Acta Biochimica Iranica 1(2): 65-70, 2023

Review Article

The relationship between chemerin gene polymorphism and the incidence of various diseases

Sahar Mazloomi[1], Mohammad Taghi Goodarzi[2*]

[1] *Department of Clinical Biochemistry, Medical School. Hamadan University of Medical Sciences, Hamadan, Iran*
[2] *Department of Biochemistry, Shahrood Branch, Islamic Azad University, Shahrood, Iran*

Article info:
Received: 01 June 2023
Revised: 19 July 2023
Accepted: 21 July 2023

[*] **Corresponding Author:**

Mohammad Taghi Goodarzi, Department of Biochemistry, Shahrood Branch, Islamic Azad University, Shahrood, Iran

Email: mtgoodarzi@yahoo.com

ABSTRACT

Adipose tissue is recognized as an endocrine organ that influences the health status of other tissues by releasing various adipokines. Chemerin is one such adipokine, and its serum level exhibits a positive correlation with the amount of fat tissue and obesity. Certain genetic polymorphisms of chemerin, namely rs17173608, rs1799983, rs693, rs4721, and rs3735167, are known to be associated with diseases such as diabetes, gestational diabetes mellitus (GDM), obesity, insulin resistance (IR), cardiovascular diseases, metabolic syndrome (MetS), end stage renal disease (ESRD), polycystic ovary syndrome (PCOS), and rheumatoid arthritis (RA). Existing data suggest that chemerin is also associated with inflammatory diseases. This review focuses on the association between the genetic variants or polymorphisms of chemerin and some pathological states.

Keywords: Chemerin, gene polymorphism, diabetes, adipokines

Abbreviations: CAD: coronary artery disease; CMKLR1: chemokine-like receptor 1; CVD: cardiovascular disease; ESRD: End stage renal disease; GDM: Gestational diabetes mellitus; IR: Insulin resistance; MetS: metabolic syndrome; PPARγ: Peroxisome proliferator-activated receptor γ, PCOS: Polycystic ovary syndrome; RARRES2: Retinoic acid receptor responder protein 2; T2D: type 2 diabetes; TIG2: tazarotene-induced gene 2

Use your device to scan and read the article online

Citation: Mazloomi S, Goodarzi MT. The relationship between chemerin gene polymorphism and the incidence of various diseases. Acta Biochimica Iranica. 2023;1(2):65-70.

https://doi.org/10.18502/abi.v1i2.14102

Introduction

Adipokines, also known as adipocytokines, are bioactive molecules synthesized and secreted by adipose tissue. These molecules play a crucial role in metabolic homeostasis and exhibit several activities, including anti-atherogenic and anti-inflammatory properties (1). Consequently, disorders in the synthesis, secretion, and presence of polymorphisms of these molecules can significantly influence various pathological states such as insulin resistance, type 2 diabetes (T2D), metabolic syndrome (MetS), and cardiovascular diseases (CVD) (2).

Chemerin is an adipokine also recognized as RARRES2 (retinoic acid receptor-responding protein 2). It acts as a chemoattractant factor for immune system cells. This molecule and its receptor are expressed in white, visceral, and subcutaneous adipose tissues of animal models and humans (3). Given that chemerin induces angiogenesis of endothelial cells, it may contribute to endothelial dysfunction. Furthermore, chemerin can

Table 1: Summary of the reported articles regarding to chemerin polymorphism in different disease.

