ISSN: 1343-4292
Volume 140, Issue 03, June, 2022

Assessment of the serum levels of chemerin and Omentin in among Iraqi patients as early Predictors markers of the Severity COVID-19

Lama Jawad Hussain[1], Hanaa Addai Ali[2*], Rawaa Adday Ali[3], Fadhil Abass Naser[4], Mohauman Mohammad Majeed AL Rufaie[5*]

Department of Chemistry, Faculty of Science, University of Kufa, Najaf, Iraq[1,2]
Microbiology Department, College of Veterinary Medicine, AL-Qasim Green University, Babylon, Iraq[3]
Department of Clinical Laboratory Sciences, Faculty of Pharmacy, Jabir Ibn Hayyan Medical University, Najaf, Iraq[4]

Corresponding Author: 2*,5*

ABSTRACT— Coronavirus disease 2019 (COVID-19) is a worldwide epidemic generated by the severe acute respiratory syndrome coronavirus 2 coronavirus ((SARS-CoV-2)). The cell entry system of COVID-19 is stimulated by the viral spike protein bonded to the angiotensin-converting enzyme 2 receptor. Adipokines' actions contribute to infection pathogenesis. The researchers wanted to look at levels of chemerin and omentin in COVID19 patients, including linkage among both adipokine, the severity of disease (mild, severe, critical). Chemerin and omentin are reported to have inflammatory and metabolic effects, and have been implicated in the development of chronic diseases. However, results are still limited regarding role of chemerin in chronic diseases. Chemerin and omentin in COVID19 patients suggest that these adipokines have a role in influencing disease severity. Chemerin and omentin are reported to have inflammatory and metabolic effects, and have been implicated in the development of chronic diseases. However, results are still limited regarding the role of chemerin in chronic diseases. Our study focused on Chemerin, and Omentin levels in COVID-19 patients to demonstrate a roles in influencing disease severity. This is a case-control study design consisting of COVID-19 patients before any treatment was recruited from the Intensive Care Unit hospitalization ICU department of the AL-Amal Hospital in AL-Najaf City, Iraq compared with apparently healthy volunteers as control group. The patients were divided into three groups: mild/moderate, severe, and critically ill cases. The enzyme-linked immunosorbent assay (ELISA) kit used to measure plasma chemerin and Omentin levels in all patient groups. COVID-19 patients' clinical symptoms, diagnostic tests, and outcomes were studied chronologically. Serum chemerin was significantly increased in COVID-19 patients but Omentin concentrations was significantly decreased compared to healthy volunteers (2.1± 0.48 and 5.65± 2.7;$P < 0.05$ vs. 1.36± 0.49 and 11.43± 2.42; ($P < 0.050$) respectively). The serum chemerin was significantly higher but and Omentin levels was significantly lower in critically ill patients than that in severe patients cases ($P < 0.00010$). Circulating chemerin and omentin levels are early predicators markers It has been linked to the severity of COVID-19 disease, may be risk of death in COVID-19 patients.

KEYWORDS: Chemerin, Omentin, COVID-19, severity

1. INTRODUCTION

The (2019) Coronavirus Disease (COVID-19) has evolved into a major threat to modern healthcare systems, with over 177 million cases reported and approximately 4 million deaths [1], [2]. SARS-CoV-2

disease can spread and attack multiple organs resulting in a wide range of symptoms [3], [4].

Severe acute respiratory syndrome coronavirus 2 was the name given to the new coronavirus (SARS-CoV-2). As a result, the World Health Organization designated the virus-caused disease as coronavirus disease 2019 (COVID-19) [5], [6].

One of the COVID-19 clinical features is the cytokine storm or cytokine release syndrome (CRS). The release of proinflammatory cytokines and chemokines is involved in the development of critical cases, multiple organ damage and functional failure [7].

Chemerin (molecular mass=14-kDa) is one of the chemoattractant protein released during certain diseases such as infections. It is a known immunomodulator acting by binding to the its receptor (chemerin receptor 23 or ChemR23) [8]. after being released as It is liberated as an inactive form (prochemerin), it is activated. Activation of prochemerin is mediated by the effect of serine protease through cleavage of the C-terminus. The main tissues responsible for secretion include visceral adipose tissue, placenta and liver. In addition, it can be released -in a lesser extent- from lungs, heart, ovaries, kidneys and pancreas [9], [10].

As a proinflammatory adipokine, chemerin is involved in immunity, inflammation and obesity-related pathophysiological conditions. It acts as a chemoattractant and participated in both adaptive and innate immunity [11]. In addition, chemerin is one of molecules that regulate angiogenesis, adipogenesis, and energy metabolism [12].

Omentin is a novel 313 amino acid that is hydrophilic (35 kDa), contains a secretory signal sequence and a fibrinogen-associated domain, and occurs as a glycolized trimer with a molecular weight of 120 kDa as negative. Omentin1 is the major circulating form with human plasma concentrations and has been studied more extensively than omentin2. Omentin1 is the primary circulating form. It also has the reciprocal design of omentin2 [13].

Substantial progress has been achieved in determining and characterizing the effects of omentin on various diseases in recent years [14]. Omentin/intelectin-1, on the other hand, is an adipocytokine found in the blood [15]. Omentin is highly expressed in visceral fat tissue. As a result, obese people have lower levels of circulating omentin [16].

