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Differential Effects of Atorvastatin and Rosuvastatin on Inflammatory Biomarkers and Adipokines in Type 2 Diabetes Mellitus with Dyslipidemia

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) with dyslipidemia is characterized by chronic low-grade inflammation and adipokine dysregulation, which contribute significantly to increased cardiovascular risk. In addition to lipid lowering, statins exert pleiotropic effects on inflammatory pathways and adipose tissue function. However, comparative evidence regarding the effects of atorvastatin and rosuvastatin on inflammatory biomarkers and adipokines in patients with T2DM remains limited, particularly in the Indian population.

Materials and Methods: This Randomized comparative prospective study included 196 patients with T2DM and newly diagnosed dyslipidemia, allocated equally to receive atorvastatin (n = 98) or rosuvastatin (n = 98). Serum levels of high-sensitivity C-reactive protein (hs-CRP), adiponectin, and leptin were measured at baseline and after six months of statin therapy. Intragroup and intergroup comparisons were performed using paired and unpaired t-tests, respectively. Multivariate linear regression analysis was conducted to assess the independent effect of statin type on biomarker changes after adjusting for age, sex, and body mass index.

Results: Baseline inflammatory and adipokine parameters were comparable between the two groups. After six months, both statins produced significant reductions in hs-CRP and leptin levels and significant increases in adiponectin ($p < 0.001$ for all intragroup comparisons). However, rosuvastatin demonstrated significantly greater reductions in hs-CRP (-125.02 ± 51.49 ng/mL vs -106.94 ± 45.22 ng/mL; $p = 0.010$) and leptin (-3.42 ± 2.24 ng/mL vs -2.07 ± 2.16 ng/mL; $p < 0.001$), along with a significantly higher increase in adiponectin levels at follow-up ($p = 0.005$). Regression analysis confirmed statin type as an independent predictor of hs-CRP and leptin reduction.

Conclusion: Both atorvastatin and rosuvastatin significantly improve inflammatory and adipokine profiles in patients with T2DM and dyslipidemia; however, rosuvastatin exerts superior pleiotropic effects, characterized by greater reductions in hs-CRP and leptin and a more pronounced increase in adiponectin. These findings suggest that rosuvastatin may offer additional cardiometabolic benefits in patients with heightened inflammatory burden.

Keywords: *Type 2 diabetes mellitus; Dyslipidemia; Rosuvastatin; Atorvastatin; hs-CRP; Adiponectin; Leptin; Inflammation.*

INTRODUCTION

Type 2 diabetes mellitus (T2DM) and dyslipidemia frequently coexist and together represent a major contributor to cardiovascular morbidity and mortality worldwide. Beyond abnormalities in lipid and glucose metabolism, these conditions are characterized by chronic low-grade inflammation and adipose tissue dysfunction, which play a central role in the development of insulin resistance, endothelial dysfunction, and atherosclerosis [1–3]. Inflammatory biomarkers and adipokines have therefore emerged as important mediators linking metabolic disturbances to cardiovascular disease.

High-sensitivity C-reactive protein (hs-CRP) is a well-established marker of systemic inflammation and an independent predictor of cardiovascular events. Elevated hs-CRP levels are commonly observed in patients with T2DM and dyslipidemia and reflect underlying vascular inflammation and endothelial injury [4,5]. In parallel, dysregulation of adipokines—particularly adiponectin and leptin—contributes significantly to metabolic and inflammatory imbalance. Adiponectin exerts anti-inflammatory, insulin-sensitizing, and anti-atherogenic effects, whereas leptin is associated with pro-inflammatory signaling, oxidative stress, and increased cardiovascular risk when present at elevated levels [6–8]. Reduced adiponectin and increased leptin concentrations are consistently reported in patients with diabetes and dyslipidemia, underscoring their relevance as biomarkers of cardiometabolic risk.