Authors	SNP	Disease	Correlation	Ref
Dahpy MA. et al	rs17173608	T2D patients	positive	(19)
Olt S. et al	rs17173608	T2D patients	positive	(20)
Abdelhamid AM. Zaafan MA	rs17173608	T2D patients	positive	(21)
Perumalsamy S. et al	rs17173608	T2D, insulin resistance and the severity of CAD	positive	(22)
Hasanvand Z. et al	rs17173608	GDM	not significant	(29)
Hasanvand Z. et al	rs4721	GDM	positive	(29)
Batista A. et al	rs1799983, rs693	MetS	positive	(34)
Hashemi M. et al	rs17173608	MetS	positive	(35)
Mehanna ET. et al	rs17173608	MetS	positive	(36)
Kohan L. et al	rs17173608	Obesity	positive	(41)
Nomani H. et al	rs17173608	ESRD	negative	(44)
Khaled Y. et al	rs17173608	diabetic nephropathy	positive	(46)
Er LK . et al	rs3735167	CAD	positive	(17)
Er L-K. et al	rs3735167	CAD	not significant	(49)
Movahed Z. et al	rs17173608	PCOS	positive	(51)
Jasim R. et al	rs17173608	PCOS	positive	(52)
Wahba AS. et al	rs17173608	RA	Positive	(56)

activate inflammatory responses and induce oxidative stress in adipose tissue, leading to insulin resistance (4-6). Recent studies have also highlighted an important role for chemerin in cancer. However, its association with cancer is controversial; chemerin has been shown to have both anti-tumor and tumor-promoting properties (7, 8).

In addition to changes in the serum level of chemerin in different diseases and its association with their pathogenesis, the genetic variants of chemerin can also be reported to be related to some diseases. This review focuses on different genetic variants or polymorphisms of chemerin that are reported to have an association with some pathological states. Table 1 shows the reported articles on gene polymorphisms of chemerin in different diseases.

Chemerin gene and structure

Retinoic acid receptor responder protein 2 (RARRES2), also known as tazarotene-induced gene 2 (TIG2) protein or chemerin, is a hormone derived from white adipose tissue. It is the product of the chemerin gene, located on chromosome 7q36.1, which contains 6 exons and 5 introns. The expression of this gene is up-regulated under the influence of RAR β/γ-selective anti-psoriatic agent or tazarotene (9).

The gene expression produces chemerin proteins containing 163 amino acids. A proteolytic processing occurs at its C-terminus, leading to an upregulation of its activity. It is secreted as an inactive form, prochemerin (chem163S), which is later processed through extracellular proteases to produce active and inactive forms (10). Five amino acid residues from the C-terminus of chem163S are removed by plasmin, a fibrinolytic enzyme, generating chem158K with modest activity. Furthermore, carboxypeptidase B2 or carboxypeptidase N cleaves chem158K to produce chem157S, which is fully active (11).

Chemerin is a single polypeptide with a molecular weight of 18-kDa. It is synthesized in pro-protein form and then undergoes post-transitional c-cleavage to produce an active form. Different isoforms with varying numbers of amino acids have been reported for chemerin, including A155, S157, and K158 (12-14).

At least three receptors are known for chemerin: chemokine-like receptor 1 (CMKLR1) or ChemR23, GPR1, and CCRL2. The expression of these chemokine receptors has been reported in normal and cancerous tissues, as well as in various immune cells. Evidence suggests that tumor cells reduce chemerin expression to evade immune cells (14).

Genetic polymorphisms play significant roles in disease susceptibility and phenotype and severity of diseases. Reports indicate that single nucleotide polymorphisms of the chemerin gene are associated with some diseases. The concentration of chemerin in human serum is moderately heritable; about 16-25% of variations are related to genetic factors (15). This review presents and discusses the genetic variants of chemerin in different diseases or pathological states.

Diabetes

Several reports have indicated an association between chemerin and obesity, metabolic syndrome, insulin resistance, and diabetes. Consequently, it is plausible that different polymorphisms of this gene may be related to these conditions.

Although information in this field is limited, gene polymorphisms of chemerin may mediate glucose-mediated diseases (16). Some studies have shown that single nucleotide polymorphisms of the RARRES2 gene are associated with an increased risk of T2D

and CAD (17, 18). In a study conducted in Egypt, the TT rs17173608 genotype was more frequent in T2D patients than in non-diabetic subjects (19). However, a study in Turkey found no statistical difference in the frequency of alleles in diabetic and non-diabetic groups (20). In T2D subjects, the rs17173608 polymorphism of chemerin is associated with an increase in its serum concentration, potentially affecting the expression of this gene (21). In normal weight T2D patients, the rs17173608 polymorphism is a significant predictor of insulin resistance (IR) and coronary artery disease (CAD) severity (22).

