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Effect of Metformin on Lipid Profiles of T2DM Mellitus

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Abstract **Original Research Article**

Introduction: T2DM mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance, leading to deregulated blood glucose levels and associated metabolic abnormalities. The standard management of T2DM includes pharmacological interventions, such as metformin, and lifestyle modifications like dietary changes. Metformin is widely prescribed for its glucose-lowering effects and potential benefits on lipid profiles. Dietary interventions, particularly those emphasizing low glycemic index foods and reduced saturated fat intake, are also critical in managing metabolic parameters in T2DM. Despite the known benefits of both interventions, limited data is available on their combined effects on haemoglobin levels, cholesterol, and triglycerides in real-world settings. This study aims to retrospectively evaluate the effects of metformin and dietary patterns on haemoglobin, cholesterol, and triglyceride levels in T2DM patients by analysing existing medical records. ***Methodology:*** A retrospective cohort study was conducted at the internal medicine department at King Hussein Medical Centre in The Royal Medical Services, Amman, Jordan. The study was conducted by obtaining Data for haemoglobin, cholesterol, and triglyceride levels from electronic medical records (Hakeem) of 200 T2DM patients who attended the outpatient diabetes clinic. Laboratory results were obtained from June 2024 to December 2024. Patients were divided to two groups: T2DM group used metformin without diet (group I) and a T2DM group also used metformin but with diet (group II). The parameters were assessed at day 0, after 3 months and after 6 months of treatment with metformin. Hb, TC and TGs, were measured. ***Results:*** There was a significant ($p<0.05$) drop in the Hb concentration in the blood between group I and group II, according to the results. Data analysis revealed that group I had a significantly higher cholesterol level. The results of the statistical analysis indicated that group I and group II differed significantly, with group I's triglyceride levels being lower than group II's. ***Conclusion:*** In individuals with type 2 diabetes, metformin positively influences lipid profiles while also enhancing glycaemic control. This capability to reduce cardiovascular risk a significant issue for diabetic patients is enabled by these impacts.

Keywords: T2DM (Type 2 Diabetes Mellitus), Metformin, Dietary Intervention, Lipid Profile (Cholesterol, Triglycerides), Hemoglobin (Hb).

INTRODUCTION

Dyslipidaemia is one of the main risk factors for cardiovascular disease in diabetes mellitus (DM), which is the world's principal cause of morbidity and death. Among dyslipidaemia, hypercholesterolaemia is the most prevalent type [1]. Both short-term and long-term complications are more likely to occur in patients with type 2 diabetes (T2DM), including microvascular conditions like retinopathy, nephropathy, and neuropathy, as well as cancers and macrovascular conditions like hypertension, hyperlipidaemia, heart attacks, coronary artery disease, strokes, cerebral vascular disease, and peripheral vascular disease [2]. Atherogenic dyslipidaemia, which is the most prevalent kind of dyslipidaemia in people with T2DM, is typified by increased levels of small dense LDL (sdLDL), decreased HDL cholesterol, and elevated triglycerides (TGs) [3]. Patients now have more options to reach their desired cholesterol levels because to the availability of numerous lipid-lowering medications and supplements. Even in diabetic patients receiving the best care, triglyceride-rich lipoproteins both fasting and non-fasting are increasingly thought to play a direct role in atherosclerosis, even when low-density lipoprotein cholesterol levels are sufficiently managed by statins and/or ezetimibe [4]. High triglycerides (TGs), high sdLDL cholesterol, and low HDL cholesterol are the hallmarks of atherogenic dyslipidaemia, the most

prevalent kind of dyslipidaemia in people with T2DM [5]. Numerous lipid-lowering medications and supplements are now available, giving patients more chances to reach their desired lipid levels. Low-density lipoprotein cholesterol levels that are adequately controlled by statins and/or ezetimibe are among the triglyceride-rich lipoproteins that are increasingly thought to be a direct cause of atherosclerosis in diabetic patients, even in those who are receiving the best care [6]. The excess free fatty acids that are mostly generated by subcutaneous fat can lead to cell malfunction and death. They can also build up as TGs in non-adipose tissues, such as the liver, heart, pancreas, and muscle [7]. Lower HDL-C concentrations, the production of tiny, dense LDL particles, and increased TG levels are the last symptoms of dyslipidaemia. Insulin resistance, hyperinsulinemia, and vascular calcification are present in the majority of diabetes individuals [8]. In addition to encouraging atherosclerosis, they might hasten the development of unstable plaques or rupture of existing plaques, which can result in thrombosis, acute coronary syndrome, and even death, especially if treatment is postponed [9]. In atherogenesis and its thrombotic consequences, platelets are essential. Insulin resistance, insufficient insulin secretion, and excessive or incorrect glucagon production all contribute to type 2 diabetes, which is characterised by hyperglycemia [10]. Numerous neuropathy, macrovascular, and microvascular problems are linked to poorly managed type 2 diabetes. Retinal, renal, and perhaps neuropathic diseases are examples of microvascular consequences of diabetes [11]. Peripheral vascular disease and coronary artery disease are examples of macrovascular problems. Peripheral and autonomic nerves are impacted by diabetic neuropathy [12].

