Assessment of Lipid Profile and Clinical Manifestation of Obese Patients with Type 2 Diabetes

Ammar Issa Taresh
Department of Community Health Technical, Technical Institute of Basra, Southern Technical University, Iraq

Abstract
This case-control study involved 356 diabetic patients and 384 apparently healthy individuals, matched for age and sex, who attended the outpatient department at Al-Zahrawi Private Hospital in Mosul from January to December 2004. The study aimed to evaluate changes in serum lipid profile among type 2 diabetics in relation to body mass index (BMI) and determine the extent and pattern of dyslipidemia in obese diabetics. Fasting plasma glucose and serum lipid profile were compared between type 2 diabetics and control subjects based on BMI. Data analysis utilized chi-square, Z, ANOVA, and Duncan tests. Fasting plasma glucose levels were highest in obese diabetics, and the frequency of poorly controlled diabetics increased with higher BMI. There was a significant positive association between BMI and serum triglyceride (TG) (p < 0.01), total cholesterol (TC) (p < 0.001), LDL-C (p < 0.001), and VLDL-C (p < 0.01). Serum HDL-C levels significantly decreased (p < 0.01) with increasing BMI. The prevalence of dyslipidemia increased with higher BMI levels in both genders. In conclusion, several lipid abnormalities in type 2 diabetics underscore the importance of diabetic control, regular lipid profile monitoring, and obesity management.

Introduction
The world is witnessing a significant increase in the prevalence of obesity and type 2 diabetes, which pose major challenges to healthcare systems due to their association with numerous severe health complications. Obesity, characterized by the abnormal or excessive accumulation of fat, is a primary factor that increases the risk of developing type 2 diabetes. An unhealthy lifestyle, including an unbalanced diet and lack of physical activity, exacerbates obesity rates and consequently the incidence of diabetes. Obesity is defined as an excessive accumulation of body fat, presenting a significant health risk. Its association with type 2 diabetes mellitus is well established, either directly or indirectly. Moreover, changes in body fat distribution are linked to alterations in lipids and lipoproteins, contributing to an increased risk of coronary heart disease (CHD). Additionally, obesity is considered a component of the metabolic syndrome in the pathogenesis of type 2 diabetes. Various methods are employed to measure obesity, including body mass index (BMI), skinfold thickness, waist-hip ratio, fat cell size and number, and body density. Among these methods, BMI has gained popularity as a preferred measure for adiposity particularly in large-scale epidemiological studies. The objective of the present study is to assess changes in serum lipid profile and the prevalence of dyslipidemia among three groups of patients with type 2 diabetes mellitus categorized according to their BMI.

Significance of the Study
This study holds great importance as it focuses on assessing the lipid profile and clinical manifestations in obese patients with type 2 diabetes. A thorough understanding of these aspects can contribute to the improvement of treatment strategies and disease management, positively impacting the quality of life of the patients. The lipid profile, which includes levels of cholesterol and triglycerides, serves as an important indicator of metabolic health and can illustrate the physiological changes resulting from obesity and diabetes.
**Objectives of the Study**

1. Assessing the Lipid Profile: Analyze the levels of total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides in obese patients with type 2 diabetes.
2. Describing Clinical Manifestations: Identify common clinical symptoms and their impact on the quality of life and disease management in these patients.

This study aims to provide a comprehensive overview of the health status of obese patients with type 2 diabetes, focusing on changes in the lipid profile and clinical manifestations, with the goal of improving treatment outcomes and reducing disease-related complications.

**The Concept of Obesity**

Obesity is defined as an excessive accumulation of body fat that poses a risk to health. It is commonly measured using the Body Mass Index (BMI), which is calculated by dividing a person’s weight in kilograms by the square of their height in meters. According to the World Health Organization (WHO), a BMI of 30 or higher is classified as obese. Obesity is a complex condition resulting from a combination of genetic, behavioral, and environmental factors. It is associated with numerous health risks, including cardiovascular diseases, hypertension, and type 2 diabetes [1].

**The Concept of Type 2 Diabetes**

Type 2 diabetes is a chronic condition that affects the way the body processes blood sugar (glucose). It is characterized by insulin resistance, where the body’s cells do not respond effectively to insulin, and eventually, the body may not produce enough insulin. This leads to elevated blood glucose levels, which can cause various health complications over time, such as heart disease, kidney failure, and nerve damage. Type 2 diabetes is often associated with obesity, physical inactivity, and poor dietary habits [2].

