Original Article
DOI: https://doi.org/10.70749/ijbr.v3i5.1218

INDUS JOURNAL OF BIOSCIENCE RESEARCH
https://induspublishers.com/IJBR
ISSN: 2960-2793/ 2960-2807

Crossref

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Effect of Statins on Liver Function Tests (LFTs) in Patients with Diabetes Presenting in CMH Rawalakot

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ARTICLE INFO

Keywords: Diabetes, Liver Function Tests, Statins.

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Declaration
Author's Contribution: Sole author.
Conflict of Interest: No conflict of interest.
Funding: No funding received by the authors.

Article History
Received: 06-04-2025, Revised: 29-04-2025
Accepted: 03-05-2025, Published: 08-05-2025

ABSTRACT

Objectives: To find the effect of statin therapy on liver function tests in diabetic patients presenting at CMH Rawalakot. **Study design:** Qausi-experimental study. **Place and duration of study:** Department of Medicine, CMH, Rawalakot, from October 2024 to March 2025. **Methodology:** A total of 100 patients, aging between 40 to 70 years, diagnosed with type 2 diabetes since ≥1 year, and was not previously on statin therapy, were included in this study using consecutive sampling. All the demographics and related medical history was recorded. Baseline liver function tests (ALT, AST, ALP, GGT, and total bilirubin) and the blood glucose levels were recorded. Patients were recommended Rosuvastatin 20 mg/day for 3 months. The primary objectives of the study was to find the impact of statin therapy on liver function tests in diabetic patients presenting at our hospital. Values of Pre- and post-treatment LFT were compared using the paired t-test, with a p-value <0.05 taken as statistically significant. **Results:** The mean age in this study was 50.38±6.89 years (ranging from 36 to 64 years). The male gender was 58% of total study population while female gender was 42%. Comparison between baseline and post-treatment liver function test values after 3 months of statin therapy with Rosuvastatin 20 mg/day showed no statistically significant change in all the parameters of LFTS including ALT (p=0.14), AST (p=0.79), ALP (p=0.11), GGT (p=0.88) and total bilirubin levels (p= 0.17). The analysis of sub-group of patients with HbA1C levels >7% also showed no statistically significant change in LFTs. **Conclusion:** Statins are hepatically safe in diabetic patients, with no significant changes in liver function tests, supporting its clinical use for managing dyslipidemia in these patients.

INTRODUCTION

Liver disease, characterized by damage to liver cells, represents a significant global health concern. The disease is manifested by impaired liver function and encompass a broad spectrum of symptoms that include physical signs, digestive disturbances, blood sugar abnormalities, immune disorders, abnormal fat absorption, and metabolic derangements.[1,2]

The damage to the liver is reflected by the elevated levels of liver enzymes like alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), and total bilirubin (TB). In this context, liver function tests (LFTs) serve as critical diagnostic tools to evaluate any hepatocellular injury, cholestasis, and overall liver health.[1,3]

Type II diabetes mellitus (T2DM) is a metabolic disorder which is marked by hyperglycemia, insulin resistance, and insulin deficiency. Global prevalence of diabetes is on rise, with a high number of 537 million adults reported to be affected in 2021, and the projected figure reaches up to 783 million by 2045. T2DM is found to drive systemic inflammation and oxidative stress and worsen the metabolic dysfunction.[4]

The interplay between insulin resistance, dyslipidemia, and chronic inflammation contributes to the development of cardiovascular (CV) and hepatic complications in diabetic patients. Emerging evidence suggests diabetes as a risk factor for the development of non-alcoholic fatty liver disease (NAFLD) and its progression can cause severe conditions like steatohepatitis, fibrosis, cirrhosis, and hepatocellular carcinoma.[5,6]

Diabetic patients frequently need lipid lowering treatment to reduce their CV risk and HMG-CoA reductase inhibitors (Statins) are among the commonly used medicines for managing dyslipidemia in diabetics. Statins are proven to reduce low-density lipoprotein cholesterol (LDL-C) levels by inhibiting the rate-limiting enzyme in cholesterol synthesis and

consequently decrease the atherosclerotic CV risk (ACVD).[7]