2. Materials and Methods

A total of 90 Iraqi volunteers as case-control study design in age range (min.-max.:45-60 years), 60 COVID-19 patients divided into three groups. (30) had mild/moderate symptoms, (18) had severe symptoms, and (12) had critical cases. Those patients were matched to 30 apparently healthy individuals in age and BMI, and sex as control group. During the period from December 2021 to January 2022, samples were taken. The research was carried out in the laboratories of the AL-Amal Teaching Hospital in Najaf.

After receiving clearance from the Iraqi Ministry of Health and Environment's Ethics Committee, and all participants gave informed consent before the study began. According to the inclusion criteria, were included in the sample COVID-19 diagnosis was defined as a SARS-CoV-2 positive real-time reverse-transcriptase polymerase chain reaction (RT-PCR) from a nose and/or throat swab specimen of patients combined with a chest X-ray or chest tomography (CT) scan that suggested COVID-19 infection. Before the therapy procedure, blood samples were taken from the patients after the investigation of the subjects' blood samples.

ISSN: 1343-4292
Volume 140, Issue 03, June, 2022

COVID-19 patients were clinically diagnosed criteria for inclusion: COVID-19 cases with no other disease. They were then categorized based on their severity (mild/moderate, sever and critical) [17].

The following are some of the study's exclusion criteria: Diabetes mellitus, cardiovascular diseases, renal disease, hepatic disorders, and autoimmune disease, smoker, and pregnant women.

The body mass index (BMI) was calculated by: BMI=Weight/(height m)^2

Patients and control groups had their venous blood samples taken. Two tubes were used to separate blood sample. 3ml allowed to clot at room temperature for 10-15 minutes before centrifugation at (3000X g) for 10 minutes to get serum. The serum samples were then divided into three tubes and kept at -80°C for future examination. Complete blood count (CBC) was tested using an autohematology analyzer with the remaining blood (2ml) (linear, Spain). Fluorescence immunoassay was used to quantify serum ferritin and D-dimer levels (ichromaTM) Human CHEM (Chemerin) ELISA Kit, Catalog No. E-EL-H0698, is a double-antibody sandwich enzyme-linked immunosorbent test kit.) Human ITLN1 (Interlactin 1/Omentin) was estimated using an Elabseience USA (Catalog No.E-EL-H2028) commercial ELISA kit.

Data were analysed using SPSS program and presented as Mean±SD. Student's t-test was used to test the significance level (t-test is used to compare between two groups, for more than two groups we need to use One Way ANOVA with Post hoc test). Data with p value less than 0.05 was considered significantly different.

3. Results and discussion

The findings showed significant differences in PO_2, SBP (systolic blood pressure) and non significant in Age and BMI,DBP diastolic blood pressure) between group patient and healthy individual group as shown in Table 1.

Table (1) Comparison of the demographical and clinical characteristics of categories of patients with COVID-19 and healthy group.

Parameters	Healthy control group mean± SD	COVID patients group			P-value
		Mild /Moderate(n=30) mean± SD	Sever(n=18) mean± SD	Critical (n=12) mean± SD	
Sex (F/M)	15/15	12/18	10/8	7/5	_
Age (years)	55.7±3.61	53.51±3.54	54.6±2.21	57.1±4.22	0.064
BMI (kg/m^2)	24.5±1.69	24.33±1.12	24.21±1.12	27.42±1.11	0.060
PO_2	99.06 ±0.69	95.89 ±3.50	88.31 ±3.45	65.60 ±9.38	0.000
SBP(mmHg)	129.32 ± 5.13	122.33± 3.66	136.64± 5.48	137.92± 4.57	0.010
DBP(mmHg)	79.44± 9.47	80.11 ± 6.42	83.61± 6.74	83.81 ± 6.46	0.155
NEUT%	49.20±10.14	75.12±10.12	80.13±8.14	85.11±12.11	0.000
LYM%	21.81±9.60	15.21±1.104	.411.24±1 1	10.22±1.105	0.000
N/L Ratio	2.25±1.05	7.35±9.15	7.12±5.77	5.59±10.96	0.32
D.dimer ng/mL	398.43±74.66	2252.4±2134.51	2212.8±2632.41	5212.6±2933.61	0.000

Ferretin ng/mL	117.5±33.52	1416.23±182.41	1318.24±111.51	1519.22±193.31	0.000
Chemerin ng/mL	1.36± 0.49	1.7± 0.42	2.1± 0.60	2.7± 0.44	0.000
Omentin ng/ml	13.34± 2.42	11.24± 2.62	10.46± 1.22	9.33± 3.42	0.0001

The critical illness patients of COVID-19 have higher mean ages, BMI compared to patients with mild/moderate illness (57.1±4.2 vs. 54.51±3.1 years, respectively), (27.42±1.11 vs. 24.33±1.12 respectively).

The data of ferritin, D-dimer, NLR were significantly higher. but, significantly lower Lymphocytes percent in severe and critical covid-19 patient's groups when compared with mild cases in patients group.

