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Micro-RNA Expression of Cutaneous Leishmaniasis in Patients Recovered from COVID 19 Infection

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Abstract

In this study, blood samples were taken from (100) leishmania-infected patients who were recovered from COVID-19 and attended Baghdad teaching Hospital, and (100) samples were also taken from healthy individuals as a control group during the period from 1st June to 1st April 2021. The results showed that the mean Leishmania IgM was (11.74±8.90) in the leishmaniasis group compared to the control group which was (0.05±0.10) with a highly significant difference, while the mean COVID IgM was (1.91±1.06) compared to the controls (0.04±0.03) with a highly significant difference. The mean Leish IgG was (8.37±8.36) in comparison with the control group (0.04±0.07), and the mean COVID IgG was (14.35±6.68) compared to the controls (0.04±0.05) with highly significant differences. The comparison between Leish IgM which was (5.77±8.94) and the control group IgM which was (6.02±8.27), and between COVID IgM which was (0.88±1.17) and the control group IgM which was (1.07±1.23) with non-significant differences. Also the comparison between Leish IgG which was (4.82±7.90) and the control IgG which was (3.60±6.46), and between COVID IgG which was (6.65±8.06) and the control group IgG which was (7.74±9.90) showed non-significant differences, while the comparison between CRP levels between the patient group (43.68±54.57) and the control group (43.43±52.19) showed no significant difference. There was a highly significant correlation between Leish IgM and CRP (p=1.000), and a highly significant correlation between COVID IgM and CRP (p=1.000). The correlation between Leish IgG and CRP showed a highly significant relationship (p=1.000), also the correlation between COVID IgG and CRP showed a highly significant relationship (p=1.000). The ROC analysis of HSV2 IgG showed a highly sensitivity (0.641) and specificity (0.807), while the COVID IgG showed a highly sensitivity (0. 971) and specificity (1.000). Also CRP showed a highly sensitivity (0.923) and specificity (0.995). Out of the (50) serum samples from infected patients 33(66.0%) had positive MicroRNA-21, while 0(0.00%) of the control group had negative MicroRNA-21.

Keywords: *Micro-RNA expression, cutaneous Leishmaniasis, COVID 19.*

Introduction

COVID 19 is one of the Corona viruses that is widespread in all parts of the world and causes serious diseases that may lead to death [1]. The evolution of SARS 2 with this change in the genetic sequence led to this virus having the ability to invade the human body [2]. It was called the emerging virus because it renewed genetic mutation, which is more virulent [3]. The evolution in the genes of this virus that continues for short and

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successive periods has led it to be a guide wherever it invades the human respiratory system [4]. The modified SARS 2 virus that killed millions of people, may be man-made [5]. Creating a vaccine against this virus may reduce its spread in the world if this virus mutates into a new genetic sequence [6]. Those who recover from infection with the virus may show several cases or signs of disease that may be complicated by the weak immune system of the infected patients [7]. Cutaneous leishmaniasis is a parasite that infects humans and transmitted by sand flies, causing skin defects that distort the body of infected people [8]. This study was conducted to determine whether the changes that occur are direct or inverse proportional to infection with COVID 19. Cutaneous leishmaniasis may be of a mucous type or a dry type and several complications may occur accompanying the infection [9]. The development in the examination of cutaneous nematodes by PCR method or by the method of genetic sequencing, and the results of gene expression have become easy and accurate, in addition to the examination of antibodies using ELISA technique [10].

Materials and methods

In the current study, blood samples were taken from (100) leishmania-infected patients who were recovered from COVID-19 and attended Baghdad teaching Hospital, and (100) samples were also taken from healthy individuals as a control group during the period from 1st June to 1st April 2021. Anti- COVID-19 IgM and IgG antibodies were measured using Afias technique, with normal value ≥ 1 ml/dl. The HSV2-, IgM and IgG kit is based on the ELISA technique. In this assay, controls and unknowns are incubated in micro-titration wells coated with HSV2- recombinant derived GD2-protein /antigen. Also CRP titer was measured by afias technique, and the normal value was up 10 ml/L.

Statistical analysis

For the statistical analysis, the SPSS program version 22 was used. The Chi- square test was used to compare between percentages (0.05 and 0.01) probability. The t-test was used to signify the comparison between means of this study.

Results

Table (1) showed that the mean Leish IgM was (11.74±8.90) and the mean IgM in the controls was (0.05±0.10), while the mean COVID IgM was (1.91±1.06) and the mean controls IgM was (0.04±0.03) with highly significant differences (P<0.01).

Table (1): Comparison between the studied group IgM and the control group IgM

Parameters	Groups	Mean± Std.	P-Value (Sig.)
Leish IgM	Study	11.74±8.90	P=.000
	Control	0.05±0.10	P<0.01 (Highly Sig.)
COVID IgM	Study	1.91±1.06	P=.000
	Control	0.04±0.03	P<0.01 (Highly Sig.)

