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Chemerin Novel Biomarker As a Prognostic Factor for Cardiovascular Complications in Type 2 Diabetic Patients

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ABSTRACT

Objective:the present study was aimed to assess chemerin as prognostic factor forcardiovascular complications in type2 diabetic patients.

Patients and methods:forty type 2 diabetic patients without cardiovascular disease, forty type 2 diabetic patients with cardiovascular disease and twenty healthy control counterparts were included in thepresent study.Chemerinlevels were assayed and correlated with clinical pathological parameters.ROC curve analysis was also done for this biochemical marker.

Results:the mean level of chemerinwas 57.65± 15.69 ng/l in diabetic subjects versus 93.97 ± 26.62 ng/l for the cardio-diabetic subjects ($P < 0.0001$).The chemerin levels were significantly elevated in the cardio-diabetic patients with increasing-reactive protein(CRP), triglycerides(TG), fasting blood glucose (FBG), glycated hemoglbin(HbA1C), micro-albumin and cholesterol ($P < 0.0001$, $P < 0.0001$, $P = 0.005$, $P=0.04$, $P=0.011$and$P=0.0001$ respectively). From the ROC curve analysis, it was observed that the area under curve for chemerin was 0.877. This finding indicates the good validity of the above biomarker as aprognostic factor for cardiovascular complication in type 2 diabetic patients.

Conclusion:it could be concluded that chemerin can be used as prognostic biomarker for cardiovascular complications in type 2 diabetic patients.

Keywords:chemerin , diabetes mellitus,cardiovascular complication,prognosis

INTRODUCTION

Diabetes mellitus is a chronic disease that affects 415 million people worldwide and 5 million people died from diabetes-related complications[1].Type 2 diabetes mellitus(T2DM) is characterized by hyperglycemia,that results from lack of endogenous insulin or resistance to the action of insulin in fat, muscle, and liver in addition to an insufficient pancreatic beta cell response [2].

T2DM is considered as a risk factor for cardiovascular disease (CVD). This is due to a complex group of risk factors associated withT2DMincluding hypertension, insulin resistance, hyperglycemia, hyperinsulinemia, diabetic dyslipidemia, systemic inflammation and adipose tissue-derived factors [3,4,5].Worthmentioning,the Changes in the mass and metabolism of adipose tissue may be accompanied with visceral obesity and insulin resistance commonly associated with T2DM[6].

Adipocyte is considered as an active endocrine organ and secretes a large number of bioactive mediators (adipokines)that signal to the brain, liver, skeletal muscle, and the immune system, the important metabolic organs in the body [7,8]. These adipokines include omentin-1, visfatin, and chemerin[8, 9]. Dysregulation of pro-inflammatory and antiinflammatory adipokines secretion in obesity may serve as a pathogenic link between obesity, insulin resistance and cardiovascular diseases [10, 11].

Chemerin is considered a proinflammatory cytokine that activates immune cells and contributes to inflammation by activating macrophage adhesion to vascular cell adhesion molecule-1(VCAM-1) and fibronectin[12]. It is not only a marker of vascular damage[13, 14] but also a prognostic predictor [15]. In addition,chemerin is related to glucose, and lipid metabolism, inflammation, and adipogenesis. All of these lead to the development of cardio-vascular complications in diabetic patients,especially atherosclerosis [11,16,17].

PATIENTS AND METHODS

Forty type 2 diabetic patients with cardiovascular disease (cardio-diabetic group) and forty type 2 diabetic patients without evidence of CVD (diabetic group) were included in the current studyand collected from clinic's national institute of diabetes and endocrinology. In addition, , twenty apparently healthy subjects with no history of type 2 DM, other endocrine dysfunctions, hyperlipidemia, hypertension, or coronary heart diseases were enrolled in the study and served as controls. Patients in the group without vascular disease were T2DM patients who had no history of

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vascular disease and those with normal ECG findings at exercise and normal peripheral artery Doppler ultrasonography findings. Exclusion criteria involved the presence of sustained type 1 DM, acute and chronic infections, malignancy, hepatic or renal disease, diabetic retinopathy and nephropathy, and other endocrine dysfunctions.This study was approved by Ethical Committee of Ethics commission and Scientific Research of the General Authority for hospitals and educational institutes.