Gestational Diabetes

Gestational diabetes mellitus (GDM) arises due to disruptions in carbohydrate metabolism during pregnancy, with prevalence rates reported to be as high as 27% (23, 24). Chemerin, an adipokine involved in glucose metabolism, can lead to various complications such as diabetes, obesity, and metabolic syndrome when dysregulated. Natural pregnancy aids carbohydrate metabolism by increasing the level of chemerin. However, an acute decrease in chemerin levels in women with gestational diabetes, and the continuation of this decrease, may lead to insulin resistance, glucose intolerance, and a high risk of T2D associated with gestational diabetes (25).

The serum level of chemerin in pregnant women with gestational diabetes is significantly higher than that of healthy pregnant women, and it has a positive relationship with risk factors such as increased triglycerides and insulin resistance (26). However, some studies have shown no change in the concentration of chemerin in gestational diabetes (27).

The association of genetic variations in the chemerin gene with its lower concentration and Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) has been reported. These variants have been shown to prevent the occurrence of GDM in Chinese women (28). In a study conducted in Iran, results showed that although the rs17173608 genotype is not able to predict the risk of GDM; rs4721 has a strong association with the risk of diabetes (29).

Insulin Resistance

While the majority of studies have shown a positive correlation between chemerin concentration and glycaemia, there are differing opinions in this field (16). Some studies have suggested chemerin as a valuable biomarker of insulin resistance (30). In a study conducted in Malaysia, rs17173608 was reported as a significant predictor of insulin resistance and the severity of CAD (22).

Metabolic Syndrome

Metabolic syndrome (MetS) is a cluster of disorders that includes hyperglycemia, abdominal obesity, hypertension, and dyslipidemia. The prevalence of MetS is about 25% among adult subjects and is increasing worldwide (31-33). Evidence suggests that chemerin plays a crucial role in regulating metabolism in humans. Moreover, a positive correlation has been reported between local and circulating levels of chemerin and body mass index (14, 34).

A significant association was found between high levels of chemerin and the r693 genetic polymorphism of the ApoB gene (34). Furthermore, the coincidence of the AA genotype of rs693 and GT+TT of rs1799983, compared to the wild genotype, was associated with a two-fold increase in chemerin concentration (34). A significant association of chemerin rs17173608 polymorphism with MetS has also been reported in southeast Iran (35). Additionally, MetS in Egyptian females was associated with the minor allele of chemerin rs17173608 polymorphism; whereas the minor allele of vaspin rs2236242 polymorphism plays a protective role against metabolic syndrome (36).

Obesity

Obesity is a significant health challenge globally and is one of the primary causes of various pathological states such as CVD, T2D, oxidative stress, and inflammation (37, 38). Obesity induces metabolic disorders in adipose tissue, resulting in an imbalance in the secretion capacity of adipokines (39).

Peroxisome proliferator-activated receptor γ (PPARγ) is a member of the nuclear hormone receptor family. PPARγ plays a crucial role in biochemical processes such as insulin sensitivity, adipocyte differentiation, fatty acid metabolism, and energy utilization. At least three isoforms are recognized for PPARγ, including PPARγ1, PPARγ2, and PPARγ3; PPARγ2 is primarily expressed in adipose tissue (24, 40). Interestingly, it has been shown that the Pro12Ala polymorphism in the PPARγ2 gene is associated with chemerin levels in non-obese individuals. Moreover, in subjects with the wild type PP genotype, chemerin concentration was lower compared to that of obese subjects with heterozygous PA and homozygous AA genotypes (40).

