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EFFECT OF SITAGLIPTIN ON LIPID PROFILE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS.

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ABSTRACT

BACKGROUND: Dyslipidemia has been identified as a major risk factor for the development of macrovascular disease; hence, disturbed lipid metabolism and altered serum lipid levels exacerbate the chances of cardiovascular disease and stroke. Sitagliptin, one of the emerging antidiabetic drugs was selected to investigate its effect on the lipid profile in type 2 diabetes. **METHODS:** This prospective study was conducted on patients diagnosed with type 2 diabetes. The patients were recruited according to the inclusion and exclusion criteria and were monitored for a period ranging from 18 to 36 weeks. Blood samples were taken and analyzed for lipid and blood parameters using the standardized enzymatic method. A paired sample t-test and chi-square test were applied to identify the mean difference in pre- and post-findings using SPSS version 15. The level of significance was set at a *p*-value of ≤ 0.05. **RESULTS:** Out of 110 patients, only 100 were selected for the study. Among these, males accounted for 54.50% and females for 45.50%, with a mean age of 50.35 years. The mean fasting blood glucose level prior to therapy was 163.65±32.0 mg/dl, and post-therapy it was 106.20±17.74 mg/dl. At baseline, HbA_1C was 9.08±0.97%, which reduced to 6.26±0.87% after therapy. After 36 weeks of treatment with sitagliptin, triglycerides were reduced from 291.32±71.58 to 145.83±36.18 mg/dl. Initially, total cholesterol was found to be 250.30±57.71 mg/dl, which decreased to 131.89±12.80 mg/dl. Upon further analysis, VLDL-C changed from 35.98±7.65 mg/dl to 24.70±7.71 mg/dl. LDL-C levels showed a highly significant reduction from baseline 136.98±20.77 to 119.87±9.24 mg/dl, while HDL-C was found to have increased to 43.63±7.21 mg/dl from 25.38±5.33 mg/dl. **CONCLUSION:** The results showed statistical significant difference in lipid and blood profiles after treatment with sitagliptin for 36 weeks. It significantly reduced the levels of triglycerides, cholesterol, LDL-C, and VLDL-C, while also improving HDL-C levels. **KEYWORDS:** Sitagliptin, dyslipidemia, glycemic index; metabolic syndrome, lipids, lipoproteins.

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INTRODUCTION

Diabetes mellitus is referred to as an endocrine metabolic disorder characterized by increased blood glucose levels along with diminished fat and/or protein metabolism [1]. The most predominant feature of type II diabetes is impaired insulin sensitivity, secretion, or both. Type II diabetes is now considered a serious

health concern that affects the population worldwide, resulting in a high rate of diabetes-related morbidity and mortality [2]. According to the International Diabetes Federation, the prevalence of type II diabetes will rise to 350 million people in 2030 [3]. In fact, studies have shown that it may lead to chronic complications, such as macrovascular, microvascular, and even neuropathic disorders. One of the prevalent metabolic changes associated with diabetes is dyslipidemia. This condition is characterized by lipid irregularities such as increased levels of triglycerides, decreased levels of HDL, elevated serum cholesterol, and changes in low-density lipoprotein LDL cholesterol [4,5]. Although extensive evidence from clinical interventional studies has investigated that low-density lipoprotein LDL and higher triglyceride levels are major risk factors for cardiovascular disease [6], thus, antidiabetic agents that have cardioprotective effects would be a preferred option for diabetic patients [6]. Recently, dipeptidyl peptidase-4 inhibitors DPP4 have been proven to be safe not only for glycemic control but for prevention of cardiac complications as well [7]. Sitagliptin, belonging to the class of DPP-4 inhibitors, is effective in the management of type II diabetes. It has been found to be efficacious in reducing HbA_1C, comparable to pioglitazone or sulfonylurea. Besides the hypoglycemic effect, sitagliptin also has favorable effects on lowering plasma lipid levels by inhibiting the enzyme DPP-4 and increasing the concentration of DPP4 substrates [8, 9]. Pakistan is an underdeveloped country and the increased number of cases of diabetes mellitus with altered lipid profiles is an alarming signal for cardiovascular disease. Thus, there remains a clinical need to investigate the effect of the widely prescribed DPP-4 inhibitor on diabetic patients. The present study aims to evaluate the influence of sitagliptin on the lipid status of type II diabetic patients.

METHODS

This was a prospective study conducted at the Outpatient Department of Peoples University of Medical & Health Sciences for Women PUMHSW Hospital, Nawabshah Shaheed Benazirabad from November 2023 to December 2023. A sample size of 100 patients was calculated at a 95% confidence level. A non-probability consecutive sampling technique was applied for sample selection. Patients meeting the inclusion criteria were those diagnosed with type II diabetes and an altered lipid profile, whereas the exclusion criteria covered patients: 1 diagnosed with co-morbid conditions such as renal impairment, liver cirrhosis, endocrine disorders, pulmonary tuberculosis, and systemic hypertension; 2 those with normal lipid levels; and 3 patients aged <40 and >60 years, as these could adversely impact the participants' health or disrupt the study's assessment **Figure-1**.