**The Relationship Between Obesity and Type 2 Diabetes**

The link between obesity and type 2 diabetes is well-documented and multifaceted. Obesity, particularly central or abdominal obesity, is a major risk factor for the development of insulin resistance, a key feature of type 2 diabetes. This section explores the physiological mechanisms underlying this relationship and the implications for disease management.

**Mechanisms Linking Obesity and Type 2 Diabetes**

1. Insulin Resistance: Insulin resistance is a condition where cells in the body become less responsive to the insulin hormone, which is crucial for regulating blood glucose levels. Adipose tissue, especially when accumulated in excess, secretes various substances such as free fatty acids, pro-inflammatory cytokines, and hormones that interfere with insulin signaling pathways. This interference leads to decreased glucose uptake by muscle and liver cells, resulting in elevated blood glucose levels [3].
2. Chronic Inflammation: Obesity is associated with a state of chronic, low-grade inflammation. Adipose tissue in obese individuals releases inflammatory mediators such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), which contribute to the development of insulin resistance. These inflammatory mediators impair insulin signaling and disrupt metabolic processes, further promoting hyperglycemia [4].
3. Lipid Metabolism: Obesity alters lipid metabolism, leading to an increase in circulating free fatty acids. High levels of free fatty acids can accumulate in tissues not suited for fat storage, such as the liver and muscles, causing lipotoxicity. This condition exacerbates insulin resistance by interfering with insulin signaling and glucose transport mechanisms [5].

4. Adipokines: Adipose tissue secretes various bioactive peptides known as adipokines, including leptin, adiponectin, and resistin. In obesity, the secretion of these adipokines is dysregulated. For instance, decreased levels of adiponectin, which has anti-inflammatory and insulin-sensitizing properties, are often observed in obese individuals, contributing to insulin resistance and the pathogenesis of type 2 diabetes [6].

**Implications for Disease Management**

Understanding the intricate relationship between obesity and type 2 diabetes highlights the importance of weight management in preventing and controlling diabetes. Strategies for managing obesity and type 2 diabetes typically include lifestyle interventions such as diet modification, increased physical activity, and behavioral therapy. In some cases, pharmacological treatments and bariatric surgery may be considered for weight reduction and metabolic improvement [7].

**Lipid Profile Components**

The lipid profile is an essential aspect of metabolic health evaluation, particularly in patients with type 2 diabetes. It includes the measurement of various lipids in the blood, which are critical indicators of cardiovascular risk and overall metabolic status. The key components of the lipid profile are:

1. Total Cholesterol: Represents the total amount of cholesterol in the blood. High levels of total cholesterol are associated with an increased risk of cardiovascular disease (CVD) [8].
2. Low-Density Lipoprotein (LDL) Cholesterol: Often referred to as "bad cholesterol," LDL carries cholesterol to tissues, including the arteries. Elevated levels of LDL cholesterol contribute to the development of atherosclerosis, a condition characterized by the hardening and narrowing of the arteries [9].
3. High-Density Lipoprotein (HDL) Cholesterol: Known as "good cholesterol," HDL helps remove cholesterol
from the bloodstream by transporting it to the liver for excretion. Higher levels of HDL cholesterol are generally protective against CVD [10].

4. Triglycerides: These are the most common type of fat in the body, stored in fat cells and used for energy. High levels of triglycerides are associated with an increased risk of CVD and can be a sign of metabolic syndrome, which is often seen in patients with type 2 diabetes [11].

**Lipid Profile Alterations in Type 2 Diabetes**

Patients with type 2 diabetes frequently exhibit dyslipidemia, a disorder of lipoprotein metabolism that is often characterized by:

1. Increased LDL Cholesterol: Diabetic patients tend to have smaller, denser LDL particles, which are more atherogenic than larger LDL particles [12].

2. Decreased HDL Cholesterol: Lower levels of HDL cholesterol are common in individuals with type 2 diabetes, reducing the protective effects against atherosclerosis [13].

3. Elevated Triglycerides: Hypertriglyceridemia is prevalent among diabetic patients, contributing to the formation of small, dense LDL particles and increasing cardiovascular risk [14].

