Analysis of Advanced Glycated End Products with Serum Omentin in Type 2 Diabetes Mellitus Subjects

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ABSTRACT:

Objectives: The purpose of the current study is to figure out the association between the level of serum AGEs and serum Omentin in type 2 DM subjects.

Methods: This study utilized a cross-sectional design and involved 62 subjects with type 2 DM, comprising 23 males and 39 females.

Results: Based on statistical analysis, the research findings displayed that there was no substantial relation between the level of serum AGEs and the level of serum Omentin in overall type 2 DM patients (p=0.054, r=0.246). Furthermore, no notable relationship was discovered between serum level of AGEs and serum Omentin levels in male subjects with type 2 DM (p=0.485, r=0.153). Similarly, no significant relationship was also found between serum level of AGEs and serum Omentin levels in female subjects with type 2 DM (p=0.478, r=0.117).

Conclusions: No discernible association was found between the level of serum AGEs and serum Omentin in subjects suffering from type 2 diabetes mellitus (DM), including both male and female subjects. In addition, no correlation was observed between the value of Intima-Media Thickness (IMT) and the level of serum Omentin in male and female subjects with type 2 DM.

1. Introduction

Diabetes mellitus is a long-term metabolic disease, causing complications in individuals with diabetes. Each year, the occurrence of diabetes mellitus shows a consistent upward trend. Individuals with diabetes mellitus may experience various dangerous complications, including microvascular and macrovascular complications, as well as nervous system disorders (neuropathy). Furthermore, diabetes mellitus is one among the immunocompromised conditions, signifying a weakened immune system that heightens susceptibility to complications and increases vulnerability to infections in individuals. During the current COVID-19 pandemic, individuals diagnosed with DM also tend to be more vulnerable to infections, and worsening inflammatory reactions. An increase in the levels of Advanced Glycated End Products (AGEs) in the body is regarded as one among the factors that can exacerbate complications in type 2 diabetes mellitus, and measuring serum AGEs levels is considered a highly accurate method for evaluating the true impact of chronic hyperglycemia. Over a certain period, glucose molecules interact with proteins or lipids. When blood glucose levels remain...
consistently high, the likelihood of glycation reactions increases, ultimately leading to an elevated formation of Advanced Glycated End Products (AGEs). Consequently, more AGEs are formed within the body. The increased accumulation of AGEs can play a part in the onset of complications which is affiliated with diabetes, including eye diseases, nerve damage, kidney diseases, and cardiovascular problems. Advanced Glycated End Products serve as pro-inflammatory agents, affecting the normal function of proteins and triggering inflammatory responses and oxidative stress in the body, all of which are risk factors associated with type 2 diabetes.  

Omentin is a protein classified as an adipokine, possessing anti-inflammatory properties within the body. Numerous studies have indicated a decline in the level of omentin among individuals with insulin resistance and obesity. A meta-analysis revealed a significant reduction in serum Omentin levels among patients diagnosed with type 2 diabetes mellitus (DM) . This implies that with increasing insulin resistance, the body tends to produce less Omentin, leading to reduced responsiveness of body cells to insulin. This condition can impact the production and function of Omentin. Inflammation caused by adiposity can disrupt the production and release of omentin by adipose tissues, affecting the ability of adipose tissues to function properly. 

Earlier investigations have primarily centered on exploring the correlation between AGEs and DM, as well as Omentin and obesity. As far as the researcher’s observations go, there is no study connecting the surge in the level of serum AGEs with the reduction in the level of serum Omentin among individuals suffering type 2 diabetes mellitus (DM).

2. Objectives

Therefore, the objective of the current study is to investigate a potential association between the elevation of serum AGEs levels and the reduction of serum Omentin levels in type 2 DM subjects, which could exacerbate type 2 DM complications.

3. Methods

Study Design and Population

The current research employed an analytical observational method and a cross-sectional study design. Type 2 diabetes mellitus (DM) patients visiting Dr. Wahidin Sudirohusodo General Hospital, Makassar, for treatment were determined as the study population. The inclusion criteria were male and female patients with type 2 DM aged >18 years, who received information and willingly participated in the research by providing informed consent. Meanwhile, the exclusion criteria included patients taking corticosteroids, those with genetic polymorphisms, those experiencing infections or malignancies, and those exhibiting serum jaundice, lipemia, or hemolysis. There were 62 samples involved in the study, comprising 23 male subjects and 39 female subjects. This study was carried out at the Laboratory of Hasanuddin University Medical Research Center (HUMRC), Makassar. Ethical approval for the study was obtained from the Health Research Ethics Committee (KEPK), Faculty of Medicine, Hasanuddin University, RSPTN-UH, with Ethical Approval Number 826/UN4.6.4.5.31/PP36/2023.

