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Research Article

Evaluation of a Few Biomarkers among COVID-19 Patients

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I N F O

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A B S T R A C T

Introduction: In the present study, the mean differences of Lactate Dehydrogenase (LDH), D-dimer, C-reactive protein, interleukin-6 and ferritin levels concentrations between study groups (patients with severe COVID-19 symptoms and patients with mild symptoms) compared tothe control group. The results showed that there were significant increased concentrations of biomarkers levels in group A as compared with group B and control.

Objective: This present study aims to evaluate the COVID-19 biomarkers(Lactate Dehydrogenase (LDH), D-dimer, C-reactive protein, IL-6 and ferritin concentrations) among COVID-19 patients.

Methodology: A total of 75 blood samples were collected from male patients with age groups ranging between 30 and 75 years who were suffering from coronavirus. Three groups were included in this study; each group includes 25 patients. Group A patients suffering from coronavirus with severe symptoms, group B patients suffering from coronavirus with mild symptoms and group C with healthy patients as control. All parameters were measured according to standard procedures. Data were analysed in SPSS version 20 by using mean ± SD.Significant association was established by chi-square test taking p-value<0.05.

Results: Increased LDH values were linked to an increase in COVID-19 toxicity. On the basis of D-dimer, the probability of mortality can be determined. C-responsive protein and ferritin serum exercises were significantly increased in COVID-19 patients compared to those with mild side effects of COVID-19. IL-6 is a key immunomodulatory cytokine in both normal and infected tissues.

Conclusion: LDH, D-dimer, C-reactive protein and serum ferritin are good predictors of COVID-19 severity and may be used for the assessment of clinical outcome.

Keywords: COVID-19, Lactate Dehydrogenase (LDH), IL-6, D-dimer, C-reactive Protein, Ferritin

Introduction

The coronavirus disease 2019 (COVID-19) is a profoundly irresistible sickness where the primary tainted case was revealed in Wuhan city-China from where it spread around the world.[1] The causative operator has a place with novel encompassed single straight positive-sense abandoned RNA Coronavirus, which is likewise called SARS-CoV-2 and has a fondness forlung cells.[2]The hereditary examination of SARS-CoV-2 proposed that this novelty HGN l strain might be created from the creature. Root by recombination between a bat SARS-like CoV and a coronavirus of obscure birthplace.[3] The capacity of fast spread of SARS-CoV-2 infection from individual to other is comparable or much more than to other human infections like flu or plague prompting to be declared as a pandemic by WHO in 2020.[4]The realities in this audit lead to propose that as a rule, the demise in SARS-CoV-2 may happen through loss of fundamental fiery reaction control which prompts lung injury followed by pneumonia, intense respiratory misery condition (ARDS) and respiratory disappointment, thus passing particularly in old patients with incessant infection.[5] Individuals with hypertension are likewise marginally bound to bite the dust from coronavirus.Theyare at a 6% higher riskthan the general populace.[6]Numerous patients with extreme COVID-19 are those with coinciding, constant conditions, including hypertension and diabetes.[7] Both of these conditions expands the danger of kidney infection. Like other respiratory malady prompting infections, for example, SARS, MERS, and network gained pneumonia (CAP), COVID-19 typically first influences the lungs. Early side effects incorporate fever, cold, restlessness and difficulty in breathing.[8] These side effects can show up within two days or as long as 14 days after contact with the infection.[9] The COVID-19 seriousness shifts from mellow or asymptomatic to extreme or deadly. More established individuals and those with interminable maladies have all the earmarks of being at a higher danger of genuine manifestations.[10] This fluctuation is additionally found in the impact of COVID-19 on the lungs.[11] A few people may have just mellow respiratory side effects while others may create pneumonia, which doesn't compromise an individual's life.[12] Few people additionally experience the ill effects of extreme lung problems. As indicated by look into, what we regularly find in individuals who are seriously contaminated with COVID-19 is respiratory pain disorder.[13] Non-specific symptoms admire fever, fatigue, cough (with or while not liquid body substance production), anorexia, malaise, muscle pain, sore throat, dyspnea, nasal congestion, or headache might occur in patients with uncomplicated higher tract infection; seldom can there be diarrhoea, fatigue, and disgorgement in patients too. Grownup and immunological disorder patients with uncommon symptoms will show up.[14] Symptoms from pregnancy physiological changes or adverse effects during pregnancy (e.g., dyspnoea, fever, gastrointestinal indications, weariness) can relate tothis disease.[15] Pneumonia without signs of severe pneumonia and no requirement for more oxygen.[16]

