Circulating Level of Serum Chemerin and CRP in Type 2 Diabetes Mellitus Patients with and Without Hypertension in Menopauses Women

Hussein Jasim AL-Harbi
Bio. Dept, College of Scince ,University of Babylon
hussein1967@gmail.com

Abstract

Chemerin may play a role in connecting inflammation and metabolic syndrome(MS), C-reactive protein(CRP) level is markedly rising during infectious and inflammatory diseases . The aimed of this study to evaluate both C- reactive protein (CRP) and Chemerin as subclinical markers in diabetic patients women. A total of 90 women, including, 24 healthy women (as control group), 66 women patients with diabetes mellitus type 2 (T2DM) (22diabetics with hypertension, 22 diabetics without hypertension and 22 hypertension only),there ages ranged between49-64 years. The result showed that significant increase ($p \leq 0.05$) in mean chemerin level in the diabetes group (8.766 ±0.648 ng/ml) in comparison with control group(4.042±0.320 ng/ml). Also, the result, revealed that significant increase ($P<0.05$) in the level of chemerin in women suffering from hypertension and diabetes (14.108 ± 0.577 ng/ml) in comparison to the women suffering from diabetic only which reached (8.766 ± 0.648 ng/ml). The data pointed out that the serum CRP level significant increase in T2DM group (6.176±0.1905) compared with control group (2.20±0.15 ng/ml) . Also, the result revealed that significant increase ($P<0.05$) of the CRP level with hypertension women patients (4.45 ± 0.131ng/ml) compared with the control group(2.20±0.15 ng/ml) and significant increase($P<0.05$) in diabetic with hypertension women group patients comparison with the women suffering from diabetic only. The chemerin and C-RP in hypertensive and normotensive patients with T2DM may be play an important role in activation of Immune Response in these patients .

Key words: Women, , Chemerin , CRP, Hypertension,T2DM.

الخلاصة

يلعب الكمرين د وراً في ربط المتلازمة الأيضية والالتهابات ، أذ يرتفع مستوى بروتين التفاعل سي ارتفاعا ملحوظا في الأمراض المعدية والالتهابات .هدفت هذه الدراسة الى تقييم كل من بروتين سي التفاعلي (CRP) والكمرين كعلامات سريرية مساعدة في تشخيص مرض السكري في النساء. شملت الدراسة 90 امراة ، تراوحت أعمارهن بين (47–64) سنة، 24 امراة صحيحة (مجموعة سيطرة)، 66 امراة يعانين من مرض السكري النوع الثاني type2diabetics (T2DM) ،(22 امراة يعانين من داء السكري مع ارتفاع ضغط الدم و22 مريضات بالسكري دون ارتفاع ضغط الدم و22 يعانين من ارتفاع ضغط الدم فقط). أظهرت النتائج وجود زيادة معنوية ($p \leq 0.05$) في مستوى الكمرين في مجموعة السكري (0.648 ±8.766 نانوغرام/ملليلتر) مقارنة بمجموعة السيطرة (4.042±0.320 ng/ml) وكذلك زيادة معنوية ($P<0.05$) في مستوى الكمرين في النساء اللائي يعانين من ارتفاع ضغط الدم والسكري (14.108 ± 0.577ng/ml) بالمقارنة مع النساء اللائي يعانين من السكري فقط (8.766 ± 0.648ng/ml). بينت نتائج مستوى بروتين التفاعل سي حصول زيادة معنوية ($P<0.05$) في مجموعة النساء اللائي يعانين من داء السكري (6.176±0.190ng/ml) مقارنة مع مجموعة السيطرة (2.2±0.15 ng/ml). كذلك، بينت النتائج زيادة معنوية ($P<0.05$) في مستوى بروتين التفاعل سي في النساء المصابات بارتفاع ضغط الدم فقط (4.45 ± 0.131ng/ml) مقارنة مع مجموعة السيطرة (2.2±0.15 ng/ml) وزيادة معنوية ($P<0.05$) في مريضات

السكري مع ارتفاع ضغط الدم مقارنة مع النساء اللاتي يعانين من داء السكري فقط .قد تكون مستويات الكمرين وبروتين التفاعل سي ا في مرضى ارتفاع ضغط الدم وضغط الدم الطبيعي مع داء السكري ربما تلعب دورا مهما في تنشيط الاستجابة المناعية لدى هؤلاء المرضى.