The mean serum chemerin and Omentin levels of the patients with mild/moderate and severe COVID-19 were (1.7±0.42 and 2.1±0.60 ng/mL, respectively (p=0.009) and (11.24±2.62 and 10.46±1.22 ng/mL, respectively (p=0.25) Comparison of all laboratory data of the patients with COVID-19 was demonstrated in table (1).

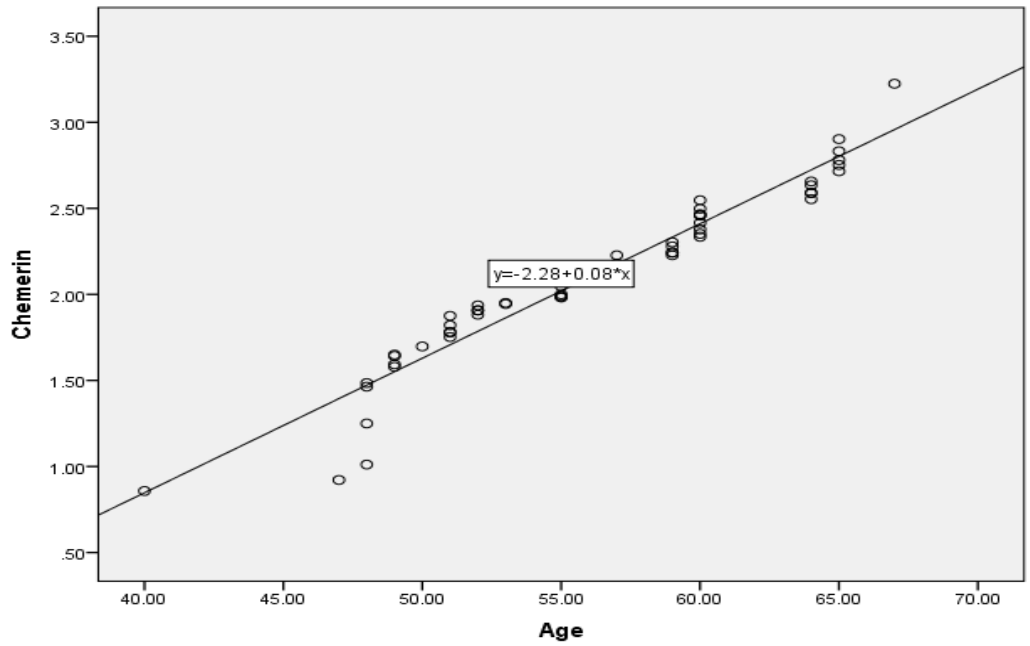
In the analyses, it was observed that serum chemerin positively correlated with Age, BMI,NUT% and negatively with LYM% ($p<0.05$) were shown in table (2) , fig (1)

Table (2) the Correlations between serum chemerin with clinical parameters in COVID-19 patients group.

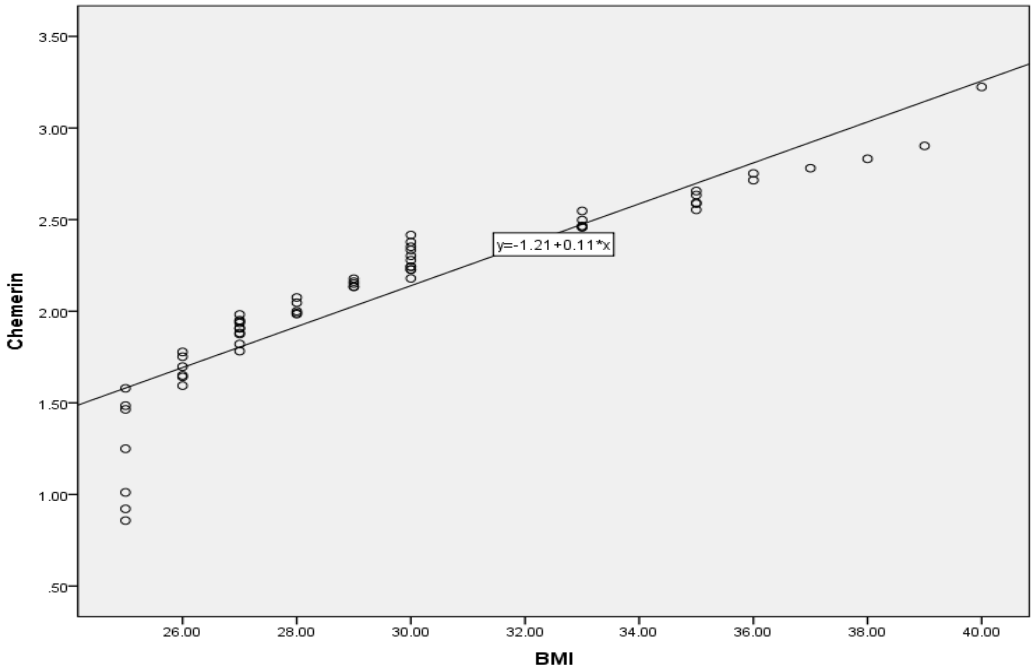
Parameters	r	p-value
Age(years)	0.525	0.000
BMI(kg/m²)	0.514	0.000
SPO_2	0.378	0.041
SBP(mmHg)	-0.063	0.75
DBP(mmHg)	-0.0463	0.841
NEUT%	0.398	0.035
LYM%	-0.671	0.000
NLR	0.964	0.0001
D. dimer (ng/ml)	0.082	0.533
ferritin (ng/mL)	0.042	0.748
Omentin (ng/mL)	- 0.001	0.992