In general, statins are well tolerated with a low side –effect profile, however, their impact on liver function remains a topic of ongoing clinical discussion. Studies with the commonly prescribed statins, simvastatin, atorvastatin and rosuvastatin and have reported to cause asymptomatic elevations in liver enzymes in some diabetic patients. This hepatotoxic potential of statins therefore requires a careful monitoring, especially in a population segment already at the risk of liver disease.[8]

The international studies exploring the effect of statin use on liver enzymes in diabetics have reported mixed findings. Some researchers have suggested transient, non-clinically significant increases in transaminases, while others have indicated no substantial alteration in LFTs and supported the hepatic safety of statins.[9,10]

Additionally, a gap of knowledge regarding the impact of satins on LFTs in diabetic persists in different regional and ethnic groups. Therefore, finding the potential adverse effects of statins, such as liver dysfunction, myopathy, and elevated liver enzymes, in specific regions with limited healthcare infrastructure and lack of research work like, Azad Jammu and Kashmir (AJK), can benefit in improving the overall outcomes in diabetic patients with dyslipidemia in population with distinct dietary patterns and life styles.

This research was therefore planned to evaluate the impact of statin therapy on LFTs in diabetic patients presenting at CMH Rawalakot. These findings will help our clinicians to make informed, region-specific clinical decision for diabetic patients taking lipid lowering therapies.

METHODOLOGY

This Quasi-experimental study was conducted at the department of Medicine, CMH, Rawalakot, Azad Kashmir from October 2024 to March 2025 over a period of 6 months after getting approval from the ethical committee of the hospital.

The sample size was calculated as per following assumptions using WHO sample size calculator:

m1 (Serum ALT levels before treatment) = 55.85±20.71 IU/L

m2 (Serum ALT levels after treatment with statin) = 48.4±9.23 IU/L.

With (α): 0.05 (two-tailed), and Power: 90% the estimated sample size n=98.[11]

A total of 100 patients, aging between 40 to 70 years, diagnosed with type 2 diabetes since ≥11 year, and was not previously on statin therapy, were included in this study using consecutive sampling.

Patients with a known history of chronic liver disease from causes other than diabetes, were excluded. Additionally, individuals with a history of alcohol use, pancreatitis, or prior use of medications known to damage the liver or induce hepatic steatosis were not included in the study. The study also excluded those who were currently using drugs that alter lipid metabolism or liver function, such as systemic steroids, immunosuppressants, or medications known to increase the risk of rhabdomyolysis when taken alongside statins (e.g., cyclosporine, erythromycin).

A written informed consent was taken from each patient prior to their inclusion.

All the demographics and related medical history was recorded. Baseline liver function tests (ALT, AST, ALP, GGT, and total bilirubin) and the blood glucose levels were recorded. Patients were recommended Rosuvastatin 20 mg/day for 3 months.

Blood samples were collected from each patient with 12 hours of fasting. Blood glucose was measured using the colorimetric enzymatic method. All these biochemical analyses were conducted in the same laboratory settings. For liver enzyme testing, 5 ml of serum was taken from each patient and stored at -70 °C. AST and ALT levels were measured using the photometric enzymatic method. All the data was recorded using a pre-designed proforma.

All the above investigations were repeated after 3 month of treatment with statins.

The primary objectives of the study was to find the impact of statin therapy on liver function tests in diabetic patients presenting at CMH Rawalakot.

All data was analyzed using SPSS version 26. Quantitative variables such as age, BMI, duration of diabetes, and LFTs were presented as mean ± standard deviation, while qualitative variables like gender, and socioeconomic status were summarized using frequencies and percentages. Pre- and post-treatment LFT values were compared using the paired t-test, with a p-value <0.05 taken as statistically significant. We further compared the pre- and post-treatment LFTs in sub-group of patients with uncontrolled diabetes (HbA1C>7%) by applying paired t-test with significance taken at <0.05.

