Original Article

Alteration of Thyroid Function Tests and Evaluation of Serum Zinc, IgG and IgM Levels in non-hospitalized Iraqi Patients with Corona Virus

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Abstract

Background: SARS-CoV-2 is a novel corona virus that would be responsible for COVID-19 infection and has provoked a worldwide epidemic.

Objective: To investigate alteration of thyroid function tests and evaluation of serum zinc, IgG and IgM levels in Iraqi patients with corona virus.

Methods: A total of 166 sera, 83 from non-hospitalized asymptomatic patients diagnosed with COVID-19 (aged 17–78 years) and 83(aged 18–70 years) from negative healthy individuals, were evaluated for thyroid hormones T_3,T_4 and TSH, trace element of zinc, IgM and IgG antibodies.

Results: recent study described non-hospitalized COVID-19 patients who developed argumentative results related to thyroid function test, signs of hypozincemia, disturbances in IgG, and IgM levels were started in some of them as compared with healthy group.

Conclusion: current study discovered that non-hospitalized patients diagnosed with COVID-19 can develop a non-critical state of thyroid function.

Keywords: Corona Virus, zinc, thyroid function tests, IgG, IgM.

Introduction

Corona Virus is a severe acute respiratory disease caused by SARS coronavirus 2 (SARS CoV2), which was discovered in Wuhan, China. This pandemic has spread rapidly in US, Spain, Italy, and even more than 70 countries [1, 2]. Despite best efforts of numerous experts, the genesis of corona virus remains unclear.[3]. Coronaviruses (CoVs) are classified into four groups:α,β,γandδ. Among these genera, αand β infect mammals, whereas γ and δ mostly infect birds. There are four lineages of beta coronaviruses: A, B, C, and D. [4] . Initially, because of location and pneumonia symptoms, disease was once dubbed "Wuhan pneumonia". causal agent of this

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outbreak, according to whole-genome sequencing, is a new coronavirus [5].

Little is known about complete spectrum of COVID-19 effects in connection to autoimmune endocrine illnesses, but endocrine engagement is becoming more common [6–8]. COVID-19, on other hand, has recently been shown to have massive impacts throughout body, with many pathological changes including the endocrine glands, which can be impaired by various mechanisms such like direct virus impairment to gland or a mediating influence on hypothalamus–pituitary gland axis, systemic inflammatory condition due to cytokine and chemokine secretion, vasculature derangement, and autoimmune responses [9,10].

Zinc is one of human body's "vital minerals". Hypozincemia refers to a lack of zinc in body caused by a variety of factors [11]. Hypozincemia is common in individuals infected with severe acute respiratory syndrome coronavirus-2 (SARS-COV-2) and has been identified as a potential cause in severe coronavirus disease-2019 (COVID-19). While zinc may impair SARS-COV-2 proliferation and cell entrance, association between zinc shortage and COVID-19 severity may also be due to COVID-19's effects on body metabolism and immune function. Lately, a link was discovered between low zinc levels and the intensity of acute respiratory distress syndrome in people with severe COVID-19 [12].

Virus infection normally results in creation of IgM, which is followed by development of IgG after a few weeks. As a result, detecting IgM and IgG antibodies simultaneously will offer additional information about the stage of infection in positive individuals [13]. Upon these different impacts of the disease, the recent study attempts to evaluate changes in thyroid function tests, zinc concentration level, and IgG and IgM in non-hospitalized patients whose affected with virus.

Materials and Methods

Study population and Data collection:

Data were collected from the 1st of September to the 1st of October in 2021, 100 not hospitalized patients who attended to different private laboratories in Iraq, with Corona virus positive tests, were voluntered to participate in this study after their verbal consent agreement. Then 13 patients were excluded due to known hypothyroidism, and 4 pregnant patients were excluded, 83 patients (aged 17–78 years) were included. Same number of (83 healthy individuals), aged (18-70 years) were also included as a control group.

Demographic information was recorded including age, gender, and residence status (Figures 1,2, and 3), In the morning of the day of declaring the PCR positive test, the patient's venous blood was collected for thyroid hormone function test, zinc, IgG, and IgM Levels measurement.

