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Relation Between Clinical Presentation and Laboratory Findings (CRP, D dimer, LDH) and Imaging In Patients With COVID 19

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Abstract

Background: The COVID19 pandemic is a scientific, medical, and societal problem. Because the clinical course of this disease is very unpredictable and can proceed quickly, resulting in major problems, it's critical to find laboratory biomarkers that can help define the patient's severity during initial stage.

Patients and methods: This prospective cohort study was carried out at El Salalm Hospital and outpatient clinics in in El-Salm City, at the period from March 2019 to February 2021. This study included 100 individuals presented with manifestations which were suspicious to be due to COVID 19 and proved to have COVID19 by COVID19 test using reverse transcriptase polymerase chain reaction (RTPCR) technique.

Results: There was significant relation between high CRP value and D dimer, and LDH, also significant relation between high CRP values and imaging data (CT chest showed ground glass appearance), also Chest pain is significantly related to high values of D dimer and LDH.

Conclusion: Current study showed significant relation between levels of inflammatory markers such as CRP and D Dimer, LDH in patients with COVID-19 so can be used as reliable indicators that can help in diagnosis of patients with COVID19.

KEYWORDS

COVID-19, C-reactive protein, D-dimer,LDH, Chest pain.

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Introduction:

COVID19 patients are divided into four categories according on the severity of their illness: mild, moderate, severe, and critical. There is an urgent need for accurate biomarkers associated to coronavirus disease 2019 (COVID19) progression in order to stratify high-risk individuals. Novel biomarkers are also needed to distinguish between individuals who have a rapid illness progression and those who have serious sequelae, such as mortality. Several haematological markers, such as lymphopenia, and some biochemical parameters, such as D Dimer and LDH, have already been linked to COVID-19 severity [(1)].

C-reactive protein (CRP) is a pentameric protein produced largely in the liver by the cytokine interleukin 6 (IL-6) (IL6). CRP levels more than 50 mg/dL have been linked to infections, while higher levels are also detected in injuries, cardiovascular disorders, and other inflammatory conditions [(2)].

D dimer is a breakdown product, a tiny protein fragment seen in the blood after a blood clot is dissolved by fibrinolysis[(3)]. Higher D dimer levels indicate that coagulation has been activated and that the fibrinolytic process has been completed [(4)].

Coronavirus disease 2019 (COVID19) is a new viral illness that the World Health Organization has labelled a worldwide public health emergency (WHO). Over 3,500,000 cases and 243,403 deaths have been reported globally since its debut in Wuhan, China [(5)].

Despite the fact that the majority of COVID19 patients present with mild or asymptomatic influenza-like illness, a small percentage of patients develop severe pneumonia, acute respiratory distress syndrome (ARDS), multi-organ failure and even death [(6)].

The reason why some people become seriously ill while others do not is still a mystery. For risk stratification, comorbidities and laboratory indicators have been proposed [(7)].

There is emerging evidence that there are hyperinflammatory features in critically sick individuals, including increased blood C-reactive protein (CRP) and D dimer. These data show that cytokine storm may play an important role in COVID19 pathogenesis [(8)].

Laboratory indicators to predict the severity of COVID19 are critical because resource allocation in a pandemic must be meticulously planned. We used a systematic review and met analysis to look at the relationship between many biomarkers, such as serum CRP and D dimer, and the severity of COVID-19 in this study [(9)].

Patients and methods:

This study included 100 individuals presented with manifestations which were suspicious to be due to COVID 19 and proved to have COVID19 by COVID19 test using reverse transcriptase polymerase chain reaction (RTPCR) technique. Patients' data were collected from March 2019 to February 2021.

The Patient demographic data were collected and reported. Risk factors,clinical presentations and vital signs were reported. All medical

laboratory data including the CBC, ESR, C-reactive protein, D-dimer, and LDH were performed at EL Salam Hospital (Vidas, French device). CT chest was done via machine (canon, Aquilion start 16 slice).

