The Impact of Anti-Diabetic Medications on Lipid Profiles in Diabetic Patients in White Nile State, Sudan

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Background: Diabetes mellitus, commonly referred to as diabetes, is indeed a complex group of diseases that affect the processing of glucose in the body. Glucose, being the important source of energy for the cells, is considered to be a vital component of one's health. The underlying cause of diabetes varies by type, leading to an increase in blood sugar level and giving rise to serious health problems. Type 1 and type 2 diabetes are related to chronic conditions. Initially, the management of diabetes involves maintaining healthy blood sugar levels through regular monitoring, insulin therapy, diet, and lifestyle choices. Later, antidiabetic medicines are prescribed, which are found to have varied adverse effects on individuals.

Methodology: The study includes (105) participants, whose ages ranged from 27 to 66 years. The

study group represents 85 diabetic patients. They were divided into four groups according to their type of anti-diabetic therapy: (20) with insulin therapy (Group 1), (27) with metformin therapy (Group 2), (07) with metformin plus Glimepiride therapies (Group 3), (31) with Glimepiride therapy (Group 4), and (20) as control (Group 5). In the study, lipid profile levels and fasting blood glucose were determined by enzymatic methods.
Result: There is a significant increase in the level of lipid profile in the patients' group except for the TC and HDL-c; it was in a normal range within control. While metformin plus Glimepiride showed a significant increase in VLDL-c within the control P-value (.049).
Conclusion: Many medications widely prescribed for diabetic patients influence, to varying degrees, selected components of the routine lipid profile (LDL-C, HDL-C, and TG levels) and, consequently, potentially the risk for atherosclerotic cardiovascular disease (ASCVD).

Keywords: Diabetic Medications, Lipid Profiles, Diabetes Mellitus.

1. Introduction

Diabetes mellitus (DM) is defined as a collection of metabolic disorders characterized by high blood sugar levels due to either inadequate insulin secretion, improper insulin action, or both.

It comprises four etiological types: type 1 diabetes (due to β-cell destruction, usually leading to absolute insulin deficiency), type 2 diabetes (due to a progressive insulin secretory defect on the background of insulin resistance), and gestational diabetes mellitus (GDM) (diabetes diagnosed in the second or third trimester of pregnancy that is not overt diabetes). (1)

Patients with diabetes are more likely to experience dyslipidemia, hypertension, and obesity. Early detection and immediate treatment can lessen the impact of diabetes and its associated complications, making diabetes screening advisable in certain situations.

Epidemiological studies have demonstrated that type 2 diabetes mellitus (DM) is a well-known risk factor for the development of cardiovascular disease, cerebrovascular disease, and peripheral vascular diseases. Dyslipidemia is a risk factor for coronary artery disease, a leading cause of mortality in patients with diabetes mellitus.

Although many patients carefully deal with their disease management, many studies revealed a bad progression of the disease. Here we will focus on the effect of some anti-diabetic drugs used in White Nile State patients on their lipid profiles (9).

Diabetes mellitus is a chronic, lifelong disease caused by a deficiency or resistance to the hormone insulin, which regulates the level of glucose in the blood. The marked hyperglycemia associated with diabetes gives rise to serious microvascular and macrovascular complications and damage to many body systems. The three primary forms of diabetes are Type 1, Type 2, and gestational diabetes. The chronic types of diabetes (type 1 and type 2) have different etiological factors. (10)

Other types include (i) diabetes related to specific single genetic mutations that may lead to rare forms of diabetes, for instance, Maturity Onset Diabetes of the Young (MODY); (ii) diabetes secondary to other pathological conditions or diseases (because of pancreatitis, trauma, or surgery of pancreas); (iii) drug- or chemically-induced diabetes. (11)

Diabetes is a systemic disease that affects most of the body's organs, especially the heart, blood vessels, kidneys, eyes, nerves, and teeth. In high-income countries, diabetes is the leading cause of chronic heart disease, renal failure, blindness, and non-traumatic lower limb amputation. (12)

