**Long-Term Impact of Saroglitazar on Advanced Hepatic Fibrosis and Metabolic Dysfunction in MASLD patients: A Two-Year Case Series**

**Abstract**

**Background:**

Metabolic dysfunction-associated steatotic liver disease (MASLD) is highly prevalent in individuals with type 2 diabetes mellitus (T2DM). However, it remains an often overlooked hepatic comorbidity in this population. This case series contributes to the literature by presenting real-world, longitudinal evidence of hepatic fibrosis regression and glucometabolic improvement with saroglitazar, a dual PPAR-α/γ agonist in combination with oral semaglutide (7 mg or 14 mg as tolerated), a GLP-1 receptor agonist in T2DM patients with MASLD over a 2-year follow-up period.

**Case Summary:**

Saroglitazar 4 mg once daily was initiated in four adult patients with T2DM and imaging-confirmed MASLD. Baseline assessments revealed elevated HbA1c (6.4–8.2%), hypertriglyceridemia, and evidence of hepatic steatosis and fibrosis on transient elastography. CAP values ranged from 257 to 347 dB/m, corresponding to S1–S3 steatosis grades, while LSM values ranged from 14.3 to 38.5 kPa, indicative of F3–F4 fibrosis stages. No other hepatoprotective or antidiabetic agents with hepatic benefit were used. All patients experienced marked reductions in HbA1c, triglycerides, ALT, and AST after two years of Saroglitazar 4 mg therapy. Three patients demonstrated improvement in hepatic steatosis (from S2–S3 to S0–S1) and fibrosis (from F2–F3 to F0–F1); notably, one patient showed marked regression from advanced fibrosis (F3) to no fibrosis (F0). The therapy was well tolerated, with no adverse effects reported.

**Conclusion:**

This case series highlights the potential of saroglitazar as a dual PPAR agent with semaglutide addressing both metabolic and hepatic derangements in MASLD associated with T2DM. The observed improvements in liver stiffness and glycemic-lipid profiles over two years, independent of weight loss or adjunct therapies, suggest a disease-modifying role. Clinicians managing diabetic patients should be vigilant for coexisting MASLD and consider saroglitazar as a promising therapeutic option pending further confirmatory trials.

**Keywords:** PPAR agonist, liver stiffness measurement, transient elastography, diabetic dyslipidemia, non-invasive biomarkers, fibrosis regression, GLP-1 receptor agonist

**INTRODUCTION**

Type 2 diabetes mellitus (T2DM) is a rapidly escalating global health concern, projected to affect over 629 million individuals by 2045 [1]. Characterized by chronic hyperglycemia and insulin resistance, T2DM not only predisposes individuals to cardiovascular, renal, and neuropathic complications but also significantly increases the risk of hepatic involvement. One of the most frequent and underrecognized hepatic manifestations is steatotic liver disease SLD [2]. Over the past decade, substantial evidence has emerged linking type 2 diabetes mellitus (T2DM) with steatotic liver disease through overlapping metabolic mechanisms such as insulin resistance and dyslipidemia. In this context, metabolic dysfunction-associated steatotic liver disease (MASLD) is being increasingly recognized as the most common hepatic manifestation of metabolic syndrome. [3,4]

There are substantial therapeutic gaps in the management of MASLD, primarily due to lack of approved treatments. While lifestyle interventions including caloric restriction, physical activity, and weight reduction remain the cornerstone of therapy, real-world adherence and long-term sustainability are often suboptimal. [5,6] American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL), acknowledge this challenge and recommend adjunctive pharmacotherapy in high-risk populations, particularly those with T2DM and hepatic fibrosis [7].

Given the limited long-term success of lifestyle interventions, therapeutic focus has shifted toward molecular targets that address the core metabolic dysfunctions of MASLD. Among these, peroxisome proliferator-activated receptors (PPARs) are of particular interest. PPAR-α enhances fatty acid oxidation and reduces hepatic steatosis, while PPAR-γ improves insulin sensitivity and regulates adipokine activity. Saroglitazar, a dual PPAR α/γ agonist, offers a unified approach to these pathways and has shown benefits in glycemic control, lipid modulation, and liver-related biomarkers [8] . First approved in India in 2013 for the treatment of diabetic dyslipidemia, saroglitazar was subsequently granted regulatory approval in 2020 for MASLD and metabolic dysfunction-associated steatohepatitis (MASH), reflecting growing recognition of its multi-targeted therapeutic potential [9]. This case series aims to present real-world, longitudinal evidence evaluating the hepatic and metabolic benefits of saroglitazar in patients with MASLD and type 2 diabetes, highlighting its potential role in addressing the current therapeutic gaps.

