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Case Report

# Severe Familial Hypertriglyceridemia in a Person with Type 2 Diabetes Mellitus: A Case Report

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**Abstract**

Indian population has a higher risk for the development of early onset of diabetes and associated co-morbidities like dyslipidemia, hypertension, obesity and other cardiovascular diseases. Hypertriglyceridemia is a common type of dyslipidemia pattern in the Indian population compared to Caucasians. In the given case study, it was observed that a young corporate professional presented with type 2 diabetes and severe familial hypertriglyceridemia. The patient was prescribed all required medications, and saroglitazar showed a significant reduction in elevated triglyceride.

**Keywords:** Diabetes dyslipidemia, familial hypertriglyceridemia, saroglitazar, type 2 diabetes mellitus, anti-diabetic agents

## Introduction

To date, treatment of hyperlipidemia in diabetes has centred on the management of plasma total and low-density lipoprotein (LDL) cholesterol levels. Although there is robust evidence for an association between LDL cholesterol levels and cardiovascular disease (CVD), there has been more uncertainty regarding the association between triglyceride levels and CVD.[1]

There is growing support for unadjusted elevated triglyceride levels as an independent CVD risk factor. However, the extent to which elevated triglycerides constitute a direct risk for CVD and whether treating elevated triglyceride levels, especially in patients with diabetes have reduced the CV events have been heavily debated. This scenario is even more interesting, especially in the Indian subcontinent where hypertriglyceridemia is more common compared to the western counterparts.[2] A great deal of attention has been recently given to Asian Indians because of the high prevalence of coronary heart disease (CHD) in this ethnic group.[3]

Not only hypertriglyceridemia (>150 mg/dL), but it has been established that severe (> 500 mg/dL) and very severe hypertriglyceridemia (1000 mg/dL) increase the risk for pancreatitis and need to be treated. However, considering epidemiological data together, both moderate and severe hypertriglyceridemia are linked with increased risk of CV disease and related mortality as long-term complications.[4]

Herein, we report an interesting case of a young (33-year-old) type 2 diabetes patient with severe familial hypertriglyceridemia managed by a lipid-lowering agent with the addition of saroglitazar and other medications.

## Case Study

### Visit 1: Case Presentation

A 33-year-old information technology (IT) professional from Bhubaneswar, Odisha, India having type 2 diabetes mellitus past two years with a history of regular alcohol intake but not on any regular medications. He had chief complaints of pain, weakness and balanoposthitis, and visited for regular comprehensive health checkups. He had a positive family history of his father with diabetes mellitus and coronary artery disease (CAD). He had no history of hypothyroidism, chronic liver disease or chronic kidney disease and abdomen pain s/o pancreatitis. On clinical examination, his body mass index (BMI) was 28 $kg/m^2$, acanthosis nigricans was present, xanthomas were absent, goitre was absent, and the rest of his systemic examination was normal.

**Table 1.** Various laboratory parameters at baseline and follow-up 2 weeks and 6 weeks

| Parameter | Visit 1 (Baseline) | Visit 2 (At 2 weeks) | Visit 3 (At 6 weeks) |
|---|---|---|---|
| Glycated hemoglobin (HbA1c, %) | 10.4 | - | 8.2 |
| Fasting blood sugar | | | |
| (FBS, mg/dL) | 289 | 180 | 128 |
| Postprandial blood sugar | | | |
| (PPBS, mg/dL) | 404 | 220 | 172 |
| Total cholesterol | | | |
| (TC, mg/dL) | 557 | 220 | 190 |
| Triglyceride | | | |
| (TG, mg/dL) | 4895 | 1200 | 410 |
| Low-density lipoprotein cholesterol | | | |
| (LDL-C, mg/dL) | 194 | 120 | 72 |
| High-density lipoprotein cholesterol | | | |
| (HDL-C, mg/dL) | 31 | 34 | 36 |
| Non-HDL-C | | | |
| (mg/dL) | 526 | 186 | 154 |
| Serum creatinine | | | |
| (mg, %) | 0.84 | - | 0.84 |
| Serum thyroid stimulating hormone | | | |
| (TSH, mIU/L) | 1.8 | - | 2.1 |

The investigations revealed significant abnormal level of blood sugar and lipid level (**Table 1**) including triglyceride (TG) level (4895 mg/dL) and LDL-C (194 mg/dL). This patient's treatment was started as classical case of T2DM with familial hypertriglyceridemia.