الكلمات المفتاحية: النساء، الكمرين، بروتين التفاعل –سي، داء السكري النوع الثاني،ضغط الدم

Introduction

The pervasiveness type 2 diabetes Mellitus (T2DM)is increasing rapidly increasing worldwide (WILd *et al*., 2004) Hypertension is extremely Common nearly 70% of patients with diabetes. (Klein *et al*., 1996).

Therefore, hypertension and Diabetes, have a significantly impact on public health **,** life quality and clinical care, (Neuparth *et al*., 2014). Chemerin, one of the adipokines, was found to enhance insulin signaling, to increase insulin-stimulated glucose transport, and to regulate insulin sensitivity in the adipose tissue (Wang *et al*. 2013); it is originaly well-known as a chemoattractant to Immune cells(Wittamer *et al*. 2003) that may have a role in adaptive and innate Immunity (Ernst and Sinal, 2010). However, The chemerin actions, stay unclear. pro-chemerin processing could lead to activation form with inflammatory properties or with anti- inflammation (Du and Leung, 2009).

There has been an increase importance in the contribution of low grade Inflammation In the pathogens of T2DM (Pickup, 2004). Interleukins 1 and 6 and tumor necrosis factor- are cytokines, stimulation an inflammatory marker CRP producing and releasing via the liver, Also Inflammation may be assumed to be playing an important role in the pathogenesis of T2DM. Recently,the studies had proposed that raised CRP level is connected with an increased risk of the Diabetes Mellitus evolution (Laaksonen *et al*., 2004; Jager , *et al*. 1999) . The circulating chemerin levels and CRP in hypertensive and normotensive patients with T2DM were evaluated (Neuparth *et al*. 2014).

Material and *Subjects*

90 menopausal women involved in this study, aged between (47-64) years ,24 menopausal women healthy subjects as control group , and 66 menopause women patients with type 2 diabetic divided into three groups {Diabetic normotensive n=22, Diabetic with Hypertensive 22,and Hypertensive only 22} , Blood pressure was estimated with mercury sphygmomanometer .

Estimation of the level of Fasting Blood Glucose

Glucose in serum blood was estimated by Glucose kit supplied via Bio Marieux , France.

Estimation of the level Chemerin.

The human Chemerin was estimated by ELISA according to the kit was suppling By Ray Biotech, Inc. U. S. A. (Cat#: ELH-Chemerin-001))

Determination of Serum CRP.

The human C-RP concentrations was estimated by ELISA kit was supplied by Elabscience Biotechnology Co., Ltd.(Catalog No: E-EL-0043).

Statistical Analysis

The data were analyzed using completely randomized design (CRD) , and the value at least significant difference (LSD) and T-test (student).

The means of the groups and Standard Error were compared at a significant level ($p<0.05$). The correlation between study parameters were done.

Results

The result of current study for blood sugar level in women suffering from DM , pressure and DM with pressure showed that significant increase ($p < 0.05$) of blood sugar in women patients with DM and DM with pressure when compared with healthy women and pressure only ,also there was a significant increase ($p< 0.05$) in women DM with pressure comparison with DM only (Fig. 1). There was a significantly differe between the 2 group according to the level of serum chemerin , being greater in the DM pat ients than in the healthy women ($p < 0.5$), (Fig. 2).

The CRP levels in DM women were more significant difference when compared to their non diabetic group ($P < 0.05$) level of CRP being greater in the DM patients with pressure than with diabetic patients only (Fig. 3).