Blood and urine samples: venous blood was collected from all participants and each blood sample was divided into two portions. The small portion was collected on EDTA coated tube for determination of $HbA1_{C,}$ and the large portion was collected on plain tube for separation of serum. Serum samples were obtained for determination of other parameters. All biochemical variables were measured on the same day of the blood collection. Remaining serum specimens were stored at -20˚C until analysis of chemerin. Urine was collected for determination of microalbumin.

Quantitative determination of glucose was carried out colorimetrically using method of Thomas[18].Quantitative estimation ofserum cholesterol was done colorimetrically using method of Richmond[19.] Serum HDL-cholesterol was assayedcolorimetrically using method ofAssmann[20].LDL-cholesterol was quantified in serum using method of Okadaet al.[21].Triglycerides in serum was measured colorimetrically using method of Jacobs and Van Denmark [22].Glycated hemoglobin was determined using method described by Trivelli *et al*.[23].Chemerinwas evaluated by solid-phase enzyme-linked immunosorbent assay (ELISA kit) using method ofAronis *et al*[24].Serum C-reactive protein (CRP) was measured byELISA using method of Hedlund[25].Quantitative estimation of microalbuminin urine was done by immunoturbidimetric assay using method of Mogensen and Schmitz[26].

STATISTICAL ANALYSIS

Data were expressed as mean ± SD and analyzed using MedCalc software, version 11. The Student's t test was used to assess the significance of difference in the levels of chemerin between the patient groups (diabetic and cardio-diabetic) and the control group. The correlation analysis between serum chemerin level and other measured parameters in the different studied groups was performed by correlation coefficient test.The cut-off value was determined for chemerin in the current study according to the best discrimination between diabetic patients and cardio-diabetic patients regarding optimal values of sensitivity and specificity using ROC curves analysis. AUC of the ROC curve was calculated for chemerin. $P< 0.05$ was accepted as significant.

RESULTS

Laboratory assessments of chemerin in the different submitted groups are presented in Table (1).Chemerin levels were significantly higher in diabetic patients than in healthy subjects (P<0.0001). likewise,chemerin levels were significantly higher in cardio-diabetic patients than in healthy subjects and diabetic patients (P< 0.0001).

Correlation between serum chemerin level and metabolic parameters in different studied groups were depicted in Table (2)**.**Significant positive correlation between serum chemerin level and cholesterol, TG, CRP, FBG, andHbA1c has been recorded in diabetic patients (P=0.007, P=0.001, P<0.0001, P<0.0001, and P=0.031 respectively) and cardio-diabetic patients(P=0.0001, P<0.0001, P<0.0001, P=0.005, and P=0.040 respectively), but negative correlation between chemerin level and micro-albumin in diabetic patients (P=0.026). Moreover, a significant positive correlations has been observed between chemerin level and LDL in diabetic patients(P=0.045),also, between chemerin and micro-albumin in cardio-diabetic patients (P=0.011).

The receiving operating characteristic (ROC) curve was designed for chemerin, (Fig.1). The cut-off values for chemerin, was75 ng/l**.**Area under curve (AUC) for chemerin was 0.877. This result indicates the good validity of the above biochemical markerto discriminate diabetic patients than cardio-diabetic patients**.**

DISCUSSION

Diabetes mellitus is a disease that occurs when the body cannot produce sufficient amount of insulin or defect of action of insulin.Patients with type 2 diabetes mellitus have a high risk of cardiovascular morbidity and mortality compared with individuals without diabetes, and are affected by cardiovascular disease. Most of this high risk is related to theprevalence of some risk factors such as dyslipidaemia, obesity and

hypertension in these patients. However the improved cardiovascular disease in patients with type 2 diabetes mellitus cannot be related to the higher prevalence of traditional risk factors only,but, other non-traditional risk factors are important in type 2 diabetic patients. Increased cardiovascular disease in patient with type 2 diabetes mellitus is due to a complex combination of different traditional and non-traditional risk factors that have an important role in the beginning and the evolution of atherosclerosis over its long natural history from endothelial function of clinical events [27].
The objective of this review is to assess chemerin as prognostic factors forcardiovascular complication in type2 diabetic patients.