**Table 2.** Various medications prescribed at baseline and follow-up of 2 weeks and 6 weeks

| Prescribed Medications | | |
|---|---|---|
| **Visit 1 (Baseline)** | **Visit 2 (At 2 weeks)** | **Visit 3 (At 6 weeks)** |
| Inj. Insulin Aspart (30%) + Insulin Aspart Protamine (70%)<br>14 U before breakfast<br>8 U before dinner | Same dose continued | Same dose continued |
| Tab. Metformin SR (1 g) OD | Same dose continued | Same dose continued |
| Tab. Atorvastatin (20 mg) OD | Tab. Atorvastatin (40 mg) OD | Tab. Atorvastatin (80 mg) OD |
| Tab. Saroglitazar (4 mg) OD | Same dose continued | Same dose continued |
| Fixed dose combination Tab. Of | | |
| Pregabalin (75 mg) + Methylcobalamin (1500 mcg) + Vitamin B6 (Pyridoxine) (20 mg) + Folic Acid (5 mg); OD | Same dose continued | Same dose continued |

## Visit 1: Treatment

This patient was ideal case study of familial hypertriglyceridemia with T2DM. Accordingly, patient was briefed about lifestyle modification including, hypocaloric diet (up to 1600 kcal/day) with simple carbohydrates and low in fat. To control elevated HbA1c and sugar level; insulin and metformin therapy were started as mentioned in **Table 2**. Apart from medications for control of diabetes mellitus, the patient was advised a moderate dose of atorvastatin (20 mg) and saroglitazar (4 mg). In this case, TG level was more than 4800 mg/dL and as per international guideline recommendation, to avoid acute pancreatitis; TG-lowering agent – saroglitazar was added along with statin.

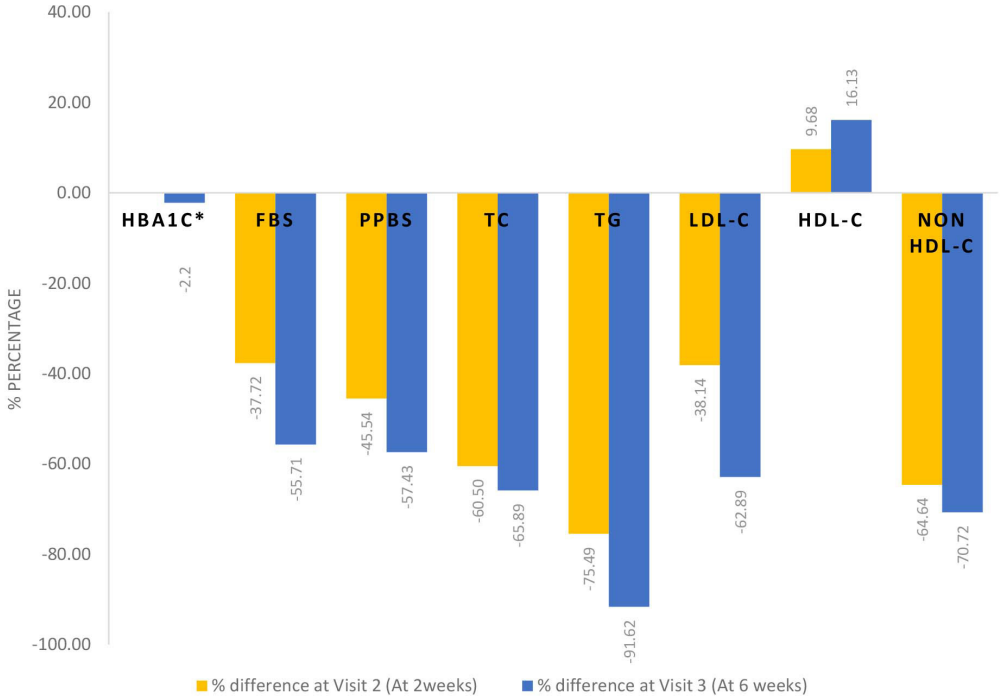


**Figure 1.** Change in laboratory parameters at visit 2 and visit 3 from baseline

[All difference values are relatively compared with baseline. HbA1c difference is absolute difference.]

### Follow-up visits:

The first follow-up was scheduled after 2 weeks with lipid and sugar profile to evaluate medication response and a significant reduction in lipid and glucose parameters were observed (**Table 1 and Figure 1**). In second, visit dose of atorvastatin was increased to 40 mg and saroglitazar 4 mg continued along with other anti-diabetic drugs. The second follow up was scheduled after 6 weeks again with glucose and lipid profile. In laboratory parameters, improvement was observed, and the atorvastatin dose was increased up to 80 mg and continued with saroglitazar 4 mg and other anti-diabetic drugs.

In this patient, liver enzyme assessment was not done. Serum lipase level and ultrasonography for the pancreas were done, and both were normal. For this patient, family genetic screening and first-degree relative lipid were not evaluated.

