatory marker monitoring is necessary.

Conclusion:

In conclusion, our findings show that positive statistical difference of means in inflammatory markers. Except procalcitonin other all markers had significant statistical association with the severity of disease.

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Declaration of Competing Interest

We have no conflict of interest to declare.