Data represented as Pearson Correlation Coefficient (r): BMI: Body Mass Index, SPO2: Saturated Partial Oxygen SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, NEUT: neutrophil. LYM: Lymphocyte, NLR:

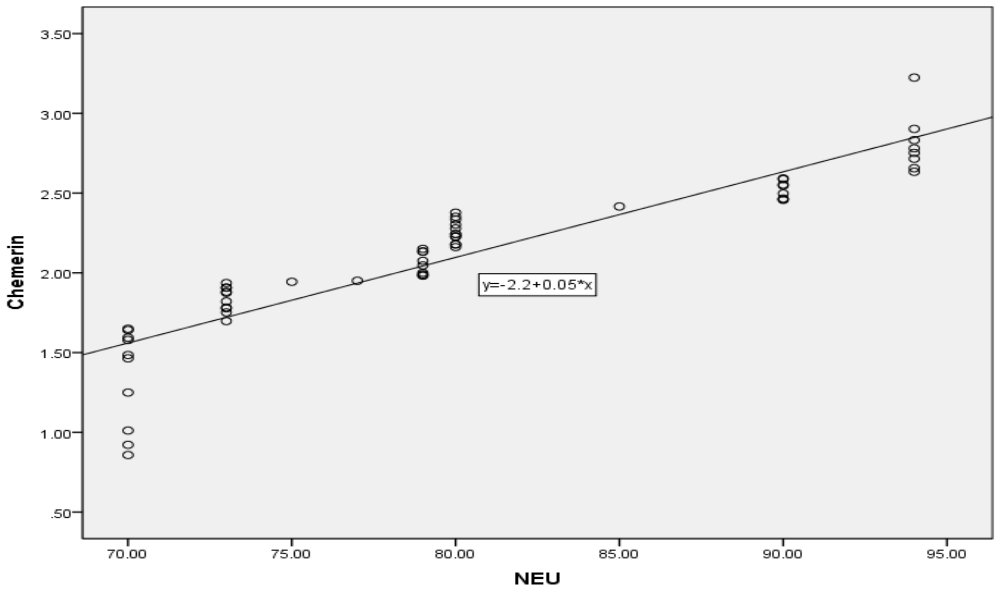
ISSN: 1343-4292
Volume 140, Issue 03, June, 2022