## Discussion

This is a case of type 2 diabetes mellitus with obesity and severe hypertriglyceridemia. According to the Fredrickson Classification of Hyperlipoproteinemias, this case can be classified under phenotype IIb, which goes by the genetic nomenclature of Familial Combined Hyperlipidemia (FCHL). FCHL is dominantly inherited, occurs in at least 1% of the population, and is responsible for about 20% of premature coronary artery disease (CAD) at age <60 years.[5] This is a classical case of predominant hypertriglyceridemia type of familial combined hyperlipidemia having predominant high triglycerides, high cholesterol and high LDL with metabolic syndrome phenotype in 80% cases with no xanthomas.[6]

This patient was having uncontrolled HbA1c and LDL-C levels for that required anti-diabetic medications and Atorvastatin 20 mg was started. Severe hypertriglyceridemia (TG >500 mg/dL) is certainly a risk factor for the development of cardiovascular disease (CVD) and acute pancreatitis. There is growing support for unadjusted elevated triglyceride levels as an independent CVD risk factor, however, the extent to which elevated triglycerides constitute a direct risk for CVD and whether treating elevated triglyceride level especially in patients with diabetes have reduced the CV events have been heavily debated. Various international societies have recommended that severe and very severe hypertriglyceridemia increase the risk for pancreatitis and need to be treated at the same time mild or moderate hypertriglyceridemia may be a risk factor for cardiovascular disease.[7,8]

For elevated TG reduction statins are first-line agents, but as per revised guidelines, if TG level is more than 135 mg/dL in patients with a high risk of CVD, TG lowering agents should be added to statins.8 Fibrates are universally approved medications for the reduction of elevated TG. In various meta-analysis reports, fibrate reduced TG in the range of 36%-43% in various populations like Asians and Americans.[9] Fenofibrate usage is associated with myopathies in patients diagnosed with diabetes mellitus, thyroid disorder, or a renal disorder. Gemfibrozil is associated with an increased risk of cholelithiasis and cholecystitis due to more saturation cholesterol in bile. Fibrates should be used cautiously in patients with renal dysfunction and along with coumarin-type anticoagulant therapy.[10]

Saroglitazar is a unique PPAR alpha and gamma agonist that reduces TG by 45-46.7%, non-HDL-C by 32.5%, and apolipoprotein B by 32% and HbA1c by 0.3% in phase 3 clinical studies. Saroglitazar was found to be safe in cardiac parameters (ECG and 2D Echo), ultrasonography, and liver enzyme parameters. Its effect on serum creatinine and body weight was neutral.[11,12] Moreover, in post-observational studies; saroglitazar's effect on TG and other lipid and sugar parameters was as similar as in phase III studies. Apart from that in the GLIDDER[13] study of ~100 patients, saroglitazar showed a reduction of small-dense LDL-C (sdLDL-C) by 20.3%, which is more atherogenic and apart from this it reduces elevated alanine transaminase (ALT) level from 28% - 67% in integrated review analysis of 18 real-world evidence studies.[14]

Saroglitazar is approved for management of type 2 diabetes (T2D) in India by the Drug Controlled General of India (DCGI) based on PRESS XII study, in which saroglitazar 4 mg along with metformin reduced HbA1c by 1.47% from baseline in T2D patients after 56 weeks of treatment.[15] In addition to this, saroglitazar is also approved for the treatment of nonalcoholic fatty liver disease with various co-morbidities like obesity, T2D, metabolic syndrome, dyslipidemia and non-cirrhotic nonalcoholic steatohepatitis (NASH). It reduced ALT level by 45.2% in NAFLD patients[16] and in 52.3% patients decreased NAS ≥2 spread across at least 2 of the NAS components without worsening of fibrosis at week 52.17 since last almost 8 years, our experience with Saroglitazar in diabetic dyslipidemia patients with high TG is significantly positive and safe as well. So, considering these all-clinical evidences and experience, saroglitazar was prescribed as TG lowering agent since the first visit and continued; due to observance of significant reducing effect on TG level.

In this case, apart from saroglitazar, statin and controlling in blood sugar certainly may have potentiated further reduction of TG.

## Conclusion

In type 2 diabetes patients, hypertriglyceridemia is commonly observed. Very severe hypertriglyceridemia, especially in a young person may be due to familial hypertriglyceridemia that may lead to pancreatitis and premature CAD. Along with lifestyle modifications, pharmacological management should be started as early as possible. Along with statin, for predominant hypertriglyceridemia, saroglitazar could be an effective option in India. In this case, it is associated with a significant decline of elevated TG in the duration of 6 weeks without any significant adverse events. The clinical experience of saroglitazar is also safe but yet to prove its cardiovascular safety in the Indian population.

## Declaration of conflicting interest

The authors declare no conflict of interest.

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## Ethics approval

Not applicable.

## Informed consent

Written informed consent was obtained from the patient.

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