Comparative study of some biochemical parameters among of COVID-19 symptoms and non COVID-19 symptoms individuals

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Abstract :
Nowadays in the Kurdistan region of Iraq, the number of patients have common symptoms with COVID-19 infection rapidly increased. 123 patients which they had common symptoms with COVID-19 and 94 healthy control individuals (non-COVID-19) were subjected for quantitative analysis for each one of the following biochemical parameters, Lactate dehydrogenase (LDH), Creatine Phosphokinase (CPK), and C-reactive protein (CRP) in Erbil, Kurdistan Region of Iraq. We analyze clinical features and compared the differences between COVID-19 and non-COVID-19 symptoms. Among the healthy control individuals, the absolute value of LDH, CPK Creatine Kinase and CRP were determined in between the normal range, and in compare with patients with COVID-19 symptoms their values were smaller and, the P value was (P < 0.05). All three biochemical parameters increased among patients with COVID-19 symptoms, but more significantly, steadily increase was observed only in LDH value in age above and under 40 years (284.43±10.29 and 321.23±16.32 U/L), and p-value was (0.0488). Male patients had higher levels of LDH (299.32±11.42 U/L), CPK Creatine Kinase (195.90±26.65 mg/L), and C-Reactive Protein (5.86±3.96 mg/L) in compared with the female patients. Our study suggested that among patients who have COVID 19 symptoms, increased LDH is the advised and helpful biochemical marker among routine panel for COVID-19 infection evaluation. Also, CRP levels were positively correlated with male patients when compared with the healthy control.
Keywords: Biochemical parameters; biochemical markers; COVID 19 symptoms; healthy control; Serological tests

1. Introduction

Millions of individuals worldwide have been infected by Coronavirus disease (COVID-19) [1]. The disease has spread to more than 199 countries and territories worldwide as of 29 March 2020 [2]. Urgent identification of clinical and laboratory predictors of progression towards serious and lethal forms is urgently needed in the battle against coronavirus disease 2019 (COVID-19), now coronavirus is a worldwide pandemic disease [3].

This disease is caused by a new zoonotic virus infection known as Extreme Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Coronavirus infection was previously documented in 2002 in China in the form of SARS-CoV, and later in 2012 in Saudi Arabia in the form of Middle East Respiratory Syndrome (MERS-CoV) [4]. Most of them target the viral glycoprotein (S) spike. S is located on the surface of virions and mediates the recognition of angiotensin-converting enzyme 2 (ACE2) cellular receptor [5]. Due to the lack of specific antiviral drugs and vaccinations, one of the most significant factor influencing disease development and prognosis is its immune status [6]. SARS-CoV-2 belongs to the β coronavirus class of the coronavirus family, which is a new independent branch of Extreme Acute Respiratory Syndrome-Related Coronavirus (SARS-CoV) and Middle East Respiratory Syndrome-Related Coronavirus (MERS-CoV) and has 79% SARS-CoV and 51.8% MERS-CoV genetic homology [7].

Positive relationship discovered in between CD4+ T cells and CD8+ T cells, IL-6, and IL-10 in a mild group, but not in a group of patients with severe COVID-19 [8]. Immune responses to SARS-CoV-2 infection vary from mild reactions to life-threatening cytokine storms in extreme COVID-19 following asymptomatic infection. To

capture the full spectrum of immunophenotypic changes, it elicited in examining of white blood cells in infected patients [9]. There has been a lot of data indicating that the levels of serum lactate dehydrogenase (LDH) represent the degree of different pathophysiological processes. The recent information on powerful change of LDH in COVID-19 pneumonia has not been well studied [10].

Due to its high transmission potential as well as high mobility and mortality, the virus has raised global concern [11]. Serological tests may be used as monitoring test to better understand SARS-CoV-2 epidemiology and possibly warn the individual risk of potential disease [12]. It was important to explore other sensitive indicators capable of representing changes in lung lesions and the seriousness of the disease. For early diagnosis of pneumonia, C-reactive protein (CRP) levels may be used, and patients with serious pneumonia have elevated levels of CRP [13]. IL-6 and CRP serum levels will effectively determine the severity of the disease and predict the outcome in patients with COVID-19 [14]. The aims of this study were to determine the relationship of the three biochemical parameters, Lactate dehydrogenase (LDH), Creatine Phosphokinase (CPK), and C-reactive protein (CRP) in patients who have exact similar symptoms with COVID 19, in compared with healthy control individuals.