Table 2 showed that the mean Leish IgG was (8.37±8.36) and the control group IgG was (0.04±0.07), while the mean COVID IgG was (14.35±6.68) and the control group IgG was (0.04±0.05) with highly significant differences (P<0.01).

Table (2): Comparison between the studied group IgG and the control group IgG

Parameters	Groups	Mean ±Std.	P-Value (Sig.)
Leish IgG	Study	8.37±8.36	P=.001
	Control	0.04±0.07	P<0.01 (Highly Sig.)
COVID IgG	Study	14.35±6.68	P=.000
	Control	0.04±0.05	P<0.01 (Highly Sig.)

Table (3) illustrated the comparison between Leish IgM which was (5.77±8.94) and the control group IgM which was (6.02±8.27), and between COVID IgM which was (0.88±1.17) and the control group IgM which was (1.07±1.23) with non-significant differences (p>0.05). Also the comparison between Leish IgG which was (4.82±7.90) and the control IgG which was (3.60±6.46), and between COVID IgG which was (6.65±8.06) and the control group IgG which was (7.74±9.90) showed non-significant differences (p>0.05), while the comparison between CRP levels between the patient group (43.68±54.57) and the control group (43.43±52.19) showed no significant difference (P>0.05).

Table (3): Comparisons of Leish IgM, IgG, COVID IgM, IgG and CRP levels between the study group and the control Group

Parameters	Groups	Mean± Std.	P-Value (Sig.)
Leish IgM	Study	5.77±8.94	P=.850
	Control	6.02±8.27	P>0.05 (Non Sig.)
COVID IgM	Study	0.88±1.17	P=.318
	Control	1.07±1.23	P>0.05 (Non Sig.)
Leish IgG	Study	4.82±7.90	P=.276
	Control	3.60±6.46	P>0.05 (Non Sig.)
COVID IgG	Study	6.65±8.06	P=.417
	Control	7.74±9.90	P>0.05 (Non Sig.)
CRP	Study	43.68±54.57	P=.976
	Control	43.43±52.19	P>0.05 (Non Sig.)

There was a highly significant correlation between Leish IgM and CRP (p=1.000), and a highly significant correlation between COVID IgM and CRP (p=1.000) as shown in table (4).

Table (4): Correlations between Leish IgM, COVID IgM and CRP among the studied group

Parameters		Lesh IgM	COVID IgM	CRP
Lesh IgM	r			
	P-Value			
Lesh IgM	r	1		
	P-Value			

COVID IgM	r	.147	1	
	P-Value	.184		
CRP	r	-.013	.169	1
	P-Value	.895	.906	.126

The correlation between Leish IgG and CRP showed a highly significant relationship (p=1.000), also the correlation between COVID IgG and CRP showed a highly significant relationship (p=1.000) as shown in table (5).

Table (5): Correlations between Leish IgG, COVID IgG and CRP among the studied group

Parameters		Leish IgG	COVID IgG	CRP
Leish IgG	r	1		
	P-Value			
COVID IgG	r	.095	1	
	P-Value	.392		
CRP	r	.197	.184	1
	P-Value	.075	.097	

The Receiver Operating Characteristic Curve (ROC) Leish analysis of HSV2 IgG showed a highly sensitivity (0.641) and specificity (0.807), while the COVID IgG showed a highly sensitivity (0. 971) and specificity (1.000). Also CRP showed a highly sensitivity (0.923) and specificity (0.995) as shown in table (6) and figure (1).

Table (6): Receiver Operating Characteristic Curve analysis (ROC) of Leish IGG, COVID IgG and CRP

Parameter	Area	Sig.(P-Value)	Cut off	Sensitivity	Specificity
Leish IgG	1.000	.000	<15.050	1.000	1.000
COVID IgG	.990	.000	<0.930	.971	1.000
CRP	.959	.000	<92.440	.923	.995

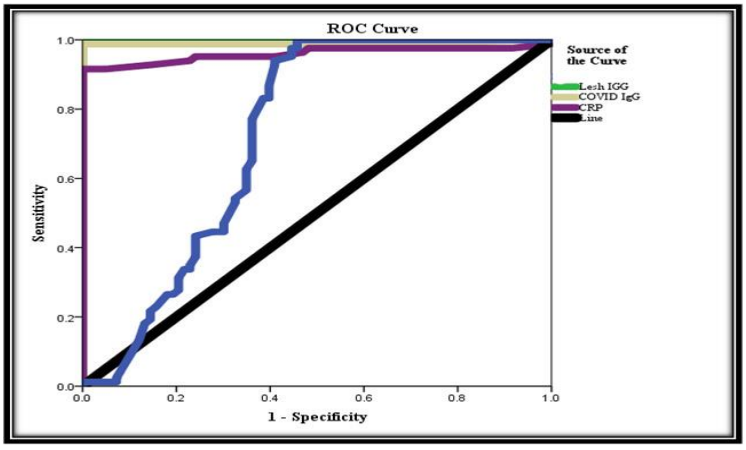

Figure (1): Receiver Operating Characteristic curve analysis (ROC) of Leish, COVID IgG and CRP

As shown in table (7) and figure (2), out of (50) serum samples from infected patients 33(66.0%) were positive for MicroRNA-21, while 0(0.00%) of the controls was negative (P= 0.005).