Laboratory test:

T_3, T_4, and TSH levels were determined using a Roche Cobas e602 electrochemical luminescence analyzer (Roche, Germany). A colorimetric approach was used to examine the zinc levels in serum (Sentinel Diagnostics, Milano, Italy). And Prima COVID-19 IgG/IgM Rapid Test (PRIMA Lab SA, Balerna, Switzerland) was evaluated against same panels of serology specimens from COVID-19 cases and a samples of negative control group.

Diagnostic criteria for Corona virus:

The Corona virus was diagnosis based on symptoms include fever, cough, and breathlessness. Detection of nucleic acid by PCR technique in respiratory tract was used to confirm the presence of Corona virus.

Statistical analysis:

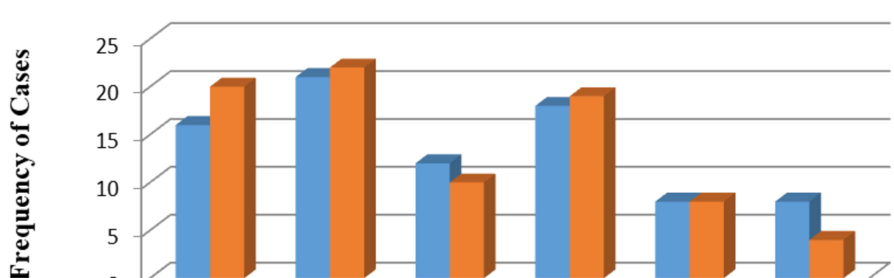
To compare percentages, the data were analyzed using the Chi-square (X2) test. For independent samples, a t-test was employed to compare two numerical variables. (Mean SD) was used to describe numerical data. The test employed a significance threshold of =0.05. To examine current data, the (SPSS 24) application was employed.

Results

This study involved (83) individuals diagnosed with COVID-19, and (83) healthy individuals served as control group. Table 1 documented that the average mean of ages (years) of COVID-19 group was (42.22±16.13) versus control group (39.56±14.15), statistically this difference is non-significant (*P*-value=0.26). Statistically the differences between the average means of IgG, IgM, Zinc, T3and TSH of COVID-19 groups versus control group, are highly significant (*P*-value=0.00). Whereas the difference between the average mean of T4 of COVID-19 group versus control group is non-significant (P-value=0.096). Table 2 shows the differences were statistically highly significant between the average mean of IgG and IgM levels among males and females of COVID-19 groups versus in males of control groups. This table also documented that there are no differences in the levels of IgG and IgM among both gender of COVID-19 and control groups respectively.

Table 3 elaborated that the difference is statistically highly significant in the average mean of zinc levels among (39) males and (44) females of COVID-19 group versus in (36) males and (47) females of control group. This table also documented that there were no differences in the levels of zinc among both gender of COVID-19 and control groups respectively. Table 4 investigated the average mean of T3 and TSH levels among (39) males and (44) females of COVID-19 groups versus (36) males and (47) females of control groups, and the differences between them are statistically highly significant. The difference in the average mean of T4 levels among males and females of COVID-19 group versus males and females of control group, is statistically non-significant. This table also documented that there were no differences in the levels of T3, T4, and TSH among both gender of COVID-19 and control groups respectively.