In addition to diet and exercise, hydroxymethylglutaryl-CoA (HMG-CoA) reductase inhibitors, commonly referred to as "statins," are used to treat hypercholesterolaemia by increasing the concentration of HDL-C and decreasing the concentrations of triglycerides (TG), total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-C) [13]. The most often given oral antidiabetic drug is metformin. Among other things, the molecular mechanisms of action of metformin are thought to be explained by the direct or indirect activation of Adenosine Monophosphate-activated protein kinase (AMPK) and non-AMPK pathways [14].

Metformin is a prominent antihyperglycemic agent that is sensitive to insulin receptors, exhibiting remarkable safety and efficacy profiles. It is also quite reasonably priced. According to new clinical and experimental data, metformin may have pleiotropic non-glycemic effects [15]. In the management of patients with type 2 diabetes mellitus (TDM2), metformin is the preferred initial glucose-lowering agent owing to its efficacy, safety profile, beneficial cardiovascular and metabolic benefits, and compatibility with other antidiabetic drugs [16].

The effects of taking metformin and statins together on lipid profiles and cardiovascular outcomes in individuals with T2DM were covered in earlier research [17]. In contrast to treatment with either medication alone, research by Ahmed *et al.,* showed that the combination of metformin and statins dramatically improved lipid profiles [18]. In a different trial, Smith *et al.,* discovered that individuals on statins and metformin together had higher HDL-C levels and lower triglycerides and LDL-C than those on metformin alone [19]. These results imply that the combined treatment might provide better cardiovascular protection and cholesterol control. This inquiry primarily examines the effect of metformin on the lipid profile in individuals with type II diabetes.

Goals

1. To assess the impact of metformin and dietary practices on triglyceride, total cholesterol, and haemoglobin levels in patients with type 2 diabetes mellitus (T2DM).
2. To compare the lipid profiles (triglycerides and cholesterol) of T2DM patients undergoing metformin plus dietary intervention against those receiving metformin only.
3. To examine variations in haemoglobin levels among T2DM patients utilising metformin based on dietary adherence.

METHODOLOGY

A retrospective cohort study was conducted at the internal medicine department at King Hussein Medical Centre in The Royal Medical Services, Amman, Jordan. The study was conducted by obtaining Data for haemoglobin, cholesterol, and triglyceride levels from electronic medical records (Hakeem) of 200 T2DM patients who attended the outpatient diabetes clinic. Laboratory results were obtained from June 2024 to December 2024. Patients were divided to two groups: T2DM group used metformin without diet (group I) and a T2DM group also used metformin but with diet (group II). The parameters were assessed at day 0, after 3 months and after 6 months of treatment with metformin. Hb, TC, TGs, HDL-C, and LDL-C were measured.

Statistical Analysis:

Standard analysis of the data of different studied group was performed using the computerized statistical program: The SPSS program (Statistical Program for Social Sciences 25). All values expressed as Mean±SD and analysis of variance (ANOVA) was used to compare the results of different groups. The differences are considered to be significant at ($P \leq 0.05$).

Inclusion and Exclusion Criteria

Adults with T2DM who were 18 years of age or older, taking metformin for at least six months, had recent lipid profile data, haemoglobin, and verified dietary adherence (based on nutritionist notes or patient self-reports) were eligible to participate. Type 1 diabetes, severe comorbidities, anaemia, pregnancy, and the use of additional cholesterol-lowering medications or any medications known to influence lipid profiles were among the exclusion criteria.

RESULTS

Although the two groups' average age and BMI differ somewhat, they are not statistically significant (p = 0.15 and p = 0.08, respectively). This implies that the ages and body compositions of the two groups are somewhat comparable. HbA1c levels are the sole statistically significant difference between the two groups (p = 0.04), with Group II exhibiting higher values. This would suggest that Group II's glycaemic control is worse.

Other demographic and medical characteristics are illustrated in Table 1.

