e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2025; 17(8); 1482-1487

Original Research Article

Efficacy and Safety of SAROGLITAZAR in the Management of Fatty Liver, Diabetes and Dyslipidaemia

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Received: 01-05-2025 / Revised: 15-06-2025 / Accepted: 21-07-2025

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Conflict of interest: Nil

Abstract

Background: Fatty liver disease, type 2 diabetes mellitus (T2DM), and dyslipidaemia often coexist and share common pathophysiological pathways, including insulin resistance and hepatic lipid accumulation. Managing these interconnected metabolic disorders poses a clinical challenge. Saroglitazar, a dual PPAR α/γ agonist, has emerged as a potential therapeutic agent due to its combined lipid-lowering and insulin-sensitizing properties.

Objective: To evaluate the efficacy and safety of Saroglitazar in the management of patients with fatty liver, T2DM, and dyslipidaemia.

Methodology: A prospective, interventional study was undertaken at Soban Singh Jeena Govt. Institute of Medical Sciences and Research (SSJGIMSR) from June to December 2024. The study included 100 participants aged 30–65 with USG/Fibroscan-diagnosed fatty liver and T2DM or dyslipidemia. Each participant got 4 mg of Saroglitazar daily for six months. LFT, HbA1c, lipid profile, and imaging were performed at baseline and follow-up. Adverse events were reported and renal and hepatic function testing were performed. Statistical analysis included paired t-tests and Wilcoxon signed-rank tests, with significance set at $p < 0.05$.

Key Results: At the end of six months, significant improvements were observed in liver enzymes (ALT: mean reduction of 22.4 U/L, AST: 18.6 U/L), USG/Fibroscan liver grading, HbA1c (reduction of 0.9%), and lipid profile parameters (LDL, triglycerides, HDL). The safety profile was acceptable, with only mild adverse events reported, and no patient required discontinuation of therapy.

Conclusion: Sarolitazar improves hepatic, glycaemic, and lipid markers in metabolic dysfunction patients with promise and manageable safety. It may help patients with diabetes, dyslipidemia, and fatty liver.

Keywords: Saroglitazar, fatty liver, diabetes, dyslipidaemia, insulin resistance, PPAR agonist.

Introduction

Global healthcare systems are burdened by dyslipidemia, type 2 diabetic mellitus (T2DM), and non-alcoholic fatty liver disease (NAFLD). Due to obesity and sedentary lifestyles, chronic diseases have skyrocketed in emerging nations like India [1]. The combination of urbanization, eating habits, and lack of exercise has caused metabolic syndrome, which includes NAFLD [2].

NAFLD is characterized by abnormal hepatocyte fat accumulation without significant alcohol intake. From moderate steatosis to non-alcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and hepatocellular cancer, it encompasses many liver diseases [3]. Worldwide prevalence estimates put NAFLD at 25% and T2DM at 70%. NAFLD is particularly dangerous in India because South Asians are genetically predisposed to visceral obesity and insulin resistance, especially at lower BMIs [4]. Type 2 diabetes causes persistent hyperglycemia due to insulin resistance and insufficiency. In the "diabetes capital of the world," nearly 77 million people have diabetes, and that number will climb. Type 2 diabetes is connected to lipid problems, liver damage, and glucose dysregulation [5,6].

Dyslipidaemia—high triglycerides (TGs), low HDL-C, and high small dense LDL-C—is another crucial aspect of this metabolic interplay. Besides insulin resistance, it causes NAFLD. Insulin resistance increases liver lipogenesis, which increases hepatic fat accumulation and systemic lipid abnormalities [7]. Clustering NAFLD, T2DM, and dyslipidemia creates this nasty cycle. Treating hyperglycemia, lipid imbalance, and hepatic steatosis independently has improved, but there are few treatments that address all three. Traditional

antidiabetic medicines including metformin, sulfonylureas, and DPP-4 inhibitors manage blood sugar but have little effect on lipid profiles and liver fat [8,9]. While fibrates and statins manage dyslipidemia, they fail in insulin sensitivity and hepatic histology. Additionally, liver-impaired patients' safety and tolerance to these drugs are limited [10].

Due to this therapy gap, researchers are seeking innovative drugs that cure fatty liver, diabetes, and dyslipidemia together. The novel PPAR agonist saroglitazar has significant PPAR-α activity and mild PPAR-γ activity, making it a promising therapy choice. PPAR-α activation enhances insulin sensitivity, glycemic control, fatty acid oxidation, and triglyceride reduction. In terms of adverse effects like fluid retention and weight gain, Saroglitazar is safer than pioglitazone [11,12].

