INDONESIAN JOURNAL OF
CLINICAL PATHOLOGY AND MEDICAL LABORATORY
Majalah Patologi Klinik Indonesia dan Laboratorium Medik

PAGE 39
2023 November; 30 (1): 39-42
p-ISSN 0854-4263 e-ISSN 2477-4685
Available at www.indonesianjournalofclinicalpathology.org

Analysis of Serum Chemerin Levels in Type 2 Diabetes Mellitus Patients

Fauziah[1], Suci Aprianti[1,2], Liong Boy Kurniawan[1,3]

[1] Department of Clinical Pathology, Faculty of Medicine, Hasanuddin University/Dr. Wahidin Sudirohusodo Hospital, Makassar, Indonesia. E-mail: fauziah_dr@yahoo.com
[2] Haji Regional Hospital, Makassar, Indonesia
[3] Clinical Pathology Laboratory, Hasanuddin University Hospital, Makassar, Indonesia

ABSTRACT

Chemerin is an adipokine involved in inflammation, adipogenesis, angiogenesis, and energy metabolism. Diabetes Mellitus (DM) is a group of metabolic diseases with hyperglycemia characteristics that occur due to abnormalities in insulin secretion, insulin action, or both. This study aimed to determine serum chemerin levels in patients with Type 2 Diabetes Mellitus (T2DM) between controlled and uncontrolled groups. This study was an analytical observational study with a cross-sectional approach. The study samples were all patients diagnosed with T2DM who had HbA1c test results and met the inclusion and exclusion criteria. Serum chemerin was measured using the ELISA method. The Kolmogorov-Smirnov, Chi-Square, Pearson, and independent T-test statistically analyzed the data. The subjects were 60 controlled and uncontrolled DM patients, 29 males and 31 females. There was a difference in serum chemerin levels in the controlled and uncontrolled DM group (5.73±2.3 ng/mL with 6.87±1.7 ng/mL, p=0.40). There was a positive correlation between chemerin levels and HbA1c (r=0.266; p=0.040). Serum chemerin levels of patients with uncontrolled DM were higher than in patients with controlled DM. Serum chemerin will increase along with the increase of HbA1c level.

Keywords: Chemerin, diabetes mellitus, HbA1c

INTRODUCTION

Hyperglycemia is a medical condition in which blood glucose levels increase beyond normal value, a characteristic of several diseases, especially Diabetes Mellitus (DM) and other conditions. According to the American Diabetes Association (ADA) in 2022, DM is a group of metabolic diseases characterized by hyperglycemia due to abnormalities in insulin secretion, insulin action or both. Based on the cause, DM can be classified into four groups, namely type 1 DM, type 2 DM, gestational DM, and other types of DM.[1,2]

Based on the pattern of population growth, it is estimated that in 2030, there will be 194 million people aged over 20 years, and the prevalence of DM in urban and rural areas will be 14.7% and 7.2%, respectively. It is also estimated that there will be 28 and 13.9 million diabetes patients in urban and rural areas, respectively. Basic Health Research Report (RISKESDAS) by the Ministry of Health in 2018, using data from the 2015 PERKENI Consensus, estimates that the prevalence of DM in 2018 will be 9%.[1,3]

It has been proven in the last few decades that there was a relationship between obesity and insulin resistance to inflammation. This fact highlights the vital role of inflammation in the pathogenesis of Type 2 DM (T2DM). The Retinoic Acid Receptor Responder Protein 2 (Rarres2) gene is a newly discovered adipokine involved in inflammation, adipogenesis, angiogenesis, and energy metabolism.[4-6]

Adipose tissue is an endocrine organ that secretes several bioactive molecules known as adipokines. Adipokines have an essential role in glucose metabolism and systemic energy balance. It is known that adipocytes alter circulating adipokine levels. This condition may coexist with obesity and contribute to the metabolic changes that eventually lead to T2DM. Another mechanism by which fluctuating adipokine levels contribute to T2DM involves inflammation-mediated insulin resistance. Insulin resistance causes an increase in glucose concentration by decreasing glucose uptake in peripheral tissues and increasing glucose production in the liver. Insulin resistance induces increased lipolysis, release of free fatty acids in adipocytes, and increased synthesis of lipids in the liver.[7]

A collection of clinical studies shows a correlation between chemerin levels and diabetes. Chemerin in T2DM patients increased significantly compared to controls with normal weight in the Caucasian population. This finding was in line with T2DM patients without other metabolic complications in Asia.[4] A prospective study showed that an increase in systemic chemerin preceded the onset of T2DM,

consistent with the results in this study, which found a relationship between high chemerin levels and more significant changes in glucose and HbA1c levels. However, research by Takashi *et al.* showed contrary findings such as a negative correlation between chemerin levels, fasting glucose, and HbA1c levels in male subjects with DM.[4,8-10]

METHODS

This study used an observational research design with a cross-sectional approach in August 2022. The research was carried out at the Clinical Pathology Laboratory Installation of Hasanuddin University Hospital for sampling and at the Hasanuddin University Faculty of Medicine Research Unit for laboratory tests. The study population was all patients diagnosed with T2DM at Hasanuddin University Hospital. The research samples were all T2DM patients whose HbA1c results met the inclusion criteria. The inclusion criteria were T2DM patients who did not suffer from malignancy, infection/inflammation, impaired kidney function, poor liver function, stroke, and heart disease, according to secondary diagnoses reported in the medical record.

