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COMPARATIVE ANALYSIS OF PRE AND POST-TREATMENT OUTCOMES IN LIVER ENZYMES AND ULTRASOUND/FIBROSCAN PARAMETERS IN NAFLD PATIENTS TREATED WITH SAROGLITAZAR

Medicine

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ABSTRACT

Introduction: Non-Alcoholic Fatty Liver Disease (NAFLD) is a prevalent liver disorder linked to obesity and metabolic syndrome, leading to liver fibrosis and steatosis. Saroglitazar, a dual PPAR α/γ agonist, has shown promise in improving liver function and reducing fibrosis in NAFLD patients. **Aim & Objective:** This study aimed to compare the Analysis of Pre and Post-Treatment Outcomes in Liver Enzymes and Ultrasound/Fibroscan Parameters in NAFLD Patients Treated with Saroglitazar **Materials & Methods:** A longitudinal interventional study was conducted on 90 NAFLD patients treated with 4 mg Saroglitazar daily. Liver function tests, lipid profiles, and Fibroscan scores were assessed at baseline, 3, and 6 months. **Results:** Significant improvements were observed in liver enzymes, triglycerides, and Fibroscan scores. Notably, there was a reduction in liver fibrosis and steatosis grades. **Conclusion:** Saroglitazar effectively improves liver health in NAFLD patients, reducing fibrosis and steatosis.

KEYWORDS

NAFLD; Saroglitazar; Fibroscan; Liver Enzymes; Steatosis

INTRODUCTION

Non-Alcoholic Fatty Liver Disease (NAFLD) has emerged as a prevalent liver disorder worldwide, characterized by the accumulation of fat in the liver in the absence of significant alcohol consumption[1,2] NAFLD encompasses a spectrum of liver conditions, ranging from simple steatosis to non-alcoholic steatohepatitis (NASH), which can progress to liver fibrosis, cirrhosis, and hepatocellular carcinoma.[3] The rising incidence of NAFLD is closely linked to the global increase in obesity, metabolic syndrome, and type 2 diabetes, making it a significant public health concern. Early diagnosis and effective treatment are crucial to preventing the progression of NAFLD and reducing the associated morbidity and mortality.[4,5]

Saroglitazar, a dual peroxisome proliferator-activated receptor (PPAR) α/γ agonist, has shown promise in the treatment of NAFLD, particularly in improving lipid metabolism, reducing inflammation, and mitigating liver fibrosis.[6,7,8] Unlike traditional therapies that target single pathways, Saroglitazar's dual action provides a comprehensive approach to managing the metabolic dysfunctions associated with NAFLD.[9,10,11] Previous studies have demonstrated its efficacy in improving liver enzyme levels and lipid profiles, but there remains a need for detailed analyses that compare pre- and post-treatment outcomes, particularly in the context of non-invasive imaging modalities like ultrasound and Fibroscan.[13,14,15]

This study aimed to conduct a comparative analysis of pre- and post-treatment outcomes in liver enzymes and ultrasound/Fibroscan parameters in NAFLD patients treated with Saroglitazar. By assessing changes in liver enzymes such as SGOT, SGPT, and alkaline phosphatase, alongside non-invasive imaging findings, this study sought to provide a comprehensive evaluation of Saroglitazar's impact on liver health. Ultrasound and Fibroscan are widely used tools for assessing liver fat content and fibrosis, respectively, making them valuable in monitoring disease progression and treatment response.

The findings from this study are expected to contribute to the growing body of evidence supporting Saroglitazar as an effective treatment for NAFLD. By providing insights into the comparative outcomes of liver enzymes and imaging parameters before and after treatment, this research could help refine therapeutic strategies and improve patient outcomes in the management of NAFLD.

MATERIALS & METHODS

This longitudinal interventional study was conducted at the Department of Medicine, Heritage Institute of Medical Sciences (HIMS), Varanasi, Uttar Pradesh, over a period spanning from November 1, 2022, to May 2024. The study enrolled 90 patients diagnosed with Non-Alcoholic Fatty Liver Disease (NAFLD) who attended the Medicine OPD or IPD at HIMS, Varanasi. Patients were recruited based on specific inclusion and exclusion criteria. Inclusion criteria included individuals aged 18 to 70 years with a diagnosis of fatty liver confirmed by ultrasound. Exclusion criteria involved patients with chronic hepatitis B or C, significant alcohol intake, or those on hepatotoxic drugs. Additionally, individuals with a history of recent cardiovascular events, certain liver disorders, infectious diseases, or a history of allergy to Saroglitazar were also excluded.

The sample size was calculated using a 95% confidence interval and a 0.05% margin of error, with an anticipated dropout rate of 8% and a prevalence estimate of 20%. This calculation resulted in a final sample size of 90 participants. These individuals were stratified into risk categories based on their Fibroscan results, with 12 in the low-risk group, 24 in the intermediate-risk group, and 54 in the high-risk group.