The results obtained in this study showed thatchemerin levelswere significantly higher in diabetic patients when compared to healthy subjects.Studies of El-Mesallamy*et al.*[28], Hu and Feng [29] andTarek and Khalid[30] revealed that chemerin level was significantly higher in diabetic subjects when compared to healthy subjects.

Sell *et al.*[31]explained these findings by the fact that adipose tissue expresses chemerin and chemokine-like receptor-1, and release of chemerin is related to the volume of adipocyte. Furthermore, the release of the high concentration of chemerin is related to insulin resistance at the level of lipogenesis by its reversible binding to the extracellular domain of insulin receptor-tyrosine kinase in peripheral tissues and decreasing the rate of auto-phosphorylation and subsequent downstream intracellular signaling cascades. Also, Chemerin suppressed phosphorylation of glycogen synthase kinase, an enzyme necessary for synthesis and storage of glycogen, and suppress the uptake of glucose. In addition, chemerin activates extracellular signal-regulated kinase (ERK).Suppression of ERK prevents chemerin-induced insulin resistance, pointing to participate of this pathway in chemerin action.
Takahashi *et al*. [32]postulated that chemerin in adipocytes has the opposite effect, where it increases insulin activated glucose uptake, so, it activates insulin sensitivity. Hence, the increase in circulating chemerin level is a compensatory mechanism in patients with insulin resistance. Also, chemerin exert various actions in endocrine, autocrine and paracrine ways. Moreover, Takahashi *et al*. [33]showed that chemerin-deficient mice are glucose intolerant, and glucose intolerance was essentially due to increased production of hepatic glucose and impaired secretion of insulin. Also,They revealed that chemerin and its receptor were expressed in β-cell, and chemerin regulate function of β-cell and plays an important role in glucose homeostasis in a tissue.
Bozaoglu *et al.*[34]found that the level of circulating chemerin in diabetic subjects was not significantly higher than in healthy subjects, this because of taking antidiabetic drugs,where Tan *et al.*[35]shown that metformin (an oral hypoglycemic drug) significantly decreased level of circulating chemerin with a concomitant decrease in insulin resistance in patients with type 2 diabetes.
The serum chemerin level was significantly higher in cardio-diabetic patients when compared to healthy subjects. Study of Ying and Dongying[36] found that serum chemerin levels of coronary artery disease (CAD) patients were significantly higher than that of control subjects, and study of Xiuying *et al*.[37]found that CAD group showed significantly higher levels of chemerin. In addition**,**Liang *et al.*[38] found that the level of chemerin was significantly higher in the acute myocardial infarction(AMI)and unstable angina(UA) groups than in the stable angina (SA) and control groups. This finding explained by Wittamer *et al*.[39]who showed that chemerin promotes the migration of macrophage and immature dendritic cell. It is well-known that a macrophage- changed to-foam cell switch elicits the initiation and development of atherosclerosis, where, chemerin promote cholesterol uptake and foam cell formation, and increased accumulation of macrophages induce the rupture of plaque and the thrombus formation in advanced atherosclerosis [38]**.** Therefore, chemerin may be involved in different stages of atherosclerosis through regulating the migration of macrophage**.**
The serum chemerin level was significantly higher in cardio-diabetic patients when compared to diabetic patients. Study of Xiuying *et al.*[37] found that CAD group showed significantly higher levels of chemerin. Kim *et al*.[40] revealed that no difference in chemerin levels between asymptomatic type 2 diabetic patients with CAD and without CAD**.**
Our study revealed a significant positive correlation between serum chemerin level and cholesterol, TG, CRP, FBG, andHbA1Cin type2 diabetes mellitus group, and cardio-diabetic patients.Likewise,significant positive correlation between serum chemerin level and

