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Effect of Corona virus Disease-19 on Complement Protein C3, C4 in Khartoum State

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Abstract

***Background**: global pandemic of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The novel virus was first identified in Wuhan, China, in December 2019; The aim of this study was to determine the effect of Corona virus disease (COVID-19) on complement C3, C4 in Khartoum state.*

***Method:** The study design was case control study which was carried out during the period from February to September 2020. A total of fourty five COVID -19 patient attended to Jabbra hospital for isolation were included in the study. DiaSys response 910 fully automation diagnosic system was used to measure Complement C3 and C4 level.*

***Result**: The study showed that from total number of patient (45) there are 30 patient with normal C3 level (66.7 %) and 15 with decreasing C3 level(33.3 %). (P.value =0.4) .patient with normal C4 level 32 (71.1%) , lower than normal 10 (22.2 %) and 3 (6.9) higher than normal .(P.value = 0.03). Frequency of COVID -19 in male is (58*

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%) and in female (42 %) that means COVID-19 infection is higher in male than females.

***Conclusion**: C3 (P.value > 0.05) indicate insignificant decrease of C3 level among COVID- 19 Patiens , where C4 (p. value < 0.05) indicate significant decrease in C4 level among COVID -19 Patiens compared to healthy people , that means the virus has effect on C4 level .*

Keywords: COVID-19, SARS-CoV-2 Complement C3 and Complement C4

The complement system is an integral part of the innate immune response and acts as connect between innate and acquired immunity.

It consists of series of proteins that are mostly (although not exclusively) synthesised in the liver and exit in the plasma and on cell surfaces as inactive precursors (zymogens). Complement mediates responses to inflammatory triggers through co-ordinated sequential enzyme cascades leading to clearance of foreign cells through pathogen recognition opsonization and lysis [1] . complement also possess anti- inflammatory functions : it is binds to immune complexes and apoptotic cells , and assist in their removal from circulation and damaged tissues [2, 3] . the complement proteins are activated by , and work with IgG and IgM antibodies hence , the name " complement " .The aim of this review is to summarise current understanding of the interaction of SARS-CoV-2 virus with the complement system and examine the case for targeting the inflammatory reaction mediated by complement in severe COVID-19 disease .

The focus of scientific research was on the human body's defence against microbial infection . the [theory of Metchnikoff] proposed that phagocytes in the blood were capable of ingesting and destroying bacteria , thus providing the basis of innate cellular immunity. this phagocytic theory was challenged by many pathologist initially on the basis that the phagocytic leucocytes were truly causal in successful response to infection . [4] Buchner and Colleagues (1891) found aheat labile factor in blood that was

capable of killing bacteria , and named (alexin) in Greek means (to ward off) [5,6] . Jules Bordet supported this humeral theory (immunity conferred due to antitoxic and bactericidal substances in body fluids) by demonstrating that immune lysis required the presence of two factors : aheat labile lytic factor (similar to alexin) and heat stable factor , which he termed sensitizer (which now know was antibody) [7] . Pual Ehrlich described the side chain theory of antibody formation especially the mechanism of antibody neutralization by toxins that induced bacterial lysis with help of complement (which has replaced historical term alexin) .

According to this theory , the immune cells contained receptors that could recognize antigens , and following immunization , this receptors multiplied and were shed into the circulation as (amboceptors) now called (antibodies) this antibodies not only attached to specific antigens but also to heat labile antimicrobial component called "complement" [8,9] Ehlrichm,s theory proposed that that antibody and complement combied to form complex enzyme capable of attaching and killing cells and micro-organisms . Bordet argued that the antigen antibody union was revesible , contraindicating Ehrich ,s view that the antigen antibody union was afirm and abased on stero chemical specificity [10] . the concept that complement was not single substance was provided by Ferrata and brand , who demonstrated sepration of complement into two fractions : midpiece (renamed as C1) and endpiece (renamed as C2) [11,12] .

Materials and Methods

Study design was Case Control Study, which conducted in Khartoum state Sudan from Jabbra specialized Hospital , forty five Sudanese patient with COVID-19 and twenty five Healthy participants were included in the study . Venous blood sample will be collected by using sterile dry plastic syringes and tourniquet to make the veins more prominent the puncture sites will be clean with 70 % ethanol and amount of blood sample must be (5ml) which will be collected in plain containers . the samples were centrifuged at 4000 rpm to obtain serum and then stored in (-4) until analysis .

Complement C3 and C4 level measured by Immuno-turbidimetric test . by using DiaSys response 910 .