2. Materials and Methods

Questionnaires for patients

We constructed a simple standardized questionnaire for all patients which they visited the private clinical diagnostic sectors, in between august to September of 2020, in Erbil province, Kurdistan region of Iraq. The patients have been chosen among different age groups and different genders. The most common questions on signs and symptoms of COVID-19 infection such as presence or absence of fever, dry cough, and tiredness, were directed to patients in our standardized questionnaires. All 123 patients had the most common signs and symptoms of COVID-19 infection. For comparative study, we also selected 94 healthy controls individuals without any disease such as diabetes, hypertension from different age and sexes.

Laboratory tests

Blood samples were collected from each patients and healthy control individuals. All blood samples collected inside the (10 ml) gel tube, it contain clotting activators, after clotting, centrifuged them for 15 minutes at 5000 round per minutes (RPM). Serum samples subjected for determination of LDH, CPK Creatine Kinase and C - reactive protein (Quantitative) on automatic biochemical analyser (Cobas e311). All normal ranges for each one of the biochemical parameters have been derived from the ROCHE kits manufacture leaflets instructions. Normal range for 1.LDH : Male (135-225 U/L) , Female (135-214 U/L) ,for 2. CPK: Male (39-308 mg/L) and Female (26-192 mg/L), 3- for both genders CRP (0-0.5 mg/L).

Statistical analysis

All data from all groups were represents as a Mean ± SEM. An unpaired t-test was used to compare results between the two groups. determine if there is a significant difference between the means of two groups, which may be related in certain featuresA P value of < 0.05 was determined to be significant.

3. Results and Discussion

Biochemical parameter values in between healthy control and patients individuals:

Results of Biochemical parameters (LDH, CPK Creatine Kinase and CRP) for healthy control individuals were determined in between the normal ranges. However, in compare with patients with COVID-19 symptoms their values were smaller, and the P value was (P ＜0.05). All three biochemical parameters increased among patients with COVID-19 symptoms, but more significantly, steadily increase observed only in LDH value in age above and under 40 years (284.43±10.29 and 321.23±16.32 U/L), and p-value was (0.0488). Table (1) illustrate the means and P values for biochemical parameters of healthy controls and patients with COVID-19 symptoms.

Biochemical parameter values in between male and female patients

All biochemical parameter values showed higher values in male patients in compared with the female patients. All P-values were nonsignificant, table (2) represent the biochemical parameter values in between males and females patients.

Biochemical parameter values in between two differ aged groups (over and under 40) years patients

Significant result observed in LDH value in between over and under 40 years patients, in such way that the P-value was (0.0488), while the P-values for each one of CPK Creatine Kinase and C - reactive protein were nonsignificant. Table (3) clarifying the results and P-values in between two differed aged groups.

Biochemical parameter values of male and female in both aged groups (over and under 40) years patients:

Only significant result observed in LDH P-value among biochemical parameters in both aged groups (over and under 40 years), with males patients, in such way that the P-value was (0.0128) table (4). While the P-values for all parameters LDH, CPK Creatine Kinase and C - reactive protein were nonsignificant in both aged groups (over and under 40 years), with female patients table (5).

Table: 1 Biochemical parameter level values in healthy controls and patients individuals

Parameters		Mean ± SEM of healthy Control	Mean ± SEM of Patients	P value
Gender	Male	N=63	N=74	
	Female	N=31	N= 49	
Age		36.54±3.11	36.61±1.21	0.9817
LDH(U/L)		185.90±5.99	297±8.87	0.0001
CPK Creatine Kinase (mg/L)		80.81±6.76	164.93±23.97	0.0030
C-Reactive Protein (Quantitative) (mg/L)		0.26±0.04	3.83±2.38	0.1914