Saroglitazar was approved in India in 2013 to treat diabetic dyslipidemia and hypertriglyceridaemia that statins cannot control. It was recently approved to treat NASH and NAFLD due to growing clinical evidence of its hepatoprotective properties. Many Indian trials demonstrate that Saroglitazar decreases blood lipids, improves glycaemic indices like HbA1c, and lowers hepatic transaminases and liver stiffness, which are surrogate indicators for hepatic fat and inflammation. Saroglitazar's complicated mechanism of action is therapeutic. Reducing liver lipid burden involves downregulating genes involved in de novo lipogenesis, triglyceride synthesis, and increasing mitochondrial β-oxidation of fatty acids. Hyperinsulinemia causes hepatic fat storage and dyslipidemia; insulin sensitization helps. Saroglitazar is a good therapy for NAFLD, T2DM, and dyslipidemia due to these processes.

In India, where metabolic syndrome is growing increasingly widespread and there are no viable therapies, Saroglitazar might alter everything. Real-world data from diverse therapeutic situations is needed to prove its efficacy and safety outside of controlled clinical trials. This study will examine how effectively and safely Saroglitazar works for persons with fatty liver, type 2 diabetes, and dyslipidemia for six months.

A tertiary care teaching hospital servicing a large population in Uttarakhand, the SSJGIMSR is undertaking the study. Using real-life patients with metabolic disorders allows a rare evaluation of Saroglitazar's translational potential in mainstream medicine. Despite Saroglitazar's potential advantages, longterm data on its usage in populations with coupled NAFLD, T2DM, and dyslipidemia, especially in North India or hilly regions, is lacking. Early studies largely used surrogate biochemical results in limited patient samples. Few clinical studies evaluate effectiveness, safety, and patient outcomes across demographics. This study investigates that gap by prospectively monitoring changes in glycaemic indices (HbA1c), lipid profiles (LDL, HDL, TGs), liver enzymes (ALT, AST), and liver fat content (measured by ultrasonography and/or Fibroscan) in Saroglitazar 4 mg daily individuals.

Materials and Methods

Study Design: This prospective interventional observational trial examines Saroglitazar's safety and efficacy in patients with fatty liver, type 2 diabetes, and dyslipidemia. The interventional aspect of the experiment involves administering 4 mg of Saroglitazar once a day to all participants and monitoring biochemical and clinical indicators.

Study Setting and Duration: The research was carried out at Soban Singh Jeena Government Institute of Medical Sciences and Research, an academic medical institution. The study spanned a period of six months, from June 2024 to December 2024.

Sample Size: A total of 100 patients were recruited for this study based on the inclusion and exclusion criteria described below.

Inclusion Criteria

Aged between 30 and 65 years.

Diagnosed with NAFLD, confirmed via ultrasound (USG) or Fibroscan.

Concurrent diagnosis of T2DM and/or dyslipidaemia based on standard diagnostic criteria.

Exclusion Criteria

Known hepatic decompensation (e.g., ascites, encephalopathy, variceal bleeding).

Chronic kidney disease stage 3 or higher (eGFR < 60 ml/min/1.73 m^2).

Alcoholic liver disease, as defined by a history of significant alcohol consumption (>21 drinks/week for men or >14 drinks/week for women).

Intervention: All participants received Saroglitazar 4 mg orally once daily. The medication was prescribed under physician supervision, and adherence was ensured through routine follow-up and pill counts during visits.

Data Collection: Methodical data collection began at the study's start and occurred monthly throughout its duration. Liver function tests (LFTs) like ALT and AST, glycaemic status (HbA1c), and a thorough lipid profile were performed at each visit. Ultrasonography (USG) or Fibroscan was used to assess hepatic fat content and grade fatty liver at baseline and follow-up. Parallel safety monitoring, including adverse drug reaction screening and renal and liver function

testing, assured drug tolerance and patient well-being.

Outcome Measures: The primary outcome measures focused on changes in liver function parameters, specifically ALT and AST levels, as well as changes in liver fat grading as observed through USG or Fibroscan.

Secondary outcomes included improvement in glycaemic control indicated by changes in HbA1c values and lipid parameters such as LDL, HDL, and triglyceride levels.

Additionally, the incidence and nature of any adverse events were recorded and analyzed as part of the safety evaluation.