4. Increased Total Cholesterol: While not always elevated, total cholesterol levels can be higher in some diabetic patients, further compounding their cardiovascular risk [2].

**Impact of Dyslipidemia on Cardiovascular Health**

Dyslipidemia in type 2 diabetes significantly heightens the risk of cardiovascular diseases. The interplay between hyperglycemia, insulin resistance, and lipid abnormalities accelerates the process of atherosclerosis, leading to higher incidences of coronary artery disease, stroke, and peripheral vascular disease in diabetic patients.

**Management of Dyslipidemia in Type 2 Diabetes**

Effective management of dyslipidemia in patients with type 2 diabetes includes:

1. **Lifestyle Modifications**: Diet changes (such as reducing saturated fat intake), increased physical activity, and weight loss can significantly improve lipid profiles [15].

2. **Pharmacotherapy**: Medications such as statins are commonly prescribed to lower LDL cholesterol levels. Other lipid-lowering agents, including fibrates and niacin, can be used to manage triglycerides and HDL cholesterol levels [16].

3. **Glycemic Control**: Improving blood glucose control through medications and lifestyle interventions can also positively affect lipid levels, reducing cardiovascular risk [17].

**Subjects and Methods**

The study was conducted over a period of 12 months from January to December 2004 and focused on diabetic patients with fasting plasma glucose levels >7.0 mmol/L. Only patients with type 2 diabetes were included, while those with other diseases were excluded. Three hundred and fifty-six diabetic patients, comprising 184 males and 172 females aged between 37 and 75 years (mean ± SD, 52.5 ± 6.4 years), who were attending the Al-Zahrawi Private Hospital Outpatient Department in Mosul, were enrolled in the study. All patients were receiving oral sulfonylureas tablets in addition to dietary restrictions. The control group consisted of 384 apparently healthy individuals (182 males, 202 females) aged between 38 and 72 years (mean ± SD, 48.4 ± 6.5 years). A general physical examination included the measurement of height and weight for the calculation of body mass index (BMI).

Patients and controls were categorized into non-obese (BMI < 25 kg/m²), overweight (BMI 25-29.9 kg/m²), and obese (BMI > 30 kg/m²) groups. Blood samples (10 ml) were collected after an overnight fast and divided into two aliquots for plasma glucose and serum lipid profile measurements. Fasting plasma glucose was measured using the glucose oxidase peroxidase method, while total cholesterol (TC), high-density lipoprotein cholesterol (HDLC), and triglycerides (TG) were determined using enzymatic methods. Low-density lipoprotein cholesterol (LDL-C) was calculated using the Friedewald formula for subjects with triglycerides <4.5 mmol/L.

The classification of hyperlipidemia and dyslipidemia followed the recommendations of the British Hyperlipidaemia Association (1998). Statistical analyses included the Z test, analysis of variance (ANOVA), Duncan test, and chi-square test. A p-value <0.05 was considered significant.

In summary, the study aimed to investigate changes in serum lipid profile and the frequency of dyslipidemia among diabetic patients classified based on their BMI, with comprehensive biochemical analyses and statistical assessments to elucidate associations and differences among the study groups.

**Results**

The mean age ± SD of non-obese, overweight, and obese diabetic patients were 50.4 ± 7.0, 52.0 ± 6.0, and 53.9 ± 6.4 years, respectively. In comparison, the mean age ± SD of non-obese, overweight, and obese control subjects were 47.9 ± 6.4, 48.3 ± 7.1, and 49.5 ± 5.8 years, respectively. Similarly, the mean BMI ± SD of non-obese, overweight, and obese diabetic patients were 23.9 ± 0.9, 27.7 ± 1.4, and 32.1 ± 1.6 kg/m², respectively, while the mean BMI ± SD of non-obese, overweight, and obese control subjects were 22.7 ± 1.1, 26.7 ± 1.3, and 32.0 ± 1.6 kg/m², respectively.