Table 5 shows that 45 case out of 83 has IgG concentration (>1) in contrast to 38 of 83 has IgG concentration (<1), while all healthy control group 83 has IgG concentration (<1). On the other hand, 23 case out of 83 has IgM concentration (>1) in contrast to 60 of 83 has IgM concentration (<1), while all healthy control group 83 has IgM concentration (<1). Statistically this difference in both IgG concentration and IgM concentration was highly significant (Chi-square=26.69, *p*-value=0.00). Table 6 shows that 47 case out of 83 has zinc concentration (<70 decrease) in contrast to 36 of 83 has zinc concentration (70-114 within normal), while all 83 healthy control group has zinc concentration (70-114 within normal). Statistically this difference was highly significant (Chi-square=65.5, *p*-value=0.00).Table 7 shows that 25 case out of 83 has T3 concentration (<3.1 increase) in contrast to 11 of 83 has T3concentration (<3.1 decrease), and 47 case out of 83 has T3 concentration (1.3-3.1 within normal), while 83 control group has T3concentration (1.3-3.1 within normal). Statistically this difference was highly significant (Chi-square=45.9, *p*-value=0.00). Table 8 shows that 65 case out of 83 has T4 concentration (3-10 within normal) and 18 of 83 has T4 concentration (<3 Decrease), while 83 control group has T4concentration (3-10 within normal). Statistically this difference was highly significant (Chi-square=20.1, *p*-value=0.00). Finally, table 9 shows no statistical differences in TSH levels between COVID-19 group and control group.



	(17-26)	(27-36)	(37-46)	47-56	57-66	>66
COVID-19	16	21	12	18	8	8
Control	20	22	10	19	8	4

Figure 1: Categorial of Age Group (Years)

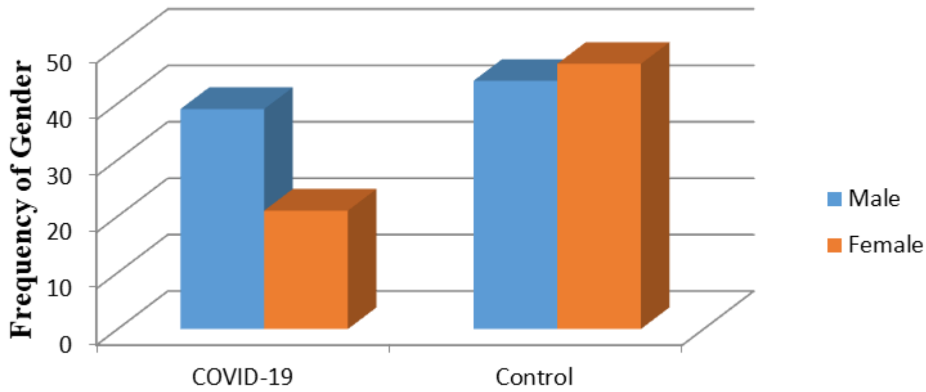


Figure 2: Categorial of Gender

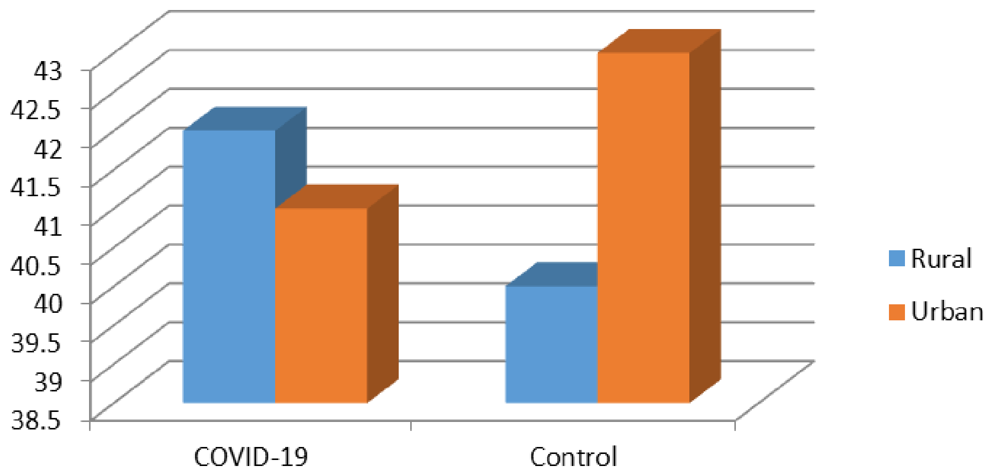


Figure 3: Categorial of Residency status

Table 1: Means value of studied parameters in and COVID-19 group versus control group