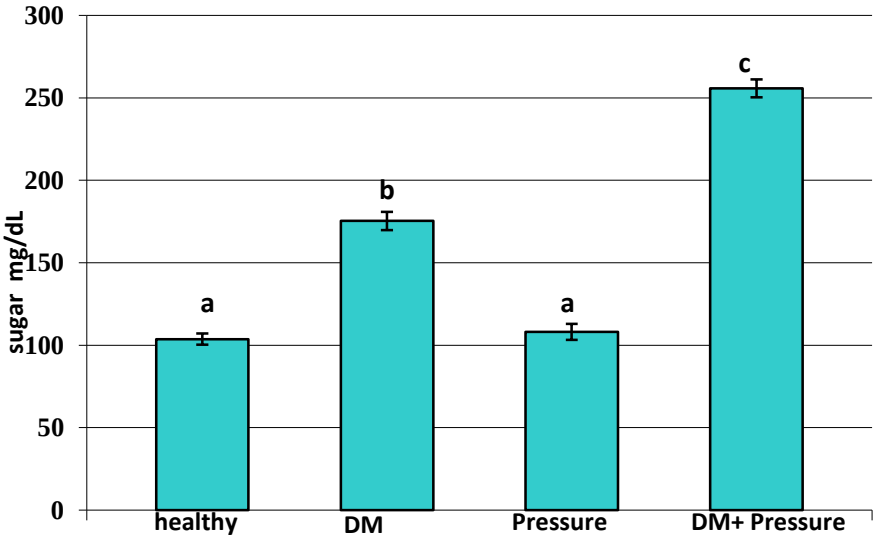

Figure 1: Serum sugar level in women patients in DM, pressure and DM with pressure and healthy group.

Different symbols (abcd) mean significant at (P<0.05)

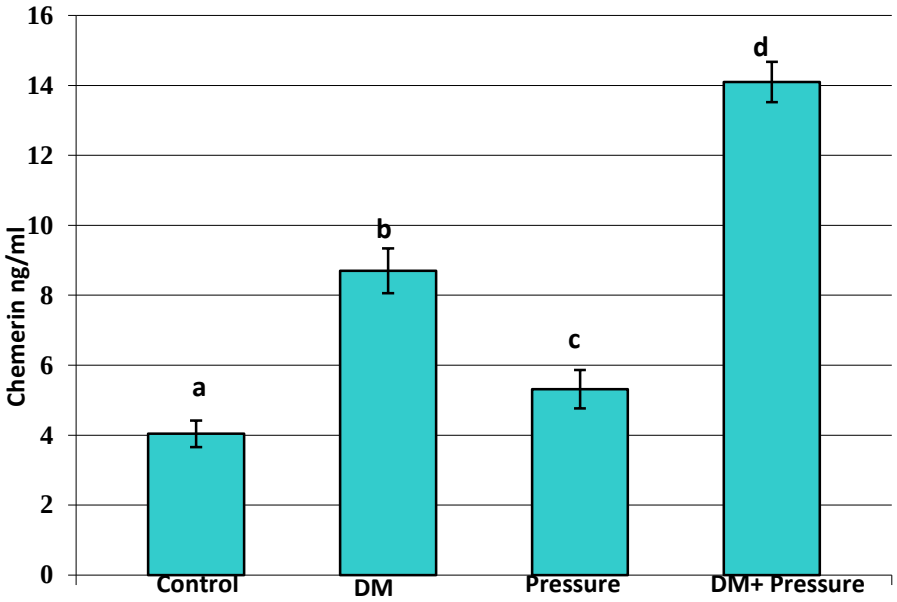

Fig. 2: Serum Chemerin level in women patients in DM, pressure and DM with pressure and healthy group.

Different symbols (abcd) mean significant at (P<0.05)