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COVID19 test were done using reverse transcriptase polymerase chain reaction (RTPCR) technique.

Ethical permission was taken from patients (or their relatives) and explained this study to them to obtain their consent.

Inclusion criteria:

Patients with clinical manifestations suspicious to be due to COVID 19 and proved by COVID19 test using reverse transcriptase polymerase chain reaction (RTPCR) technique and are able to give informed consent or from relatives.

Exclusion criteria:

Patients who refused to participate in the study or inability to give informed consent or relative's refusal to participate in the study.

Statistical Analysis:

Data were collected, demographic data, risk factors, clinical presentation, laboratory data included (CBC, D-dimer,CRP, ESR, LDH) were included. ECG and CT chest was done.

Data analysis:

SPSS version 18 was used to analyze the collected data (SPSS Inc., Chicago, IL, USA). Statistics such as mean and standard deviation (SD) were used for quantitative information, and percentages were used for qualitative information. Analysis of variance (ANOVA) tests.

1. Mean = $\frac{\Sigma x}{n}$ Where Σ = sum & n = number of observations.
2. Standard Deviation (SD): $SD = \sqrt{\frac{\Sigma |x - x|^2}{n-1}}$

Standard Error (SE): $SE = \frac{SD}{\sqrt{n}}$

On the other hand, the Chi square or Fisher's exact test was employed to establish whether or not the difference was statistically significant for quantitative variables. It was considered statistically significant when the P-value was 0.05 or lower.

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Results:

Patient population data

The study included 100 patients from March 2019 to February 2021.

Table (1): Basic demographic data and risk factors

Age	Range	20-76	
	Mean ±SD	50.040±14.944	
		N	%
Sex	Female	75	75.00
	Male	25	25.00
HTN	No	43	43.00
	Yes	57	57.00
Dyslipidemia	No	54	54.00
	Yes	46	46.00
DM	No	60	60.00
	Yes	40	40.00
Smoking	No	79	79.00
	Yes	21	21.00

The mean age of the study group was 50.040±14.944 and 75 patients were female. In our populations 57 patients were hypertensive (57%), 40 patients were diabetic (40%), 46 patients were dyslipaedemic (46%), twenty one patients were smoker (21%).

Clinical presentation

Table (2): Showing clinical presentations

		N	%
Fever	No	3	3.00
	Yes	97	97.00
Sore throat	No	2	2.00
	Yes	98	98.00
Diarrhea	No	52	52.00
	Yes	48	48.00
Abdominal pain	No	52	52.00
	Yes	48	48.00
Dyspnea	No	13	13.00
	Yes	87	87.00
Cough	No	2	2.00
	Yes	98	98.00
Loss of smell	No	32	32.00
	Yes	68	68.00
Loss of appetite	No	5	5.00
	Yes	95	95.00
Loss of taste	No	32	32.00
	Yes	68	68.00
Chest pain	No	30	30.00
	Yes	70	70.00
Palpitation	No	32	32.00
	Yes	68	68.00

The study included one hundred patients, ninety seven patients (97%) presented with fever, ninety eight patients (98%) presented with sore throat, fourty eight patients (48%) presented with diarrhea, fourty eight patients (48%) presented with abdominal pain, eighty seven patients (87%) presented with dyspnea, ninety eight patients (98%)

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presented with couph, sixty eight patients (68%) presented with loss of smell, ninety five patients (95%) presented with loss of appetite, sixty eight patients (68%) presented with loss of taste, seventy patients (70%) presented with chest pain, sixty eight patients (68%) presented with awareness of heart beats (palpitations).