RESULTS

The mean age in this study was 50.38±6.89 years (ranging from 36 to 64 years). The male gender was 58% of total study population while female gender was 42%. The details of demographics and related clinical features are shared in Table-I.

Table I

Demographics and related clinical features (n=100)

Demographics and related clinical features		
Age (Mean±SD) years		50.38±6.89
Gender	Male n (%)	58 (58)
	Female n (%)	42 (42)
BMI (Mean±SD) Kg/m^2		27.48±3.72

Duration of Diabetes (Mean±SD) years		5.31±2.35
HbA1C levels (Mean±SD) %		7.82±0.95
Fasting blood glucose levels (Mean±SD) mg/dL		142.03±10.39
Co-morbidities	Hypertension n (%)	35 (35)
	Obesity (BMI ≥30) n (%)	28 (28)
	Dyslipidemia n (%)	79 (79)

Baseline and post-treatment liver function test (LFT) values were analyzed after 3 months of statin therapy with Rosuvastatin 20 mg/day. No statistically significant change was observed in all the parameters of LFTS including ALT (p=0.14), AST (p=0.79), ALP (p=0.11), GGT (p=0.05) and total Bilirubin levels (p= 0.17) as shown in Table-II.

Table II

Comparison of Pre- and Post-Treatment Liver Function Tests (n=100)

Parameters	Baseline (Mean ± SD)	Post-Treatment (Mean ± SD)	p-value*
ALT (U/L)	49.57 ± 4.12	48.08 ± 4.86	0.14
AST (IU/L)	38.48±2.92	38.38 ± 2.22	0.79
ALP (IU/L)	97.71±7.98	96.31± 6.43	0.11
GGT (IU/L)	49.98±3.73	49.74±3.14	0.05
Total Bilirubin (mg/dL)	0.93 ± 0.12	0.92 ± 0.10	0.17

*Paired t-test

We also studied the impact of statin treatment on patients where HbA1C levels were >7% (58% of total study population), to find any impact of this lipid lowering treatment in uncontrolled diabetics. This comparison also showed no statistically significant change in all the parameters of LFTs including ALT (p=0.11), AST (p=0.7), ALP (p=0.05), GGT (p=0.88) and total Bilirubin levels (p= 0.24) as shown in Table-II.

Table III

Comparison of pre- and post-treatment liver function tests in diabetics with HbA1C >7% (n=58)

Parameters	Baseline (Mean ± SD)	Post-Treatment (Mean ± SD)	p-value*
ALT (U/L)	48.61 ± 5.11	49.10 ± 4.03	0.11
AST (IU/L)	38.25±2.82	38.14 ± 2.04	0.70
ALP (IU/L)	96.77±7.17	96.31± 6.43	0.05
GGT (IU/L)	49.95±4	49.81±3.46	0.88
Total Bilirubin (mg/dL)	0.93 ± 0.12	0.92 ± 0.09	0.24

*Paired t-test

DISCUSSION

The mean in this study was 50.38±6.89 years, and patients had a 5.31±2.35 years as mean duration of diabetes. In these diabetic patients dyslipidemia (79%), hypertension (35%), and obesity (28%), were the most common comorbidities. Comparison between baseline and post-treatment LFTs after 3 months treatment with Rosuvastatin 20mg/day showed no statistically significant change in the parameters including ALT (p=0.14), AST (p=0.79), ALP (p=0.11), GGT (p=0.88) and total bilirubin levels (p= 0.17), indicating the treatment had no impact on liver function. The analysis of sub-group of patients with HbA1C levels >7% also showed no statistically significant change in pre- and post-treatment LFTs.

The effect of statins on LFTs have been discussed in a number of research publication with different perspectives and varying objectives.