Materials and Method

A total of 75 blood samples were collected from male patients with age group range between (30-75 years) who were suffering from coronavirus. Samples were collected from patients during the period from January 2021 to March 2021 from the Marjan Medical City and private laboratories in Hilla, Iraq.

Study Groups

Three groups were included in this study; each group includes 25 patients. Group A patients suffering from coronavirus with severe symptoms, group B patients suffering from coronavirus with mild symptoms and group C with healthy patients as control. All patients and control were from the same ethnic group (Arabic).

Collection of Blood Samples

5 ml of blood was collected from each subject by vein puncture method. 2 mL of blood was kept into EDTA vials with sodium citrate for separating plasma for the estimation of D-dimer whereas, 3 mL of blood was kept into dispensable tubes containing isolating gel, and was allowed to clot at room temperature for 30 minutes. After that,it was centrifuged at 2000 rpm for more or less 10 min for serum separation. The serum was transferred into little aliquots and stored at (-20ºC) for the estimation of other biomarkers.

Determination of LDH Level Concentration

Estimation of LDH level in serum was done by using an auto analyzer for spectrometry and measured by mind ray system, China.

Determination of D-dimer Level Concentration

Estimation of D-dimer level was done using a fluorescence immunoassay that quantifies the total D-dimer concentration in plasma. The test was used as an aid in the post-therapeutic evaluation of thromboembolic disease patients. A specific kit fromBoditch Bio-technology, Francewas also used for the estimation.

Determination of C-reactive Protein Concentration

In most cases, the blood is taken from a vein in the arm. Using a rubber band to wrap around the arm, blood is drawn from the veins and the puncture site is disinfected. A vial or syringe can be used to collect a small amount of blood. Afterwards, the bandage is removed to allow blood to flow freely again. The needle is removed and the puncture site is sealed with a crushed membrane once enough blood has been extracted. Only a few minutes are needed for this rather easy procedure. Mispai2, assessed C-reactive protein using an auto-analyzersystem, Switzerland.

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Determination of IL-6 Concentration

The human IL-6enzyme-linked immunosorbent assay kit was used in this study for the quantitative determination of cytokine concentrationin adult patients' serum samples and was done according to company instruction (Elabscience, China).

Determination of Ferritin Level Concentration

Estimation of ferritin level concentration in serum was done by an auto-analyzer for spectrometry and measured by cobase e 411, Germany.

Statistical Analysis

After collection of data, it was entered in Microsoft excel sheet. Data were analysed in SPSS version 20 by using mean ±SD.Significant association was established by chi-square test taking p-value<0.05.[17]

Results

Determination of LDH Level Concentration

The mean differences of LDH level concentration between study groups A,B, and Cwere shown in Table 1 and Figure 1. The results show that there wasa significant increase in LDH level concentration in group A as compared to groups B and C (P=0.001).

Table 1.Determination of LDH Level Concentration among Study Groups

Biomarker	Study Groups			P value
LDH U/L	Group A (25)	Group B(25)	Group C (25)	0.001*
	Mean ± SD	Mean ± SD	Mean ± SD	
	630.84 ± 212.48	254.44 ± 21.25	152.63 ± 36.97	

Normal LDH levels range from 140 U/L to 280 U/L. Group A: patients suffering from coronavirus with severe symptoms; Group B: patients suffering from coronavirus with mild symptoms; and Group C: healthy patients as control. Pvalue ≤ 0.05 was significant.

