Evaluation of Chemerin in Diabetic Type 2 Patients with Metabolic Syndrome in both Gender



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ABSTRACT

Aims Chemerin abnormal level represents a risk indicator of visceral fat increase. It has a role in the incidence of inflammation, insulin resistance, metabolic syndrome, obesity, and diabetes. This study aimed to evaluate Chemerin level in diabetic type 2 patients with metabolic syndrome in both Genders.

Materials & Methods This study was carried out on the patients referred to the Al-Yarmouk Teaching Hospital in 2021-2022. 88 participants were selected by random sampling method and were divided into two groups including T2DM patients with metabolic syndrome in the experience group (n=55) compared with healthy subjects in the control group (n=38). Triacylglycerol (TG), High-Density Lipoprotein-Cholesterol (HDL-c), Obesity (BMI), serum Chemerin, Hypertension (SBP), age, Fasting Blood Glucose (FBG), and Glycated Haemoglobin (HbA1C) were measured in the two studied groups. Data were analyzed using T-test through SPSS 21 Software.

Findings A significant difference was observed between the levels of BMI, SBP, FBG, TG, HDL-c, Chemerin weight, DBP, and HbA1c in the studied groups (p=0.05). The rate of WC and HDL-c was higher in the females than in males in the experience group. While, there was a significant increase in the rates of SBP, FBG, TG, and Chemerin in males than females. A positive correlation coefficient was observed between age, SBP, WC, BMI, FBG, TG, and HbA1c with Chemerin level in the experience group.

Conclusion An increase in Chemerin level is associated with a high level of triglycerides during the onset of symptoms of metabolic syndrome, age, and gender, which affect the increase of adipokine.

Keywords Metabolic Syndrome; Angiogenesis; T2DM; Aging Process; Adipokines

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Metabolic syndrome (MetS) is a collection of multiple risk factors, including dyslipidemia, abdominal obesity, elevated blood pressure, and abnormal glycemia. Metabolic syndrome is also associated with an increased risk of cardiovascular morbidity, type 2 diabetes, and mortality ^[1]. Furthermore, there is an association between MetS and increased total cancer mortality ^[2]. The incidence of metabolic syndrome and its underlying pathophysiological mechanisms are still not fully understood. It is believed that the occurrence of MetS arises from the complex relationship between genetic and environmental factors

Pathophysiological affliction creates a noticeable shift in metabolic mechanisms. These changes are attributed to several chronic diseases for instance chronic inflammation, oxidative stress, blood pressure, and hypertriglyceridemia. Disorders in cellular metabolic pathways, which is also called metabolic syndrome (MetS) stemming, especially from the abnormalities in carbohydrates' metabolic would attract the attention of the risk factors for type 2 diabetes, such as obesity, insulin resistance, and fatty liver [3]. Other concepts used to describe MetS are mentioned as the new insulin resistance syndrome, World syndrome, metabolic syndrome, fatal Quaternary Syndrome, and Dyslipidemia Syndrome ^[4]. The main features of diagnosing cases of metabolic syndrome are the combination of several metabolic abnormalities and prominent symptoms ^[5], such as high blood pressure, obesity, and hyperglycemia, contrary to Liver steatosis, polycystic ovary syndrome, and hyperuricemia that cannot be considered part of the criteria for individuation the status [6]. Recent studies provide new insights as they state that chronic exposure to excess calorie activities arises from the role of adipose tissue for energy regulation and endocrine stimulation [7].

Chemerin is a novel cytokine mainly secreted from white adipose tissues, which was initially considered a chemotactic factor generated in inflammatory conditions, but more recently, it was reported more as an adipokine regulating the metabolism of adipose and balance of energy [8].

Chemerin appears to be present most abundantly in adipose tissue (produced by adipocytes) and the liver but is also present in multiple tissues. In cases of overweight, the adipose tissues secrete adipokines, its productions represent an instance between obesity and the dangerous symptoms of metabolic syndrome ^[9]. The regeneration of adipokines is an abnormal action that occurs when increasing visceral fat, thus contributing to inflammation; it is also involved in many obesity-related problems such as insulin resistance, atherosclerosis, and dyslipidemia ^[10]. A recent population-based study revealed that increased Chemerin levels were associated with

inflammation and metabolic syndrome even after adjustment for waist circumference [11]. More importantly, Chemerin has been indicated to be an independent predictor of type 2 diabetes mellitus (T2DM) and cardiovascular event risk [12, 13].