Variables	Study Groups	No.	Mean	SD	T-test	P-value*
Age (Years)	COVID-19	83	42.22	16.13	1.13	0.26 (N.S)
	Control	83	39.56	14.15		
IgG (ng/ml)	COVID-19	83	8.40	2.79	8.63	0.00 (H.S)
	Control	83	0.04	0.02		
IgM (ng/ml)	COVID-19	83	0.90	0.3	5.71	0.00 (H.S)
	Control	83	0.07	0.01		
Zinc (ug/dl)	COVID-19	83	65.97	22.76	6.4	0.00 (H.S)
	Control	83	86.01	16.50		
T3 (ng/ml)	COVID-19	83	2.79	0.92	10.12	0.00 (H.S)
	Control	83	1.08	0.42		
T4 (ng/ml)	COVID-19	83	3.78	1.14	1.67	0.096 (N.S)
	Control	83	4.14	1.57		
TSH (ng/ml)	COVID-19	83	2.3	1.0	10.04	0.00 (H.S)
	Control	83	0.85	0.17		

*; Independent sample test, N.S; non-significant, H.S; highly significant, SD; Standard Deviation

Table 2: Comparison of IgG (ng/ml) and IgM (ng/ml) levels among studied groups in relation to gender

parameters	Studied groups	Male (Mean±SD)	No.	Female (Mean±SD.)	No.	t- test	p- value*	C.S
IgG (ng/ml) (N.V >1)	Control	0.054±0.01	36	0.04±0.02	47	1.0	0.3	N.S
	COVID-19	9.07±6.00	39	7.80±4.66	44	0.65	0.5	N.S
	t-test	6.0		6.1				
	P*-value	0.00 (H.S)		0.00 (H.S)				
IgM (ng/ml) (N.V >1)	Control	0.05±0.01	36	0.09±0.01	47	1.0	0.28	N.S
	COVID-19	0.80±0.1	39	0.98±0.31	44	0.63	0.5	N.S
	t-test	3.7		4.3				
	P*-value	0.00 (H.S)		0.00 (H.S)				

*; Independent sample test, N.V; normal value, H.S; highly significant,
C.S; coefficient significance, SD; Standard Deviation

Table 3: Comparison of Zinc (ug/dl) levels among studied groups in relation to gender

Zinc (ug/dl) (N.V 70-114)	Male (Mean±SD)	No.	Female (Mean±SD)	No.	t- test	p- value*	C.S
Control	83.08±12.42	36	88.26±9.55	47	1.42	0.1	N.S
COVID-19	64.34±10.78	39	67.42±15.25	44	0.62	0.5	N.S
t-test	3.8		5.2				
P*-value	0.00 (H.S)		0.00 (H.S)				

*; Independent sample test, N.V; normal value, N.S; non-significant,
C.S; coefficient significance, SD; Standard Deviation

Table 4: Comparison of T3 (ng/ml), T4 (ng/ml), and TSH (ng/ml) levels among studied groups in relation to gender

Parameters	Studied groups	Male (Mean±SD)	No.	Female (Mean±SD)	No.	t- test	p- value*	C.S
T3 (ng/ml))N.V 1.3-3.1(	Control	1.03±0.414	36	1.13±0.43	47	1.02	0.3	N.S
	COVID-19	2.92±0.55	39	2.67±1.0	44	0.76	0.4	N.S
	t-test	7.09		7.16				
	P*-value	0.00 (H.S)		0.00 (H.S)				
T4 (ng/ml))N.V 3.0-10.0(	Control	3.92±1.74	36	4.31±1.42	47	1.1	0.2	N.S
	COVID-19	3.77±1.165	39	3.79±1.13	44	0.08	0.9	N.S
	t-test	0.42		1.9				
	P*-value	0.6		0.05				
TSH (ng/ml))N.V 0.4-4.0(	Control	0.82±0.14	36	0.87±0.2	47	0.27	0.7	N.S
	COVID-19	2.26±0.6	39	2.42±1.0	44	0.59	0.51	N.S
	t-test	6.3		7.8				
	P*-value	0.00 (H.S)		0.00 (H.S)				