Serum chemerin levels were measured using the Enzyme-Linked Immunosorbent Assay (ELISA) method. Chemerin levels were assessed with a 0.01 ng/mL sensitivity using the Human CHEM (Chemerin) ELISA Kit Elabscience and expressed in ng/mL. Data analysis was performed using SPSS 25. The Kolmogorov-Smirnov test was used to determine the normality of data, the Chi-Square test was used for the analysis of categorical data, the unpaired T-test was used for the analysis of continuous data, and the Pearson correlation test was used for the analysis of normal distributed data. The statistical test results with p-value <0.05 were reported as significant.

This research was carried out after obtaining ethical clearance by considering respect for the subject, beneficence, non-maleficence, and justice from the Health Research Ethics Commission (KEPK) Faculty of Medicine, Hasanuddin University/UH Hospital/Dr. Wahidin Sudirohusodo Hospital, Makassar with number 440/UN4.6.4.5.31/ PP36/2022.

RESULTS AND DISCUSSIONS

The results showed that 60 research subjects in this study consisted of 16 people with controlled DM and 44 people with uncontrolled DM. There were 29 (48.3%) males and 31 (51.7%) females with an age range of 37-84 years. There were 26 (43.3%) people suffering from T2DM for < 5 years, 10 (16.7%) people suffering from T2DM for 5-10 years, and 24 (40%) people suffering from T2DM for > 10 years. The mean fasting blood glucose, HbA1c, and chemerin levels were 172.5 mg/dL, 8.8%, and 6.57 ng/mL, respectively (Table 1).

Based on Table 2, independent T-test results found no significant difference in age between controlled and uncontrolled T2DM with a p-value of 0.676 (p > 0.05). In contrast, there was a significant difference in fasting blood glucose and HbA1C levels with p-values < 0.001 and < 0.001 (p < 0.05), respectively. The Chi-square test results found no significant difference in gender and length of suffering from T2DM between controlled and uncontrolled T2DM, with p-values of 0.459 and 0.676, respectively (p > 0.05).

This study's mean chemerin level in controlled and uncontrolled DM was 5.73 pg/mL and 6.87 pg/mL, respectively. Independent T-test results

Table 1. Characteristics of subjects suffering from type 2 DM

Criteria	n (%)	Mean±SD	Median (Min-Max)
Gender			
Male	29 (48.3)		
Female	31 (51.7)		
Type 2 DM			
Controlled	16 (26.7)		
Uncontrolled	44 (73.3)		
Length of T2DM			
< 5 years	26 (43.3)		
5 – 10 years	10 (16.7)		
>10 years	24 (40)		
Age		57.7±9.3	59 (37–84)
Fasting blood glucose (mg/dL)		172.5±67.7	165 (69 – 332)
HbA1c (%)		8.8±2.4	8.2 (5.7–15.9)
Chemerin (ng/mL)		6.57±1.9	6.64 (1.25–9.96)

Table 2. The difference in chemerin levels between controlled and uncontrolled DM

Variable	Controlled DM	Uncontrolled DM	p
Gender			
Male	9	20	0.459*
Female	7	24	
Length of T2DM			
< 5 years	9	17	0.476*
5 – 10 years	2	8	
>10 years	5	19	
Age	30.45±3.8	32.33±3.8	0.676**
Fasting blood glucose (mg/dL)	107.5±19.9	196.1±63.3	< 0.001**
HbA1C (%)	6.3±0.3	9.6±2.2	< 0.001**
Chemerin (ng/mL)	5.73±2.3	6.87±1.7	0.040*

*Chi-Square test ** Independent T-test

found a significant difference in mean chemerin levels between controlled and uncontrolled DM with a p-value of 0.040 (p <0.05). Pearson correlation test results showed that there was a significant positive correlation with a p-value of 0.040 (p <0.05) with a correlation strength of 0.266 (weak correlation), which indicated that a higher HbA1c level would lead to a higher chemerin level.

This study used a cross-sectional research design involving 60 research subjects who met the inclusion and exclusion criteria. Table 1 shows that research subjects consisted of 29 (48.3%) males and 31 (51.7%) females with an age range of 37-84 years, and 40% had suffered from DM for > 10 years. According to the International Diabetes Report Federation (IDF), referred to in INFODATIN of T2DM by the Indonesian Ministry of Health, the prevalence of DM in 2019 in females and males was 9% and 9.65%, respectively. It was estimated that this number would increase along with the increasing age of the population at 65-79 years.[11]

There were no differences in age, gender, and length of suffering from DM in the controlled and uncontrolled DM (Table 2). In contrast, there was a significant difference in fasting blood glucose and HbA1C levels with p-values < 0.001 and < 0.001 (p < 0.05), respectively. A study by Khan *et al.* showed that patients with HbA1c ≥ 6.5% had very high fasting blood glucose levels. The relationship between HbA1c and GDP is relatively strong, especially in DM subjects. Fasting blood glucose indicates current glycemic status, and HbA1c measures long-term glycemic control.[12,13]