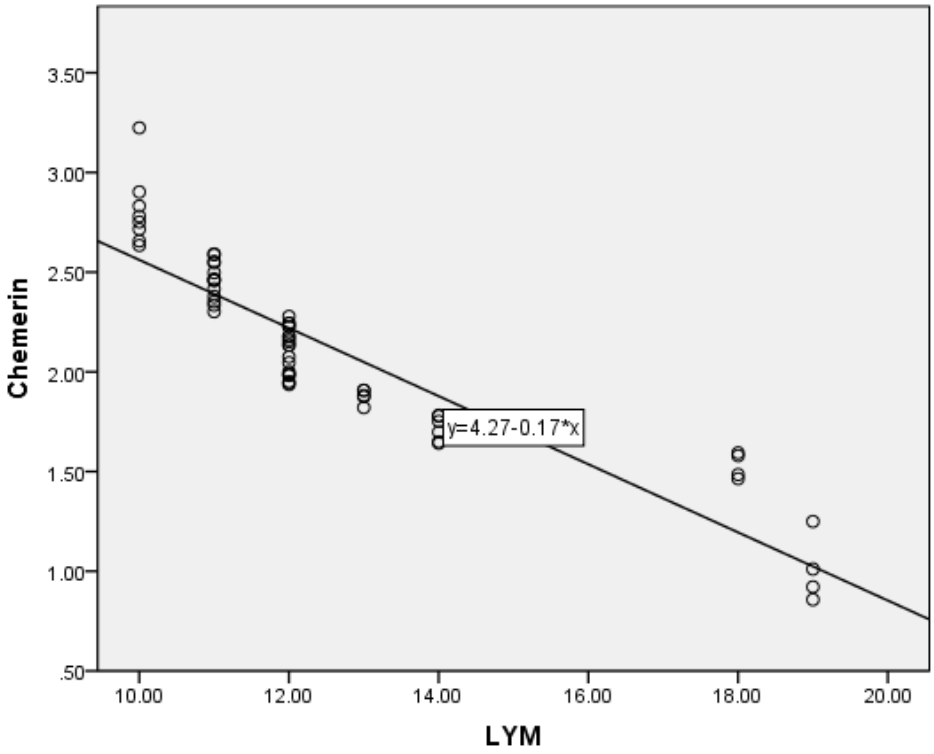
A



B

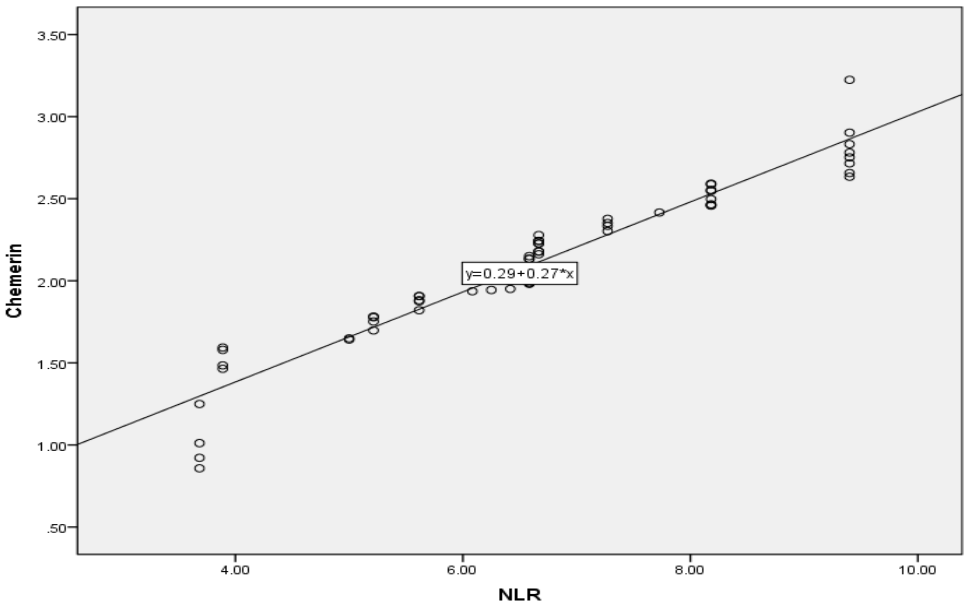

Chemerin
NEU
y=-2.2+0.05*x
3.50
3.00
2.50
2.00
1.50
1.00
.50
70.00
75.00
80.00
85.00
90.00
95.00

C


Chemerin
LYM
y=4.27-0.17*x
3.50
3.00
2.50
2.00
1.50
1.00
.50
10.00
12.00
14.00
16.00
18.00
20.00

D

ISSN: 1343-4292
Volume 140, Issue 03, June, 2022



E

Figure (1) linear regression analysis between serum level of Chemerin with A (Age), B (BMI), C (NUET), D (LYM) and E (NLR)

Table (3) The Correlations between serum Omentin with clinical parameters in COVID-19 patients group.

Parameters	r	p-value
Age(years)	-0.036	0.785
BMI(kg/m²)	-0.069	0.602
SPO_2	0.273	0.06
SBP(mmHg)	-0.170	0.377
DBP(mmHg)	-0.087	0.655
NEUT%	-0.248	0.056
LYM%	0.004	0.978
NLR	-0.381	0.042
D-dimer(ng/mL)	-0.129	0.325
Ferritin(ng/mL)	-0.120	0.362
Chemerin (ng/mL)	-0.001	0.992

Data represented as Pearson Correlation Coefficient (r): BMI: Body Mass Index, SPO2: Saturated Partial Oxygen SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, NEUT: neutrophil. LYM: Lymphocyte, NLR: Neutrophil/ Lymphocyte Ratio