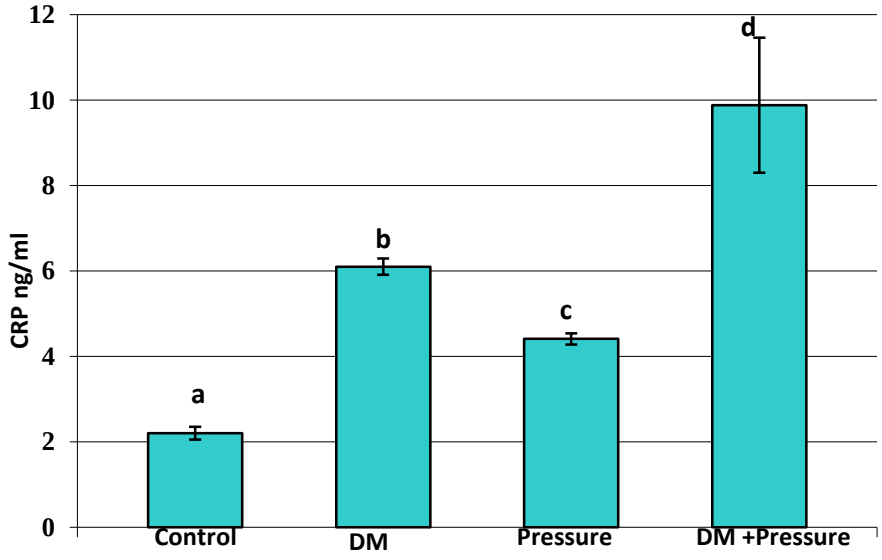

Figure. 3:The level of C - reactive protein in women patients in DM, pressure and DM with pressure and healthy group.

Different symbols (abcd) mean significant at (P<0.05)

There was positive significant correlation between the level of serum chemerin with DM, and DM plus pressure; while, there was no-significant (p>0 .05) correlation between level of serum chemerin with pressure as showen in table(1).

Farthermore, the data demonstrated that a positive significant correlation between CRP level with DM , pressure and DM plus pressure (table 2).

There was positive significant correlation between C - reactive protein and serum chemerin with DM and DM with pressure, but non-significant correlation between chemerin and CRP with pressure only (table 3).

Table (1): Correlation coffeicint between chemerin with DM, pressure and DM plus pressure in women patients.

Groups parameters	Chemerine	
	r	P
DM	+ 0.521	0.047
pressure	+0.374	0.2
DM with Pressure	+ 0.662	0.007

Table (2): Correlation coffeicint between CRP with DM, pressure and DM plus pressure in women patients.

Groups parameters	CRP	
	r	P
DM	+ 0.678	0.008
Pressure	+ 0.431	0.04
DM with Pressure	+ 0.511	0.03

Table(3): Correlation coffecient between chemerin and CRP in diabetes, pressure and diabetes with pressure patients.

Groups parameters	Chemerin+ CRP	
	r	P
DM	+ 0.596	0.02
pressure	+ 0.374	0.2
DM with Pressure	0.62	0.01

Discussion

In the present study, there were a significant increase between the diabetic patients and healthy group regarding to the serum chemerin level; being high level in T2DM patients, comparison with healthy women. These results are agreed with the findings reported by other studies that demonstrated that chemerin level were significantly increased in patient group with type2 diabetes in compared with nondiabetic individuals (Ali and Al Hadidi, 2013; el-Mesallamy *e t a l.*, 2 011; Hu And Feng, 2 011).

Whether elevated chemerin was a cause or a result of T2DM still unclear, but other studies found chemerin on murine C2CL2 myoblasts was effected by insulin resistance through nuclear f actor-κB pathway-mediated reaction of inflammatory (Huang and Xie,2015); Additionally,this proposal presumably varies with the Takahashi *et al*. (2008),chemerin which has the reverse influence ,and may be increased absorption of insulin stimulation in adipocytes through modulating and induce insulin sensitivity. And then rise in the chemerin level was a compensatory mechanisms insulin resistance patients. Also, chemerin might play a different role in endocrine function and autocrine/paracrine .In mice that deficient in chemerin is glucose intolerance and glucose intolerant was mostly owing chemerin controls beta-cell role and action an important function in hemostasis of glucose in a tissue dependent way (Takahashi e*t al.* 2011).

Also our study is consistent with a study of Mesallamy *et.al.* (2012) who found a significant increase in the level of serum chemerin in patients suffering with T2DM comparison with healthy people, as well as in our study results showed highly significant increase in the level of chemerin in patients with diabetes and blood pressure compared with patients suffering diabetes without blood pressure. The result of this study was in agreement with the study of Yang *et.al*.,(2010) who revealed that level of serum chemerin is increased markedly in patients suffering from T2DM
plus blood pressure compared with patients with T2 DM and healthy group . According to these results, this relationship of blood pressure - chemerin, might be related to the great chemerin expression with in the kidney, a key location to regulation of blood pressure. Our results suggests that, in diabetes and hypertension patients women, high levels of chemerin are not related to hypertension only, but also may be associated with diabetes itself and obesity. It appears that an adipocytes dysfunction happens (Neupart *et al*., 2014) .