Table 1 illustrates the gender distribution according to BMI among non-obese, overweight, and obese male and female diabetics. For instance, in non-obese male diabetics, 14.1%, 50.6%, and 35.3% were categorized as non-obese, overweight, and obese, respectively, while
in female diabetics, 9.8%, 54.7%, and 35.5% fell into the same BMI categories.

| Table 1: Age and Sex Distribution of Diabetics and Control Subjects According to BMI |
|-----------------------------------|-----------------------------------|-----------------------------------|
| BMI                               | Diabetics (n=356)                 | Control subjects (n=384)          |
| Age (years), Mean ± SD            | Non-obese (n=43)                 | Overweight (n=187)               |
|                                  | 50.4 ± 7.0                       | 52.0 ± 6.0                       |
|                                  | Obese (n=126)                    | 53.9 ± 6.4                       |
|                                  | 47.9 ± 6.4                       | 48.3 ± 7.1                       |
|                                  | Overweight (n=276)               | 49.5 ± 5.8                       |
|                                  | Obese (n=88)                     |                                  |
|                                  | 23.9 ± 0.9                       | 27.7 ± 1.4                       |
|                                  | 32.1 ± 1.6                       | 22.7 ± 1.1                       |
|                                  | 32.0 ± 1.6                       | 26.7 ± 1.3                       |
| Males (%)                         | 26(14.1)                         | 93 (50.6)                        |
|                                  | 65 (35.3)                        | 127(69.7)                        |
|                                  | 42 (23.3)                        | 13 (7)                           |
| Females (%)                      | 17(9.8)                          | 94 (54.7)                        |
|                                  | 61 (35.5)                        | 149(73.7)                        |
|                                  | 46(22.8)                         | 7(3.5)                            |

Based on BMI, variations in fasting plasma glucose (FPG) levels were observed among patients relative to their degree of overweight and obesity. In non-obese, overweight, and obese diabetics, the mean FPG levels ± SD were 9.9 ± 2.8, 9.7 ± 3.1, and 12.4 ± 3.7 mmol/L, respectively. Notably, the mean fasting plasma glucose level was highest in obese patients, as shown in Table 2.

Table 2: Clinical and Laboratory Characteristics of Diabetics without Obesity (D1, n=43), with Overweight (D2, n=187) and with Obesity (D3, n=126) and in Control Subjects without Obesity (C1, n=276), with Overweight (C2, n=88) and with Obesity (C3, n=20)

Note: Different letters horizontally mean a significant difference at p<0.05 level according to Duncan test (ab = not significant with either a or b); HS = Highly significant; NS = Not significant

The total number of uncontrolled diabetics was 287, distributed according to their BMI into non-obese (33 out of 43, 76.6%), overweight (148 out of 187, 78.7%), and obese (106 out of 126, 82%) diabetics, respectively. This indicates an increase in the percentage of poorly controlled diabetics with higher BMI, although specific data was not shown. No significant differences were observed based on sex in lipid profile and fasting plasma glucose (FPG) levels among the diabetic patients, as indicated by unshown data. There was a significant positive association between BMI and serum triglycerides (TG) (p < 0.01), total cholesterol (TC) (p < 0.001), LDL-C (p < 0.001), and VLDL-C (p < 0.01). Conversely, serum HDL-C levels decreased significantly.
(p < 0.01) with increasing BMI, with the lowest HDL-C observed in individuals with BMI > 30 kg/m². Additionally, all other lipid profile parameters were highest in obese diabetics compared to other BMI groups, and these differences were statistically significant. Similar trends were observed in control subjects for all parameters except HDL-C levels, which were not significant, as shown in Table 2. A subject was considered dyslipidemic when the cutoff value criteria were met according to the recommendations of the British Hyperlipidaemia Association (1998). The prevalence of dyslipidemia increased with higher BMI levels in both sexes, indicating a lower prevalence rate in non-obese and a higher rate in overweight and obese diabetics, as depicted in Table 3.

Table 3: Prevalence of Dyslipidaemia in Diabetics (in relation to BMI) According to the Recommendation of the British Hyperlipidaemia Association (1998). Results are expressed as number (%) of patients