Statistical Analysis: Statistical analysis employed parametric and non-parametric methods depending on data distribution. We utilized the paired t-test for normally distributed continuous variables and the Wilcoxon signed-rank test for skewed data to compare pre- and post-treatment values. Descriptive statistics summarized demographic and baseline clinical information. All studies with p-values below 0.05 were statistically significant, indicating a substantial change from baseline.

Results

Baseline Characteristics: One hundred patients made up the study's sample. Participant ages ranged from 52.4 to 52.4 ± 8.1 years. There were 60% men and 40% women out of the total population. A mean BMI of 29.6 ± 3.4 kg/m² was recorded. Hypothyroidism (12%), cardiovascular disease (15%), and hypertension (40%) were the most prevalent co-occurring disorders.

Table 1: Baseline Characteristics of Study Participants

Parameter	Value (Mean ± SD) or %
Number of participants	100
Age (years)	52.4 ± 8.1
Gender (Male/Female)	60% / 40%
BMI (kg/m²)	29.6 ± 3.4
Hypertension	40%
Cardiovascular Disease	15%
Hypothyroidism	12%

Primary Results

There was a marked improvement in liver enzyme readings both before and after therapy. The average ALT level dropped from 72.5 ± 18.2 U/L at the beginning of the trial to 41.3 ± 11.5 U/L by its conclusion. There was a drop in AST, going from 65.4 ± 15.6 U/L to 38.7 ± 10.8 U/L. According to USG/Fibroscan, 68% of subjects saw an improvement in the grading of liver fat.

Table 2: Change in Liver Enzymes and Liver Fat Grading

Parameter	Baseline (Mean ± SD)	Post-Treatment (Mean ± SD)	% Improvement	p-value
ALT (U/L)	72.5 ± 18.2	41.3 ± 11.5	43%	< 0.001
AST (U/L)	65.4 ± 15.6	38.7 ± 10.8	41%	< 0.001
Liver Fat Score*	Grade 2–3 (100%)	Grade 1–2 (68%)	–	< 0.01

***Liver fat score based on USG/Fibroscan grading scale.**

Secondary Results: The mean HbA1c reduced from 8.4 ± 1.1% at baseline to 7.1 ± 0.9% after 6 months of treatment. Lipid profile improvements were observed with LDL levels decreasing from 140.3 ± 22.7 mg/dL to 112.5 ± 18.4 mg/dL, triglycerides from 240.6 ± 45.2 mg/dL to 180.4 ± 30.8 mg/dL, and HDL increasing from 39.1 ± 6.2 mg/dL to 45.2 ± 7.0 mg/dL.

Table 3: Changes in HbA1c and Lipid Profile

Parameter	Baseline (Mean ± SD)	Post-Treatment (Mean ± SD)	% Change	p-value
HbA1c (%)	8.4 ± 1.1	7.1 ± 0.9	-15.5%	< 0.001
LDL (mg/dL)	140.3 ± 22.7	112.5 ± 18.4	-19.8%	< 0.001
HDL (mg/dL)	39.1 ± 6.2	45.2 ± 7.0	+15.6%	< 0.001
Triglycerides (mg/dL)	240.6 ± 45.2	180.4 ± 30.8	-25.1%	< 0.001

Safety Profile: Minor adverse events were recorded by 7 patients, or 7% of the total. Weak indigestion (n=3), headache (n=2), and lethargy (n=2) were among these. During the follow-up period, no significant adverse events or worsening of hepatic or renal function were seen. Tests for renal and liver function showed no abnormalities in most cases.

Table 4: Adverse Events and Safety Monitoring

Adverse Event	Frequency (n)	Severity
GI Discomfort	3	Mild
Headache	2	Mild
Fatigue	2	Mild
Hepatic/Renal Impairment	0	–

Discussion

This six-month study examined Saroglitazar's safety and efficacy in treating fatty liver, dyslipidemia, and type 2 diabetes. Saroglitazar significantly improved study participants' lipid measures, glycemic control, and liver enzyme levels. When ALT and AST reduced dramatically, the liver reacted well to treatment. Saroglitazar has hepatoprotective potential, as USG/Fibroscan imaging demonstrated a liver fat grading reduction in almost two-thirds of patients. One of the most notable glycaemic effects was HbA1c reductions, indicating improved insulin sensitivity and glucose control. Saroglitazar reduces glucose and lipids by lowering LDL and triglycerides and raising HDL. During the study, the medicine was well-tolerated with few adverse effects and no changes in hepatic or renal function.