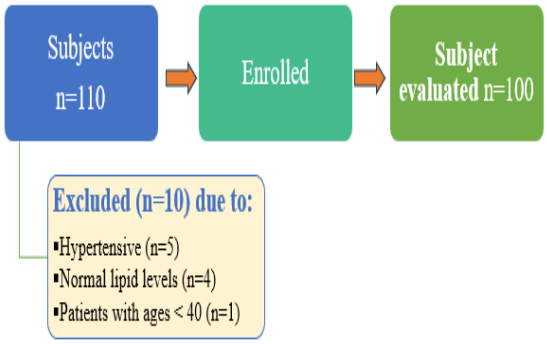

Figure 1: Study Participation

The study was approved for ethical approval by Research Review Committee of PUMHSW, and all the enrolled patients were informed prior to their participation in the study. The privacy of the data was ensured and kept confidential throughout the study. The participants underwent screening according to the protocol, including a detailed medical history and clinical examination. The diagnosis of diabetes was confirmed based on fasting blood sugar levels of >126 mg/dl and >200 mg/dl in the non-fasted state 10. Sitagliptin 50 mg twice daily was orally administered for a treatment period of 18 weeks and continued till 36 weeks. Venous blood was drawn from the patients after a 12-hour overnight fast, and the serum was separated into aliquots in glass tubes for analysis of blood glucose and lipid parameters. Fasting blood sugar was assessed using the glucose oxidation method, and HbA1c was determined using Tetra-decyl-trimethyl ammonium bromide TTAB. Total cholesterol TC and triglycerides TG were analyzed using the enzymatic colorimetric method, while the precipitant method was applied to determine HDL-C, VLDL-C, and LDL-C levels. The computed data was analyzed using SPSS version 26.0. Quantitative parameters were expressed as Mean±SD, and the difference in

diabetic and lipid profiles was examined using a paired *t*-test.

RESULTS

A total of 110 type II diabetic patients were initially recruited for the study. Among them, only 100 participants met the inclusion criteria and were enrolled. The enrolled participants comprised 60 54.50% males and 40 45.50% females. The mean age of the patients was 50.35±4.21, with a maximum and minimum age of 45 and 60 years, respectively. The baseline characteristics, such as body mass index, systolic, and diastolic blood pressure are presented in **Figure-1**. The details of fasting blood sugar FBS and glycated hemoglobin levels HbA1C in the selected participants are presented in **Table-1**. At the beginning of the study, fasting blood glucose was recorded at 163.65±32.05 mg/dl. After 18 weeks of treatment, the blood glucose level decreased significantly to 144.87±24.09 mg/dl $p<0.05$, with further reduction occurring by the end of the 36th week, which found to be 106.20±17.74 mg/dl $p<0.001$ **Table-1**. Whereas, the HbA_1C levels at baseline were observed to be 9.08±0.97%, which decreased to 8.09±0.76% at the 18th week, while a significant reduction was observed at the 36th week in comparison to its baseline value 7.26±0.87% $P<0.001$. The serum lipid profile parameters are shown in **Table-2**. Triglycerides were also significantly decreased $p<0.05$ after 18th and 36th weeks, with the reduction at 36 weeks being the highest. A significant reduction was also noted in serum total cholesterol levels $p<0.001$. However, at 36th weeks of treatment, a prominent reduction in total cholesterol was recorded as 131.89±12.80 mg/dl. Moreover, the effect of sitagliptin on VLDL-C was evaluated; it was measured at baseline as 35.98±7.56 mg/dl, and at 36 weeks of treatment, VLDL-C levels were also significantly declined, showing a highly significant reduction to 24.70±7.71 mg/dl $P<0.001$ **Table-2**. Sitagliptin also revealed a significant increase in HDL-C levels from baseline 25.38±5.33 mg/dl to 43.63±7.21 mg/dl at the 36th week of treatment. The results suggest that sitagliptin shows favorable anti-diabetic effects and helps in regulating the lipid profile in patients with type II diabetes.

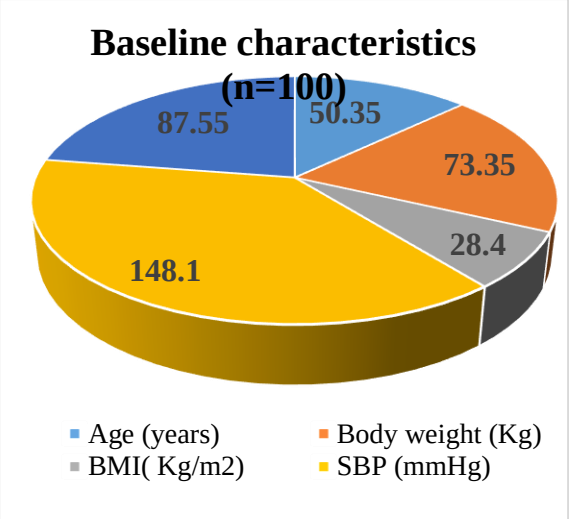

Figure 2: Baseline characteristics

Table-1 Effect of Sitagliptin on Glycemic Profile n=100

Parameter	Baseline	Time interval 18 weeks	Time interval 36 weeks	*P*-value
FBS mg/dl	163.65 ± 32.05	144.87 ± 24.09	106.20 ± 17.74	0.001
HbA_1C %	9.08± 0.97	8.09 ± 0.76	7.26 ± 0.87	0.001