Many patients with T2DM are often treated with insulin early in the disease process, despite the availability of multiple classes of anti-diabetic agents with extremely low risks of hypoglycemia. Additionally, as diabetes progresses and β-cell function continues to decline, the majority of individuals with Type 2 Diabetes Mellitus (T2DM) will ultimately need insulin therapy to maintain effective glucose control and avert complications associated with diabetes. Direct insulin-related positive effects on the lipid profile include reductions in TG levels, most apparent with the more dramatic improvement of glycemic control, along with increases in HDL-C levels; LDL-C levels remain typically unaffected. (17)

Hyperglycemia is an increase in plasma glucose level due to abnormalities in glucose metabolism that are most commonly measured with threshold criteria for fasting plasma glucose (FPG) or 2-h plasma glucose. (33)

Hypoglycemia in diabetic patients is an abnormally low concentration of glucose in the blood caused by insufficient food intake, excessive exercise, or overdosage with oral hypoglycemic agents or insulin. The development of hypoglycemia is a present possibility in all patients with diabetes treated with insulin or oral hypoglycemic medications. (35)

Proper monitoring and treatment of glycemia and its complications in diabetic patients have been the keys to reducing diabetes-related deaths. Although many diabetic patients believe that they are in the right direction in using their treatments and that their health matters are at their best, they are surprised by the instability in the level of fats in the blood, which increases their health problems, so we did this study to further clarify the effect of diabetes treatments on diabetic patients is the level of lipids in the blood.

2. Methodology:

A total of 85 diabetic patients attending the diabetic clinic of health insurance (main center) were randomly selected for the study as a case group, while 20 healthy subjects were the control. The participants were already diagnosed with diabetes and were under treatment at the diabetic clinic.

Four ml of venous blood were collected using a disposable sterile syringe and transferred into a plain container from diabetic patients after overnight fasting (10-12 hours). Blood was immediately centrifuged at 4000 rpm for 10 minutes, and serum was separated and stored at $4^{o}C$.

Statistical Analysis:

Data are expressed as means ± SE. Statistical analysis has been performed using SPSS (version 21). Differences from the baseline were assessed by a t-test. A P-value of <0.05 was considered significant.

3. Results:

A sample of 85 patients randomly selected, (32) 37.6% male and (53) 62.4% female, were divided into four groups according to their type of anti-diabetic therapy: (20) with insulin therapy (Group 1), (27) with metformin therapy (Group 2), and (07) with metformin plus Glimepiride therapies (Group 3); and (31) with Glimepiride therapy (Group4) and (20) as control (Group 5) (13) 65% male and (7) 35% as female. General characteristics among groups are studied in Table 1.

Table 1. General characteristics of a group study:

Groups	Controls		Cases	
Age	N	%	N	%
<40yrs	4	20%	4	7.7%
40-50yrs	9	45%	30	35.3%
>50yrs	7	35%	51	60%
BMI	Controls		Cases	
Average	22.805		27.852471	
Sex	N	%	N	%
Male	13	65%	32	37.6%
Female	7	35%	53	62.4%
DM Duration	Cases			
	N		%	
<5yrs	28		32.9%	
5-10yrs	42		49.5%	
>10yrs	15		17.6%	
Complication	N		%	
Retinopathy	57		52.3%	
Neuropathy	40		36.7%	
Nephropathy	4		3.7%	
Amputation	8		7.3%	

Table 2. Effects of anti-diabetic medication on lipid profiles among diabetic groups:

Parameters	Mean ± Std. Error			
	Insulin	Metformin	Glimepiride	Metformin & Glimepiride
FBG	196.3±17.8*	181.2±19.7*	189.7±13.9*	143.0±29.1
TC	234.3±12.7*	228.3±14.2*	240.2±12.9*	238.7±23.7
TG	136.9±12.4*	128.1±8.2*	149.7±12.0*	196.0±53.6*
LDL	163.7±8.6*	157.5±10.4*	163.0±8.7*	153.4±17.9*
HDL	43.8±3.7*	44.7±4.2*	46.0±3.1*	42.3±6.7*
VLDL	27.3±2.4*	25.4±1.6*	29.9±2.4*	39.1±10.7*

*Significant using t-test at P< 0.05 level of significance.