Table (3): Showing vital signs

		N	%
Temperature	**Normal**	4	4.00
	Abnormal	96	96.00
Respiratory Rate	**Normal**	31	31.00
	Abnormal	69	69.00
Blood pressure	**Normal**	47	47.00
	Abnormal	53	53.00
Pulse	**Normal**	32	32.00
	Abnormal	68	68.00

The study included one hundred patients, ninety six patients (96%) presented with fever, sixty nine patients (69%) were tachypneic, sixty eight patients (68%) had tachycardia, fifty three patients (53%) had arterial hypertension at initial assessment in our study.

Table (4): Showing laboratory data

		N	%
Leucocytic count	**Normal**	23	23.00
	Low	65	65.00
	High	12	12.00
Lymphocytic count	**Normal**	31	31.00
	Low	66	66.00
	High	3	3.00
Neutrophils	**Normal**	34	34.00
	High	66	66.00
CRP	**Negative**	3	3.00
	Positive <50	29	29.00
	Positive >50	68	68.00
D Dimer	**Normal**	31	31.00
	High	69	69.00
LDH	**Normal**	31	31.00
	High	69	69.00
ALT	**Normal**	92	92.00
	High	8	8.00
AST	**Normal**	92	92.00
	High	8	8.00
Creatinine	**Normal**	80	80.00
	High	20	20.00
Urea	**Normal**	79	79.00
	High	21	21.00

The study included one hundred patients, sixty five patients (65%) had leucopenia, twelve patients (12%) had leucocytosis, sixty six patients (66%) had lymphopenia, three patients (3%) had lymphocytosis, sixty six patients (66 %) had neutrophilia, sixty eight patients (68%) had CRP more than 50 mg/dl, twenty nine patients (29%) had CRP more than 6 mg/dl but less than 50 mg/dl, sixty nine patients (69%) had high D dimer, sixty nine patients (69%) had LDH, eight patients (8%) had

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elevated ALT, eight patients (8%) had elevated AST, twenty patients (20%) had high creatinine level, twenty one patients (21%) had high urea level.

Table (5): Showing significant relation between chest pain and LDH

LDH	Chest pain						Chi-Square	
	No		Yes		Total			
	N	%	N	%	N	%	X^2	P-value
Normal	29	96.67	2	2.86	31	31.00	86.398	<0.001*
High	1	3.33	68	97.14	69	69.00		
Total	30	100.00	70	100.00	100	100.00		

There was significant relation between presentation with chest pain and LDH level, with significant p-value (<0.001*).

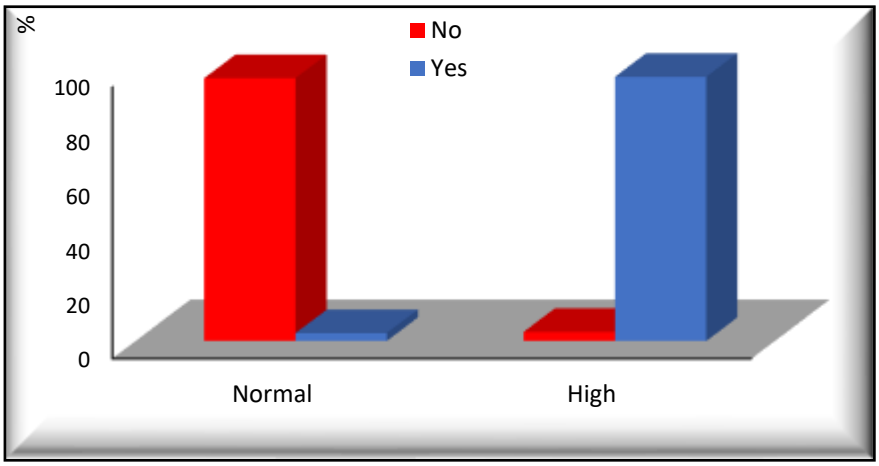

Figure (1): Showing significant relation between chest pain and LDH

Table (6): Showing significant relation between chest pain and D dimer

D Dimer	Chest pain						Chi-Square	
	No		Yes		Total			
	N	%	N	%	N	%	X^2	P-value
Normal	28	93.33	3	4.29	31	31.00	77.849	<0.001*
High	2	6.67	67	95.71	69	69.00		
Total	30	100.00	70	100.00	100	100.00		