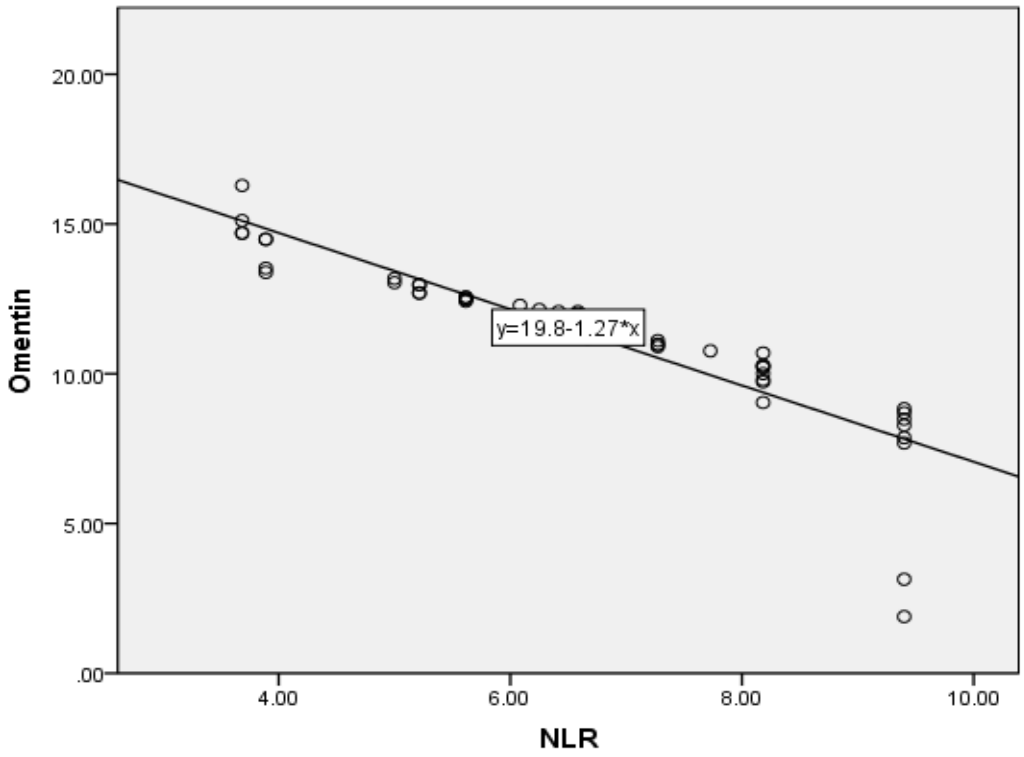


Figure (2) linear regression analysis between serum level of Omentin with NLR

Chemerin is an adipokine chemokine and growth factor [18- 20]. it is involved in inflammation. It has been suggested that adipokines are involved in the link between excess fat mass, adipose tissue inflammation and chronic diseases. Our findings are consistent with those in the previous works as they found high levels of chemerin in obese persons compared to non-obese [21] where similar link between chemerin and BMI was observed. High levels of these circulating biomarkers were noticed in inflammation and obesity [22], [23] and act in a pro-inflammatory fashion [24], [25].

It has been found that adipose tissue is one of the important sources of immune factors such as adipokines, chemokines, and cytokines, molecules that perform an important role in metabolism and immune system [26].

In both obesity and and severe COVID-19 there is a hypercoagulable state due to elevated levels of prothrombin along with reduced levels of anti-thrombin molecules [27], [28].

According to recent studies, COVID-19 is associated with dysregulation of pro-inflammatory cytosines that may result in chronic diseases/ inflammation secondary to obesity and lead to more severe disease [29].

SARS Cov-2 pathogenesity is dependent on the angiotensin-converting enzyme-2 (ACE-2) receptor for entry into cells in a variety of tissues, such as the nose lining, lungs, pancreas, kidneys, GIT, adipose, as well as the lining of blood vessels, heart muscle, and blood cells. Furthermore, ACE-2 has been found to play a significant role in obesity [30], [31].

Chemerin also encourages DCs to migrate from the circulatory system to the reactive lymph nodes [32], [33].

Therefore, chemerin not only regulates the recruitment of DC to the site of inflammation, but also plays a central role in activating innate immunity [34].

In particular, many studies have been reported on the anti-inflammatory effect of Chemerin CMKLR1 axis. Previous reports of, including a peritonitis model, showed that chemerin inhibits neutrophil and monocyte aggregation and reduces proinflammatory cytokine expression [35].

Chemerin-induced anti-inflammatory cytokine expression in MFs has also been reported [36], though this contradicts the study showing that active chemical stimulation increases inflammatory cytokine expression in MF [37].

Macrophages are classified as M1 or M2 based on their polarization type. The former is primarily responsible for the production of proinflammatory cytokines, whereas the latter is responsible for the production of anti-inflammatory cytokines. These two polar macrophages coexist in atherosclerotic lesions [38], implying that abnormal lipid metabolism may result in the transformation of M2 to M1 [39].

Adipokineomentin may be involved in the etiology of asthma. However, it may also protect lung endothelial function and reduce lung permeability and inflammation. Decreased levels of omentin, ghrelin, and adiponectin have been observed in people who suffer from obstructive sleep apnea [40].

The present study is the firs that links between the low level of circulating omentin and a number of metabolic risk factors. Omentin is produced by several types of human tissues, among them is the visceral adipose tissue which produces a large amount of it. In addition, reduced gene expression of omentin has been reported obese patients [41]. Low levels of omentin may be linked to other metabolic disorders such as insulin resistance and glucose intolerance [42]. Omentin may perform perform other effects such as vasodilation suppression of adhesion molecule expression, and attenuation of inflammatory response in vascular endothelial cells [43].

According to our findings suggest a beneficial effect of omentin in several pathologies including infections and insulin sensitivity. Future studies are required to investigate the role of omentin in other metabolic diseases.

4. Conclusion

In conclusion, serum chemerin rates were increased in patients with severe and critical COVID-19 patients compared to mild/moderate patients and were relevant to disease severity in this investigation. But the omentin levels were decreased with critical severity than mild cases in COVID-19.

5. Acknowledgements

The authors thank the patients for their cooperation and the medical staffs in the laboratories of the AL-Amal Hospital AL-Najaf city -Iraq

6. References

[1] Lambert H, Gupte J, Fletcher H, Hammond L, Lowe N, Pelling M, et al. (2020) COVID-19 as a Global Challenge: Towards an Inclusive and Sustainable Future. Lancet Planet Health 4(8):e312–e4.

[2] The World Health Organization. WHO Coronavirus Disease (COVID-19) Dashboard (2021).

[3] Shafi AMA, Shaikh SA, Shirke MM, Iddawela S, Harky A. (2020) Cardiac Manifestations in COVID-19 Patients—A Systematic Review. J Cardiac Surg (2020) 35(8):1988–2008.

[4] Seyed ASA, Karimi A, Shobeiri P, Nowroozi A, Mehraeen E, Afsahi AM, et al. (2020) Psychological Symptoms of COVID-19 Epidemic: A Systematic Review of Current Evidence. Psihologija (2020) 54(2)173–92.

[5] Vieira JM, Ricardo OMP, Hannas CM, Kanadani TCM, Prata TDS, Kanadani FN. (2020) What do we know about COVID-19? A review article. Rev Assoc Med Bras (1992). 2020;66(4):534-40.

[6] World Health Organization. Naming the coronavirus disease (COVID-19) and the virus that causes it [cited on May 24, 2021].