Statins remain the cornerstone of dyslipidemia management and have demonstrated substantial benefits in reducing cardiovascular events in high-risk populations. In addition to their lipid-lowering properties, statins exert pleiotropic effects, including modulation of inflammatory pathways, improvement of endothelial function, and regulation of adipokine secretion [9,10]. These non-lipid effects are increasingly recognized as contributors to cardiovascular risk reduction. However, accumulating evidence suggests that individual statins may differ in the magnitude and direction of their effects on inflammatory biomarkers and adipokines.

Atorvastatin and rosuvastatin are among the most commonly prescribed statins and are widely used in patients with T2DM. Several studies have demonstrated that both agents reduce hs-CRP levels, although rosuvastatin has been reported to produce a more pronounced anti-inflammatory effect in certain populations [11,12]. Similarly, statin therapy has been associated with increased adiponectin and reduced leptin levels, but comparative data between atorvastatin and rosuvastatin remain limited and inconsistent, particularly in patients with diabetes and dyslipidemia [13,14]. Most existing studies have focused primarily on lipid or cardiovascular outcomes, with inflammatory biomarkers and adipokines often assessed as secondary endpoints.

Furthermore, data from Indian and other South Asian populations are scarce, despite the high prevalence of diabetes-related dyslipidemia and heightened cardiometabolic risk in these regions. Genetic, lifestyle, and environmental factors unique to these populations may influence inflammatory and adipokine responses to statin therapy, highlighting the need for region-specific evidence.

In this context, the present study was undertaken to compare the effects of atorvastatin and rosuvastatin on inflammatory biomarker hs-CRP and adipokines (adiponectin and leptin) in patients with T2DM and dyslipidemia. Understanding these differential pleiotropic effects may aid clinicians in selecting statin therapy that optimally addresses not only lipid abnormalities but also underlying inflammation and adipose tissue dysfunction, thereby improving overall cardiometabolic outcomes.

MATERIALS AND METHODS

Study Design

The present study was designed as a randomized comparative prospective study with the objective of evaluating the differential effects of atorvastatin and rosuvastatin on inflammatory biomarker hs-CRP and adipokines, namely adiponectin and leptin, in patients with type 2 diabetes mellitus (T2DM) and dyslipidemia.

Place of Study

The study was conducted in the Outpatient Departments of Medicine and ENT of a tertiary care teaching hospital in India. The hospital caters to patients from rural, suburban, and urban regions, thereby providing a diverse and representative population of individuals with T2DM and dyslipidemia.

Methodology

Patients with type 2 diabetes mellitus attending the outpatient clinics were screened for eligibility. Individuals aged between 30 and 65 years who were newly diagnosed with dyslipidemia and had not previously received statin therapy were included after obtaining written informed consent. Patients with chronic inflammatory or autoimmune diseases, hepatic or renal impairment, malignancy, pregnancy, lactation, or those receiving medications known to influence inflammatory markers or adipokine levels were excluded from the study. The sample size was 196 participants, with 98 patients allocated to each treatment group. Participants were randomly assigned to receive either atorvastatin or rosuvastatin as per standard clinical practice. Baseline demographic and clinical data were recorded at enrollment. Blood samples were collected at baseline and after six months of statin therapy for estimation of hs-CRP, adiponectin, and leptin using standardized and validated

laboratory assay methods. Relevant data were obtained from laboratory reports, electronic medical records, and manual patient records.

Statistical Analysis

All collected data were entered into Microsoft Excel and analyzed using SPSS version 29. Continuous variables were expressed as mean ± standard deviation. Intragroup comparisons of baseline and follow-up values were performed using the paired t-test, while intergroup comparisons were analyzed using the unpaired t-test. Multivariate linear regression analysis was carried out to assess the independent effect of statin type on changes in inflammatory and adipokine parameters after adjusting for potential confounders such as age, sex, and body mass index. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations

Ethical approval for the study was obtained from the Institutional Ethics Committee prior to its commencement (Ethical number……..). The study was conducted in accordance with the ethical principles outlined in the Indian Council of Medical Research guidelines and Good Clinical Practice standards. Written informed consent was obtained from all participants before enrollment. Confidentiality of patient information was maintained by anonymizing data and securely storing records with access limited to the research team.