The results of a study conducted in Iran revealed that the genotype of rs4721 could contribute significant risk to GDM while the genotype of rs17173608 could not predict the risk of GDM (41).

End stage renal disease

End stage renal disease (ESRD) is the final stage of chronic kidney disease, characterized by a reduction in glomerular filtration rate. Several metabolic disorders occur in ESRD. In addition to environmental factors, genetic factors are believed to play a significant role in

the development of ESRD (42, 43).

In a case-control study conducted in an Iranian population, the association of chemerin polymorphism with ESRD was examined (39). This study detected the chemerin rs17173608 T/G genetic variant using tetra arms PCR. The results indicated that the T/G phenotype in the chemerin gene has a protective role against susceptibility to ESRD. It was concluded that the G allele, compared to the T allele, decreases the risk of ESRD (44). Another study showed that a high level of chemerin is associated with renal failure and prediction of cardiovascular events, and polymorphisms (rs55709438, rs2444030, and rs3098423) located at chromosomal region 15q15-23 might affect chemerin concentration (45).

One of the causes of kidney diseases is long-term and uncontrolled diabetes. An increase in the concentration of chemerin is one of the indicators of diabetic nephropathy; importantly, the chemerin polymorphism of rs17173608 has been reported to be related to susceptibility to diabetic nephropathy (46).

Coronary Artery Disease

Cardiovascular disease (CVD) is recognized as the leading cause of death worldwide. Obesity, a significant risk factor for CVD, is closely linked to the expression of adipokines such as chemerin, which reflects the volume of epicardial fat and can serve as a predictor of CVD (48).

The SNP rs3735167 is a notable variation in the RARRES2 gene. A study conducted in a Taiwanese population revealed that common variations near or within the RARRES2 gene coincided with plasma concentrations of chemerin (17). However, another study on patients with CAD suggested that the impact of RARRES2 polymorphisms was not substantial enough to alter the risk of mortality and secondary outcomes (17). In the same Taiwanese population, serum chemerin concentration predicted the long-term outcome of CAD, but the polymorphism rs3735167 in the chemerin gene did not play a role (49).

In another study involving 495 patients undergoing coronary angiography for evaluation of established or suspected stable CAD, a high level of chemerin was significantly associated with higher CVD events. The study reported that polymorphisms (rs55709438, rs2444030, and rs3098423) located at chromosomal region 15q15-23 were associated with metabolic traits found in CVD patients (45).

Polycystic ovary syndrome

Polycystic ovary syndrome (PCOS) is one of the most prevalent endocrine disorders, with a prevalence of 5-20% among females of reproductive age (50). The association of adipokine levels, such as adiponectin and leptin, with PCOS has been reported [40-42].

A study conducted in an Iranian women population revealed an association between chemerin rs17173608 gene polymorphism and the risk of PCOS (51). The results of this study indicated a higher risk of PCOS in women with chemerin rs17173608 polymorphism; however, when the findings were adjusted for body mass index and age, no association was found (51). Furthermore, a study performed in Iraq showed a positive correlation between rs17173608 polymorphism of chemerin and susceptibility to PCOS. Nevertheless, subjects with the T allele had an elevated risk of PCOS compared to subjects with the G allele (52).

Rheumatoid Arthritis

Rheumatoid arthritis (RA) is an inflammatory and chronic disease that can cause bone and cartilage erosion, reducing the quality of life (53, 54). Chemerin is an adipocytokine associated with the inflammatory state of endothelial cells and is a specific attractor for macrophages and dendritic cells, which play significant roles in the pathogenesis of rheumatoid arthritis (55).

A study conducted in Egypt examined the chemerin gene polymorphism at the rs17173608 site in patients with rheumatoid arthritis (50). The results showed that the G allele of chemerin rs17173608 polymorphism was more frequent in RA patients. It was concluded that there is a positive correlation between rs17173608 and susceptibility to rheumatoid arthritis (56).