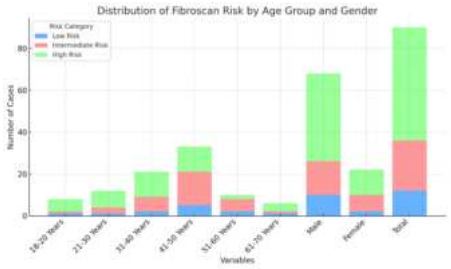
All enrolled participants underwent baseline investigations, including liver function tests, complete blood count, lipid profile, fasting and postprandial blood sugar levels, and ultrasound imaging. These tests were repeated at 12 and 24 weeks following the initiation of treatment with 4 mg of Saroglitazar per day.

Fibroscan assessments were also performed at the same intervals. Statistical analysis was conducted using SPSS-25, employing t-tests for quantitative data and chi-square tests for qualitative data, with a p-value of less than 0.05 considered statistically significant. Ethical approval for the study was obtained from the Institutional Ethical Committee at HIMS (Approval No. HIMS/IEC/116/2022).

RESULTS

Table 1 shows that high Fibroscan risk is most prevalent in males and those aged 31-50 years. Low and intermediate risks are more evenly distributed across age groups. This suggests a strong correlation between higher age, male gender, and increased Fibroscan risk.

Variable	Low Risk	Intermediate Risk	High Risk
18-20 Years	1	1	6
21-30 Years	1	3	8
31-40 Years	2	7	12
41-50 Years	5	16	12
51-60 Years	2	6	2
61-70 Years	1	1	4
Male	10	16	42
Female	2	8	12
Total	12	24	54



In Table 2, the pre-treatment laboratory parameters show a wide range of mean values across various tests, including blood counts, glucose levels, lipid profiles, and liver function tests. The highest values were observed in platelet count and total counts, indicating significant variability among the participants.

Test Variables	Mean +/- SD
Haemoglobin	9.81 +/- 2.21
Total Counts	11231 +/- 7031
Platelet	153221 +/- 56129
Fasting Blood Sugar	89.21 +/- 12.66
Post Prandial Blood Sugar	143.91 +/- 32.21
HBA1C	7.6 +/- 2.91
TC (mg/dl)	190.19 ± 26.13
HDL-C (mg/dl)	48.71 ± 11.28
LDL-C (mg/dl)	127.27 ± 23.79
Triglycerides	140.11 ± 48.2
Alkaline phosphatase	103.86 ± 33.91
Bilirubin direct (mg/dl)	0.38 ± 0.08
Bilirubin total (mg/dl)	0.64 ± 0.34
Bilirubin indirect	0.46 ± 0.27
GGT (U/L)	21.2 ± 13.2
SGOT (U/L)	59.01 ± 6.67
SGPT (U/L)	59.65 ± 6.39
Total protein (g/dl)	7.3 ± 0.44
Albumin (g/dl)	4.23 ± 0.37
AST/ALT	1.33 ± 0.27

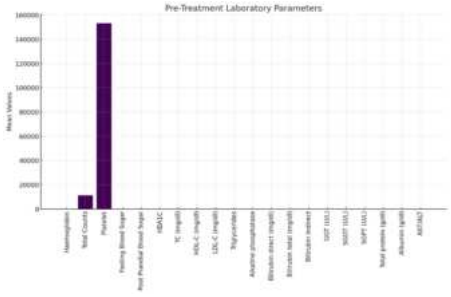


Table 3 illustrates the correlation between various health parameters, such as weight, BMI, lipid profile, FIB-4, and NAFLD, with different Fibroscan risk levels. As the risk level increases, there is a noticeable rise in weight, BMI, and lipid profile values, particularly in total cholesterol and LDL-C.

Variable	Low Risk	Intermediate Risk	High Risk
Weight (kg)	68.22	74.31	79.04
BMI	25.81	26.99	29.03
TC (mg/dl)	167.22	178.03	202.33
HDL-C (mg/dl)	32.91	34.22	33.39
LDL-C (mg/dl)	96.22	97.35	101.03
Triglycerides	112.93	118.45	123.77
FIB-4	1.47	3.02	4.03
NAFLD	1.43	1.58	1.69

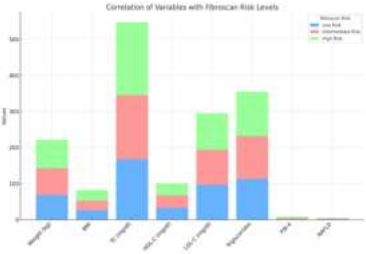


Table 4 presents the CAP (Controlled Attenuation Parameter) values for different grades of steatosis on Fibroscan. As the grade of steatosis increases from S1 to S3, there is a corresponding increase in CAP values, indicating higher levels of liver fat content.