[7] Ying-yi Luan, Cheng-hong Yin and Yong-ming Yao. (2021). "Update Advances on C-Reactive Protein in COVID-19 and Other Viral Infections",J Frontiers in Immunology,12: 720363 .

[8] Cash JL, Hart R, Russ A, Dixon JP, Colledge WH, Doran J, Hendrick AG, Carlton MB & Greaves DR (2008). Synthetic chemerin-derived peptides suppress inflammation through ChemR23. Journal of Experimental Medicine 205 767–775.

[9] Bozaoglu K, Bolton K, McMillan J, Zimmet P, Jowett J, Collier G, Walder K & Segal D.(2007) Chemerin is a novel adipokine associated with obesity and metabolic syndrome. Endocrinology 148 4687–4694.

[10] Goralski KB, McCarthy TC, Hanniman EA, Zabel BA, Butcher EC, Parlee SD, Muruganandan S & Sinal CJ(2007). Chemerin, a novel adipokine that regulates adipogenesis and adipocyte metabolism. Journal of Biological Chemistry 282 28175–28188.

[11] Rourke, J.L.; Dranse, H.J.; Sinal, C.J. (2013). Towards an integrative approach to understanding the role of chemerin in human health and disease". Obes. Rev. 14, 245–262.

[12] Zabel, B.A.; Kwitniewski, M.; Banas, M.; Zabieglo, K.; Murzyn, K.; Cichy, J. (2014).Chemerin regulation and role in host defense". Am. J. Clin. Exp. Immunol.3, 1–19.

[13] Yang RZ, Lee MJ, Hu H, Pray J, Wu HB, Hansen BC, Shuldiner AR, Fried SK, McLenithan JC, Gong DW: (2006). Identification of omentin as a novel depot-specific adipokine in human adipose tissue: possible role in modulating insulin action". Am J Physiol Endocrinol Metab 290:E1253–E1261.

[14] De Souza Batista CM, Yang RZ, Lee MJ, Glynn NM, Yu DZ, Pray J, Ndubuizu K, Patil S, Schwartz A, Kligman M, Fried SK, Gong DW, Shuldiner AR, Pollin TI,McLenithan JC(2007): Omentin plasma levels and gene expression are decreased in obesity. Diabetes, 56:1655–1661.

[15] Yang RZ, Lee MJ, Hu H, Pray J, Wu HB, Hansen BC, Shuldiner AR, Fried SK, McLenithan JC, Gong DW(2006): Identification of omentin as a novel depotspecific adipokine in human adipose tissue: Possible role in modulating insulin action. Am J Physiol Endocrinol Metab, 290:E1253–E1261.

[16] Tsuji S, Uehori J, Matsumoto M, Suzuki Y, Matsuhisa A, Toyoshima K, Seya T(2001): Human

intelectin is a novel soluble lectin that recognizes galactofuranose in carbohydrate chains of bacterial cell wall. J Biol Chem, 276:23456–23463.

[17] National Institute of Health. Coronavirus disease 2019 (COVID-19) treatment guidelines [cited on Dec 17, 2020].

[18] Roh SG, Song SH, Choi KC, Katoh K, Wittamer V, Parmentier M & Sasaki S.(2007) Chemerin – a new adipokine that modulates adipogenesis via its own receptor. Biochemical and Biophysical Research Communications 362 1013–1018.

[19] Wittamer V, Franssen JD, Vulcano M, Mirjolet JF, Le Poul E, Migeotte I, Brezillon S, Tyldesley R, Blanpain C, Detheux M, et al(2003). Specific recruitment of antigen-presenting cells by chemerin, a novel processed ligand from human inflammatory fluids. Journal of Experimental Medicine 198 977–985.

[20] Bozaoglu K, Curran JE, Stocker CJ, Zaibi MS, Segal D, Konstantopoulos N, Morrison S, Carless M, Dyer TD, Cole SA, et al(2010). Chemerin, a novel adipokine in the regulation of angiogenesis. Journal of Clinical Endocrinology and Metabolism 95 2476–2485.

[21] Zylla S, Pietzner M, Kuhn JP, Volzke H, Dorr M, Nauck M & Friedrich N.(2017) Serum chemerin is associated with inflammatory and metabolic parameters-results of a population-based study. Obesity 25 468–475.

[22] Hotamisligil GS & Bernlohr DA(2015). Metabolic functions of FABPsmechanisms and therapeutic implications. Nature Reviews Endocrinology 11 592–605.

[23] Jian JL, Konopka J & Liu CJ(2013). Insights into the role of progranulin in immunity, infection, and inflammation. Journal of Leukocyte Biology 93 199–208.

[24] Hui X, Li H, Zhou Z, Lam KS, Xiao Y, Wu D, Ding K, Wang Y, Vanhoutte PM & Xu A.(2010) Adipocyte fatty acid-binding protein modulates inflammatory responses in macrophages through a positive feedback loop involving c-Jun NH2-terminal kinases and activator protein-1. Journal of Biological Chemistry 285 10273–10280.

[25] Youn BS, Bang SI, Kloting N, Park JW, Lee N, Oh JE, Pi KB, Lee TH, Ruschke K, Fasshauer M, et al(2009). Serum progranulin concentrations may be associated with macrophage infiltration into omental adipose tissue. Diabetes 58 627–636.

