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# Investigation of the Lipid Profile Level Fluctuation in Diabetes Mellitus Patients in Iraq.

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**ABSTRACT**

Diabetes Mellitus is regarded as one of the commonest metabolic disorder all over the world. It can cause various endocrine disorders by affecting the secretion, metabolism, clearance or bioavailability of hormones. This study includes eighty-four (84) subjects, twenty (20) of them are healthy subjects chosen as control group, and the other sixty-four (64) are patients with Type 2 Diabetes Mellitus. The level of Glucose (FBS) is found to be significantly higher in diabetic patients compared with healthy control groups. Type 2 Diabetes Mellitus has significant correlation with lipid profile: by which Triglycerides, Cholesterol, Low-Density-Lipoprotein (LDL), Very-Low-Density Lipoprotein (VLDL) level was found to be significantly higher in patients with Type 2 Diabetics that have low level of High-Density Lipoprotein (HDL) when compared with healthy nondiabetic patients.

**Keywords:** Diabetes Mellitus, Lipid Profile.

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## INTRODUCTION

Diabetes mellitus (DM) has been defined as a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both [1]. Insulin is a hormone produced in pancreas that enable body cells to absorb glucose to turn into energy, if the body cell do not absorb the glucose, it will accumulates in its blood "hyperglycemia". The chronic hyperglycemia leading to various potential complications [2]. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels. The new classification of DM has been proposed by American Diabetes Association (ADA) and World Health Organization (WHO). They comprise four etiological types: Type 1 Diabetes (due to b-cell destruction, usually leading to absolute insulin deficiency), Type 2 Diabetes (due to a progressive insulin secretary defect on the background of insulin resistance), Gestational Diabetes Mellitus/GDM (diabetes diagnosed in the second or third trimester of pregnancy that is not clearly overt diabetes). Other specific types of diabetes due to other causes, e.g., Monogenic Diabetes Syndromes (such as neonatal diabetes and maturity-onset diabetes of the young [MODY]), diseases of the Exocrine Pancreas (such as Cystic Fibrosis), and drug -or chemical-induced diabetes (such as in the treatment of HIV/AIDS or after organ transplantation) [3-5].

## PATIENTS AND METHODS

Sixty-four patients with Type 2 Diabetes Mellitus were selected according to convenient non-random one and carried out by consecutive pooling of diabetic patients attending the National center of Diabetes (in AL-Mustansiria University) between November 2015 and February 2016, with type of drug divided patients to three groups (Group one: newly diagnosed/without therapy) 23; Group two: with metformin therapy (MT.)(20); Group three with metformin plus glibenclamide (MT. plus Glib.)(21) and 20 healthy subjects were included in the study as a control group). All patients were clinically examined, levels of Fasting Plasma Glucose (FPG), Glycated Hemoglobin (HbA1c%), Lipid Profile. From each subjects, 10 ml of blood were obtained by vein puncture, using a 10 ml disposable syringe. The blood sample was divided into two aliquots; 2 & 8 ml. The first aliquot blood was dispensed in a tube containing Ethylene Diamine Tetraacetic Acid (EDTA), this blood mixed gently and used for HbA1c estimation, while the second aliquot was dispensed in a plain tube and left for around 2-3 minutes (at room temperature) to clot at room temperature (25 °C), and then separated by centrifuge at (3000 rpm) for ten minutes (10 min) to collect serum. The serum was divided into two Eppendorf tubes and stored in the deep Freeze (-20 $^{0}$ C) until the assay day. The parameters measured be enzymatic methods: glucose kit supplied by Spinreact, Spain, Glycated hemoglobin (GHb) from Infopia, Korea, HDL-Cholesterol, Total Cholesterol and Triglyceride from Randox, U.K.