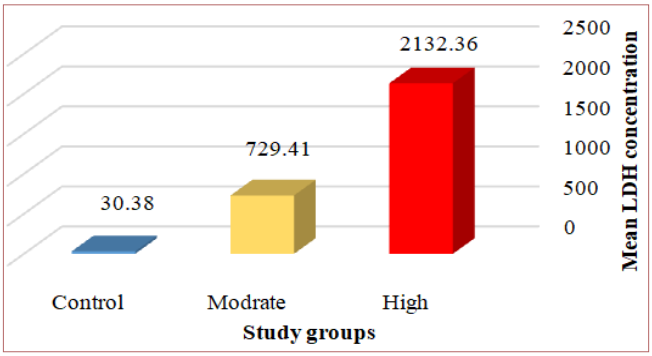

Figure 1.Bar Diagram showing LDH Level Concentration among Study Groups

Determination of D-dimer Level Concentration

Table 2 and Figure 2 shows D-dimer level concentration, which is significantlyhigherin group A as compared to groups B and C (P=0.004).

Table 2.Determination of D-dimerLevel Concentration among Study Groups

Biomarker	Study Groups			P value
D-dimerng/L	Group A (25)	Group B (25)	Group C (25)	0.004*
	Mean ± SD	Mean ± SD	Mean ± SD	
	1531.57 ± 2423.89	528.91 ± 10.73	203.94 ± 66.69	

Normal D-dimer levels < 500 ng/L. Group A: patients suffering from coronavirus with severe symptoms; Group B: patients suffering from coronavirus with mild symptoms; and Group C: healthy patients as control. Pvalue ≤ 0.05 was significant.

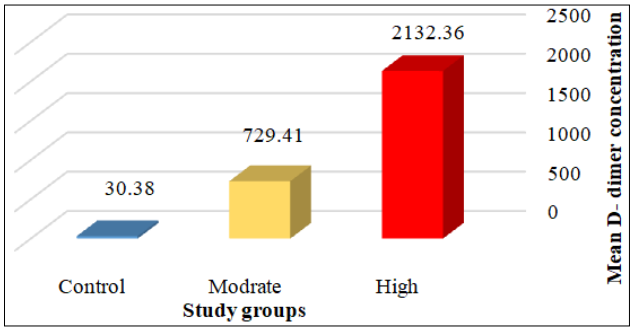

Figure 2.Bar diagram showing D-dimer Level Concentration among Study Groups

Table 3.Determination of C-reactive Protein Level Concentration among Study Groups

Biomarker	Study Groups			P value
CRP mg/L	Group A (25)	Group B(25)	Group C (25)	0.001*
	Mean ± SD	Mean ± SD	Mean ± SD	
	17.77 ± 4.44	2.20 ± 0.62	0.43 ±0.28	

Normal CRP levels< 6.0 mg/L. Group A: patients suffering from coronavirus with severe symptoms; Group B: patients suffering from coronavirus with mild symptoms; and Group C: healthy patients as control. P value ≤ 0.05 was significant.

Determination of C-reactive Protein Level Concentration

Table 3 and Figure 3 show C-reactive protein level concentration. It shows a significant increase in C-reactive protein level concentration in group A as compared to groups B andC(P=0.001).

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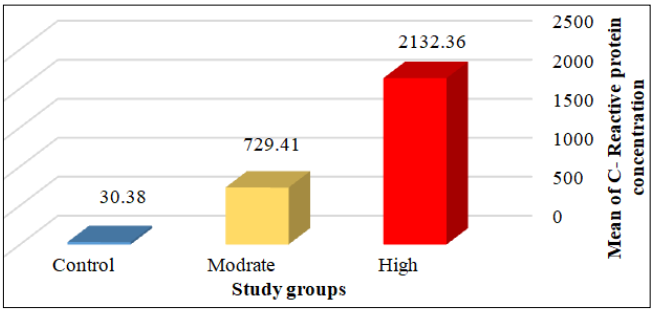

Figure 3.Bar Diagram showing Comparison between C-reactive ProteinLevel Concentration among Study Groups

Determination of IL-6 Level Concentration

Table 4 and Figure 4 show IL-6 level concentration among study and control groups. There is a significant increase in IL-6 level in group A compared as compared to groups B and C (P=0.001).