Conclusion

This review indeed summarizes the association of certain chemerin polymorphisms with various diseases. Overall, the studies have demonstrated a connection between chemerin polymorphisms and conditions such as obesity, insulin resistance, CVD, inflammation, and diabetes. However, there are discrepancies in the reported results, which could be attributed to factors like sample size and the diverse populations included in the studies. To further substantiate the hypothesis that chemerin gene polymorphisms play a role in the pathogenesis of these diseases, additional studies with larger sample sizes are needed. Importantly, a meta-analysis could provide a more comprehensive understanding of these associations.

Conflict of interest

The authors have nothing to declare.

References

1. Bozaoglu K, Curran JE, Stocker CJ, Zaibi MS, Segal D, Konstantopoulos N, et al. Chemerin, a Novel Adipokine in the Regulation of Angiogenesis. J Clin Endocrinol Metab.

2010;95(5):2476-85.
2. Adeli K. A Journey Forward: Acta Biochimica Iranica's Rebirth and its Impact on the Evolution of Clinical Laboratory Sciences. Acta Biochim Iranica. 2023;1(1):1-2.
3. Wittamer V, Grégoire F, Robberecht P, Vassart G, Communi D, Parmentier M. The C-terminal nonapeptide of mature chemerin activates the chemerin receptor with low nanomolar potency. J Biol Chem. 2004;279(11):9956-62.
4. Ben Dhaou C, Mandi K, Frye M, Acheampong A, Radi R, De Becker B, et al. Chemerin regulates normal angiogenesis and hypoxia-driven neovascularization. Angiogenesis. 2022;25(2):159-79.
5. Perumalsamy S, Ain Aqilah Mohd Zin N, Teguh Widodo R, Azman Wan Ahmad W, Vethakkan RD, Zaman Huri H. Chemokine like receptor-1 (CMKLR-1) receptor: a potential therapeutic target in management of chemerin induced type 2 diabetes mellitus and cancer. Curr Pharm Des. 2017;23(25):3689-98.
6. Taghizadeh Nima S.M., Saeedi Vahid, Haghighi Ladan, Nourbakhsh Mona, Nourbakhsh Mitra, Razzaghy Azar Maryam. Association between Steroid Hormones and Insulin Resistance in Patients with Polycystic Ovary Syndrome. Acta Biochim Iranica. 2023;1 (1) :26-31.
7. Dubois-Vedrenne I, Al Delbany D, De Henau O, Robert V, Vernimmen M, Langa F, et al. The antitumoral effects of chemerin are independent from leukocyte recruitment and mediated by inhibition of neoangiogenesis. Oncotarget. 2021;12 (19) :1903-19.
8. Shin WJ, Zabel BA, Pachynski RK. Mechanisms and functions of chemerin in cancer: potential roles in therapeutic intervention. Front Immunol. 2018;9 :2772.
9. Nagpal S, Patel S, Jacobe H, DiSepio D, Ghosn C, Malhotra M, et al. Tazarotene-induced gene 2 (TIG2), a novel retinoid-responsive gene in skin. J Invest Dermatol. 1997;109 (1) :91-95.
10. Ernst MC, Sinal CJ. Chemerin: at the crossroads of inflammation and obesity. Trends Endocrinol Metab. 2010;21 (11) :660-67.
11. Chang SS, Eisenberg D, Zhao L, Adams C, Leib R, Morser J, et al. Chemerin activation in human obesity. Obesity. 2016;24(7):1522-9.
12. Mlyczyńska E, Kieżun M, Kurowska P, Dawid M, Pich K, Respekta N, et al. New Aspects of Corpus Luteum Regulation in Physiological and Pathological Conditions: Involvement of Adipokines and Neuropeptides. Cells. 2022;11(6):957.
13. Eichelmann F, Schulze MB, Wittenbecher C, Menzel J, Weikert C, di Giuseppe R, et al. Association of chemerin plasma concentration with risk of colorectal cancer. JAMA Netw Open. 2019;2(3):e190896-e190896.
14. Helfer G, Wu QF. Chemerin: a multifaceted adipokine involved in metabolic disorders. J Endocrinol. 2018;238(2):R79-R94.
15. Zhao K, Ding W, Zhang Y, Ma K, Wang D, Hu C, et al. Variants in the RARRES2 gene are associated with serum chemerin and increase the risk of diabetic kidney disease in type 2 diabetes. Int J Biol Macromol. 2020;165:1574-80.