Table :2 Biochemical parameter values in male and female patients

Parameter	Mean ± SEM of male N=74	Mean ± SEM of female N=49	P value
LDH(U/L)	299.32±11.42	293.48±14.23	0.7488
CPK Creatine Kinase (mg/L)	195.90±26.65	118.17±44.27	0.1128
C-Reactive Protein (Quantitative) (mg/L)	5.86±3.96	0.76±0.17	0.2976

Table :3 Biochemical parameter values in patients over and under 40 years

Parameter	Age under 40 .N=81	Age above 40.N=42	P value
LDH(U/L)	284.43±10.29	321.23±16.32	0.0488
CPK Creatine Kinase (mg/L)	137.15±20.00	218.52±58.28	0.1078
C-Reactive Protein (Quantitative) (mg/L)	1.13±0.37	9.03±6.94	0.1171

Table :4 Biochemical parameter values in both aged groups and in male patients

Parameter	Age under 40 .N=50	Age above 40 .N=24	P value
LDH(U/L)	279.84±12.35	339.91±22.22	0.0128
CPK Creatine Kinase (mg/L)	180.38±23.38	228.25±66.76	0.4042
C-Reactive Protein (Quantitative) (mg/L)	1.92±0.49	14.07±12.17	0.1523

Table :5 Biochemical parameter values in both aged groups and in female patients

Parameter	Age under 40.N=31	Age above 40.N=18	P value
LDH(U/L)	290.29±16.3	327.5±23.59	0.1891
CPK Creatine Kinase (mg/L)	152.26±42.85	236.72±123.51	0.4429
C-Reactive Protein (Quantitative) (mg/L)	0.77±0.36	17.67±16.20	0.1745

Biochemical parameter values between healthy control individuals and female patients:

Like previous results, significant P-value has been recorded for LDH value, it was (0.0001). Other biochemical parameter P-values were nonsignificant in between healthy control individuals and female patients table (6).

Biochemical parameter values between healthy control individuals and male patients:

Unlike all previous results, significant P-value results have been noticed for all biochemical parameters in between healthy control individuals and male patients table (7). The P-values for (LDH: 0.0001, CPK Creatine Kinase: 0.0043, and C-Reactive Protein: 0.003) were recorded respectively.

Table :6 Biochemical parameter values in healthy control individuals and female patients

Parameter	Mean ± SEM of female control N=31	Mean ± SEM of female patient N=49	P value
LDH(U/L)	190.75±6.31	303.95±13.59	0.0001
CPK Creatine Kinase (mg/L)	75±4.37	183.29±52.39	0.1055
C-Reactive Protein (Quantitative) (mg/L)	0.27±0.07	6.98±5.96	0.3744

Table :7 Biochemical parameter values in healthy control individuals and male patients

Parameter	Mean ± SEM of male control N=63	Mean ± SEM of male patients N=74	P value
LDH(U/L)	183.14±8.90	292.39±11.73	0.0001
CPK Creatine Kinase (mg/L)	84.14±10.45	152.78±19.90	0.0043
C-Reactive Protein (Quantitative) (mg/L)	0.26±0.05	1.74±0.45	0.0030

The aim of this research was to determine the relationship between patients with common COVID-19 symptoms and health control individuals. In patients with similar symptoms of COVID-19, biochemical parameters such as LDH, CPK Creatine Kinase and C-Reactive Protein (Quantitative) typically increased. Data showed that LDH result was (185.90 ± 5.99 U/L) in healthy control individuals and significantly increased to 297 ± 8.87 U/L in patients with COVID-19 symptoms, the P-value was (0.0001) which statistically important. However, CPK Creatine Kinase result was (80.81 ± 6.76 mg/L) in healthy control individuals and the P-value was 0.0030. No significant difference was observed in results of C-Reactive Protein (Quantitative) parameter values between (healthy and patients) groups (table 1). Remarkable increase in results of LDH, CPK and CRP, were seen in primary laboratory workups [15]. The results showed that in COVID-19 patients, the value of LDH was increased [16], as well as significantly increased of LDH values has been noticed in our patients with COVID-19 symptoms. [17] reported that plenty rise have been observed in values of creatine phosphokinase (CPK) and lactate dehydrogenase (LDH). Beside of elevated C-reactive protein (CRP), and except in those with no signs or mild illness, the computerized tomographic chest scan is normally abnormal, [18] noticed the normal or low white blood cell counts as a typical laboratory findings.