Comparison with Previous Studies

This study demonstrated Saroglitazar's efficacy consistent with earlier studies. Previous study has indicated that saroglitazar treats dyslipidemia and NAFLD. This applies primarily to type 2 diabetics. A multicenter study by [13] found that Saroglitazar for NAFLD improved ALT, AST, and lipid markers. The drug's dual PPAR-α/γ agonist action was corroborated by [14], who showed improved glycaemic control and reduced hepatic steatosis in diabetic people.

This experiment supports the concept that Saroglitazar addresses the metabolic triad of fatty liver, diabetes, and dyslipidemia by targeting the same pathophysiological mechanisms. Our cohort's liver enzyme and liver fat grading decreases complement prior imaging-based studies revealing histological improvements with Saroglitazar.

Mechanism of Saroglitazar's Effect

PPAR-α activity dominates, whereas PPAR-γ activity is moderate, making Saroglitazar a novel PPAR agonist. PPAR-α agonism enhances fatty acid oxidation in the liver, reducing hepatic triglyceride accumulation and lowering blood triglycerides, making it effective in treating dyslipidemia and fatty liver. PPAR-γ activation improves glycaemic control, reduces hepatic glucose production, and improves insulin sensitivity [15]. The dual process is much more critical when insulin resistance and hepatic fat storage occur concurrently, as in metabolic syndrome. Sarolitazar reduces hepatic lipotoxicity by enhancing mitochondrial β-oxidation and reducing de novo lipogenesis. Together, these interventions improve liver function and decrease NAFLD and NASH development. Improved adipocyte function and decreased systemic inflammation may mediate systemic insulin sensitization, evidenced by HbA1c reduction.

Implications for Clinical Practice

There are several clinical implications from this study. Because fatty liver, type 2 diabetes, and dyslipidaemia often coexist, saroglitazar may be an effective therapy for all three. Saroglitazar affects glucose and lipid metabolism, two metabolic syndrome components, giving it an advantage over monotherapy. Real-world polypharmacy for metabolic disease patients increases the risk of adverse drug responses and noncompliance. Since Saroglitazar is dual-action, clinicians can obtain complete metabolic control with a streamlined therapy plan. Given the rising number of diabetics with NAFLD, saroglitazar may prevent liver issues, delay cirrhosis, and maybe improve cardiovascular outcomes. Adding Saroglitazar to diabetes treatment strategies may reduce the cost of end-stage liver disease, cardiovascular events, and liver-related morbidity.

Strengths of the Study

The prospective design of the study allowed systematic data collection throughout time, reducing memory bias and improving data quality. Objective clinical criteria including liver enzyme levels, USG/Fibroscan imaging, and standardized laboratory testing improved the study's internal validity. Patient group was well-defined. Safety and efficacy were followed throughout the experiment to fairly assess Saroglitazar's therapeutic potential. The results are more reliable since they were tested using many endpoints (ALT, AST, HbA1c, LDL, HDL, triglycerides) and the positive findings were constant. The absence of major adverse events justifies Saroglitazar's continued use in wider patient groups, indicating a good risk-benefit ratio.

Limitations

This study has some limitations that reduce its promising outcomes. The study was conducted at SSJGIMSR, therefore the results may not apply to other areas with different demographics or healthcare availability. Small sample size (n =

100) limits statistical power, making it difficult to uncover moderate subgroup differences or occasional adverse occurrences.

The short follow-up is another negative. After six months, biochemical parameters improved, but more research is needed to determine if these improvements will last and if Saroglitazar is safe to use, especially for cardiovascular endpoints and hepatic fibrosis. Since there was no control group or comparator medicine, it is impossible to establish that Saroglitazar was the only active element in the study's good outcomes. Randomized controlled trials (RCTs) are needed to prove causality, although pre-post designs establish linkage. Finally, USG/Fibroscan is less invasive and more practical than liver biopsy, but it cannot investigate histological changes and reduces liver fat estimation precision.

Conclusion

This study found that Saroglitazar is safe and beneficial for fatty liver, dyslipidemia, and type 2 diabetes.

ALT, AST, hepatic fat grading, HbA1c, and lipid markers (LDL, HDL, and triglycerides) improved significantly throughout the six-month medication period with few side effects and no substantial safety problems. Our research suggests that saroglitazar may address this patient group's shared metabolic dysfunctions.

Given the study's single-center design, moderate sample size, and short duration, larger, multicentric randomized controlled trials with extended follow-up are needed to validate and investigate long-term outcomes like histological liver improvements and cardiovascular benefits.

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