This study found a significant difference in chemerin levels between controlled and uncontrolled DM with a p-value of 0.040 (p <0.05) with higher mean chemerin levels in uncontrolled DM compared to that of controlled DM. In line with a study by Bobbert *et al.*, chemerin levels are associated with changes in glucose and HbA1c levels, which support the idea of chemerin as a mediator of insulin resistance.[8]

Chemerin is a recently discovered adipokine that has been considered a regulator of many biological processes, including adipocyte formation, glucose homeostasis, immune function, and inflammation. Chemerin levels are positively related to Body Mass Index (BMI), blood pressure, HbA1c, triglyceride levels, fasting blood glucose, insulin resistance, and cholesterol levels, indicating their vital role in obesity and their association with comorbid metabolic syndrome and DM.[8,13]

This study also found a significant correlation between chemerin and HbA1C levels, which indicated that higher HbA1C levels would lead to higher chemerin levels. This result was in line with previous studies showing that chemerin levels are related to the degree of glycemia and insulin resistance based on fasting glucose, HbA1c, and insulin.[13,14]

Due to a cross-sectional approach, this study could only perform analysis at a specific time. Therefore, it was impossible to establish a causal relationship between chemerin levels and T2DM. It was also challenging to determine whether high chemerin levels contribute to T2DM or whether T2DM causes elevated chemerin levels.

CONCLUSIONS AND SUGGESTIONS

Serum chemerin levels were higher in uncontrolled DM patients than in controlled DM patients. Higher HbA1c levels would lead to higher chemerin levels. Further research is needed using a

larger sample with different subjects, adding research variables, and using a longitudinal approach to understand changes in chemerin levels over time and its effect on developing type 2 diabetes complications.

REFERENCES

1. Soelistijo S, Lindarto D, Decroli E, Permana H, Sucipto K, dkk. Pedoman pengelolaan dan pencegahan diabetes melitus tipe 2 dewasa di Indonesia. Pengurus besar Perkumpulan Endokrinologi Indonesia, 2019; 12-13: 1-183.
2. Addendum. Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes-2021. Diabetes Care, 2021; 44(Suppl 1): S15-S33.
3. Perkumpulan Endokrinologi Indonesia. Konsensus Pengelolaan dan pencegahan diabetes melitus tipe 2 di Indonesia. Jakarta, PB PERKENI, 2015; 10-51, 113.
4. Helfer G, Wu QF. Chemerin: A multifaceted adipokine involved in metabolic disorders. J. Endocrinol, 2018; 238: R79-R94.
5. Jialal I. Chemerin levels in metabolic syndrome: A promising biomarker. Arch Physiol Biochem, 2021; 1-3. Epub ahead of print. PMID: 33843397.
6. Tan L, Lu X, Danser AHJ, Verdonk K. The role of chemerin in metabolic and cardiovascular disease: A literature review of its physiology and pathology from a nutritional perspective. Nutrients 2023, 15: 2878. Available from: https://doi.org/10.3390/nu15132878 (accessed Augst 8, 2023).
7. Balaban YA, Yilmaz N, Kalayci M, Unal M, Turhan T. Irisin and chemerin levels in patients with type 2 diabetes mellitus. Acta Endocrinol. (Copenh), 2019; 15: 442-446.
8. Bobbert T, Schwarz F, Rosinsky A, Maurer L, Mohlig M, *et al.* Chemerin and prediction of diabetes mellitus type 2. Clin. Endocrinol. (Oxf), 2015; 82: 838-843.
9. Ekpe EE, Ekpe VE. Chemical pathology of chemerin and its link to obesity and type 2 diabetes mellitus: A review. Biochemistry and Molecular Biology, 2017; 2(4): 37-39.
10. Zylla S, Pietzner M, Kühn JP, Völzke H, Dörr M, Nauck M, *et al.* Serum chemerin is associated with inflammatory and metabolic parameters-results of a population-based study. Obesity, 2017; 25(2): 468-75.
11. Kementerian Kesehatan RI. Infodatin tetap produktif, cegah, dan atasi diabetes melitus 2020. Pusat Data dan Informasi Kementerian Kesehatan RI, 2020; 1-10.
12. Indranila KS. Glycated hemoglobin a1c as a biomarker predictor for diabetes mellitus, cardiovascular disease, and inflammation. Indonesian Journal of Clinical Pathology and Medical Laboratory, 2017; 23(2): 191-196.
13. Khan HA, Sobki SH, Alhomida AS. Regression analysis for testing association between fasting blood sugar and glycated hemoglobin in diabetic patients. Biomed. Res, 2015; 26: 604-606.
14. Szpakowicz A, Szpakowicz, M, Lapinska M, Paniczko M, Lawicki S, *et al.* Serum chemerin concentration is associated with proinflammatory status in chronic coronary syndrome. Biomolecules, 2021; 11: 1-13.