Table 4.Determination of IL-6 Level Concentration among Study and Control Groups

Biomarker	Study Groups			P value
IL-6 pg/L	Group A (25)	Group B(25)	Group C (25)	0.001*
	Mean ± SD	Mean ± SD	Mean ± SD	
	960.08 ± 170.24	729.41 ± 15.09	190.86 ± 79.63	

Normal IL-6levels < 7.0 pg/L. Group A: patients suffering from coronavirus with severe symptoms; Group B: patients suffering from coronavirus with mild symptoms; and Group C: healthy patients as control. P value ≤ 0.05 was significant.

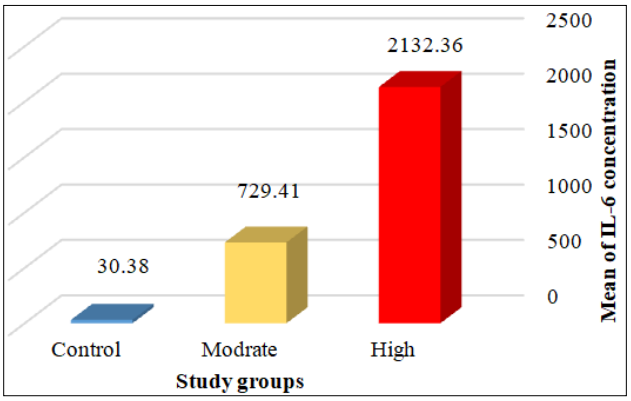

Figure 4.Bar Diagram showing Comparison of IL-6 Level Concentration among Study and Control Groups

Determination of Ferritin Level Concentration

Table 5 and Figure 5 show ferritin level concentrationamong study and control groups. Thereisa significant increasein ferritin level concentration in group A as compared to groups B and C (P=0.001).

Table 5.Determination of Ferritin Level Concentration among Study and Control Groups

Biomarker	Study Groups			P value
Ferritinng/L	Group A (25)	Group B (25)	Group C (25)	0.001*
	Mean ± SD	Mean ± SD	Mean ± SD	
	2132.36 ± 1309.35	729.41 ± 15.09	30.38 ± 11.03	

Normal male ferritin levels range from 25-350 ng/L. Group A: patients suffering from coronavirus with severe symptoms; Group B: patients suffering from coronavirus with mild symptoms; and Group C: healthy patients as control. Pvalue ≤ 0.05 was significant.

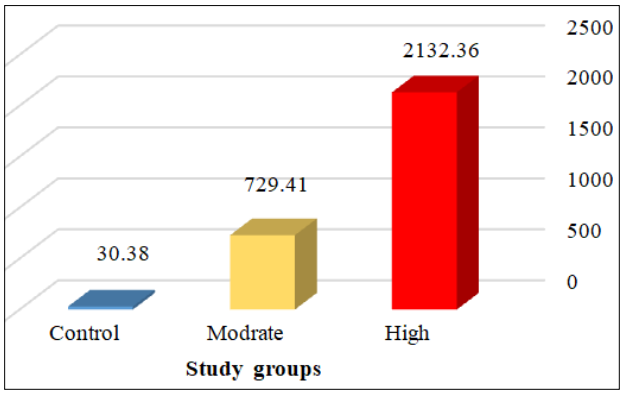

Figure 5.Bar Diagram showing Comparison of Ferritin Level Concentration among Study Control Groups