LDL in diabetic group. Study of Ying and Dongying[36] found a significant positive association between serum chemerin and triglycerides, and high-sensitivity CRP in CAD patients, and Osman *et al.*[41]found that serum chemerin level was positively correlated with total cholesterol, LDL-C and triglycerides in type 2 diabetes mellitus group.In addition, Qingwei *et al*.[42] demonstrated that CRP, which is an established marker of inflammation, was positively correlated with chemerin in acute coronary syndrome (ACS) patients**.** Moreover, Yu-Jin *et al*.[43] found significant but weak correlations between serum chemerin concentrations and fasting glucose, triglyceride, total cholesterol, LDL-cholesterol and hsCRP in CAD patients.

Our results revealed anegative association between microalbumin and chemerin level in diabetic subjects,but positive association between microalbumin and chemerin level in cardio-diabetic subjects.Wenchao andPing[44] postulated that no differences were found in the level of serum chemerin between diabetic patients with normo-albuminuria and micro-albuminuria and control subjects**.** In addition, Christiane and Gunter[45] found that serum chemerin was significantly elevated in type 2 diabetic patients with macro-albuminuria compared with control subjects and diabetic patients with normo-albuminuria and micro-albuminuria.

ROC curve was done to detect the best cut off value of serum chemerin in diabetic and cardio-diabetic patients was 75ng/l with 80% sensitivity and 90% specificity .Studies such as Yan *et al.*[46] and Lin *et al.*[47]reported high levels of circulating chemerin in CAD patients, alsoEl-Mesallamy*et al*.[28] and Hu and Feng [29]found that level ofchemerinwas significantly elevated in diabetic patients and in diabetic patients with ischaemic heart diseaseompared with healthy subjects. Moreover,Kadoglou *et al*.[48] found that acute myocardial infraction (AMI) group appeared with significantly higher concentrations of chemerin compared with healthy controls . These findings suggesting that chemerin is a biomarker of CAD in patients with type 2diabetes mellitus.

Measurement of chemerin might provide useful diagnostic and prognostic tools for cardiovascular complication in patients with type 2 diabetes mellitus.

REFERENCES

1-International Diabetes Federation(2015): IDF Diabetes Atlas, 7 ed. Brussels, Belgium: International Diabetes Federation.

2-Wolfs MGM, Hofker MH, Wijmenga C, van Haeften TW(2009): Type 2 diabetes mellitus: New genetic insights will lead to new therapeutics. Curr Genomics, 10(2):110e8.

3-Bartels DW, Davidson MH and Gong WC (2007): Type 2 diabetes and cardiovascular disease: Reducing the risk. J Manag Care Pharm., 13: S2-S15.

4-Fox Caroline S , GoldenSherita H , Anderson Cheryl , Bray George A , Burke Lora E , de Boer Ian H ,Deedwania Prakash ,Eckel Robert H , Ershow Abby G, Fradkin Judith ,Inzucchi Silvio E ,Osiborod Mikhail K, Nelson Robert G, Patel MaheshJ , Pignone Michael , Quinn Laurie ,Schauer Philip R ,Selvin Elizabeth ,Vafiadis Dorothea K(2015) : Update on preventation of cardiovascular disease in adults with type 2diabetes mellitus in light of recent evidence:A scientific statement from American Heart Association and American Diabetes Association, Cardiovascular Disease & Diabetes, Diabetes Care, 38 (9) 1777-1803.

5-Bakker W, Eringa EC, Sipkema P and van Hinsbergh VW(2009): Endothelial dysfunction and diabetes: Roles of hyperglycemia, impaired insulin signaling and obesity. Cell Tissue Res., 335: 165-189.

6-Lebovitz HE(2006): Insulin resistance – A common link between type 2 diabetes and cardiovascular disease. Diabetes Obes Metab.,8: 237-249.

7- Gijs HGoossens and Ellen EBlaak(2015): Adipose tissue dysfunction and impaired metabolic health in human obesity: A matter of oxygen?, Front. Endocrinol., 6:55 .