## RESULTS AND DISCUSSION

The present study included 84 subjects divided into four groups. Group 1: newly diagnosed (without therapy) (23); Group 2: with Metformin Therapy (MT.)(21); Group 3: with Metformin plus Glibenclamide Therapy (MT. plus Glib.)(20), and 20 Healthy subjects were included in the study as a control group. Duration of diabetes, and FPG were evaluated in the Sera of Type 2 Diabetic subjects and control, the result was revealed:

### Duration of Diabetes and Duration of Taking Treatment

The duration of diabetes and duration of taking treatment in Group 2 showed a nonsignificant difference when compared with Group 3 as shown in table (1), also revealed that mean of FPG for Group 1 (newly diagnosed), Group 2 (with Metformin Therapy), Group 3 (with Metformin plus Glibenclamide Therapy) and control group were (12.00 ± 0.49), (6.96 ± 0.28), (7.70 ± 0.28) and (4.67 ± 0.09) respectively. The difference was highly statistically significant between the four groups. In Group 1, FPG was higher than Group 2 and Group 3, this could be due to anti-diabetic drugs which reduce FPG. Metformin reduces blood glucose levels by inhibiting hepatic glucose production and reducing insulin resistance, particularly in liver and skeletal muscle(4). Glibenclamide enhances insulin secretion from the pancreas blocking hepatic glucose production and reduce glucose levels(5). There was a nonsignificant difference between Group 2 and Group 3. This result was in agreement with Marwan M. [6] who had demonstrated that there were a nonsignificant differences between fasting glucose of metformin treated group and those treated by a combination therapy of metformin plus glibenclamide.

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**Table (1): Clinical Characteristics of Three Groups Diabetic Patients and Control Group.**

| Parameters | Mean ± SE | | | | P-value |
|---|---|---|---|---|---|
| | Control group | Group1 Newly diagnosed | Group 2 MT. | Group 3 MT. plus Glib. | |
| Duration of diabetic (years) | --- | --- | 3.09 ± 0.23 a | 3.38 ± 0.24 a | 0.4030 |
| Duration of taking treatment(years) | --- | --- | 2.14 ± 0.23 a | 2.70 ± 0.25 a | 0.1059 |
| FPG(mmole/L) | 4.67 ± 0.09 c | 12.00 ± 0.49 a | 6.96 ± 0.28 b | 7.70 ± 0.28 b | 0.0001* |

*significant using ANOVA test at 0.05 level of significance.
Similar letters indicated there is no significant difference while different letters indicated there is a significant difference (P<0.05).

The results of Table (2) showed that mean cholesterol was found to be statistically significant (p<0.05) in Group 1 (newly diagnosed group) when compared with control group. This result was in agreement with Al-Naama *et al.* (2010) who found that patients with T2DM have significantly higher serum concentrations of cholesterol [7]. Group 1 showed a nonsignificant difference when compared with Group 2 and was a significant difference when compared with Group 3, so this result found that using Metformin plus Glibenclamide Treatment showed a favorable effect on cholesterol than using Metformin alone. A nonsignificant difference was observed in Group 2 (with Metformin Therapy) and Group 3 (with Metformin plus Glibenclamide Therapy) when compared with control group. This result was in agreement with Reyadh *et al.* (2012) who found that use of Metformin/Glibenclamide combination or Metformin alone in the treatment of T2DM maintained cholesterol levels closer to normal levels and in combination therapy serum, TC level was lower than Metformin used alone(8).

**Table (2): Mean Values of Serum Cholesterol in Three Groups Diabetic Patients and Control Group**.

| Parameter | Mean ± SE | | | | P-Value |
|---|---|---|---|---|---|
| | Control Group | Group1 Newly diagnosed | Group 2 MT. | Group 3 MT. plus Glib. | |
| Cholesterol (mmole/L) | 4.06 ± 0.20 b | 5.13 ± 0.24 a | 4.45 ± 0.32 a b | 3.78 ± 0.29 b | 0.0029* |
| Triglyceride (mmole/L) | 1.36 ± 0.10 c | 2.09 ± 0.20 a | 1.64 ± 0.16 a b c | 1.81 ± 0.13 a b c | 0.0111* |
| HDL(mmole/L) | 1.40 ± 0.07 a | 1.08 ± 0.03 b | 1.21 ± 0.04 b | 1.11 ± 0.04 b | 0.0001* |
| LDL(mmole/L) | 1.80 ± 0.11 b | 2.98 ± 0.18 a | 2.57 ± 0.27 a | 1.82 ± 0.28 b | 0.0003* |
| VLDL (mmole/L) | 0.273 ± 0.02 c | 0.419 ± 0.04 a | 0.328 ± 0.03 a b c | 0.362 ± 0.032 a b c | 0.0111* |

*significant using ANOVA test at 0.05 level of significance.
Similar letters indicated there is no significant difference while different letters indicated there is a significant difference (P<0.05).