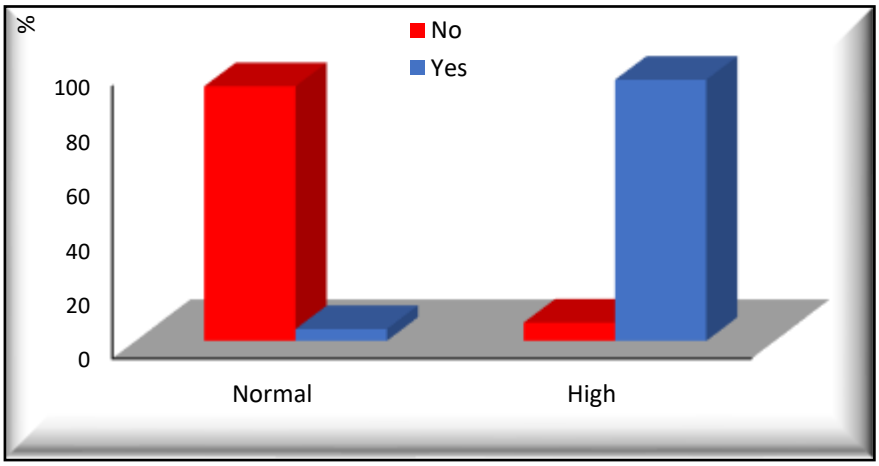

Figure (2): Showing significant relation between chest pain and D dimer

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Table (7): Showing significant relation between CRP and chest pain

Chest pain	CRP								Chi-Square	
	Negative		Positive <50		Positive >50		Total			
	N	%	N	%	N	%	N	%	X^2	P-value
No	3	100.00	26	89.66	1	1.47	30	30.00	82.500	<0.001*
Yes	0	0.00	3	10.34	67	98.53	70	70.00		
Total	3	100.00	29	100.00	68	100.00	100	100.00		

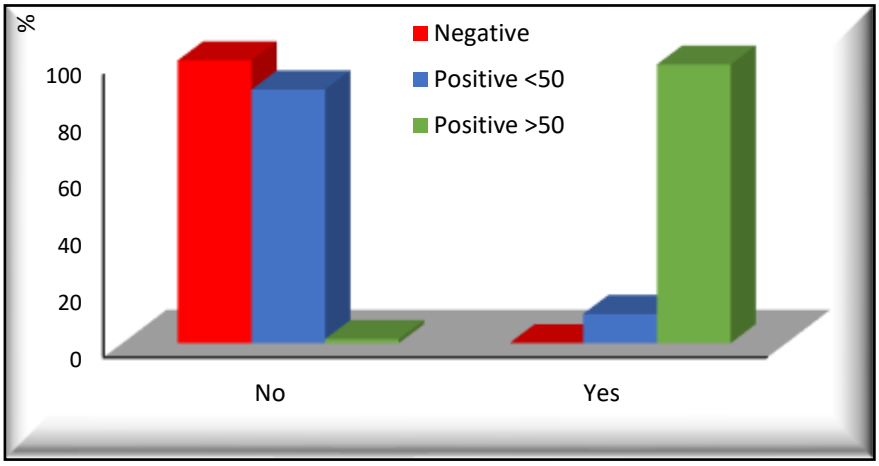

Figure (3): Showing significant relation between CRP and chest pain

Table (8): Showing significant relation between CRP and LDH

LDH	CRP								Chi-Square	
	Negative		Positive <50		Positive >50		Total			
	N	%	N	%	N	%	N	%	X^2	P-value
Normal	3	100.00	28	96.55	0	0.00	31	31.00	95.486	<0.001*
High	0	0.00	1	3.45	68	100.00	69	69.00		
Total	3	100.00	29	100.00	68	100.00	100	100.00		

There was significant relation between CRP level and LDH, with significant p-value (<0.001*).