8-Yan Q, Zhang Y, Hong J, Gu W, Dai M, Shi J, ZhaiY,WangW,Li X(2012): The association of serum chemerin level with risk of coronary artery disease in Chinese adults. Endocrine., 41(2):281e-8.

9- Yang R, Xu A, Pray J, Hu H, Jadhao S, Hansen B(2003): Cloning of omentin, a new adipocytokine from omental fat tissue in humans. Diabetes, 52: A1

10-Roh S, Song SH, Choi KC, Katoh K, Wittamer V, Parmentier M(2007): Chemerin e a new adipokine that modulates adipogenesis via its own receptor. BiochemBiophys Res Commun.,362:1013e-8.

11-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. J BiolChem.,282:28175-88.

12-Ouchi N, Parker JL, Lugus JJ, Walsh K(2011): Adipokines in inflammation and metabolic disease. Nat Rev Immunol.,11(2):85e-97.

13- Cohn JN(1999): Vascular wall function as a risk marker for cardiovascular disease. J Hypertens.,17:S41e-4

14-Van Popele NM, Grobbee DE, Bots ML(2001): Association between arterial stiffness and atherosclerosis: The Rotterdam study.Stroke,32:454-460.

15- Cruickshank K, Riste L, Anderson SG, Wright JS, Dunn G,Gosling RG(2002): Aortic pulse-wave velocity and its relationship to mortality in diabetes and glucose intolerance: An integrated index of vascular function? Circulation, 106:2085e-90

16-Zabel BA, Silverio AM, Butcher EC (2005): Chemokine-like receptor 1 expression and chemerin-directed chemotaxis distinguish plasmacytoid from myeloid dendritic cells in human blood. J Immunol.,174:244-51.

17-ErifiliHatziagelaki, Christian Herder, Anastasia Tsiavou , Tom Teichert, AthinaChounta , Peter Nowotny, Giovanni Pacini , George Dimitriadis , Michael Roden(2015): Serum Chemerin Concentrations Associate with Beta-Cell Function, but Not with Insulin Resistance in Individuals with non-alcoholic fatty liver disease (NAFLD), plos one, 10(5).

18- Thomas L (1998): Clinical Laboratory Diagnostics, 1st ed. Frankfurt: TH-Books Verlagsgesellschaft, 131 -137.

19-Richmond N(1973): Preparation and properties of a cholesterol oxidase from Nocardia sp. and its application to the enzymatic assay of total cholesterol in serum.Clin .Chem., 19:1350-1356**.**

20-Assmann G (1979): HDL-cholesterol precipitant. Randox Labs. Ltd. Crumlin Co. Antrim, N. Ireland. Internist., 20: 559-564.

21- Okada M,MatsuiH,ItoY,FujiwaraA,Inano K(1998):low-density lipoprotein cholesterol can be chemically measured.J Lab.Clin.Med.,132:195-201.

22-Jacobs NJ and Van Denmark PJ (1960): Triglyceridliquicolor,ARCHBiochem Biophys,88: 250-255.

23-Trivelli LA, Ranney HM, and Lai HT(1971): Hemoglobin components in patients with diabetes mellitus,New Eng. J. Med.,284,353.

24-Aronis KN, Sahin-Efe A, Chamberland JP, Spiro A, Vokonas P, Mantzoros CS (2014): Chemerin levels as predictor of acute coronary events: A case-control study nested within the veterans affairs normative aging study. Metabolism,63 (6):760-6

25-HedlundP(1961): Clinical and experimental studies on C-reactive protein (acute phase protein). Thesis Acta Med Scand., 128 (361):1-71.

26-Mogensen CE, Schmitz A(1988): Microalbumin for the quantitative determination of albumin in urine. Med. Clin. North Amer.,72:1465-92.

27-Iciar Martín-Timón, Cristina Sevillano-Collantes, Amparo Segura-Galindo, Francisco Javier del Cañizo-Gómez(2014): Type 2 diabetes and cardiovascular disease: Have all risk factors the same strength?**,** World J Diabetes,15(4): 444-470

28- El-Mesallamy HO, El-Derany MO and Hamdy NM(2011): Serum omentin-1 and chemerin levels are interrelated in patients with Type 2 diabetes mellitus with or without ischaemic heart disease. Diabet Med.,28 (10):1194-200.