**Serum Triglyceride**

The mean triglyceride was found to be significantly elevated (p<0.05) in Group 1 (newly diagnosed group) when compared with control group as shown in table (1). This result in agreement with Attalah (2007) [9] who found increase level of serum triglycerides in diabetic patients, which could be due to the increase of hepatic triglyceride synthesis. Group 2 (with Metformin Therapy) and Group 3 (with Metformin plus

Glibenclamide therapy) showed a nonsignificant difference when compared with Group 1 and control group. These results were in agreement with Kassim (2011) who found that Metformin and Glibenclamide therapies produces a nonsignificant favorable effect on serum triglyceride [10].

**Serum High Density Lipid (HDL)**

The results of Serum High Density Lipoprotein for three groups diabetics and control group as shown in Table (2) revealed that mean HDL-C was found to be significantly different ($p<0.05$) in diabetic patients in three groups when compared with control group. Type 2 diabetes is characterized by low HDL cholesterol (HDL-C) and HDL dysfunction [11]. The precise cause of the low HDL-C in Type 2 Diabetes is not known but may be the consequence of insulin resistance, augmented very low density lipoprotein production and increased activities of cholesteryl ester transfer protein and hepatic lipase(12). Group 2 (with Metformin Therapy) and Group 3 (with Metformin plus Glibenclamide Therapy) showed a nonsignificant difference when compared with Group 1. This result was in agreement with Cagatay *et al*. (2011) who found that using Metformin as a monotherapy or combination with Glibenclamide in Type 2 Diabetics produce a nonsignificant effect on HDL-C [12-13].

**Serum Low Density Lipid (LDL)**

The results of Serum Low Density Lipoprotein for Group 1 and Group 2 diabetic patients was found to be significantly different ($p<0.05$) when compared with control group. Singh and Kumar (2011) found that the level of LDL significantly higher in Type 2 Diabetics [14]. Increased elimination of Lipids and Apolipoproteins from VLDL particles results in the increased production of Intermediate Density Lipoprotein (IDL) and LDL [15]. Group 1 showed a nonsignificant difference when compared with Group 2 and show a significant difference when compared with Group 3, so this result found that using Metformin plus Glibenclamide Treatment showed a favorable effect on LDL than using Metformin alone. Dailey et al. (2002) found that combination therapy of Metformin and Glibenclamide shows a favorable effect on LDL-C levels and closer to that of nondiabetic subjects [16-20].

**Very Low Density Lipoprotein (VLDL)**

The results of Serum Very Low Density Lipoprotein for three groups diabetic and control group as shown in Table (2) revealed that mean VLDL-C in Group 1(newly diagnosed group) was found to be significantly elevated ($p<0.05$) when compared with control group. This result was in agreement with Petrovic *et al.* (2010) who showed a significant elevation in VLDL-C when compared diabetic patients with controls. This may be due to insulin resistance has striking effects on lipoprotein size and subclass particle concentrations for VLDL and that lead to increased hepatic secretion of VLDL-C in Type 2 Diabetic patients [17-20]. Comparing Group 2 (with Metformin Therapy) and Group 3 (with Metformin plus Glibenclamide Therapy) with the control group showed a nonsignificant difference. This result was in agreement with Reyadh *et al.* (2012) [8] who found a nonsignificant difference between Metformin and Metformin plus Glibenclamide treated groups compared with control group(8).

## CONCLUSIONS

- Using Metformin as monotherapy or combination with Glibenclamide can reduce FPG and HbA1c% levels in Type 2 Diabetic patients.
- Metformin alone produces a nonsignificant favorable effect on all lipid profile parameters while Metformin plus Glibenclamide showed a significant reduction in TC and LDL-C.
- In comparison with healthy control groups, the level of glucose (FBS) is found to be higher in diabetic patients.
- In comparison between healthy nondiabetic patients and Type 2 Diabetic patients, a low level of (HDL) seen in the diabetic patients with significantly a higher level of Triglycerides, Cholesterol , Low-Density-Lipoprotein (LDL), Very-Low-Density Lipoprotein (VLDL).

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