Ethical consideration

This study was approved by Ethical committee of faculty of medial laboratory sciences –Al-Zaiem Al-Ezhari University, Sudan ministry of health , management of Jabbra hospital for isolation and participant .

Data analysis

Data were analyzed by using Statistical Package Social of Science (SPSS) computer software Version 2021. [P. value > 0.05 indicate insignificant, where p. value < 0.05 indicate significant] .

Results

Study was conducted on 45 patients infected with COVID -19 (25--41 year) in Jabbra hospital for isolation , the aim of this study to determine the effect of COVID -19 on complement system .

The result showed that the frequency of COVID -19 in male (58 %) and in female (42 %) .Normal complement C3 level 30 . (66.7 %) and C3 lower than normal 15 (33.3 %).

Normal Complement C4 level 32 (71.1 %) and lower than normal 10 (22 .2 %) and in higher than normal 3 (6.9 %). Total (N: 45).

Table (1): Descriptive Statistics of healthy participants

	N	Minimum	Maximum	Mean	Std –deviation
Age (year)	25	28	39	32.7	3.285

Table (2): Descriptive Statistics of COVID -19 Patient

	N	Minimum	Maximum	Mean	Std – deviation
Age (year)	45	29	41	33.40	3.557

Table (3): frequency of Complement C3 level among COVID -19 patients

C3	Frequency	Percentage
Normal	30	66.7
Lower than normal	15	33.3
Total	45	100

Table (4) frequency of complement C4 level among COVID -19 Patients

C4	frequency	Percentage
Normal	32	71.1
Lower than normal	10	22.2
Higher than normal	3	6.7
Total	45	100

Table (5): Comparison of C3 and C4 between healthy participants and COVID- 19 patients:

	Study group	N	Mean	Std. deviation	P. value
C3(mg/dl)	Healthy participants	25	100.04	13.562	0.4
C3(mg/dl)	COVID -19 participants	46	106.00	37.994	0.4
C4(mg/dl)	Healthy participant	25	16.28	4.861	0.03
C4(mg/dl)	Healthy participant	46	20.58	11.953	0.03

Table (6) Comparison of C3 and C4 between healthy participants and covid 19 patients(after random selection of equal count of healthy participants and covid 19 patients) :

	Study group	N	Mean	Std. deviation	P. value
C3(mg/dl)	Healthy participants	25	100.04	13.562	0.4
C3(mg/dl)	COVID -19 participants	25	106.16	36.227	0.4
C4(mg/dl)	Healthy participant	25	16.28	4.861	0.02
C4(mg/dl)	Healthy participant	25	23.4	13.581	0.02

Table (7): Comparison of C3 and C4 within gender among COVID-19 patients:

	Gender	N	Mean	Std.deviation	P.value
C3(mg/dl)	Male	26	106.54	34.858	0.9
C3(mg/dl)	Female	19	105.26	42.896	0.9
C4(mg/dl)	Male	26	20.81	12.123	0.8
C4(mg/dl)	Female	19	20.26	12.041	0.8

Table (8): Correlation of age to C3 and C4 level in covid 19 patients

		C3(mg/dl)	C4 (mg/dl)
Age (year)	Pearson correlation	0.17	0.06
	P.value	0.24	0.6
	N	45	45

Discussion

One study was conducted in Turkey (23), one in Spain (33), and the remaining 17 in China (22, 24–32, 34–40). Seventeen studies reported C3 and C4 concentrations measured within the first 24-48 h from admission (22–27, 30–40), whilst the remaining two did not specify the collection time (28, 29). In this systematic review and meta-analysis, we observed that the serum concentrations of complement C3 and C4 were significantly lower in COVID-19 patients with more severe disease or who died during follow up when compared to those with milder disease or survivor status.

This study showed insignificant decrease in the mean level of complement C3 in COVID-19 patients campared to control group(P.value = 0.4) and significant decrease mean level of complement C4 level campared to control group (P.value=0.03).

In this study the frequency of COVID -19 is higher in males than females.

There is insignificant correlation between the age and and C3 and C4 level in study group (P.value for C3= 0.24 and for C4 =0.6.

In this study there is significant decrease in C4 level in COVID -19 patient that agreement to above studies conducted in Turkey , spain and china and insignificant decrease in C3 level that disagreement to above studies . this disagreement may be due to small sample size , and severity of disease, difference in environmental changes .

Conclusions

This study conclude that there was significant decrease in Complement C4 level while the was insignificant decrease in Complement C3level in COVID-19 patients when compared to control group.

There was insignificant correlation between C3 and C4 level and age of study group .

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