Table 1: Demographic and Medical Characteristics of the two study groups

Characteristics	Group I (N=100)	Group II (N=100)	P value
Age (Mean ± SD, years)	58.4 ± 9.6	60.2 ± 10.3	0.15
Gender			
Male	55 (55%)	45 (45%)	0.21
Female	45 (45%)	55 (55%)	
BMI (Mean ± SD, kg/m²)	28.9 ± 4.7	30.3 ± 5.0	0.08
Diabetes Duration (Mean ± SD, years)	8.1 ± 5.1	9.5 ± 5.8	0.09
HbA1c (Mean ± SD, %)	7.9 ± 1.1	7.6 ± 1.3	0.04 (*)
Hypertension	60 (60%)	70 (70%)	0.19
Dyslipidemia	45 (45%)	50 (50%)	0.54
Smoking History			
Current Smoker	15 (15%)	20 (20%)	0.41
Former Smoker	30 (30%)	35 (35%)	0.52
Never Smoked	55 (55%)	45 (45%)	
Exercise Habits			
Yes	45	48	0.071
No	55	52	

p-value interpretation: **(*) Statistically significant if p < 0.05.**

Effects of metformin, on Hb, serum cholesterol and serum triglyceride concentration

There was a significant (p<0.05) drop in the Hb concentration in the blood between group I and group II, according to the results. Data analysis revealed that group I had a significantly higher cholesterol level. The results of the statistical analysis indicated that group I and group II differed significantly, with group I's triglyceride levels being lower than group II's (Table 2).

Table 2: Effect of Metformin on Lipid Profiles and Hemoglobin

Parameter	Group 1 (n=100, Mean ± SD)			Group II (n=100, Mean ± SD)			p-value
Time Point	**Day 0**	**3 Months**	**6 Months**	**Day 0**	**3 Months**	**6 Months**	
Total Cholesterol (mg/dL)	205.5 ± 25.6	197.6 ± 22.8	185.4 ± 20.5	212.1 ± 24.9	175.6 ± 23.1	156.9 ± 21.2	0.021*
Triglycerides (mg/dL)	180.7 ± 28.4	160.3 ± 25.6	145.2 ± 22.9	182.5 ± 27.9	165.1 ± 24.7	150.4 ± 21.8	0.034*
Hemoglobin (g/dL)	12.4 ± 1.5	12.1± 1.4	11.2 ± 1.4	11.5 ± 1.23	12.7 ± 1.26	13.94 ± 1.4	0.032*

p-value interpretation: **(*) Statistically significant if p < 0.05.**

DISCUSSION

The World Health Organisation (WHO) defines diabetes mellitus as a long-term metabolic condition marked by high blood glucose levels that eventually damages the heart, blood vessels, eyes, kidneys, and nerves. T2DM, which accounts for more than 90% of cases of diabetes mellitus, is characterised by tissue insulin resistance (IR), insufficient compensatory insulin secretory response, and insufficient insulin secretion by pancreatic islet β-cells [20]. The most significant therapy approach for metabolic syndrome that has been shown to be successful is lifestyle adjustment, with an emphasis

on food and physical activity changes. Another popular treatment for metabolic syndrome is medication therapy. Despite its mild side effects, metformin has been demonstrated to increase insulin sensitivity and aid in weight loss [21]. One of the most common and widespread blood-related disorders that affects diabetic people is anaemia. Patients with DM who also have renal impairment are most likely to experience it. Research suggests that the kidney's inability to produce enough erythropoietin is usually linked to anaemia in patients with T2DM [22,23]. So there are a number of studies are consistent with our study which indicating that metformin causes a decrease in the level of hemoglobin [24,25]. In the current study, data analysis revealed that group I had a significantly higher cholesterol level. The results of the statistical analysis indicated that group I and group II differed significantly, with group I's triglyceride levels being lower than group II's Interestingly, similar findings has been reported with diabetic patients treated with Metformin respectively in previous study by Zannah *et al.*, (2014) [27]. This may be the result of increased hepatic breakdown of cholesterol and lower chylomicron absorption of cholesterol because α-glucosidase enzymes are inhibited. According to the aforementioned finding, using metformin may help with lipid dysfunction and hence postpone the onset of problems from diabetes. Their encouragement of glucose utilisation and thus decreased fat mobilisation may be the cause of this. It is commonly known that untreated diabetes mellitus causes a drop in HDL-C and an increase in total cholesterol and triglycerides, all of which are risk factors for coronary artery disease [28]. In people with type 2 diabetes, metformin dramatically lowers serum triglyceride and cholesterol levels. A typical characteristic of diabetic dyslipidaemia is elevated triglycerides and cholesterol, which are linked to insulin resistance. Metformin stimulates AMP-activated protein kinase (AMPK), which promotes fatty acid oxidation and suppresses the liver's fatty acid production, or lipogenesis. Additionally, it decreases the liver's synthesis of very-low-density lipoprotein (VLDL), a lipoprotein that is rich in triglycerides.

CONCLUSION

Metformin's main therapeutic benefits stem from its capacity to reverse the effects of insulin resistance, lowering blood sugar levels without raising basal insulin levels or producing clinically significant hypoglycemia or weight gain. Metformin has a number of additional clinical advantages beyond glycaemic control that are very pertinent to type 2 diabetes, namely an enhanced blood lipid profile, decreased blood coagulability, and decreased inflammation, all of which contribute to a lower risk of cardiovascular disease.

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