RESULTS

A total of 196 patients with type 2 diabetes mellitus and dyslipidemia were included in the study, with 98 patients in each treatment group receiving atorvastatin or rosuvastatin. Baseline inflammatory and adipokine parameters were comparable between the two groups, confirming adequate randomization and baseline homogeneity.

At baseline, serum hs-CRP levels did not differ significantly between the atorvastatin and rosuvastatin groups, with mean values of 556.00 ± 28.20 ng/mL and 552.60 ± 37.75 ng/mL, respectively ($p = 0.476$). After six months of therapy, a significant reduction in hs-CRP was observed in both groups. In the atorvastatin group, hs-CRP decreased to 449.06 ± 35.14 ng/mL, while in the rosuvastatin group it declined further to 427.58 ± 41.26 ng/mL. The intragroup reductions were highly significant in both groups ($p < 0.001$). Intergroup comparison at follow-up demonstrated a significantly greater reduction in hs-CRP levels with rosuvastatin compared to atorvastatin ($p < 0.001$), indicating a superior anti-inflammatory effect of rosuvastatin (Table 1).

Table 1. Intergroup and Intragroup Comparison of hs-CRP Levels (ng/mL)

Parameter	Atorvastatin (Mean ± SD)	Rosuvastatin (Mean ± SD)	p-value
Baseline	556.00 ± 28.20	552.60 ± 37.75	0.476
6 months	449.06 ± 35.14	427.58 ± 41.26	<0.001*
Intragroup	t=23.41, **p<0.001**	t=24.04, **p<0.001**	

Baseline adiponectin levels were comparable between the two groups, with mean values of 1.40 ± 0.43 µg/mL in the atorvastatin group and 1.53 ± 0.46 µg/mL in the rosuvastatin group ($p = 0.058$). After six months of statin therapy, adiponectin levels increased significantly in both groups. The atorvastatin group showed an increase to 2.53 ± 0.60 µg/mL, while the rosuvastatin group demonstrated a greater increase to 2.81 ± 0.76 µg/mL. The intragroup improvements were statistically significant in both groups ($p < 0.001$). Intergroup comparison at follow-up revealed a significantly higher adiponectin level in the rosuvastatin group ($p = 0.005$), suggesting a more favorable effect on adipokine modulation (Figure 1).