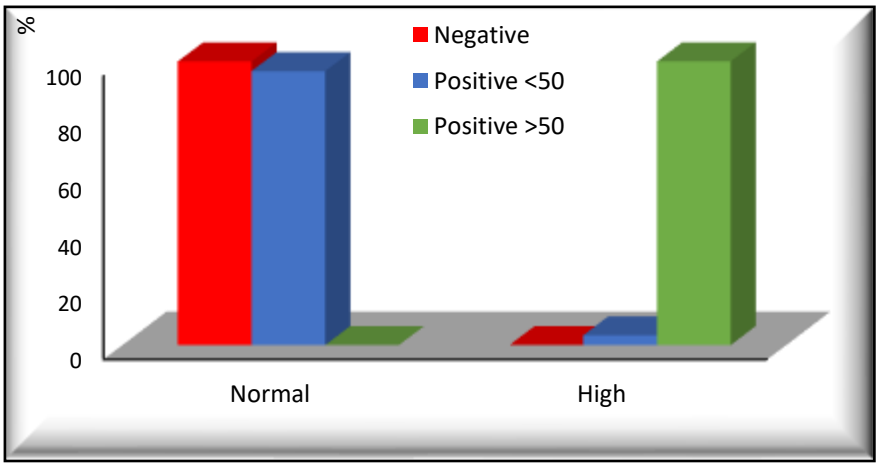

Figure (4): Showing significant relation between CRP and LDH

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Table (9): Showing significant relation between CRP and D dimer

D Dimer		CRP								Chi-Square	
		Negative		Positive <50		Positive >50		Total			
		N	%	N	%	N	%	N	%	X^2	P-value
Normal		3	100.00	27	93.10	1	1.47	31	31.00	86.688	<0.001*
High		0	0.00	2	6.90	67	98.53	69	69.00		
Total		3	100.00	29	100.00	68	100.00	100	100.00		

There was significant relation between CRP level and D dimer, with significant p-value (<0.001*).

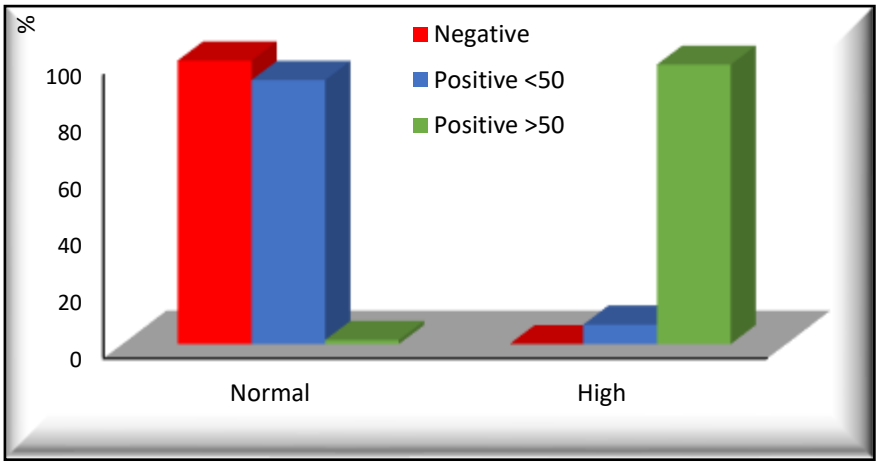

Figure (5): Showing significant relation between CRP and D dimer

Table (10): Showing significant relation between CRP and CT chest findings (Ground Glass appearance)

CT chest	CRP								Chi-Square	
	Negative		Positive <50		Positive >50		Total			
	N	%	N	%	N	%	N	%	X^2	P-value
Normal	3	100.00	18	62.07	13	19.12	34	34.00	22.717	<0.001*
Abnormal	0	0.00	11	37.93	55	80.88	66	66.00		
Total	3	100.00	29	100.00	68	100.00	100	100.00		

There was significant relation between high CRP and CT chest findings (Ground Glass appearance) , with significant p-value (<0.001*).