*; Independent sample test, N.V; normal value, H.S; highly significant,
N.S; non-significant, C.S; coefficient significance, SD; Standard Deviation

Table 5: Categorial levels of IgG (ng/ml) and IgM (ng/ml) in COVID-19 group and control group according to the cutoff point

Categorial Count		COVID-19		Total Count	Control		Total	Chi-sequare	P-value*
		%			%				
IgG (ng/ml)	<1 normal	38	45.8%	83	83	100.0%	83	61.73	0.00 (H.S)
	>1 increase	45	54.2%	100.0%	0	0.0%	100.0%		
IgM (ng/ml)	<1 normal	60	72.3%	83	83	100.0%	83	26.69	0.00 (H.S)
	>1 increase	23	27.7%	100.0%	0	0.0%	100.0%		

*; Independent sample test, H.S; highly significant

Table 6: Categorial levels of Zinc in COVID-19 group and control group according to the cutoff point of Zinc (ug/dl)

Study Groups		Categorial Zinc (ug/dl)		Total
		70-114 normal	**<70 decrease**	
COVID-19	Count	36	47	83
	%	43.4%	56.6%	100.0%
Control	Count	83	0	83
	%	100.0%	100.0%	100.0%
Total	Count	119	47	166
	%	71.7%	28.3%	100.0%
Chi-square	65.5			
P*-value	0.00 (H.S)			

*; Independent sample test, H.S; highly significant

Table 7: Categorial levels of T3 in COVID-19 group and control group according to the cutoff point of T3 (ng/ml)

Study Groups		Categorial T3 (ng\ml)			Total
		Normal 1.3-3.1	**Decrease <1.3**	**Increase <3.1**	
COVID-19	Count	47	11	25	83
	%	56.6%	13.3%	30.1%	100.0%
Control	Count	83	0	0	83
	%	100.0%	0.0%	0.0%	100.0%
Total	Count	130	11	25	166
	%	78.3%	6.6%	15.1%	100.0%
Chi-square	45.9				
P*-value	0.00 (H.S)				

*; Independent sample test, H.S; highly significant

Table 8: Categorial levels of T4 in COVID-19 group and control group according to the cutoff point of T4 (ng\ml)

Study Groups		Categorial T4 (ng/ml)		Total
		3-10 Normal	<3 Decrease	
COVID-19	Count	65	18	83
	%	78.3%	21.7%	1000.0%
Control	Count	83	0	83
	%	100.0%	00.0%	100.0%
Total	Count	148	18	166
	%	89.2%	10.8%	100.0%
Chi-square	20.1			
P*-value	0.00 (H.S)			

*; Independent sample test, H.S; highly significant

Table 9: Categorial levels of TSH in COVID-19 group and control group according to the cutoff point of TSH (ng\ml)

Study Groups		Categorial TSH (ng/ml)	Total
		(0.4-4 Normal)	
COVID-19	Count	83	83
	%	100.0%	100.0%
Control	Count	83	83
	%	100.0%	100.0%
Total	Count	166	166
	%	100.0%	100.0%

No statistics are computed because TSH is a constant.

