

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

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## 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 aim of this study was to evaluate both C-reactive protein (CRP) and Chemerin as subclinical markers in diabetic patients with and without hypertension. A total of 90 women, including 24 healthy women (as control group), 66 women patients with diabetes mellitus type 2 (T2DM) (22 diabetics with hypertension, 22 diabetics without hypertension and 22 hypertension only), their ages ranged between 49-64 years. The result showed that significant increase ( $p \leq 0.05$ ) in mean chemerin level in the diabetes group ( $8.766 \pm 0.648$  ng/ml) in comparison with control group ( $4.042 \pm 0.320$  ng/ml). Also, the result revealed that significant increase ( $P < 0.05$ ) in the level of chemerin in women suffering from hypertension and diabetes ( $14.108 \pm 0.577$  ng/ml) in comparison to the women suffering from diabetic only which reached ( $8.766 \pm 0.648$  ng/ml). The data pointed out that the serum CRP level significant increase in T2DM group ( $6.176 \pm 0.1905$ ) compared with control group ( $2.20 \pm 0.15$  ng/ml). Also, the result revealed that significant increase ( $P < 0.05$ ) of the CRP level with hypertension women patients ( $4.45 \pm 0.131$  ng/ml) compared with the control group ( $2.20 \pm 0.15$  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 play an important role in activation of Immune Response in these patients.

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

## الخلاصة

يلعب الكمرين دوراً في ربط المتلازمة الأيضية والالتهابات، إذ يرتفع مستوى بروتين التفاعل سي ارتفاعاً ملحوظاً في الأمراض المعدية والالتهابات. هدفت هذه الدراسة إلى تقييم كل من بروتين سي التفاعلي (CRP) والكمرين كعلامات سريرية مساعدة في تشخيص مرض السكري في النساء. شملت الدراسة 90 امرأة، تراوحت أعمارهن بين (47-64) سنة، 24 امرأة صحية (مجموعة سيطرة)، 66 امرأة يعانين من مرض السكري النوع الثاني (T2DM) type 2 diabetics، (22 امرأة 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 ( $8.766 \pm 0.648$  نانوغرام/ملييلتر) مقارنة بمجموعة السيطرة ( $4.042 \pm 0.320$  ng/ml) وكذلك زيادة معنوية ( $P < 0.05$ ) في مستوى الكمرين في النساء اللاتي يعانين من ارتفاع ضغط الدم والسكري ( $14.108 \pm 0.577$  ng/ml) بالمقارنة مع النساء اللاتي يعانين من السكري فقط ( $8.766 \pm 0.648$  ng/ml). بينت نتائج مستوى بروتين التفاعل سي حصول زيادة معنوية ( $P < 0.05$ ) في مجموعة النساء اللاتي يعانين من داء السكري ( $6.176 \pm 0.190$  ng/ml) مقارنة مع مجموعة السيطرة ( $2.2 \pm 0.15$  ng/ml). كذلك، بينت النتائج زيادة معنوية ( $P < 0.05$ ) في مستوى بروتين التفاعل سي في النساء المصابات بارتفاع ضغط الدم فقط ( $4.45 \pm 0.131$  ng/ml) مقارنة مع مجموعة السيطرة ( $2.2 \pm 0.15$  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 originally 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 supplying 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 significant difference between the 2 group according to the level of serum chemerin, being greater in the DM patients 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).

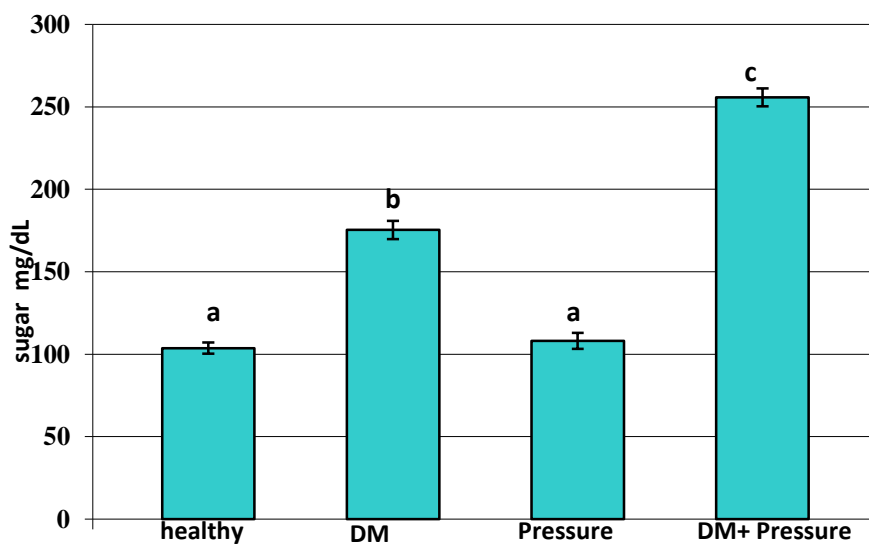


Figure 1: Serum sugar level in women patients in DM, pressure and DM with pressure and healthy group.