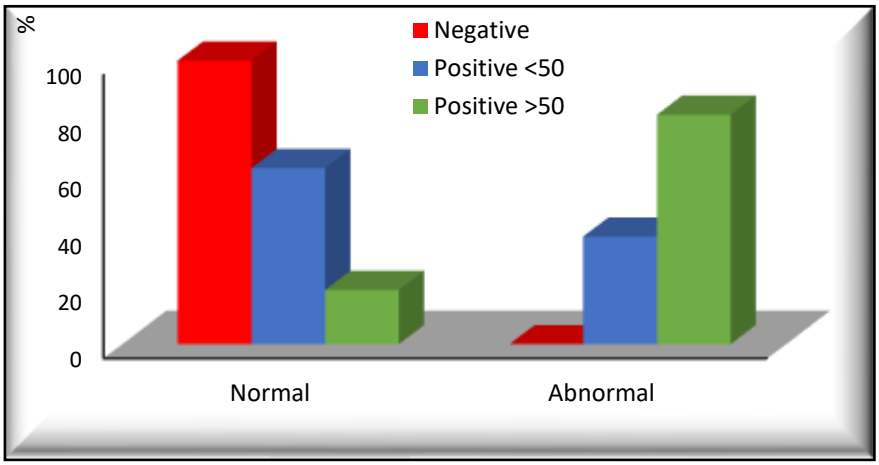

Figure (6): Showing significant relation between CRP and CT chest findings (Ground Glass appearance)

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Discussion:

Corona virus disease 2019 (COVID-19) is characterised by systemic inflammation triggered by a cytokine storm [(10)].

COVID19 has expanded fast over the world since its breakout in Wuhan, with symptoms ranging from asymptomatic to serious disease [(11)].

COVID19, which caused the Severe Acute Respiratory Syndrome (SARS) and the Middle East Respiratory Syndrome (MERS), has a clinical course and pathological characteristic in common with SARS and MERS. Although the majority of COVID-19 patients were mild and recovered within two weeks, roughly 15-20% of them had severe interstitial pneumonia [(12)].

In our study, There was significant relation between CRP level and LDH, with significant P-value (<0.001*).

So our results agree with Wei et al. [(13)] who reported that there was significant relation between elevated inflammatory markers (CRP and LDH) and both are highly associated with moderate and severe COVID infection.

Also agree with Huang et al. [(14)] who reported that there was significant relation between CRP,LDH and both are highly associated chest pain and palpitations.

Also agree with Shi et al. [(15)] who reported that there was direct relation between inflammatory markers such as CRP and (D dimer, LDH), which are associated with recurrent chest pain.

In our study, There was significant relation between CRP level and D dimer, with significant p-value (<0.001*). Also There was significant relation between lymphopenia and high LDH with significant p-value (<0.001*).

So our results agree with Wan et al. [(16)] who showed Relationships among inflammatory markers such CRP and lymphocytic count, and cardiac involvement in coronavirus (COVID-19) infected patients.

In our study, there was significant relation between high CRP valued and CT chest findings (Ground Glass appearance).

So our results agree with Li et al. [(17)] who reported that the high inflammatory markers such as high CRP, high D dimer and high LDH are correlated to CORAD classification of pulmonary affection.

In our study there was significant relation between presentation with chest pain and LDH level, with significant p-value (<0.001*).

Wei et al.[(13)] proved the relation between high CRP and recurrent persistent chest pain and post COVID syndrome.

Conclusion:

Current study showed significant relation between levels of inflammatory markers such as CRP, D Dimer, LDH in patiens proved to have COVID-19 so can be used as reliable indicators that can help in diagnosis of patients with COVID 19.

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