Level Measurement

In this study, patient identities were recorded. Before blood collection, patients underwent fasting and anthropometric examinations. Complete blood samples were collected in red-capped tubes without anticoagulants for the examination of the level of serum AGEs and serum Omentin. Subsequently, the blood samples were allowed to stand for 15-30 minutes inside the vacuum tubes and then left to clot. The samples were centrifuged at a speed of 3000 rpm for 10 minutes. After centrifugation, transfer the separated serum from the blood cells to sample cups using a disposable pipette, with a volume of 150 µl for each serum cup. The serum was stored in a calibrated freezer at a temperature of -20°C to ensure sample stability. Then, to examine the serum AGEs level and Omentin level, the Enzyme-Linked Immunosorbent Assay (ELISA) kit from MyBioSource was utilized on the Thermo ELISA Reader instrument.

Data Analysis

Version 22 of the SPSS software was employed to analyze the obtained data. The analysis involved entering all variables, including gender, age, and the result of laboratory test. Kolmogorov-Smirnov as well as Shapiro-Wilk tests were conducted to determine the normality of the data distribution, utilizing a significance level (α) of 0.05. Spearman and Pearson correlation tests were performed in this study.
4. Results
As can be seen in Table 1, the current research involved 62 type 2 diabetes mellitus individuals, consisting of 23 male and 39 female subjects.

Table 1. Frequency Distribution of Gender Variables in Research Subjects

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Category</th>
<th>Type 2 DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>39</td>
</tr>
</tbody>
</table>

Individuals suffering from type 2 diabetes mellitus ranged in age from 22 to 83 years, with an average Body Mass Index (BMI) of 24.95 kg/m², an average HbA1c of 8.56%, an average Fasting Blood Glucose (FBG) of 149.74 mg/dL, an average serum Omentin level of 5.05 ng/mL, and an average serum AGEs level of 22.37 ng/mL (Table 2).

Table 2. Descriptive Analysis of Age, Serum AGEs Levels, and Serum Omentin Levels in Subjects of the Research

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n</th>
<th>Mean±SD</th>
<th>Median</th>
<th>Min-Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td>62</td>
<td>58.00±11.87</td>
<td>58</td>
<td>22-83</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>62</td>
<td>24.95±4.01</td>
<td>24.14</td>
<td>17.78-36.89</td>
</tr>
<tr>
<td>HbA1c(%)</td>
<td>62</td>
<td>8.56±1.38</td>
<td>8.5</td>
<td>5.7-14.1</td>
</tr>
<tr>
<td>FBS (mg/dL)</td>
<td>62</td>
<td>149.74±40.18</td>
<td>148</td>
<td>79-296</td>
</tr>
<tr>
<td>Serum Omentin level (ng/mL)</td>
<td>62</td>
<td>5.05±0.93</td>
<td>4.97</td>
<td>3.3075-8.9497</td>
</tr>
<tr>
<td>Serum AGEs level (ng/mL)</td>
<td>62</td>
<td>22.37±4.58</td>
<td>22.10</td>
<td>12.2075-36.8992</td>
</tr>
</tbody>
</table>

Notes:
BM = Body Mass Index, HbA1c= Hemaglobin A1c, FBS = Fasting Blood Sugar, AGEs= Advanced glycated end products

Normality Test
The findings from Table 3 demonstrate that the Kolmogorov-Smirnov and Shapiro-Wilk tests revealed that the serum Omentin levels in individuals diagnosed with type 2 diabetes mellitus exhibited a p-value of 0.009>0.05, implying that the data does not follow a normal distribution. Conversely, the distribution of serum AGEs levels in overall type 2 diabetes mellitus subjects was revealed to be normal, as indicated by a p-value of 0.200>0.05. Table 3 further illustrates that the serum Omentin levels in individuals with type 2 diabetes mellitus demonstrated a p-value of 0.132>0.05, suggesting a normal distribution of the data. Similarly, serum AGEs levels in male individuals suffering from type 2 diabetes mellitus showed a p-value of 0.134>0.05, indicating normal data distribution. Moreover, the level of serum Omentin in individuals suffering from type 2 diabetes mellitus revealed a p-value of 0.115>0.05, implying normal data distribution, and serum AGEs levels in male individuals suffering from type 2 diabetes mellitus presented a p-value of 0.090>0.05, implying normal data distribution as well.