In a study on this subject by Ather MM et al., the prevalence of asymptomatic increase in liver enzyme was determined in type II diabetic patients using statin. The results of 335 patients showed statistically non-significant increase in the levels of ALT and AST. This increase was observed in patients with increasing age, diabetes duration, BMI, FBS, or TG, but remained non-significant in all these subgroups.[12] In a cross-sectional study by Nascimbeni F., results showed no significant differences in LFTs between the groups of users and non-users of statins among diabetic patients, with AST (32 vs 31 U/L, p=0.178), ALT (42 vs 39 U/L, p=0.218), and GGT (50 vs 54 U/L, p=0.286). These results indicate that statin use did not significantly alter LFTs, supporting their hepatic safety in diabetics with NAFLD as statin users showed no increased prevalence of NASH (57% vs 56%, p=0.868). Multivariate analysis showed statins were negatively associated with NASH (OR 0.57) and SF (OR 0.47), indicating no significant LFT disturbances and potential hepatic benefit in diabetic patients.[13] Hence the findings of above mentioned studies align with the results of our study on LFTs in diabetic populations and supports the hepatic safety of statins.

Moreover, some studies have shown potential hepatoprotective effects of statins in specific diabetic populations. An important finding was shared by Rusu E et al. who studied the effect of statin on LFTs in diabetic patients. After 6 months of atorvastatin therapy in T2DM patients with chronic hepatitis C, significant reductions were observed in liver enzymes where AST and ALT levels decreased notably (p<0.05), indicating improved liver function. No elevations in liver enzymes occurred which suggested atorvastatin as safe and well-tolerated in this patient population.[14] Bril F et al. in a study of patients with nonalcoholic steatohepatitis (NASH) and prediabetes/T2DM, showed no histologic liver worsening or increased hepatic insulin resistance and confirmed that statins do not adversely affect LFTs and are safe in diabetic patients with NASH.[15] The findings of Ho A et al. also mentioned that statin therapy was not linked to elevated liver enzymes, including ALT, while LDL cholesterol and total cholesterol, lowered significantly in statin users, demonstrating its potential to reduce CV risks in NAFLD patients.[16] These studies collectively reinforce the hepatic safety profile of statins in diabetic patients, even in those with pre-existing liver conditions like NASH or NAFLD.

In contrast to the above findings, some research has yielded contradictory results that warrant these consideration. Rajabian M et al. compared liver enzyme levels in 200 type 2 diabetic patients, where statin users showed significantly higher BMI, LDL, ALT, AST, and cholesterol levels ($p < 0.05$). These results suggested that statin use may elevate liver enzymes, indicating potential hepatic risk.[17]

Cheon DY and Jo SH discussed the possible adverse effects of statins and mentioned that mild, transient elevations in liver function tests (LFTs), may be caused by these drugs, especially ALT, without any true liver damage. This was observed more commonly during the first year of use and at higher doses. In diabetics, the metabolic state of liver may be altered, heightening the susceptibility towards this damage, however, clinically significant hepatic dysfunction is rare and usually resolves without discontinuing the drug. The exact mechanism is unclear and likely involves idiosyncratic or immune-allergic reactions.[18]

All this discussion contribute to the growing set of evidence suggesting that statin therapy is generally well-tolerated in diabetic patients without significant adverse effects on liver functions, supporting their continued use for CV risk reduction.

The major limitation of our study is its short follow up time as any long term effect couldn't be recorded. Moreover, the quasi-experimental design without a control group limits the strength of conclusions of our findings. Future studies covering these limitations will add up to this useful data on the use of statins in diabetic patients.

CONCLUSION

This study shows that statin therapy doesn't significantly alter LFTs in diabetic patients over a three-month treatment period. These non-significant changes in ALT, AST, ALP, GGT, and total bilirubin levels suggest that statins are generally well-tolerated without clinically meaningful hepatotoxic effects, including those with uncontrolled diabetes (HbA1C >7%) and can be recommended in diabetic patients for their lipid lowering benefits. Regular monitoring of liver function is still recommended as per standard clinical practice, particularly in patients with other risk factors for liver dysfunction.

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