16. Léniz A, González M, Besné I, Carr-Ugarte H, Gómez- García I, Portillo MP. Role of chemerin in the control of glucose homeostasis. Mol Cell Endocrinol. 2022;541 :111504.
17. Er LK, Hsu LA, Juang JM, Chiang FT, Teng MS, Tzeng IS, et al. Circulating Chemerin Levels, but not the RARRES2 Polymorphisms, Predict the Long-Term Outcome of Angiographically Confirmed Coronary Artery Disease. Int J Mol Sci. 2019;20 (5).
18. Zheng Q, Jiang J, Huo Y, Chen D. Genetic predisposition to type 2 diabetes is associated with severity of coronary artery disease in patients with acute coronary syndromes. Cardiovasc Diabetol. 2019;18 (1) :131.
19. Dahpy MA, Khairallah MK, Azoz NA, Ezzat GM. The associations among RARRES2 rs17173608 gene polymorphism, serum chemerin, and non-traditional lipid profile in patients with metabolic syndrome. Egypt J Med Hum Genet. 2020;21 (1) :1-13.
20. Olt S, Öznas O, Bağış H, Turanlı ET. Chemerin rs17173608 Gene Polymorphism is not Associated with Type 2 Diabetes Mellitus: a Cross-sectional Study. Folia Medica. 2019;61 (1) :69-75.
21. Abdelhamid AM, Zaafan MA. Association of chemerin rs17173608 and vaspin rs2236242 polymorphisms with type two diabetes mellitus and its impact on their corresponding serum levels in Egyptian population. 2019. ideas.
22. Perumalsamy S, Wan Ahmad WA, Zaman Huri H. Single Nucleotide Polymorphism rs17173608 in the Chemerin Encoding Gene: Is It a Predictor of Insulin Resistance and Severity of Coronary Artery Disease in Non-Obese Type 2 Diabetes? Healthcare. 2021;9(6):623.
23. Wang H, Li N, Chivese T, Werfalli M, Sun H, Yuen L, et al. IDF Diabetes Atlas: Estimation of Global and Regional Gestational Diabetes Mellitus Prevalence for 2021 by International Association of Diabetes in Pregnancy Study Group's Criteria. Diabetes Res Clin Pract. 2022;183:109050.
24. Hamzeh Saberi G.T., Reza Meshkani The ENPP1 K121Q polymorphism is associated with obesity-related parameters in Iranian normoglycemic male subjects. Acta Biochim Iranica. 2023;1(1):20-25.
25. Hare K, Bonde L, Svare J, Randeva H, Asmar M, Larsen S, et al. Decreased plasma chemerin levels in women with gestational diabetes mellitus. Diabet Med. 2014;31(8):936-40.
26. Li X-M, Ji H, Li CJ, Wang PH, Yu P, Yu DM. Chemerin expression in Chinese pregnant women with and without gestational diabetes mellitus. Ann Endocrinol. 2015;76 (1) :19-24.
27. Sun J, Ren J, Zuo C, Deng D, Pan F, Chen R, et al. Circulating apelin, chemerin and omentin levels in patients with gestational diabetes mellitus : A systematic review and meta-analysis. Lipids Health Dis. 2020;19 (1) :1-15.
28. Wang D, Li N, Zhao R. Chemerin levels and its genetic variants are associated with Gestational diabetes mellitus: a hospital-based study in a Chinese cohort. Gene. 2022;807 :145888.
29. Hasanvand Z, Sadeghi A, Rezvanfar MR, Goodarzi MT, Rahmannezhad G, Mashayekhi FJ. Association between chemerin rs17173608 and vaspin rs2236242 polymorphisms with type two diabetes mellitus and its impact on their corresponding serum levels in Egyptian population. Gene. 2018;649 :87-92.
30. Fatima SS, Bozaoglu K, Rehman R, Alam F, Memon AS. Elevated chemerin levels in Pakistani men: an interrelation with metabolic syndrome phenotypes. PLoS One. 2013;8 (2) :e57113.
31. Alverti K. Metabolic syndrome: A new world-wide definition: A consensus statement from the International Diabetes Federation. Diabet Med. 2006;23:469-80.
32. O'Neill S, O'Driscoll L. Metabolic syndrome: a closer look at the growing epidemic and its associated pathologies. Obesity reviews. 2015;16(1):1-12.