***Methodology***

This observational case series was carried over a two-year period at Dr. Dang’s Diabetes Clinic, Ghaziabad, Uttar Pradesh, India. Between March 2023 to April 2025, with four adult patients presenting to the outpatient department were screened for eligibility. All four patients were also initiated on oral semaglutide in doses of 7 mg or 14 mg once daily, titrated based on individual tolerance and glycemic targets. This combination regimen of saroglitazar 4 mg with semaglutide was used consistently throughout the study period.

All participants were between 18 and 70 years of age and had a confirmed diagnosis of T2DM based on the diagnostic criteria of the American Diabetes Association (ADA) [10]. Hepatic steatosis greater than Grade I was confirmed in all enrolled individuals via abdominal ultrasonography.

Additional eligibility requirements included the presence of obesity (as per WHO Asian cut-offs), hypertriglyceridemia, and elevated hepatic fat and stiffness indices. Hepatic steatosis severity and fibrosis assessment were performed using transient elastography, with Controlled Attenuation Parameter (CAP) and Liver Stiffness Measurement (LSM) values used to quantify liver involvement. All patients provided written informed consent prior to inclusion, in compliance with institutional ethics policies.

Patients were excluded if they had a history of liver injury attributable to chemical agents or hepatotoxic medications within the 9 months preceding assessment. Use of glucagon-like peptide-1 receptor agonists (GLP-1 RAs), sodium-glucose co-transporter-2 (SGLT2) inhibitors, or pioglitazone within 3 months prior to enrollment or during the study period was also a contraindication for participation. Individuals with positive serology for hepatitis B surface antigen or hepatitis C virus antibodies were excluded. Any other comorbid conditions or factors deemed likely to interfere with study assessments or compromise patient safety were considered exclusionary.

All four patients were also initiated on oral semaglutide as part of their standard diabetic management. No other hepatoprotective or metabolic agents with known hepatic benefits were used during the observation period.

**Case Presentation:**

**Case 1**: A 39-year-old male with type 2 diabetes mellitus presented with obesity and laboratory evidence of dyslipidemia. At baseline, HbA1c was 6.4%, fasting glucose was 110 mg/dL, and triglycerides were elevated at 190 mg/dL. The CAP score was 328 dB/m and liver stiffness measurement (LSM) was 15.7 kPa at baseline, corresponding to Fibrosis Stage F3. Follow-up assessments over 32 weeks revealed progressive improvement in metabolic and hepatic parameters. HbA1c had decreased to 5.6%, triglycerides to 128 mg/dL, and LSM had normalized to 4.3 kPa (F0). The CAP score declined to 225 dB/m, reflecting reduced hepatic steatosis at 32 weeks.

**Case 2:** A 61-year-old male with poorly controlled T2DM at baseline (HbA1c 7.1%) and features suggestive of advanced hepatic fibrosis was enrolled. Initial LSM was markedly elevated at 38.5 kPa, with a CAP score of 257 dB/m. Over the 2-year follow-up, glycemic control improved substantially (HbA1c reduced to 5.5%), with corresponding declines in LSM to 25.8 kPa and CAP to 231 dB/m. Liver enzyme levels remained within normal limits throughout the study period.

**Case 3**: A 56-year-old male with long-standing T2DM and severe dyslipidemia was evaluated. At baseline, HbA1c was 8.2%, fasting glucose 163 mg/dL, triglycerides 298 mg/dL, and CAP and LSM were elevated at 347 dB/m and 14.3 kPa, respectively. After 2 years, HbA1c had reduced to 6.2%, triglycerides to 141 mg/dL, and CAP and LSM values reduced to 238 dB/m and 5 kPa, respectively. Liver enzymes also showed a consistent downward trend.

**Case 4**: A 48-year-old woman with uncontrolled T2DM (HbA1c 8.2%) and hepatic steatosis was enrolled. Baseline CAP and LSM were 321 dB/m and 28.7 kPa, respectively. After 1 year, there was an appreciable reduction in HbA1c to 7.1%, CAP to 291 dB/m, and LSM to 15.3 kPa. Liver transaminases declined progressively, and LDL cholesterol improved from 75 mg/dL to 61 mg/dL over the 8-month follow-up.