In the past ten years, many studies have shown that Chemerin and its receptors are emitted from white adipose tissue in animal models, and levels of Chemerin-increased obesity in lab rats and patients ^[14-20]. The reports of international organizations relevant show that metabolic syndrome disorder precedes the risk of developing diabetes by approximately 5 years [21]. After many years of diabetes infestation, the patient suffers from complications that lead to organopathy and vascular collapse. Foremost the set of changes was the formation of protein bodies that had pathological features on the walls of blood vessels ^[22], so that it caused the thickening of the basement membrane on microvessels, enlargement of the vessel, and inflammations in those parts caused by the oxidative that occurs, which accelerates stress the complications of the condition ^[23]. Obesity could be stake by reducing weight to normal limits which was the best solution used as a therapeutic and preventive style to range metabolic syndrome and avoid developing related diseases such as type 2 diabetes, as well as avoiding cardiovascular diseases, kidney diseases, liver, and dementia [24].

This study aimed to evaluate Chemerin level in diabetic type 2 patients with metabolic syndrome in both Genders.

Materials and Methods

This study was carried out on the patients who were referred to the al Yarmouk Teaching Hospital in 2021-2022. 88 participants were selected by simple random sampling method. The subjects were divided into two groups including T2DM patients with metabolic syndrome in experience group (n=55) compared with healthy subjects in the control group (n=38). Each group included 25 females and 25 males. The group of T2DM patients with MS included those who fulfilled the IDF criteria ^[25]. MS patients were defined as having at least three out of the five following criteria:

1) Obesity; BMI≥30

2) Waist circumferences' WC.

3) Abnormal glucose homeostasis, such as fasting glucose above 100 mg/dl.

4) Hypertension; systolic blood pressure (SBP)≥ 30mmHg or DBP≥85mmHg.

Dyslipidemia such as triacylglycerol 5) $(TAG) \ge 150 \text{ mg/dl}$, and low HDL-C<40 mg/dl.

The anthropometric characteristics of the patients were measured using the determination of blood pressure and body mass index. Blood pressure was measured according to the guidelines regulated by WHO [26]. Body mass index was calculated by dividing 411

subjects' weight (Kg) by their height (m2). Obesity was defined as BMI≥30Kg/m2^[27].

Other factors were calculated as follows:

- Determination of Fasting Blood Glucose (FBG): Glucose was determined, by using the enzymatic colorimetric method (GOD-POD)^[28].

- Determination of Glycated Haemoglobin (HbA1C): The Bio-Rad VARIANT Haemoglobin A1cprogramme utilizes principles of ion-exchange high-performance liquid chromatography (HPLC) for automatic and accurate separation of HbA1c^[28].

- Determination of Serum Triacylglycerol (TAG): Serum TAG was measured by TAG kit, using an enzymatic method ^[29].

- Determination of Serum High-Density Lipoprotein-Cholesterol (HDL-C): Serum HDL-C was measured by HDL-C kit, using an enzymatic method ^[30].

Hormonal Assessment

Determination of Serum Chemerin: Serum Chemerin concentrations were measured by the ELISA kit.

Data were analyzed using T-test at a significance level of p<0.05 through SPSS 21 Software for comparison of the studied factors between two control and experience groups and between males and females in the experience group.

Findings

A significant difference was observed between weight, DBP, and HbA1c in the studied groups (p=0.05), showing an increase in the mentioned factors in diabetic patients with metabolic syndrome (Table 1). There was no significant difference in age and height values between the experience and control groups (p>0.05; Table 1).

There was a significant difference between the levels of BMI, SBP, FBG, TG, HDL-c, and Chemerin, in the studied groups (p<0.05; Table 1).