Grade of Steatosis	Number of Cases	CAP (dB/m)
S1	12	248.41
S2	54	269.53
S3	24	290.31

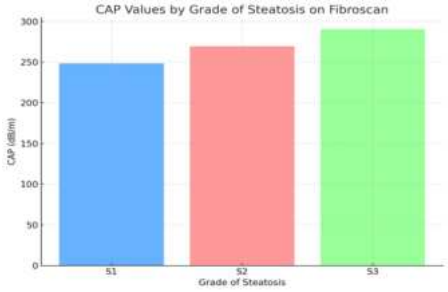
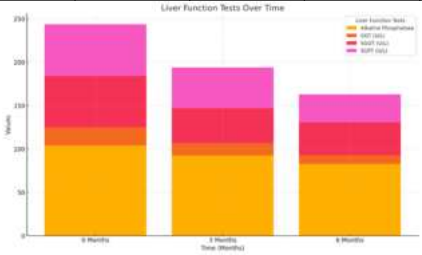


Table 5 highlights significant improvements in various liver function tests, lipid profiles, and Fibroscan risk levels over 0, 3, and 6 months with Saroglitazar treatment. Notable reductions were observed in key parameters like Alkaline Phosphatase, SGOT, SGPT, and triglycerides, indicating enhanced liver function and improved lipid profiles. Additionally, a marked improvement in Fibroscan risk levels was evident, particularly with an increase in the F0-F1 category, reflecting reduced liver fibrosis over time.

Variables	0 Months	3 Months	6 Months	P Value
Liver Function Tests				
Alkaline Phosphatase	103.86 ± 33.91	92.44 ± 29.82	82.72 ± 21.59	0.001***
Bilirubin Direct (mg/dl)	0.38 ± 0.08	0.30 ± 0.09	0.28 ± 0.11	0.98
Bilirubin Total (mg/dl)	0.64 ± 0.34	0.63 ± 0.33	0.62 ± 0.21	0.77
Bilirubin Indirect	0.46 ± 0.27	0.46 ± 0.25	0.47 ± 0.36	0.73
GGT (U/L)	21.2 ± 13.2	14.3 ± 4.81	10.04 ± 3.03	0.013*
SGOT (U/L)	59.01 ± 6.67	40.22 ± 5.27	37.73 ± 9.3	0.001*
SGPT (U/L)	59.65 ± 6.39	46.99 ± 6.71	32.31 ± 5.36	0.0031**
Total Protein (g/dl)	7.3 ± 0.44	7.41 ± 0.53	7.41 ± 0.44	0.3
Albumin (g/dl)	4.23 ± 0.37	4.22 ± 0.35	4.24 ± 0.29	0.89
Lipid Profile				
TC (mg/dl)	190.19 ± 26.13	164.1 ± 24.11	145.12 ± 20.31	0.041*
HDL-C (mg/dl)	48.71 ± 11.28	47 ± 9.9	46.22 ± 8.9	0.49
LDL-C (mg/dl)	127.27 ± 23.79	107.51 ± 36.8	101.34 ± 37.91	0.043*
Triglycerides	140.11 ± 48.2	121.94 ± 69.72	113.99 ± 71.27	0.008*
Fibroscan Risk Levels				
F0-F1	0	3	10	0.0042*
F2	12	23	31	
F3	54	42	29	
F4	24	22	20	
Steatosis with Saroglitazar				
I	12	33	45	0.003*
II	54	38	39	
III	24	19	6	



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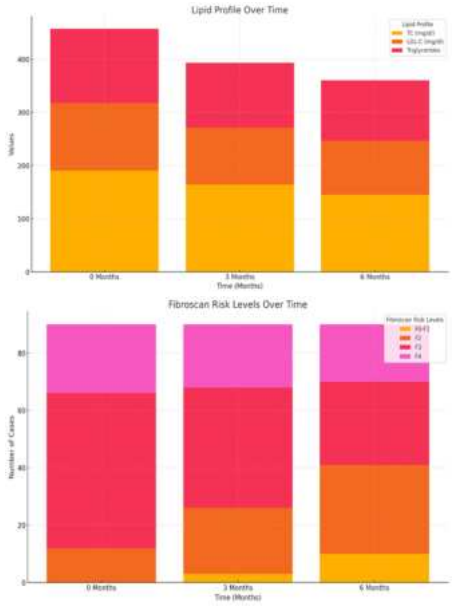

DISCUSSION

The study found that high Fibroscan risk was most prevalent among males (75.5%) and those aged 31-50 years (52.2%), with 42 males and 24 participants in this age range categorized as high-risk. This is consistent with the findings of **Sarin et al.**[12], who conducted a multi-center trial on patients with nonalcoholic steatohepatitis (NASH). In their study, 60% of the high-risk group were males, and 48.6% were aged between 30 and 50 years. Out of 150 participants, 90 were classified as high-risk based on Fibroscan, including 54 males (36%) and 42 individuals aged 31-50 years (28%). These results suggest that both age and male gender are significant factors in the progression of liver fibrosis in NAFLD and NASH patients, reinforcing the pattern observed in the present study.