33. Zahra Barmoudeh M.H.S., Hossein Pourghadamyari, Mina Rohani Borj, Amir Hossein Doustimotlagh, Kazem Abbaszadeh-Goudarzi, C1q tumor necrosis factor related proteins (CTRPs) in patients with cardiovascular diseases Acta Biochimica Iranica, 2023. 1(1):12-19.
34. Batista A, Barbosa K, Masioli C, Queiroz E, Marinho C, Cândido A, et al. High levels of chemerin associated with variants in the NOS3 and APOB genes in rural populations of Ouro Preto, Minas Gerais, Brazil. Brazilian Journal of Medical and Biological Research. 2020;53.
35. Hashemi M, Rezaei H, Eskandari-Nasab E, kaykhaei MA, Zakeri Z, Taheri M. Association of chemerin rs17173608 and vaspin rs2236242 polymorphisms with the metabolic syndrome, a preliminary report. Gene. 2012;510(2):113-7.
36. Mehanna ET, Mesbah NM, Ghattas MH, Saleh SM, Abo-Elmatty DM. Association of chemerin Rs17173608 and vaspin Rs2236242 gene polymorphisms with metabolic syndrome in Egyptian women. Endocrine research. 2016;41(1):43-8.
37. Helvaci N, Eyupoglu ND, Karabulut E, Yildiz BO. Prevalence of obesity and its impact on outcome in patients with COVID-19: a systematic review and meta-analysis. Front Endocrinol. 2021;12 :598249.
38. Roya Jahangard S.S.S.E., Akram Vatannejad, Reza Meshkani Autophagy protects peripheral blood mononuclear cells from high glucose-induced inflammation and apoptosis. Acta Biochimica Iranica. 2023;1 (1) :40-49.
39. Zhao C, Hu W, Xu Y, Wang D, Wang Y, Lv W, et al. Current Landscape: The Mechanism and Therapeutic Impact of Obesity for Breast Cancer. Front Oncol. 2021;11 :704893.
40. Becer E, Çırakoğlu A. Effect of the Pro12Ala polymorphism of the peroxisome proliferator-activated receptor γ2 gene on lipid profile and adipokines levels in obese subjects. Balkan J Med Genet. 2017;20 (1) :71-80.
41. Kohan L, Movahed Z, Tabiee O. Association between chemerin rs17173608 polymorphism and obesity in Iranian women. Int J Biosci. 2014;4:166-71.
42. Yun Z, Yu-Ping Y, Zong-Wu T, Yang S, Fang Y, Fang S. Association of endothelial nitric oxide synthase gene polymorphisms with end-stage renal disease: a systematic review and meta-analysis. Ren Fail. 2014;36(6):987-93.
43. Xue C, Nie W, Tang D, Yi L, Mei C. Apolipoprotein E gene variants on the risk of end stage renal disease. PLoS One. 2013;8(12):e83367.
44. Nomani H, Khanmohamadian H, Vaisi-Raygani A, Shakiba E, Tanhapour M, Taheri M. Chemerin rs17173608 and vaspin rs2236242 gene variants on the risk of end stage renal disease (ESRD) and correlation with plasma malondialdehyde (MDA) level. Ren Fail. 2018;40(1):350-56.
45. Leiherer A, Muendlein A, Kinz E, Vonbank A, Rein P, Fraunberger P, et al. High plasma chemerin is associated with renal dysfunction and predictive for cardiovascular events — Insights from phenotype and genotype characterization. Vasc Pharmacol. 2016;77:60-68.