There was no high increase in male and female patient with COVID-19 symptoms. In female patients, LDH dramatically increased. The LDH value was (299.32 ± 11.42 U/L) in male patients, and (293.48 ± 14.23 U/L) in female patients. The ratio of both CPK Creatine Kinase and C-Reactive Protein in male patients was higher than in female patients (195.90 ± 26.65 mg/L and 5.86 ± 3.96 mg/L). We can not find any statistically significant between male and female patients for all three parameters (table 2). [19], studied that increase in results of CRP and LDH were observed. The risk factor for serious illness and death in patients with COVID-19 has already been identified as older age and male sex [20]. The independent high-risk factors associated with the development of Covid-19 infection are age, CRP, LDH, and haemoglobin levels. Some of the findings are consistent with previous research finding multiple risk factors in patients with Covid-19 to be correlated with poor clinical results [21].

The ages of patients were divided into two separate groups, under and above 40 years of age. All three parameters were increased in patients with over 40 years of ages, while the statistically significant value was reported only for LDH parameters and the p-value was (0.0488), and the p-value were (0.4042) and (0.1523) respectively for remained parameters. No correlation was noted between ages below and above 40 years (table 3). On the other hand, similar findings were found with male patients in both aged groups, all three parameters were significantly increased, but only value of LDH ratio statically was significant and the p-value was (0.0128). higher number of LDH was reported in male patients above 40 years of age and (339.91 ± 22.22 U/L) above 40 years of age, but it was (279.84 ± 12.35 U/L) below 40 years of age. The levels of CPK Creatine Kinase and C-Reactive Protein (Quantitative) also differ from male to female in each category (Table 4). Results showed that the majority of COVID-19 deaths occurred with reduced oxygen saturation levels and elevated lactate dehydrogenase and erythrocyte sedimentation levels on admission in male

elderly people [22].

Elevated amounts of C-reactive protein (CRP) reported in laboratory test results, which suggesting the infection by COVID-19 [23]. [24] stated that poor prognosis is associated with multiple laboratory features, including LDH and CPK. Normal blood cell counts, liver function tests, serum electrolytes and glucose were seen in blood tests. There was a small rise in C-reactive protein and LDH (respectively 0.74 mg/dL, normal value 0-0.5; 261 U/L, normal value 0-248) [25]. In patients with COVID-19 biochemical markers, including elevated lactate dehydrogenase (LDH), creatinine kinase (CPK), creatinine kinase MB (CK-MB), D-dimer, high-sensitivity troponin, have been reported [26]

In female patients over and below 40 years of age, there is no difference in biochemical parameter values and all three p-values were non-significant for each of them at < 0.05, and these findings are opposite to the biochemical parameter values in male patients over and below 40 years of age (Tables 4 and 5). Although the positive SARS-CoV-2 patients appeared to have a higher neutrophil-to-lymphocyte ratio (8.9 vs. 4.1; P =.134), CPK (359.0 vs. 144.5; P =.667), CRP (24.2 vs. 13.8; P =.627), lactate dehydrogenase (576.5 vs. 338.0; P =.313), and ferritin (974.0 vs. 412.0; P =.47), these differences were not statistically significant [20].

Tables 6 and 7 showed that the Biochemical parameter levels in the healthy control individuals and male patients with COVID-19 symptoms. Our results represent that there are differences between the healthy control individuals and patients for each gender. All three parameters are increased from healthy control and patients of the males. Extremely significant increase were observed for each LDH, CPK Creatine Kinase, and C-Reactive Protein (Quantitative) while opposite results were detected in healthy control and female patients. Only LDH was significant between these two groups (healthy control individuals and female patient). The significant value for C-Reactive Protein (Quantitative) was only noted between healthy control individuals and male patient. Value in healthy males individuals was (0.26 ± 0.05 mg/L), it was lower than male patients (1.74 ± 0.45 mg/L) and the p-value was (0.0030) statistically significant (Table 7).

4. Conclusion

Our study showed that assessment of ldh as a biochemical parameter was helpful in distinguishing between healthy individuals with covid 19 symptoms from different aged groups and genders for further analysis of covid 19 infection.

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