Discussion

The thyroid's anatomic position, which is next to the upper airways, a common entry point for corona viruses, lends credence to the idea that the thyroid might be a direct target of SARS-CoV-2. SARS-COV-2, like the virus that caused SARS, employs the ACE-2 as its cellular entrance receptor, as previously explained [14]. In this study, we describe non-hospitalized COVID-19 patients who developed argumentative results related to thyroid function test, T3 level (<1.3), T4 (<3.0), and TSH (<0.4) were defined as 'decrease', and T3 level (>3.1), T4 (>10.0), and TSH (>4.0) were defined as 'increase'. 25 COVID-19 patients out of 83 have T3level more than normal value (<3.1), 11 out of 83 has T3 level lower than normal value (<3.1), and 47 case out of 83 has T3 level within normal value (1.3-3.1), statistically this difference was highly significant (Chi-square=45.9, *p*-value=0.00) as compared to healthy control group. Whereas 65 COVID-19 patients out of 83 have T4level within normal value (3-10), and 18 of 83 has T4level lower than normal value (<3), statistically this difference was highly significant (Chi-square=20.1, *p*-value=0.00)as compared to healthy control group. Thyroid hormones showed disturbances in their levels presented by high and low levels in non-hospitalized COVID-19 patients and normal levels in the same group; from clinical point of view, disturbances perhaps due to the intensity of the disease, they could be mild for patients with normal values or moderate for other values. On the other hand, no statistical differences in TSH levels between COVID-19 and control group. The results of Gao et al. discovered that in COVID-19 patients, FT3, TSH, and FT3/FT4 levels dropped with clinical worsening of COVID-19 and were lowest in patients who died. The drop in FT3 was independently related with all-cause mortality in severely or critically sick individuals. Patients with FT3 concentrations less than 3.10 pmol/L had an elevated risk of death from any cause, indicating that extensive treatment efforts should be implemented to minimize the risk of death in patients with lower FT3 concentrations[15].

A person infected with COVID-19 can: 1) acquire thyroid dysfunction because of direct and indirect thyroid gland impairment; 2) develop a low-T3 condition if hospitalized owing to severe COVID-19 infection; and 3) possibly create SAT [16]. Persons in intensive care unit are reported to have decreased T3, low thyroxine, and normal ranges or slightly lowered TSH (i.e., non-thyroidal sickness condition or low-T3 condition), even though no proof of correlation exists [17]. Patients with severe systemic illness are known to have abnormal thyroid laboratory findings [18].Moreover, thyroid hormone levels have been observed to have a role in predicting a poor prognosis in these individuals [17].

A zinc level (<70) was considered a 'decrease.' Patients with COVID-19 who were zinc deficient were identified as 'decrease'. Patients with COVID-19 who were zinc deficient were determined and compared to those who had normal zinc values.47 COVID-19 patients out of 83 have zinc level lower than (<70), while 36 of 83 has zinc level within normal value (70-114), while all 83 healthy control group has zinc level within normal value (70-114). Statistically this difference was highly significant (Chi-square=65.5, *p*-value=0.00), this compromises to the results of Jothimani et al. who discovered that a large majority of COVID-19 patients lacked zinc. These zinc-deficient individuals experienced greater problems, and the deficiency was linked to a longer hospital stay and a higher death rate [18], otherwise our patients were not hospitalized to decrease their zinc level dramatically, and perhaps for those, with zinc level within normal value, they started to intake zinc supplement as the public COVID-19 treatment protocol.

Finally, 45 COVID-19 patients out of 83 have IgG level (>1) in contrast to 38 of 83 has IgG level (<1), while all healthy control group 83 has IgG level (<1). Statistically this difference was highly significant (Chi-square=61.73, p-value=0.00). On the other hand, 23 COVID-19 out of 83 has IgM level (>1) in contrast to 60 of 83 has IgM level (<1), while all healthy control group 83 has IgM level (<1). Statistically this difference was highly significant (Chi-square=26.69, p-value=0.00).IgG and IgM analyses showed optimal sensitivity at 21 days after the onset of disease [19], with IgM showing a lower positive predictive value than IgG in this research. A prior investigation of SARS-CoV found a variation in sensitivities between IgG and IgM detection. The discrepancy might be because the concentration of IgM in blood after infection was lower than that of IgG, or it could be due to the varied capture sensitivity of the IgG and IgM regents in our test. Furthermore, earlier SARS-CoV investigations found that IgG and IgM levels rose to detectable levels in the second or third week after symptoms began[20].

Conclusions

This study focused on the alteration of thyroid function tests and evaluation of Serum Zinc, IgG, and IgM Levels in non-hospitalized Iraqi Patients with Corona Virus. According to our statistics, none of them performed better. Combined detection parameters are a viable option. However, the results were conflicting. There are some possible theories behind this issue that are worth clinical trials and further studies.

Conflicts of interest: The author declares to have no conflict.

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