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

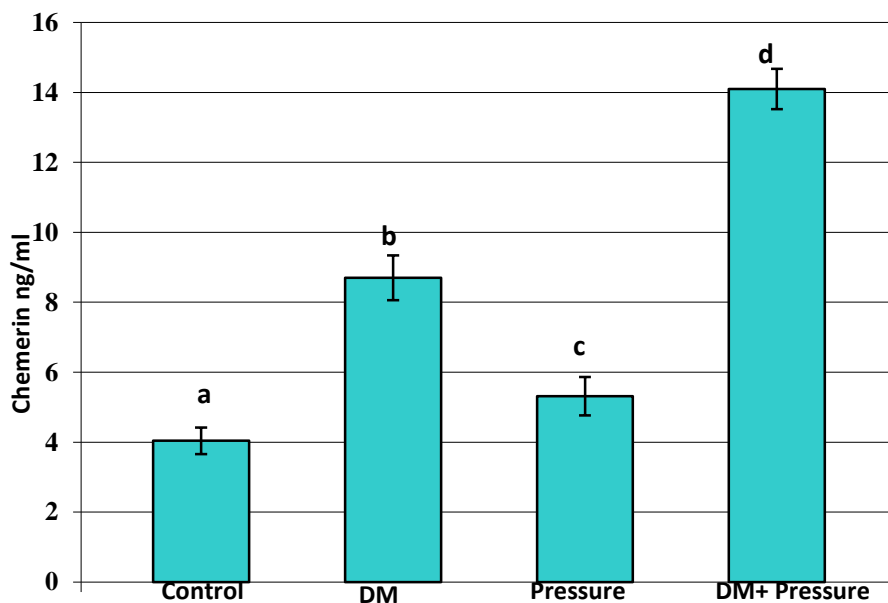


Fig. 2: Serum Chemerin level in women patients in DM, pressure and DM with pressure and healthy group.

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

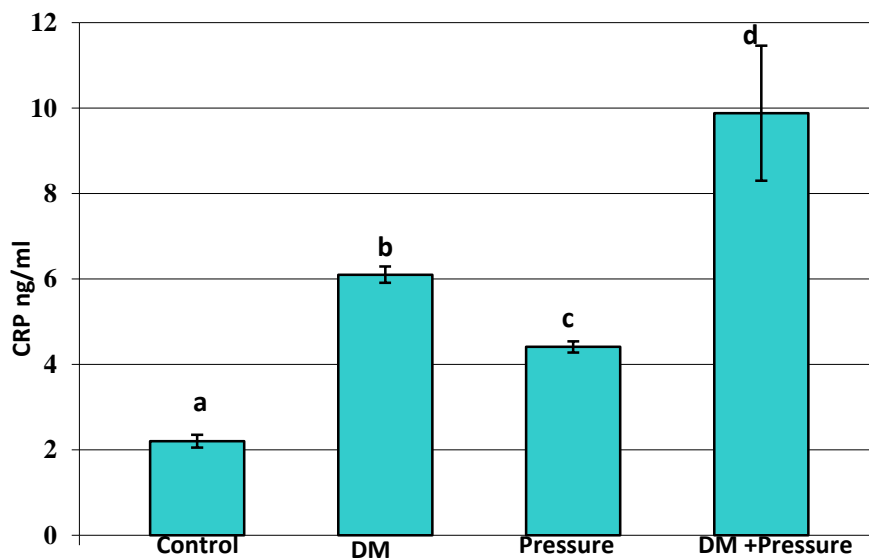


Figure. 3: The level of C - reactive protein in women patients in DM, pressure and DM with pressure and healthy group.

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 shown in table( 1).

Furthermore, 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 coefficient 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 coefficient 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 coefficient 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 *et al.*, 2011; Hu And Feng, 2011).

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 factor- $\kappa$ B 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 *et 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).

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