Table 3. Normality Test of Serum AGEs Levels and Serum Omentin Levels in Research

<table>
<thead>
<tr>
<th>Serum Omentin Levels (Overall)</th>
<th>Normality Test</th>
<th>Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Statistic</td>
<td>p</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>62</td>
</tr>
<tr>
<td></td>
<td>p</td>
<td>0.009*</td>
</tr>
<tr>
<td>Serum AGEs Levels (Overall)</td>
<td>0.08</td>
<td>0.200*</td>
</tr>
<tr>
<td>Serum Omentin Levels (Male)</td>
<td>0.93</td>
<td>0.132**</td>
</tr>
<tr>
<td>Serum AGEs Levels (Male)</td>
<td>0.93</td>
<td>0.134**</td>
</tr>
<tr>
<td>Serum Omentin Levels (Female)</td>
<td>0.95</td>
<td>0.115**</td>
</tr>
<tr>
<td>Serum AGEs Levels (Female)</td>
<td>0.95</td>
<td>0.090**</td>
</tr>
</tbody>
</table>

Notes: * Kolmogorov-Smirnov Test, ** Shappiro-Wilk Test, BMI = Body Mass Index, AGEs= Advanced glycated end products

Correlation Test
According to the Spearman correlation test conducted on serum AGEs levels and serum Omentin levels in individuals diagnosed with type 2 diabetes mellitus, a p-value of 0.054 was obtained. As 0.054 > α (0.05), the conclusion drawn is that no notable correlation was identified between serum AGEs levels and serum Omentin levels in patients diagnosed with type 2 diabetes mellitus (Table 4).

Table 4. Correlation Test of Serum AGEs Levels and Serum Omentin Levels in Overall Research Subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Serum AGEs Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Omentin Level</td>
<td>r= 0.126</td>
</tr>
<tr>
<td>p</td>
<td>0.056</td>
</tr>
</tbody>
</table>

*p = Spearman Correlation Test
Based on the scatterplot below, it can be observed that the data distribution forms a random pattern. This observation suggests the absence of a significant correlation or relationship between the variables of serum AGEs levels and serum Omentin levels (Figure 1).
Figure 1. Scatterplot of Serum AGEs Levels and Serum Omentin Levels in Overall Research Subjects

**Correlation between the Level of Serum AGEs and Serum Omentin in Male Type 2 Diabetes Mellitus Subjects**

The Pearson correlation test between the levels of serum AGEs and serum Omentin in male individuals suffering from type 2 diabetes mellitus yielded a p-value of 0.485. Given that 0.485 > α (0.05), it can be inferred that no significant association was exhibited between serum AGEs levels and serum Omentin levels in male individuals diagnosed with type 2 diabetes mellitus (Table 5).

**Table 5. Correlation Test of Serum AGEs Levels and Serum Omentin Levels in Male Subjects suffering from Type 2 Diabetes Mellitus**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Serum AGEs Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Omentin Level</td>
<td>p = 0.485</td>
</tr>
<tr>
<td>r = 0.117</td>
<td></td>
</tr>
</tbody>
</table>

According to the scatterplot below, it can be observed that the data distribution forms a random pattern. This implies that there is no notable correlation or relationship between the variables of serum AGEs levels and the level of serum Omentin in male subjects diagnosed with type 2 diabetes mellitus, as displayed in Figure 2.

Figure 2. Scatterplot of Serum AGEs levels and Serum Omentin Levels in Male Subjects

**Correlation between the Level of Serum AGEs and Serum Omentin in Female Subjects with Type 2 Diabetes Mellitus**

The Pearson correlation test between serum AGEs levels and serum Omentin levels in female subjects with type 2 diabetes mellitus yielded a p-value of 0.478. As 0.478 > α (0.05), hence, it can be inferred that no notable association was detected between serum AGEs levels and serum Omentin levels in female subjects with type 2 diabetes mellitus (Table 6).

**Table 6. Correlation Test Between the Level of Serum AGEs and Serum Omentin in Female Subjects with Type 2 Diabetes Mellitus**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Serum AGEs Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Omentin Level</td>
<td>p = 0.478</td>
</tr>
<tr>
<td>r = 0.117</td>
<td></td>
</tr>
</tbody>
</table>

*p=Pearson Correlation Test

Based on the scatterplot below, it can be observed that the data distribution forms a random pattern. This suggests no significant correlation or relationship between the variables of serum AGEs levels and serum Omentin levels in female subjects suffering from type 2 diabetes mellitus (Figure 3).
5. Discussion
The current study was conducted from October to November 2023. The levels of serum AGEs and Omentin were measured in samples from those suffering from type 2 diabetes mellitus. Multiple studies have pointed out a rise in serum AGEs levels in diabetes complications, a significant factor contributing to mortality in individuals with type 2 diabetes mellitus. For instance, Ying et al., 2021 detailed the association of AGEs with the prevalence of diabetic retinopathy severity, one of the microvascular complications. Other research has also highlighted an increase in AGEs accumulation in tissues among individuals with type 2 diabetes mellitus. The detection of circulating AGEs may serve as an indicator of the risk of future diabetes.