<table>
<thead>
<tr>
<th>BMI (Kg/m²)</th>
<th>Hypercholesterolemia TC &gt;3 mmol/L</th>
<th>Hypertriglyceridaemia TG &gt;2.4 mmol/L</th>
<th>LDL-C &gt;3 mmol/L</th>
<th>Low HDL-C &lt;1.5 mmol/L</th>
<th>TC: HDL-C ratio &gt;5.0</th>
<th>LDL-C: HDL-C ratio &gt;2.5</th>
<th>TG: HDL-C ratio &gt;3.0</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Non-obese BMI &lt;25 (n=43)</td>
<td>25</td>
<td>7.0</td>
<td>15</td>
<td>4.2</td>
<td>23</td>
<td>6.5</td>
<td>23</td>
</tr>
<tr>
<td>Overweight BMI 25-29.9 (n=187)</td>
<td>125</td>
<td>35.1</td>
<td>55</td>
<td>15.5</td>
<td>125</td>
<td>35.1</td>
<td>115</td>
</tr>
<tr>
<td>Obese BMI &gt;30 (n=126)</td>
<td>98</td>
<td>27.5</td>
<td>59</td>
<td>16.5</td>
<td>97</td>
<td>27.2</td>
<td>90</td>
</tr>
<tr>
<td>Total</td>
<td>248</td>
<td>69.6</td>
<td>129</td>
<td>36.2</td>
<td>245</td>
<td>68.8</td>
<td>228</td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;0.05 (S)</td>
<td>&lt;0.01 (S)</td>
<td>&lt;0.05 (S)</td>
<td>&gt;0.05 (NS)</td>
<td>&lt;0.001 (S)</td>
<td>&lt;0.05 (S)</td>
<td>&lt;0.01 (S)</td>
</tr>
</tbody>
</table>

Discussion
Accelerated coronary and peripheral vascular atherosclerosis stands out as one of the most prevalent and severe complications of long-term diabetes mellitus. In addition to other risk factors such as hypertension, smoking, and obesity, increasing attention has been directed towards secondary hyperlipidemia in contributing to the development of accelerated atherosclerosis.

The data presented in Table 1 indicates a positive correlation between BMI and age in diabetic individuals, which aligns with findings from previous studies.

In this study, plasma glucose concentration increased with rising BMI, and the proportion of poorly controlled diabetics rose correspondingly with increasing BMI. This suggests that obese patients exhibited a higher prevalence of poorly controlled diabetes compared to non-obese patients. This finding is significant as it underscores the close relationship between hyperglycemia and hypercholesterolemia, hypertriglyceridemia, and elevated LDL-C levels, all of which are well-documented risk factors for coronary heart disease. It is widely recognized that elevated levels of fat hinder the action of insulin or downregulate its receptors, leading to an insulin-resistant state that predisposes individuals to type 2 diabetes mellitus. This establishes a complex interplay between obesity, hyperglycemia, and dyslipidemia, contributing to the progression of cardiovascular complications in diabetic patients. The most prominent lipid abnormality observed in diabetes is hypertriglyceridemia, often accompanied by an increase in plasma cholesterol levels.

In this study, obese diabetic individuals exhibited a significant elevation in serum total cholesterol, triglycerides, LDL-C, and VLDL-C levels compared to non-obese diabetics, with notable differences in serum HDL-C levels. These findings are consistent with previous research. Earlier studies have indicated that high triglycerides and low HDL-C levels in type 2 diabetes are independent of the degree of obesity contrary to the findings of this study. However, Laakso and Pyorala...
(1990) noted that the effects of obesity, as measured by BMI, on serum lipids and lipoproteins were more pronounced in diabetics compared to non-diabetic individuals which aligns with the present study proposed that the severity of obesity plays a role in determining lipoprotein abnormalities in type 2 diabetes, in addition to the level of glycemic control. The current study clearly demonstrated that all lipid fractions (except HDL-C) were significantly elevated in obese diabetic patients compared to obese control subjects.

While some studies suggest that lipoprotein distribution in type 2 diabetes mellitus is not significantly influenced by the degree of glycemia, this study highlighted the magnitude and pattern of dyslipidemia among Iraqi adult diabetic patients. The prevalence of dyslipidemia increased with higher BMI levels in both sexes, consistent with the findings of [18].

Conclusion
The reported prevalence of dyslipidemia in diabetes varies widely, ranging from 25% to 60% This variability may be attributed to differences in the studied population, the level of glycemic control, and variations in the definition of "cut-off" values for lipid profile parameters. In conclusion, the study has identified several lipid abnormalities in type 2 diabetic patients and emphasized the importance of diabetic management in controlling these abnormalities, particularly through the management of overweight and obesity.

References