Table (7): The incidence of MicroRNA-21 in the studied groups

MicroRNA-21	Cases				P value
	Leishmania & COVID19		Control		
	Count	%	Count	%	
Negative	33	66%	60	100.0%	
Positive	17	24%	0	0.0%	0.005

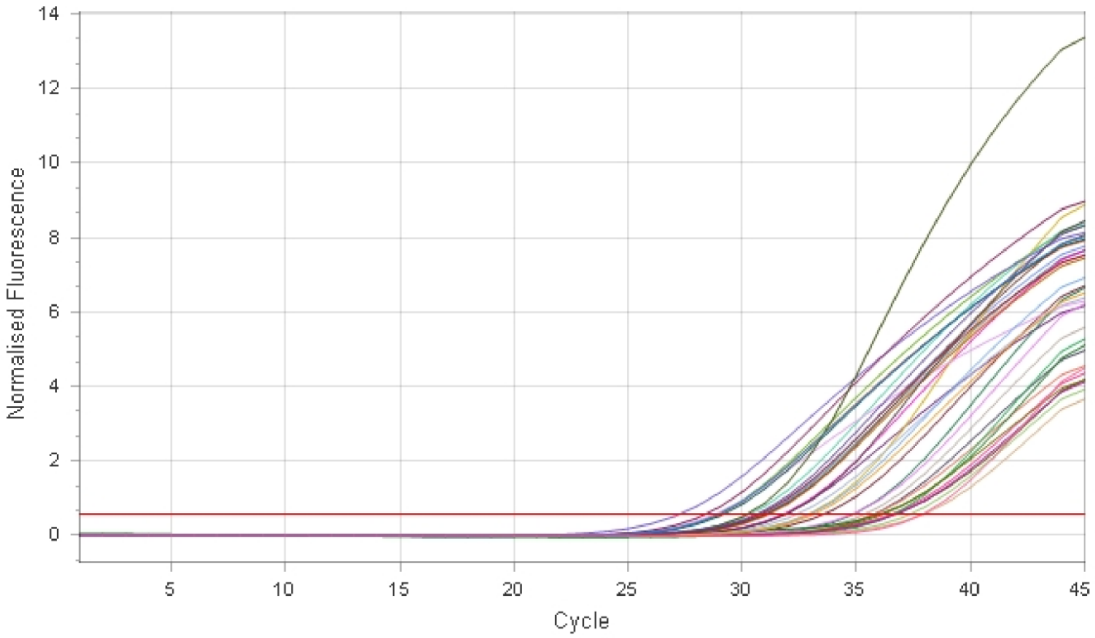

Figure (2): Evaluation of MicroRNA21 of C. Leishmania & COVID19 infections

Discussion

Cutaneous leishmaniasis has no link with COVID-19 infections but these patients who have recovered from COVD 19 also have cutaneous leishmaniasis. There is a significant difference between patients with cutaneous leishmaniasis and the control group, due to what was mentioned in previous studies. Al-Qadhi, B. N.et al, reported a significant difference between patients with cutaneous leishmaniasis and the healthy group, and this suggests that the infection is widespread in Iraq, especially the presence of vectors [11]. Also there was a highly significant difference between COVID 19 and the healthy group, and this gives an idea of the spread of this dangerous disease and its side effects on the infected patients. These findings agreed with (Coulthard, P., 2020) who demonstrated that the coronavirus (COVID-19) has challenged health professions and systems and has evoked different speeds of reactions and types of responses around the world [12]. Also there was a correlation between cutaneous leishmaniasis and CRP and a direct relationship between the parisitic infection and CRP levels, and this indicates that damage to the body of the infected person leads to an increase in this protein. (O'Daly, J. A, et al, 2013) proved that there is a direct relationship between leishmaniasis and the high levels of CRP, and that the high titer of this protein is an evidence of the damage occurring somewhere or in the infected body [13]. During COVID 19 infection, it was found that the high levels of CRP may cross the risk threshold, which was increased significantly in

this study. These results were consistent with (Wang, G. et al, 2020) who found that most of moderately or severely COVID-19 infected patients were suffering from high levels of LCR with an excessive increase [14]. Gene expression was determined for COVID-19 patients with cutaneous leishmaniasis and showed that out of (50) cases, 33(66%) had positive micro-RNA 21, which is considered high in determining infection and gene expression by Real Time technique. (Geraci, N. S. et al, 2015) revealed that there is a role for micro-RNAs in determining leishmaniasis and that the Real Time technology is able to determine the gene expression of this parasite [15]. Also, (M. A. et al, 2020) reported that the extensive Gene Expression Omnibus literature screening and drug predictive analyses showed that SARS-CoV-2 infection response pathways are closely related to those of SARS-CoV and respiratory syncytial virus infections [16].

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