**Table 1:** Changes in Hepatic and Metabolic Parameters Over a Two-Year Period Following Saroglitazar Therapy in Patients with MASLD and Type 2 Diabetes.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Parameter | Visit | Patient 1 | Patient 2 | Patient 3 | Patient 4 |
| CAP (dB/m) | ***Baseline*** | 328 | 257 | 347 | 321 |
|  | ***6 months*** | 310 | 248 | 329 | 300 |
|  | ***1 year*** | 290 | 260 | 342 | 291 |
|  | ***2 years*** | 225 | 231 | 238 | 281 |
| LSM (kPa) | ***Baseline*** | 15.7 | 38.5 | 14.3 | 28.7 |
|  | ***6 months*** | 22.03 | 52.6 | 11.8 | 25.6 |
|  | ***1 year*** | 22.03 | 33.2 | 10.7 | 18.8 |
|  | ***2 years*** | 4.3 | 25.8 | 5 | 15.3 |
| HbA1c (%) | ***Baseline*** | 6.4 | 7.1 | 8.2 | 8.2 |
|  | ***6 months*** | 5.8 | 7.0 | 7.3 | 7.6 |
|  | ***1 year*** | 5.8 | 5.6 | 6.8 | 7.1 |
|  | ***2 years*** | 5.6 | 5.5 | 6.2 | 6.9 |
| Triglycerides (mg/dL) | ***Baseline*** | 190 | 209 | 298 | 210 |
|  | ***6 months*** | 140 | 198 | 244 | 184 |
|  | ***1 year*** | 132 | 189 | 172 | 172 |
|  | ***2 years*** | 128 | 176 | 141 | 160 |
| ALT (U/L) | ***Baseline*** | 26 | 22 | 68 | 33 |
|  | ***6 months*** | 23 | 23 | 52 | 28 |
|  | ***1 year*** | 23 | 20 | 30 | 26 |
|  | ***2 years*** | 22 | 24 | 28 | 23 |
| AST (U/L) | ***Baseline*** | 22 | 30 | 54 | 44 |
|  | ***6 months*** | 18 | 32 | 41 | 39 |
|  | ***1 year*** | 18 | 27 | 32 | 34 |
|  | ***2 years*** | 19 | 24 | 29 | 28 |

**DISCUSSION**

This case series presents real-world evidence on the efficacy of saroglitazar in patients with T2DM and MASLD. Substantial improvements were observed in hepatic fibrosis, steatosis, and cardiometabolic parameters with the addition of oral semaglutide over a follow-up period extending up to two years.

Patients experienced marked reductions in LSM, with one patient showing improvement from advanced fibrosis (15.7 kPa) to no fibrosis (4.3 kPa). This trend is consistent with prior real-world studies such as Chaudhuri et al. (2023), which reported a 22% mean reduction in LSM at 52 weeks, including in patients with compensated cirrhosis (F4), and Goyal et al. (2020), who observed a smaller but statistically significant reduction of from 8.4 (7.1-9.3) to 7.5 (6.4-8.4) (p = 0.0261) over 24 weeks. [11,12] Our study further supports the emerging view that saroglitazar may contribute to fibrosis regression even in higher LSM ranges (38.5 → 25.8 kPa).

CAP improved in 3 out of 4 patients. This aligns with data from Goyal et al. (2020) (from 335 to 256 dB/m) and Chaudhuri et al. (2023) (from 328 to 287 dB/m) [11,12]. All patients demonstrated consistent and clinically meaningful reductions in ALT and AST. The enzyme declines mirror those reported by Goyal et al. and Chaudhuri et al., where ALT and AST levels decreased by 50% and 40%, respectively, over 24–52 weeks. [11,12] These improvements occurred independently of changes in BMI or weight, reinforcing that saroglitazar’s hepatic benefits are mechanistically distinct from lifestyle-induced weight loss a finding explicitly corroborated in Chaudhuri's cohort. [11]

Saroglitazar’s dual PPAR-α/γ action and semaglutide translated into notable reductions in HbA1c across all patients. Baseline HbA1c values ranged from 6.4% to 8.2%, declining to 5.5% to 6.9% at two years, with a mean reduction of 1.3%. For instance, Patient 3’s HbA1c improved from 8.2% to 6.2%. These outcomes align with the glycemic benefit seen in Dang et al. (mean HbA1c reduction from 7.56% to 6.11%) and support previous Indian data documenting improved insulin sensitivity with saroglitazar. [13] Similarly, triglyceride levels dropped by >50% in some cases, matching or exceeding the reductions reported in Chaudhuri et al. (40.6%) and Goyal et al. (48%). This emphasizes saroglitazar’s utility in addressing diabetic dyslipidemia, a key driver of both MASLD progression and cardiovascular morbidity.

The co-administration of saroglitazar and oral semaglutide may exert synergistic effects, leveraging complementary mechanisms of action. Saroglitazar’s dual PPAR-α/γ modulation targets lipid metabolism and insulin sensitivity, while semaglutide, a GLP-1 receptor agonist, improves glycemic control and reduces hepatic fat. Although the study was not designed to isolate the effects of semaglutide, the sustained metabolic and hepatic improvements observed in this cohort suggest potential additive or synergistic benefits.

**Conclusion**

This case series provides valuable real-world evidence supporting the long-term safety and efficacy of saroglitazar along with semaglutide in patients with T2DM and MASLD. Larger controlled trials with histological endpoints are warranted to further validate these observations and assess long-term outcomes. Further randomized controlled trials are warranted to explore this therapeutic synergy and its long-term safety implications.

**Ethical Approval:**

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

**Consent**

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

**Disclaimer (Artificial intelligence)**

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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