[26] Galic S, Oakhill JS, Steinberg GR. Adipose tissue as an endocrine organ. Mol Cell Endocrinol. (2010);316(2):129–39.

[27] Targher G, Zoppini G, Moghetti P, Day CP(2010). Disorders of coagulation and hemostasis in abdominal obesity: emerging role of fatty liver. Semin Thromb Hemost.;36(1):41–8.

[28] Abdollahi M, Cushman M, Rosendaal FR(2003). Obesity: risk of venous thrombosis and the interaction with coagulation factor levels and oral contraceptive use. Thromb Haemost. ;89(3):493–8.

[29] Ryan PM, Caplice NM.(2020) Is adipose tissue a reservoir for viral spread, immune activation, and

cytokine amplification in coronavirus disease 2019? Obesity (Silver Spring).;28(7):1191–4.

[30] Higham A, Singh D(2020). Increased ACE2 Expression in the Bronchial Epithelium of COPD Patients who are Overweight. Obesity (Silver Spring).;28(9): 1586–9. 122. Jia XY, Lu C, Chen S, Liu Y, Bai Q, Lu JY. Two things about COVID-19 might need attention. Preprints. 2020;2020020315.

[31] Zhou Y, Zhang B, Hao C, et al(2018). Omentin-A novel adipokine in respiratory diseases. Int J Mol Sci.;19(1):73-89.

[32] W. Vermi, E. Riboldi, V. Wittamer et al.(2018), "Role of ChemR23 in directing the migration of myeloid and plasmacytoid dendritic cells to lymphoid organs and inflamed skin," The Journal of Experimental Medicine, vol. 201, no. 4, pp. 509–515, 2005.W. Wu, X. Liu, P. Li, N. Li, and Z. Wang, "Effect of Liuzijue Exercise Combined with Elastic Band Resistance Exercise on Patients with COPD: A Randomized Controlled Trial," Evidence-Based Complementary and Alternative Medicine, vol. 2018, Article ID 2361962, 12 pages,.

[33] G. De Palma, G. Castellano, A. Del Prete et al.(2011), "The possible role of ChemR23/chemerin axis in the recruitment of dendritic cells in lupus nephritis," Kidney International, vol. 79, no. 11, pp. 1228–1235.

[34] S. Gonzalvo-Feo, A. del Prete, M. Pruenster et al.(2014), "Endothelial cell-derived chemerin promotes dendritic cell transmigration," Journal of Immunology, vol. 192, no. 5, pp. 2366–2373.

[35] S. Laranjeira, D. Regan-Komito, A. J. Iqbal, D. R. Greaves, S. J. Payne, and P(2018). Orlowski, "A model for the optimization of anti-inflammatory treatment with chemerin," Interface Focus, vol. 8, no. 1, p. 20170007.

[36] M. Herová, M(2015). Schmid, C. Gemperle, and M. Hersberger, "ChemR23, the receptor for chemerin and resolvin E1, is expressed and functional on M1 but not on M2 macrophages," Journal of Immunology, vol. 194, no. 5, pp. 2330– 2337.

[37] S. Luangsay, V. Wittamer, B. Bondue et al.(2009), "Mouse ChemR23 is expressed in dendritic cell subsets and macrophages, and mediates an anti-inflammatory activity of chemerin in a lung disease model," Journal of Immunology, vol. 183, no. 10, pp. 6489–6499.

[38] M. A. Bouhlel, B. Derudas, E. Rigamonti et al.(2007), "PPARgamma activation primes human monocytes into alternative M2 macrophages with anti-inflammatory properties," Cell Metabolism, vol. 6, no. 2, pp. 137–143.

[39] T. A. Wynn, A. Chawla, and J. W(2013). Pollard, "Macrophage biology in development, homeostasis and disease," Nature, vol. 496, no. 7446, pp. 445–455.

[40] Zhang D, Pang X, Huang R, Gong F, Zhong X, Xiao Y(2018). Adiponectin, omentin, ghrelin, and visfatin levels in obese patients with severe obstructive sleep apnoea. Biomed Res Int. 2018;2018:1-8.

[41] De Souza Batista CM, Yang RZ, Lee MJ, Glynn NM, Yu DZ, Pray J, Ndubuizu K, Patil S, Schwartz A, Kligman M, Fried SK, Gong DW, Shuldiner AR, Pollin TI,McLenithan JC(2007): Omentin plasma

levels and gene expression are decreased in obesity. Diabetes , 56:1655–1661.

[42] Pan HY, Guo L, Li Q(2010): Changes of serum omentin-1 levels in normal subjects and in patients with impaired glucose regulation and with newly diagnosed and untreated type 2 diabetes. Diabetes Res Clin Pract. 88:29–33.

[43] Maruyama, S.; Shibata, R.; Kikuchi, R.; Izumiya, Y.; Rokutanda, T.; Araki, S.; Kataoka, Y.; Ohashi, K.; Daida, H.; Kihara, S.; et al(2012). Fat-derived factor omentin stimulates endothelial cell function and ischemia-induced revascularization via endothelial nitric oxide synthase-dependentmechanism. J. Biol. Chem. , 287, 408–417.