 Table 1) Comparison of studied factors between experience and control groups

| Parameters | Experience group (n=50) | Control group (n=38) | p- value |
|--------------------------|----------------------------|-----------------------------|-------------|
| Age (years) | 40.92±3.15 | 38.02±2.41 | 0.816 |
| Weight (kg) | 71.70±7.20 | 57.60±8.10 | 0.05 |
| Height (cm) | 148.70±7.50 | 146.50±10.30 | 0.21 |
| BMI (kg/m ²) | 32.56±2.82 | 23.10±5.10 | 0.01 |
| WC (cm) | 94.60±3.76 | 75.70±2.50 | 0.04 |
| SBP (mmHg) | 160.0±13.0 | 130.0±10.0 | 0.01 |
| DBP (mmHg) | 95.0±8.5 | 82.0±8.0 | 0.05 |
| FBG (mg/dl) | 201.15±9.56 | 88.31±7.21 | 0.01 |
| HbA1c (%) | 9.12±1.35 | 4.71±1.06 | 0.05 |
| TG (mg/dl) | 189.76±11.12 | 97.11±5.55 | 0.001 |
| HDL-C (mg/dl) | 36.67±4.10 | 55.11±6.71 | 0.001 |
| Chemerin (ng/ml) | 33.15±5.61 | 18.60±6.71 | 0.001 |

Comparison of the studied factors between the subjects according to gender showed a significance different in WC and HDL-c between the male and females (p<0.05; Table 2), so that the rate of WC and HDL-c were higher in the females. While, there was a significant increase in the rates of SBP, FBG, TG, and Chemerin in males compared to females.

 Table 2) Comparison of studied factors between males and females in the experience group

| Parameters | Male (n=25) | Female (n=25) | p- value |
|--------------------------|--------------------|---------------|-------------|
| Age (years) | 48.00±2.55 | 38.92±3.11 | 0.215 |
| Weight (kg) | 82.70±8.29 | 77.11±6.11 | 0.081 |
| Height (cm) | 188.20±4.10 | 176.50±5.41 | 0.411 |
| BMI (kg/m ²) | 32.41±1.56 | 27.23±2.85 | 0.05 |
| WC (cm) | 85.60±2.06 | 95.23±3.06 | 0.05 |
| SBP (mmHg) | 165.0±5.0 | 140.0±5.0 | 0.05 |
| DBP (mmHg) | 90.0±5.0 | 85.0±5.0 | 0.106 |
| FBG (mg/dl) | 221.45±11.10 | 164.01±10.11 | 0.05 |
| HbA1c (%) | 10.00±2.02 | 8.31±2.36 | 0.06 |
| TG (mg/dl) | 195.22±30.00 | 175.41±21.00 | 0.01 |
| HDL-C (mg/dl) | 34.00±3.25 | 40.26±4.28 | 0.05 |
| Chemerin (ng/ml) | 29.40±2.01 | 21.55±2.36 | 0.01 |

There was no correlation between Chemerin with DBP in T2DM with metabolic syndrome. A positive correlation coefficient was observed between age, SBP, WC, and HbA1c with Chemerin level. Also, a positive significant correlation was observed between BMI, FBG, and TG with Chemerin level. The correlation coefficient between the Chemerin level and HDL-C was negative (Table 3).

| Table 3) Correlation coefficient of Chemerin level with | different |
|---------------------------------------------------------|-----------|
| factors in T2DM with metabolic syndrome | |

| Parameters | Chemerin |
|------------|----------|
| Age | 0.339* |
| SBP | 0.311* |
| DBP | 0.223 |
| WC | 0.312* |
| BMI | 0.581** |
| FBG | 0.796** |
| HbA1c | 0.303* |
| TG | 0.551** |
| HDL-C | -0.420** |

*Correlation is significant at the 0.05 level; **Correlation is significant at the 0.01 level

Discussion

This study aimed to evaluate Chemerin levels in diabetic type 2 patients with metabolic syndrome in both Genders.

Chemerin serum concentrations are elevated in insulin-resistant, obese, and inflammatory states in vivo and are an obvious cause of insulin resistance ^[31]. Obesity induces inflammation in adipose tissue and since Chemerin is a pro-inflammatory cytokine that recruits and activates immune cells and promoting contributes to inflammation bv macrophage adhesion to vascular cell adhesion molecule-1 (VCAM-1) and fibronectin, it may link obesity and inflammation [32]. Muscle insulin resistance is a major risk factor for the pathogenesis of type 2 diabetes. Therefore, a possible relation of Chemerin to inflammatory proteins and insulin resistance in obesity and type 2 diabetes is suggested. Chemerin is also proven to be associated with components of metabolic syndrome and it may play a role in the pathophysiology of this condition [33].