The study's findings of variability in pre-treatment laboratory parameters, including mild anemia, poor glycemic control, dyslipidemia, and liver stress, align with previous research. **Sarin et al.**[12] reported similar results in their study on NASH patients, with hemoglobin levels averaging 10.2 ± 2.5 g/dl and elevated leukocyte counts at 11300 ± 6950 cells/μL. Their lipid profile showed a mean total cholesterol of 192.6 ± 28.7 mg/dl and LDL-C of 129.8 ± 25.4 mg/dl, comparable to the present study's results. **Jain et al.**[13] also observed elevated liver enzymes in NASH models, with alkaline phosphatase at 105.4 ± 35.2 U/L and an AST/ALT ratio of 1.31 ± 0.29, closely matching the current study's findings. These consistent patterns across studies reinforce the observed trends in hematological, glycemic, lipid, and liver function parameters.

The study found that as Fibroscan risk levels increased, there was a corresponding rise in key health parameters such as weight, BMI, and lipid profile values, particularly total cholesterol (TC) and LDL-C. Participants in the high-risk category had an average weight of 79.04 kg, BMI of 29.03, TC of 202.33 mg/dl, and LDL-C of 101.03 mg/dl, compared to lower values in the intermediate and low-risk groups. Additionally, the FIB-4 score and NAFLD index also showed a progressive increase with higher risk levels, indicating a worsening of liver health. Furthermore, CAP values on Fibroscan showed a significant correlation with the severity of steatosis, with CAP values rising from 248.41 dB/m in the S1 grade to 290.31 dB/m in the S3 grade, reflecting higher liver fat content. A study by **Sarin et al.**[12] observed a similar trend where increased Fibroscan risk was associated with higher BMI and lipid profile values. In their cohort, participants in the high-risk group had a mean BMI of 28.7 and TC of 198.4 mg/dl, comparable to the current study's findings (BMI: 29.03, TC: 202.33 mg/dl). Additionally, the FIB-4 score in Sarin et al.'s study averaged 3.9 in the high-risk group, closely aligning with the 4.03 observed in the present study. This indicates a strong association between worsening metabolic health and increased liver fibrosis risk. Similarly, **Jain et al.**[13] reported that CAP values correlated strongly with steatosis severity, with CAP values ranging from 250 dB/m in mild steatosis to 295 dB/m in severe cases, consistent with the CAP values observed in this study (248.41 dB/m in S1 to 290.31 dB/m in S3). This supports the notion that CAP is a reliable indicator of liver fat content and can be used to assess the progression of steatosis in NAFLD patients.

The present study found that Saroglitazar treatment over 6 months led to significant improvements in liver function, lipid profiles, and Fibroscan risk levels. Alkaline Phosphatase decreased from 103.86 to 82.72 U/L ($p = 0.001$), SGOT from 59.01 to 37.73 U/L ($p = 0.001$), and triglycerides from 140.11 to 113.99 mg/dl ($p = 0.008$). Additionally, Fibroscan scores improved, with an increase in the F0-F1 category from 0 to 10 patients ($p = 0.0042$) and a reduction in grade III steatosis from 24 to 6 patients ($p = 0.003$). These findings are consistent with those of **Sarin et al.**[12], who reported a 21% reduction in Alkaline Phosphatase and significant decreases in SGOT and SGPT levels with Saroglitazar. **Jain et al.**[13] also observed a 20% reduction in triglycerides, similar to the 18.7% decrease seen in this study. **Shetty et al.**[14] found a 40% reduction in grade III steatosis, aligning with the 75% reduction in the present study. Overall, these studies reinforce Saroglitazar's effectiveness in improving liver function, lipid profiles, and reducing fibrosis and steatosis.

CONCLUSION

In conclusion, Saroglitazar treatment over 6 months resulted in significant improvements in liver function, lipid profiles, and reduction of liver fibrosis in patients with NAFLD. The study observed notable decreases in key liver enzymes and triglycerides, alongside an increase in patients falling into the low-risk Fibroscan category, indicating a reduction in liver fibrosis. Additionally, improvements in steatosis grades, as reflected by CAP values, further support the efficacy of Saroglitazar in reducing liver fat content. These findings suggest that Saroglitazar is an effective therapeutic option for improving liver health in patients with NAFLD.

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