Table-2 Effects of sitagliptin on plasma lipid profile before and after treatmentn=100

Parameters	Baseline	Time interval 18 weeks	Time interval 36 weeks	*P*-value
Triglycerides mg/dl	291.32 ± 71.58	189.93 ± 34.37	145.83 ± 36.18	0.001
Total Cholesterol mg/dl	250.30 ± 57.71	160.92 ± 27.89	131.89 ± 12.80	0.001
VLDL-C mg/dl	35.98 ± 7.56	34.38 ± 9.19	24.70 ± 7.71	0.001
LDL-C mg/dl	136.98 ± 20.77	129.87 ± 18.87	119.87 ± 9.24	0.001
HDL-C mg/dl	25.38 ± 5.33	38.19 ± 7.78	43.63 ± 7.21	0.001

DISCUSSION

One of the pivotal goals of treating type II diabetes is to achieve optimum glucose levels to prevent the development of diabetic complications [11.] In fact, diabetic patients have an impact on their lipid profiles, and therefore, it is recommended to use antidiabetic agents that have lipid-modulating effects [12-13.] According to research conducted, family history and the duration of diabetes pose a higher risk of dyslipidemia [14]. HbA_1C levels are routinely measured in diabetic patients to monitor their glycemic index. The target is to achieve levels not exceeding 7% [15]. In fact, HbA_1C serves as a reliable predictor, and a bidirectional relationship between Type II DM and dyslipidemia exists [16.] In our study, a reduction in HbA_1C and fasting blood glucose was observed. This is due to difference in lipid metabolism and carbohydrates [17]. Type II DM is a complex metabolic syndrome, and various findings have also been reported [18]. It is noteworthy that the potency of HbA_1C reduction relies on the baseline value of HbA_1C; studies have shown that higher baseline HbA_1C values usually result in higher reductions of HbA_1C. A study reported that sitagliptin administration for 36 weeks improved fasting blood sugar and HbA_1C levels in diabetic patients. Another study reports that a reduction in the HbA_1C level by 0.2% could decrease the mortality rate by 10% [19]. At baseline, FBS was observed to be at higher side **Table-1**. However, results of our study showed that treatment with sitagliptin led to a significant lowering of fasting blood sugar FBS at 36^{th} weeks. More recently, DPP-4 inhibitor class of oral antidiabetic agents has gained considerable attention and popularity for the treatment of type 2 diabetes [20]. In a study, the influence of DPP-4 on lipid parameters in type 2 diabetic patients has been investigated. A lower HDL level is the most common lipid abnormality encountered in patients with type 2 diabetes [21]. According to current guidelines on the treatment of blood cholesterol, there are low HDL and low TG levels in type 2 diabetic patients [22]. We observed higher triglyceride levels at the baseline, and a significant reduction was found in triglycerides level as shown in **Table-2**. These findings are consistent with the results of a previously reported study 23. Similarly, we have observed changes in HDL-C, LDL-C, VLDL-C, and total cholesterol levels, with significant changes in total cholesterol levels noted at 36^{th} weeks of therapy. In fact, type II diabetic patients experience low HDL-C dysfunction, which might result in insulin resistance, with subsequent increases in VLDL-C production along with cholesteryl ester transfer protein and hepatic lipase activity. Patients on sitagliptin therapy showed highly significant effects on both LDL-C and VLDL-C levels. Our results elucidate that there has been a significant improvement in HDL-C levels noted in patients in this study. These outcomes were found to be in agreement with previous similar research that also noticed a remarkable increase in HDL-C levels in patients [24]. The aforementioned results of our recent study suggest that sitagliptin has proved to have a significant role in ameliorating dyslipidemia in type 2 diabetes along with a glucose-regulating effect.

CONCLUSION

The study findings concluded that sitagliptin could be a promising drug in managing glycemic control along with lipid irregularities in patients with type 2 diabetes such as a reduction in serum triglycerides, low-density lipoproteins, total cholesterol and concurrent increase in high-density lipoproteins.

ETHICS APPROVAL: The ERC gave ethical review approval.

CONSENT TO PARTICIPATE: written and verbal consent was taken from subjects and next of kin.

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AUTHORS' CONTRIBUTIONS:

All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated in the work to take public responsibility of this manuscript. All authors read and approved the final manuscript.

CONFLICT OF INTEREST: No competing interest declared

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