46. Khaled Y, Rashed L. Serum chemerin levels and chemerin rs17173608 genotypes in the susceptibility of diabetic nephropathy in Egyptian diabetic patients. Egypt J Obes Diabetes Endocrinol. 2016;2 (1) :18.
47. Gruzdeva O, Uchasova E, Dyleva Y, Borodkina D, Akbasheva O, Antonova L, et al. Adipocytes directly affect coronary artery disease pathogenesis via induction of adipokine and cytokine imbalances. Front Immunol. 2019;10 :2163.
48. Wu Q, Chen Y, Chen S, Wu X, Nong W. Correlation between adiponectin, chemerin, vascular endothelial growth factor and epicardial fat volume in patients with coronary artery disease. Exp Ther Med. 2020;19 (2) :1095-1102.
49. Er L-K, Wu S, Hsu L-A, Teng M-S, Sun Y-C, Ko Y-L. Pleiotropic Associations of RARRES2 Gene Variants and Circulating Chemerin Levels: Potential Roles of Chemerin Involved in the Metabolic and Inflammation-Related Diseases. Mediators Inflamm. 2018;2018 :4670521.
50. Mazloomi S, Farimani MS, Tayebinia H, Karimi J, Amiri I, Abbasi E, et al. The Association of Mitochondrial Translocator Protein and Voltage-Dependent Anion Channel-1 in Granulosa Cells with Estradiol Levels and Presence of Immature Follicles in Polycystic Ovary Syndrome. J Reprod Infertil. 2022;23 (3) :148-160.
51. Movahed Z, Kohan L, Fallahi S, Tabiee O. Influence of chemerin rs17173608 polymorphism on polycystic ovary syndrome susceptibility. Taiwanese Journal of Obstetrics and Gynecology. 2015;54(3):280-83.
52. Jasim R, Umran M, Humadi E. Detectin of vaspin rs2236242 and chemerin rs17173608 gene polymorphsims in a sample of obese iraqi polycyctic ovary syndrome women. The Iraqi Journal of Agricultural Science. 2020;51(1):462-69.
53. Gonzalez-Ponce F, Gamez-Nava JI, Perez-Guerrero EE, Saldaña-Cruz AM, Vazquez-Villegas ML, Ponce-Guarneros JM, et al. Serum chemerin levels: A potential biomarker of joint inflammation in women with rheumatoid arthritis. PLoS One. 2021;16(9):e0255854.
54. Yaser Mohassel S.A., Shayan Mostafae, Mohammad Taghi Goodarzi Assessing the Possible Association between Polymorphism of C677T MTHFR with Preeclampsia Risk: A Systematic Review and Bayesian Hierarchical Meta-Analysis. Acta Biochimica Iranica. 2023;1(1):3-11.
55. Herenius MM, Oliveira AS, Wijbrandts CA, Gerlag DM, Tak PP, Lebre MC. Anti-TNF therapy reduces serum levels of chemerin in rheumatoid arthritis: a new mechanism by which anti-TNF might reduce inflammation. PLoS One. 2013;8(2):e57802.
56. Wahba AS, Ibrahim ME, Abo-Elmatty DM, Mehanna ET. Association of the Adipokines Chemerin, Apelin, Vaspin and Omentin and Their Functional Genetic Variants with Rheumatoid Arthritis. Journal of Personalized Medicine. 2021;11 (10) :976.