The results noted that C-RP is significantly greater in the diabetic women patients compared with a healthy group. These results are compatible with those found by Thejaswini *et al*. (2013), who described a higher hs-C-reactive protein in T2 DM patients. Since, hs-CRP is considered to be a sensitive indicator of inflammation, a higher hs-CRP level in Type 2 diabetic patients may suggest that inflammation could be involved in the pathogenesis of diabetes and early atherosclerotic processes (Nagwa *et al.* 2016),also, raised levels of C- reactive protein is related to the elevated blood pressure (Dauphinot *et al*., 2009, Davey smith *et al*., 2005) as well as with insulin resistance (XU *et al*., 2008). There was a relationship between serum chemerin and hs-CRP levels which is consistent with the findings of other studies (Weigert *et al.*, 2010; Lehrke *et al.*, 2009; Bozaoglu *et al.* 2009).The levels of chemerin were positively associated with CRP and that it may also be correlated with the development of cardiac artery disease (Dong *et al.*, 2011). Other studies have suggested that the increased serum chemerin levels could be strongly associated with the markers of inflammation such as C- reactive protein (Weigert *et al.*, 2010; Lehrke *et al* ., 2009).

References

Ali, T.,Al Hadidi, K. (2013). Chemerin is associated with markers of inflammation and predictors of atherosclerosis in Saudi subjects with metabolic syndrome and type 2 diabetes mellitus. Beni-Suef Univ J Basic Appl Sci 2: 86–95

Bozaoglu, K.; Segal, D.; Shields, K.; Cummings, N.; Curran, J.; Comuzzie, A.; et al. (2009). Chemerin is associated with metabolic syndrome phenotypes in a Mexican-American population. J. Clin. Endocrinol. Metab. 94: 3085–3088.

Dauphinot, V., Roche, F., Kossovsky, M. P., Schott, A. M., Pichot, V., Gaspoz, J. M., Gosse, P. & Barthelemy, J. C. (2009). "C-Reactive Protein Implications in New-Onset Hypertension in a Healthy Population Initially Aged 65 Years: The Proof Study," *Journal of Hypertension*, 27 (4) 736-43.

Davey Smith, G., Lawlor, D. A., Harbord, R., Timpson, N., Rumley, A., Lowe, G. D., Day, I. N. & Ebrahim, S. (2005). "Association of CReactive Protein with Blood Pressure and Hypertension: Life Course Confounding and Mendelian Randomization Tests of Causality," *Arteriosclerosis, Thrombosis, and Vascular Biology*, 25 (5) 1051-6 .

Dong, B.; Ji, W. and Zhang, Y. (2011). Elevated serum chemerin levels are associated with the presence of coronary artery disease in patients with metabolic syndrome. Intern Med 50: 1093–1097.

Du, X.Y., Leung, L.L. (2009). Proteolytic regulatory mechanism ofchemerin bioactivity. Acta Biochim Biophys Sin, 41, 973–9.

El-Mesallamy, H., El-Derany, M., Hamdy, N.(2011) Serum omentin-1 and chemerin levels are interrelated in patients with type 2 diabetes mellitus with or without ischemic heart disease. Diabet Med 28: 1194–1200

El-Mesallamy, H.O., M.O. El-Derany, N.M. Hamdy, (2012). Serum omentin-1 and chemerin levels are interrelated in patients with type 2 diabetes mellitus with or without ischemic heart disease. Diabet Med.,28(10): 1194-200.

Ernst, M.C and C.J. Sinal, (2010). Chemerin: at the crossroads of inflammation and obesity. Trends Endocrinol Metab., 21: 660-667.

Hu, W., Feng, P. (2011) Elevated serum chemerin concentrations are associated with renal dysfunction in type 2 diabetic patients. Diabetes Res Clin Pract 91: 159– 163.

Huang, Z, Xie, X. (2015). Chemerin induces insulin resistance in C2C12 cells through nuclear factor-κB pathway-mediated inflammatory reaction. PubMed, 31(6), 725-9.