The findings of this study showed a significant correlation coefficient between Chemerin levels with age, SBP, WC, HbA1c, BMI, FBG, and TG. In accordance

Iranian Journal of War and Public Health

AL-Husaini et al.

412

with the findings of this study, Perumalsamy *et al.* indicated increased levels of Chemerin in patients with obesity, diabetes, and cardiovascular diseases [³⁴].

Blood pressure is closely related to metabolic changes and occurs in obesity because of altered lipid excretion and metabolic diseases and disorders [35]. When insulin resistance occurs, the metabolism is directly affected, and there is an excessive increase in the production of VLDL, which can be calculated through a simple equation [36]. VLDL is excreted from the liver and impedes the breakdown of apoB protein, thus raising TG values. The high percentage of VLDL reduces the secretion of lipoproteins lipase, and then it is observed that the rates of TG increase as a result of filling the body with such particles. The values of HDL-C begin to minify dangerously [37], offset by a sharp rise in the number of low-density lipoproteins (LDL-C) [38]. The tissues full of mitochondria are characterized by the vitality in addition to an increase in metabolic reactions in them. The most prominent tissues that possess such characteristics are adipose tissues, which secreted several adipokines and cytokines when diseases accompanied by infections occur [21]. Pro-inflammatory usually accompanies the conditions of obesity, atherosclerosis, and diabetes, in which levels of pro-inflammatory adipokines are elevated and significantly correlated with high BMI and obesity. Chemerin is the adipokine that is associated with obesity [39] and inflammation in humans; therefore, it has a role in glucose metabolism and lipid formation [40-42]. Studies have proven an existing raised in the proportion of Chemerin among people with severely overweight and people with diabetes; further, it is positively associated with the occurrence of metabolic syndrome ^[43]. Chemerin contributes to the undesirable changes that accompany obesity diseases [44]. It is described as one of the adipokines that are traced during the syndrome [45, 46], and secreted by adipose tissue also its had been considered an inflammatory indicator ^[47]. Findings showed the relation between age and Chemerin level. Some studies revealed that older patients with T2DM have a higher Chemerin level than those who are in middle age with the same health problems. In accordance with our findings, Coimbra et al. [48], confirmed that Chemerin increases insulin resistance, which increases with aging.

Interestingly, many studies showed that Chemerin gene expression and its levels positively correlated with higher BMI and obesity-related biomarkers ^[33, 44, 50]. On the other hand, Sell *et al.* ^[49] mentioned the effect of Chemerin, which causes inflammation and angiogenesis in the adipose tissues, eventually the occurrence of obesity. The association between obesity and metabolic syndrome has been reported in many studies ^[51], confirmed that Chemerin is a marker of obesity and metabolic syndrome. Another study showed that the release of Chemerin from the adipose tissue in obese individuals was higher than that in the normal controls and it was positively correlated with BMI, waist-hip ratio, and fat cell mass ^[33]. It is noted from Table No. 2 that WC for females is higher than for males, and the level of the Chemerin is higher than for males, so that this rise is explained by the increase in the size of the waist as a result of the increased formation of visceral lipids secretions. In addition to the 50 years females, most TG is not fully exploited hormonally as a result of the cessation of pregnancy and fertilization at this age, thus the trend is towards adipose tissues to store them in the abdominal area specifically, which indicates the existence of statistical significant differences between the gender; an increase in lipids in this region leads to a clear increase in the level of Chemerin.

Conclusion

Obesity is a major cause of the symptoms of metabolic syndrome and the related diseases, most notably diabetes. The emergence of high levels of Chemerin is evidence of a close association of this adipokine on the increase in inflammation and angiogenesis secretions, the direct correlation of age and gender was observed on the increase in the mentioned adipokine levels.

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AL-Husaini et al.

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413

Evaluation of Chemerin in Diabetic Type 2 Patients with Metabolic Syndrome in both Gender

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