4. Discussion:

The current study was a cross-sectional study. Conducted in centers in Kosti, White Nile State, Sudan. A total of 85 diabetic patients attending the diabetic clinic of health insurance (main center) were randomly selected for the study as the case group, while 20 healthy subjects were the control. The participants were already diagnosed with diabetes and were under treatment at the diabetic clinic. For each patient, a questionnaire was filled out to obtain information regarding their age, sex, residence, tribe, and information about education, and occupation. Additional data, such as family history, type of therapy (natural or chemical), and nutritional program. Four ml of venous blood were collected using a disposable sterile syringe and transferred into a plain container from diabetic patients after overnight fasting (10-12 hours). Blood was immediately centrifuged at 4000 rpm for 10 minutes, and serum was separated and stored at 4 C^{o}. Fasting blood sugar and lipid parameters were estimated.

In contrast to many studies, no significant improvement regarding glycemic parameters (FBG) and lipid profiles was seen in patients treated with insulin, glimepiride, metformin, or a combination when compared with controls in our study. Although the defects in these parameters are slightly away from their normal values. Moreover, the defects for all medications chosen—insulin, glimepiride, metformin, and combination—were similar. From the findings, we attributed this event to poor management.

Type 2 diabetes is characterized by low HDL cholesterol (HDL-C) and HDL dysfunction (36). The exact reason for low HDL-C levels in type 2 diabetes remains unclear, but it could result from insulin resistance, increased production of very low-density lipoprotein, and heightened activity of cholesteryl ester transfer protein and hepatic lipase (37). Cagatay et al. (2011) found that using metformin as monotherapy or in combination with glimepiride in type 2 diabetics produced no significant effect on HDL-C. (38) The results of serum low-density lipoprotein for group 1 and group 2 diabetic patients were found to be significantly different ($p \leq 0.05$) when compared with a control group, and this result matches our findings. On the other hand,

Singh and Kumar (2011) found that lipids are not significantly improved when they focus on the level of LDL, which is significantly higher in type 2 diabetics (39). Increased elimination of lipids and apolipoproteins from VLDL particles results in increased production of intermediate-density lipoprotein (IDL) and LDL (40).

Additionally, the study by Petrovic et al. (2010) demonstrated a significant increase in VLDL-C levels when comparing diabetic patients to control subjects. This may be due to insulin resistance having striking effects on lipoprotein size and subclass particle concentrations for VLDL, and that leads to the increased hepatic secretion of VLDL-C in type 2 diabetic patients. (41), while Reyadh et al. (2012) found no significant difference between metformin and metformin plus glibenclamide-treated groups compared with the control group (42). Dailey et al. (2002), moving in the opposite direction, said the combination therapy of metformin and glibenclamide shows a favorable effect on LDL-C levels closer to that of non-diabetic subjects. (41)

5. Conclusion:

Many medications widely prescribed for diabetic patients influence, to varying degrees, selected components of the routine lipid profile (LDL-C, HDL-C, and TG levels) and, consequently, potentially the risk for ASCVD. Although some effects can be substantial, many medications are linked to minor alterations in the lipid profile, making them unlikely to independently influence ASCVD risk. However, the cumulative effect on patients taking multiple medications may be significant and should not be overlooked. The overall impact of these medications on the lipid profile, along with their effects on other cardiovascular health factors, should be anticipated, and their potential influence on ASCVD risk should be taken into account.

Ethical clearance:

On March 1, 2022, the University of El Imam El Mahdi's School of Medicine's Standing Committee for Scientific Research granted ethical approval, and all procedures were carried out in compliance with the approval's guidelines.

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Disclosure of conflict of interest:

The authors declare that they have no conflicts of interest.

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