Jager A, Van Hinsberg VW, Kostense PJ *et al*. (1999). CRP and five year mortality in diabetic subjects: The Hoorn study. *Arteioscler Throm Vasc Biol*; 12: 3071-80.

Klein, R., Klein, B. E., Lee, K. E.,Cruickshanks, K. J. & Moss, S. E. (1996)."The Incidence of Hypertension in Insulin-Dependent Diabetes," *Archives of Internal Medicine*, 156 (6) 622-7.

Laaksonen DE, Niskanen L, Nyyssonen K *et al. (2004).*C-reactive protein and the development of the metabolic syndrome and diabetes in middle-aged men. *Diabetologia*; 47: 1403-10.

Lehrke M., Becker A., Greif M., Stark R., Laubender R., von Ziegler F., et al. (2009) Chemerin is associated with markers of inflammation and components of the metabolic syndrome but does not predict coronary atherosclerosis. Eur J Endocrinol 161: 339–344. [PubMed]

Nagwa A. Lachine, Abdel Aziz Elnekiedy, Magdy Helmy Megallaa, Gihane I. Khalil, Mohamed A. Sadaka, Kamel H. Rohoma, and Heba S. Kassab(2016). Serum chemerin and high-sensitivity C reactive protein as markers of subclinical atherosclerosis in Egyptian patients with type 2 diabetes Endocrinol Metab v.7(2)

Neuparth, M.J. ; Proenca, J.B. ; Santos-Silva,A. ; and Coimbra ,S. (2014), Adipokines, C-Reactive Protein and Lipid Profile Levels in Hypertensive Type 2 Diabetic Portuguese Patients ,*Endocrinology* Vol. *9 pages*

Pickup,J.C.(2004). Inflammation and activated innate immunity in the pathogenesis of type 2 diabetes. *Diabetes Care*; 27: 813-23.

Takahashi, M.; Okimura, Y.; Iguchi, G.; Nishizawa, H.; Yamamoto, M.; Suda, K.; Kitazawa, R.; Fujimoto, W.; Takahashi, K. (2011). Chemerinregulates β-cell function in mice. Sci Rep. 1, 123.

Takahashi, M.; Takahash,i Y., Takahashi, F.N. (2008). Chemerin enhances insulin signaling and potentiates insulinstimulated glucose uptake in 3T3-L1adypocytes. FEBS Lett,582, 573–8.

Thejaswini, K., Roopakala M., Dayananda G., Chandrakala S., Prasanna K. (2013). A study of association of ankle brachial index (ABI) and the highly sensitive C-reactive protein (hsCRP) in Type 2 diabetic patients and in normal subjects. J Clin Diagn Res 7: 46–50.

Wang D., Yuan G., Wang X., Jia J., Di L., Yang L., et al. (2013) Plasma chemerin level in metabolic syndrome. Genet Mol Res 12: 5986–5991. [PubMed]

weigert J., Neumeier M., Wanninger J., Filarsky M., Bauer S., Wiest R., et al. (2010) Systemic chemerin is related to inflammation rather than obesity in type 2 diabetes. Clin Endocrinol 72:342–348. [PubMed]

Wild, S., Roglic, G., Green, A., Sicree, R. & King, H. (2004). "Global Prevalence of Diabetes: Estimates for the Year 2000 and Projections for 2030," *Diabetes Care*, 27 (5) 1047-53

Wittamer, V., Franssen, J.D., Vulcano, M. Specific.(2003).recruitment of antigen-Presenting cells by chemerin, anovel processed ligand from human inflammatory fluids.The Journal of Experimental Medicine, 198, 977–985

Xu, T., Ju, Z., Tong, W., Hu, W., Liu, Y., Zhao, L. & Zhang, Y. (2008). "Relationship of CReactive Protein with Hypertension and Interactions between Increased C-Reactive Protein and Other Risk Factors on Hypertension in Mongolian People, China," *Circulation Journal*, 72 (8) 1324-8.

Yang, M., G.; Yang, J.; Dong, Y.; Liu, H.; Zong, H.; Liu, G. and Boden, L. Li, (2010). levated plasma levels ofchemerin in newly diagnosed type 2 diabetes mellitus with hypertension. J Investig J; 58(7): 883-885.