29- Hu W and Feng P(2011): Elevated serum chemerin concentrations are associated with renal dysfunction in type 2 diabetic patients. Diabetes Res ClinPract., 91(2):159.

30- Tarek M Ali , Khalid Al Hadidi (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 University journal o f basic and Applied Sciences, (2) 86-95.

31- Sell H,Laurencikiene J, Taube A,Eckardt K, Cramer A,Horrighs A,Arner P and EckelJ(2009): Chemerin Is a novel adipocyte-derived factor inducing insulin resistance in primary human skeletal muscle cells. Diabetes,58(12): 2731-2740.

32-Takahashi M, Takahashi Y, Takahashi K,Zolotaryov FN, Hong KS,Kitazawa R,Iida K,OkimuraY(2008): Chemerin enhances insulin signaling and potentiates insulin-stimulated glucose uptake in 3T3-L1 adipocytes. FEBS Lett.,582(5): 573-578.

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

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

35- Tan B K , ChenJ,Farhatullah S,Adya R, KaurJ,Heutling D, Lewandowski K C , O'Hare J P,Lehnert H and Randeva H S(2009): Insulin andmetformin regulate circulating and adipose tissue chemerin. Diabetes,58 (9) 1971-1977.

36- Ying Wang andDongying Zhang (2014): Serum chemerin levels and risk of coronary atherosclerosis in early-onset coronary artery disease of chinese population. Journal of the American College of Cardiology,64(16):0735-1097.

37-Xiuying Gao, ShuhuaMi, Fuzhuang Zhang, Fengying Gong, Yongqiang Lai, Feng Gao, Xiaoxia Zhang, Linjie Wang and Hong Tao(2011): Association of chemerin mRNA expression in human epicardial adipose tissue with coronary atherosclerosis. Cardiovascular Diabetology,10:87

38- Liang Z , Yu K , Wu B , Zhong Y , Zeng Q(2015): The elevated levels of plasma chemerin and C-reactive protein in patients with acute coronary syndrome. Chinese Journal of Cellular and Molecular Immunology, 31(7):953-956.

39-Wittamer V, Franssen JD, Vulcano M, Mirjolet JF, Le Poul E, Migeotte I,Brézillon S, Tyldesley R, Blanpain C, Detheux M, Mantovani A, SozzaniS,Vassart G, Parmentier M, CommuniD(2003): Specific recruitment of antigenpresenting cells by chemerin, a novel

processed ligand from human inflammatory fluids. J Exp Med.,198:977–985.

40- Kim HM, Lee BW, Song YM, Kim WJ, Chang HJ, Choi DH, Yu HT, Kang E, ChaBS, Lee HC(2012): Potential association between coronary artery disease and the inflammatory biomarker YKL-40 in asymptomatic patients with type2 diabetes mellitus. CardiovascDiabetol., 11:84.

41- Osman Mona M, Abd El-mageedAbeer I, El-hadidiEman,Shahin Rania S K, and Abdel MageedNanees A(2012): Clinical Utility of serum chemerin as a novel marker of metabolic syndrome and Type 2 diabetes mellitus. Life Science Journal,9(2):1098-1108

42-Qingwei Ji, Yingzhong Lin, Zhishan Liang, Kunwu Yu, Yuyang Liu, Zhe Fang, Ling Liu, Ying Shi,Qiutang Zeng, Chao Chang, Meng Chai and YujieZhou(2014): Chemerin is a novel biomarker of acute coronary syndrome but not of stable angina pectoris. Cardiovascular Diabetology,13:145

43- Yu-Jin Hah, Nam-Keong Kim, Mi-Kyung Kim, Hye-Soon Kim, Seung-Ho Hur, Hyuck-Jun Yoon, Yoon-Nyun Kim, Keun-Gyu Park(2011): Relationship between chemerinlevels and cardiometabolicparameters and degree of coronary stenosis in koreanpatients with coronary artery disease.Diabetes Metab J.,35:248-254

44-Wenchao Hu, Ping Feng (2011):Elevated serum chemerin concentrations are associated with renal dysfunction in type 2 diabetic patients.Diabetes Research and Clinical Practice, 91(2): 159–163

45-Christiane Rüster and GunterWolf (2013): Adipokines promote chronic kidney disease Nephrol Dial Transplant,28 (4): iv8–iv14.