Discussion

When the virus enters the body, it wants a special receiver to support it into the cell, which is called the vasoconstrictive changes in the enzymes, ACE 2.[18] ACE 2 is a gift within the respiratory organ on the surface of the alveolar cells.[19] They need three sorts of alveolar cells: Type 1: accountable for gas exchange with blood vessels (gas exchange), Type 2: it's responsible for the assembly of surfactant, that may be a mixture of proteins and fats that cut back the physical phenomenon of the air sac and kind 3: immune cells, which are macrophages.[20] The coronavirus envelope contains proteins referred to as spikes and specials (S_Spike) that facilitate the virus bind to ACE2.[21] The virus' genetic material enters the cell's interior and also the cell is controlled to provide the virus' proteins, and so the virus multiplies and the cell dies.[22] After two alveolar cells have passed away, they throw out certain inflammatory mediators for alleged substances. These substances stimulate the dominant "macrophages" of the immune cells, and they secrete three immune substances called "cytokine" after stimulating the macrophages: interleukin 1, interleukin 6 and the mortification problem with the neoplasm.[23] The symptoms associated with Coronavirus infection are caused by the 3 substances when they reach the bloodstream.[24] The blood

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vessels also enlarge the cyst as permeability, vasodilation and capillary permeability of these vessels are increased exaggeratedly.[25] This leads to "alveolar oedema" leading to drive and breathlessness. Loss of a chemical substance leads to an increase of the vesicle's physicality and thus to the collapse of the Alveolar system. It also causes breathlessness and hypoxia.[26] In addition, the flow of "neutrophils" into the infectious agent infection location as an associate degree reaction to these three substances increases.[27] Cells of neutrophils kill viruses with the secretion of two substances like ROS, Proteases. However, in addition, the second article breaks down a number of alveolar cells responsible for exchanges of gas and causes a condition called "cough" consolidation.[28] The 3 substances, "IL-1, IL-6, and TNF" attend the "hypothalamus" and so increase the vital sign and cause "fever" symptoms. In extreme cases, the "SIRS" can occur. Syndrome of generalized inflammatory reaction. 29 This results in septic shock. Syndrome with multiple organ disease. Particularly the excretory organ, which results in renal failure.[30] One of these biomarkers of concern is feed dehydrogenase (LDH), particularly as higher LDH levels have been linked to worse outcomes among patients with previously different infective agent infections.[31] Early knowledge of COVID-19 patients led to significant differences in LDH levels, while not severe sickness, among patients with associated degrees.[32] A group analysis of the literature revealed was therefore conducted in order to investigate the possible connection between exaggerated LDH values for patients with COVID-19.[33] In severe, non-severe cases of COVID-19many studies compared elevated LDH values.[34,35] In almost all organs, LDH is a living catalyst found in cellular components that catalyses pyruvate and lactate interconversion with concurrent NADH and NAD+ interconversion.[36] The catalyst is comprised of 2 major sub-units (i.e., A and B) and is donated tohumans in 5 separate isozymes (CARL-1, RR-2-2, LRH-3, RCC LDH-3, RCL and PRH-2 and LDH-5).[37] The catalyst is used in the human body in the cardiomyocytes and in the panoramic system. While LDH has been used historically since the 1960s as a marker of viscus injuries, abnormal values can come out of multiple organ wounds and reduced action with glycolytic upregulation.[38] The acidic extracellular pH caused by infection feed and tissue damage triggers metalloprotease activation and increases the medium phagocyte ontogeny.[39] But the contribution to the LDH elevation determined in COVID-19 by the different LDH isoenzymes was not determined. LDH levels in nephrosis and cardiac muscle injury are also increased in thrombotic microangiopathy.[40] In addition, high dimer concentrations and blood disorder have been reported in serious COVID-19 patients, indicating that hyper coagulating conditions may also contribute to the severity of illness and deaths.[41] COVID-19 patients had main fever clinical symptoms, most of which were sensitive and many severe cases. Due to the variability of symptoms and imaging findings, and the variable level of sickness progression, the condition and prognosis for COVID-19 patients were sophisticated.[42] The dynamic changes of the peripheral blood clotting indices in patients who loved D-dimer were observed in COVID-19, which showed that level D-dimers could well be used to forecast COVID-19 severity and prognosis.[43] D-dimer is that fibrinolytic degradation product and high levels indicate that the body is hyper coagulated and the secondary decay is very useful in determining thrombosis. It has been reported that COVID-19 patients have a hypercoagulable condition.[44] Further, in patients with severe COVID-19 the incidence of blood vessel occlusion (VTE) was 25%, while embolism was diagnosed in 30% of COVID-19 patients.[45] Additional levels of D-dimer were exaggerated within the blood of COVID-19 patients with CVA.[46] The next D-dimer value also indicated that the patient's condition could be very serious, and even combined with various complications.[47] For COVID-19 patients, there are attainable reasons for increasing dimer values: The infection causes pro-inflammatory cytokines to be released so that an inflammatory storm is infected.[48] In plasma, love IL-2, IL-6, G-CSF, IP-10, MCP-1, MIP-1A and TNF-α were higher especially in severe COVID-19 patients, with apace and extremely active T cells, macrophages and natural cells, with overruns in the immunodeficiency cell or non-immune and with more than a hundred and fifty infectious cytokines and Checells and with over 100 inflammatory cells. In some COVID-19 patients, hypoxia is completely different, and inflammation leads to occlusion or over-consumption of gas.[50] The absolute demand for oxygen will increase in the whole of the abnormal hemodynamics which triggers and ends up in thrombosis, both molecular and cellular. Severe infection or acute septic inflammation could also influence coagulation of the blood, love excessive levels of proteolytic enzyme (PAI-1), and excessive tenured dissolution.[52] Serum globulin may be an inflammatory substance produced by the liver. The C-reactive protein examines how much this protein is measured in the blood. The test can help diagnose acute and chronic inflammatory conditions.[53] In COVID-19, the handwriting misunderstands the importance of high IL-6. Although IL-6 is generally greater in various inflammatory conditions, the pathophysiology of COVID-19 is restricted in this finding. Different studies have demonstrated the association between initial IL-6 levels greater than 80 pg/mL and the results of love metastasis failure and death.[54] The authors fail to discuss prognostic models such as ISARIC-4C or associated hyperinflammatory syndrome COVID-19, which underline the prognostic marks of sugar globulin and IL-6.[55] Significantly high levels of IL-6 body fluid do not appear to be the clinical reaction requirement for IL-6