Omentin, originating from visceral fat tissue, is an anti-inflammatory protein which acts as a biomarker for metabolic risk. Omentin is associated with glucose metabolism and insulin sensitivity in the body, with a relationship observed between increased serum Omentin levels and enhanced insulin sensitivity. Moreover, omentin also functions as a biomarker for metabolic risk and can be involved in proinflammatory conditions in various contexts, such as obesity, insulin resistance, or imbalanced metabolic conditions. The levels of Omentin serum in the body often decrease in these situations, and this decrease can then become a contributing factor to higher inflammation in the body, which, in turn, may contribute to various health conditions, such as cardiovascular diseases, diabetes, or autoimmune diseases. Mustafa et al., 2020, reported a noteworthy reduction in the level of serum Omentin among diabetic patients in comparison to the control group. This study also suggests that serum Omentin significantly decreases in diabetic patients diagnosed with retinopathy in comparison to those without retinopathy.

Derived from the research findings presented in Table 4, the Spearman correlation test conducted on subjects with DM shows no notable correlation between serum AGEs levels and Omentin levels, with a value of $p=0.054$, $r=0.246$. The Pearson correlation test carried out on male subjects with type 2 diabetes mellitus for serum AGEs levels and Omentin levels (Table 5) revealed a value of $p=0.485$, $r=0.153$, indicating no significant relationship between serum AGEs levels and Omentin levels in male subjects with type 2 diabetes mellitus. Meanwhile, the Pearson correlation test performed on female subjects with type 2 diabetes mellitus, examining serum AGEs levels and Omentin levels (Table 6), yielded a value of $p=0.478$, $r=0.117$, signifying no significant association between the level of serum AGEs and Omentin levels in female subjects with type 2 diabetes mellitus.

This finding contradicts the outcomes of prior research by Liang et al., 2019 [10]. Their study examined the connection between Omentin-1 levels and coronary artery disease or also abbreviated as CAD and discovered the association between low levels of Omentin-1 and CAD, along with elevated levels of AGEs in CAD individuals. Other research also indicates a decrease in Omentin-1 among individuals suffering from type 2 diabetes mellitus and peripheral artery disease, with these Omentin-1 levels being linked with the gravity of the disease [11]. On the other hand, contrasting results were presented by Yilmaz et al., 2011 [13], stating that serum Omentin levels increase in Non-alcoholic fatty liver disease (NAFLD), a disease related to obesity, even though obesity is associated with lower levels of Omentin [13].

Based on the research findings, the absence of correlation between AGEs levels and serum Omentin levels may be influenced by several factors, with the duration of suffering from diabetes mellitus (DM) being one potential factor. Before a significant decrease in Omentin levels occurs, the Omentin levels might still be relatively high. According to Abdelraour Korany et al., 2018 [14], serum Omentin, diabetes duration, and IMT (Intima Media Thickness) exhibit a negative correlation. Various medications can also affect Omentin levels; the use of medications such as metformin may increase Omentin levels [15]. Recent studies have demonstrated that atorvastatin enhances serum Omentin level in individuals diagnosed with coronary artery disease, indicating that...
there may be medications that respondents consume without the researcher's knowledge. Moreover, smoking is also associated with various hormonal and chemical changes in the body, including those related to lipid metabolism and the inflammatory system. Several studies have found a relationship between smoking and the level of serum Omentin. For instance, a study by Ansari et al. 2018 found an increase in serum Omentin levels among smokers when compared to non-smokers. Smoking is regarded as one of the primary contributors of oxidative stress. When someone smokes, various chemical compounds found in cigarette smoke can stimulate the production of Reactive Oxygen Species (ROS) within cells. This Reactive Oxygen Species are molecules which are highly reactive and can cause cellular damage and triggering responses to oxidative stress. This oxidative stress can alter gene expression and the production of adipokines, including Omentin.

6. Conclusion

No discernible association was found between the level of serum AGEs and serum Omentin in subjects suffering from type 2 diabetes mellitus (DM), including both male and female subjects. In addition, no correlation was observed between the value of Intima-Media Thickness (IMT) and the level of serum Omentin in male and female subjects with type 2 DM.

References


15. Tan BK, Adya R, Farhatullah S, Chen J, Lehnert H, Randeva HS. Metformin treatment may increase omentin-1 levels in women with polycystic ovary syndrome. *Diabetes.* 2010;59(12):3023-3031. doi:10.2337/db10-0124