46-Yan Q, Zhang Y, Hong J, Gu W, Dai M, Shi J, Zhai Y, Wang W, Li X, Ning G(2012): The association of serum chemerin level with risk of coronary artery disease in Chinese adults. Endocrine, 41:281–288.

47- Lin X, Tang X, Jiang Q, Liu Q, Lin Z, Lin J, Chen L, Hong H (2012): Elevated serum chemerin levels are associated with the presence of coronary artery disease in patients with type 2 diabetes. Clin Lab., 58:539–544

48-Kadoglou Nikolaos PE, TahmatzidisDimitrios K, Giannakoulas Christos, KapelouzouAlkistis, GkontopoulosArgirios, Parissis John, Lampropoulos Stylianos, Kottas George (2015): Serum levels of novel adipokines, omentin-1 and chemerin in patients with acute myocardial infarction: kozani study Journal of Cardiovascular Medicine,16 (5) : 341–346.

Table 1:Laboratory assessments of chemerin in the different studied groups

Parameters	Control subject (C)	Diabetic subject (D)	Cardio –diabetic subject (CD)	P1	P2	P3
Chemerin (ng/l)	28.80± 6.82	57.65± 5.69	93.97 ± 26.62	< 0.0001	< 0.0001	< 0.0001

P1:- Diabetic group compared to control group.
P2:- Cardio-diabetic group compared to control group.
P3:- Cardio-diabetic group compared to diabetic group

Table 2: Correlation between serum chemerin concentration and metabolic parameters in the different studied groups

Parameters	Serum chemerin level in control groups		Serum chemerin level in diabetic group		Serum chemerin level in cardio-diabetic groups	
	r	p	r	p	r	p
Cholesterol(mg/dl)	0.258	0.271	0.416	0.007**	0.579	0.0001**
TG (mg/dl)	0.215	0.362	0.490	0.001**	0.601	<0.0001**
HDL (mg/dl)	-0.010	0.966	-0.291	0.062	-0.067	0.671
LDL (mg/dl)	0.026	0.912	0.318	0.045*	0.062	0.694
CRP(mg/l)	0.278	0.234	0.761	<0.0001**	0.616	<0.0001**
FBG(mg/dl)	0.049	0.835	0.802	<0.0001**	0.432	0.005**
HBA1C (%)	0.211	0.370	0.340	0.031*	0.324	0.040*
Micro-alb (mg/ml)	-0.275	0.239	-0.349	0.026*	0.397	0.011*

r: Correlation coefficient, *P<0.05, **P<0.01, not significant(P >0.05)

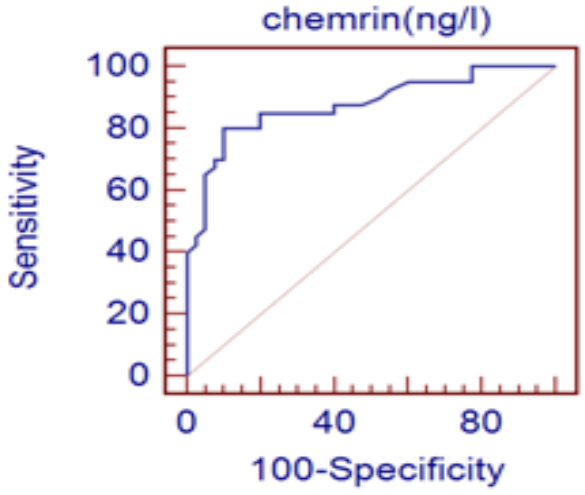

Fig.1:- ROC curves for differentiation between diabetic and cardio-diabetic subjects by chemerin (P=0.0001)