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blockage. Median IL-6 pretreatment concentrations are only moderately elevated in approved sickness indications such as multicenterCastleman's disease and large cell arteritis.[56] While the results of the IL-6 blockade irregularly controlled studies have been largely negative, various immunomodulatory therapy studies investigating each short-term outcome are being conducted.[57] COVID-19 is a heterogenic disease thatcan cause many manifestations of immune disorder in children, beginning with the protein storm, via alleged long-haul syndrome and inflammatory multisystem disorder.[58] Body fluid IL-6 remains the most effective COVID-19 severity biomarker on the market and still has good guiding potential for this disease. The COVID-19 fatal effects during cytokine storm syndrome have been reported to depend on the severity of the disease. A body fluid protein content assessment is carried out by this cytokine storm.[59] Aload of infectious agents or microorganisms in the body indicates increased amounts of ferritin or hyperferritinemia. A condition activating macrophages to secrete proteins can be hyperferritinemia or hyperferritinemic syndrome, which may be a sign of serious sickness, and in severe cases, maycausea cytokine storm.[60] During cytokine storm syndrome the fatal results of COVID-19 are present. The severity of the disease dependingon cytokine tempest syndrome has thus been reported. A complete evaluation of serum ferritin levels can be carried out in this cytokine storm.[61] The gravity of COVID-19 might best be determined by serum ferritin levels. Many people suffering from polygenic disorder have high levels of body fluid proteins, which are likely to have serious COVID-19 complications.[62] The median values of serum ferritin from several recent studies have exceeded COVID-19 detection limits during the entire hospital period, indicating that the levels of ferritin in all hospitals have been continuously exaggerated.[63]

Conclusion

Increased LDH values were linked to an increase in COVID-19 toxicity. On the basis of D-dimer, the probability of mortality can be determined. C-responsive protein and ferritin serum exercises were significantly increased in COVID-19 patients compared to those with mild side effects of COVID. IL-6 is a key immunomodulatory cytokine in both sound and infected tissues.

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Conflict of Interest: None

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