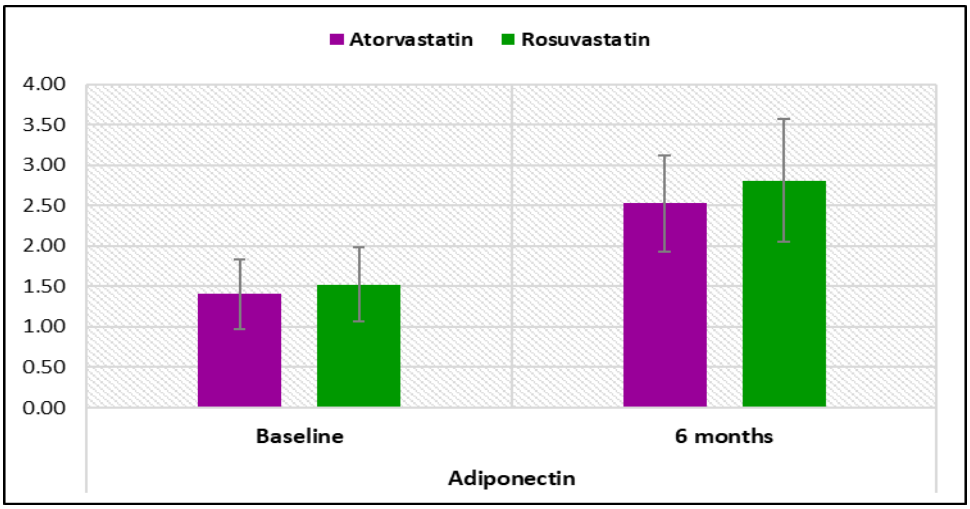

Figure – 1 : Intergroup & Intragroup Comparison of Adiponectin

With respect to leptin, baseline levels were significantly higher in the rosuvastatin group (10.48 ± 1.79 ng/mL) compared to the atorvastatin group (9.60 ± 1.62 ng/mL, $p < 0.001$). Following six months of therapy, leptin levels decreased significantly in both groups. The atorvastatin group showed a reduction to 7.53 ± 1.69 ng/mL, while the rosuvastatin group demonstrated a greater reduction to 7.06 ± 1.34 ng/mL. Both intragroup reductions were highly significant ($p < 0.001$). Intergroup comparison at follow-up showed a significantly greater reduction in leptin levels with rosuvastatin ($p = 0.030$), indicating superior improvement in leptin-mediated inflammatory signaling (Figure 2).

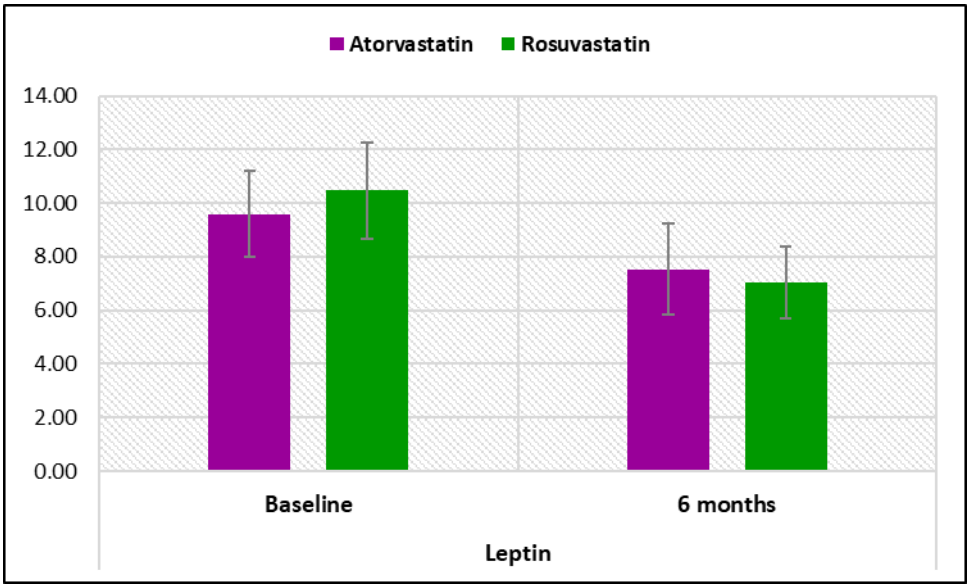

Figure 2. Intergroup and Intragroup Comparison of Leptin Levels (ng/mL)

The magnitude of change in inflammatory and adipokine parameters was further analyzed. Mean reduction in hs-CRP was −106.94 ± 45.22 ng/mL in the atorvastatin group and −125.02 ± 51.49 ng/mL in the rosuvastatin group, with the difference being statistically significant ($p = 0.010$). The increase in adiponectin was +1.12 ± 0.68 µg/mL in the atorvastatin group and +1.28 ± 0.93 µg/mL in the rosuvastatin group, though this difference was not statistically significant ($p = 0.175$). Reduction in leptin was significantly greater with rosuvastatin (−3.42 ± 2.24 ng/mL) compared to atorvastatin (−2.07 ± 2.16 ng/mL, $p < 0.001$) (Table 2).

Table 2. Comparison of Mean Change in Biomarker Levels

Parameter	Atorvastatin (Mean ± SD)	Rosuvastatin (Mean ± SD)	p-value
hs-CRP (ng/mL)	−106.94 ± 45.22	−125.02 ± 51.49	0.010*
Adiponectin (µg/mL)	+1.12 ± 0.68	+1.28 ± 0.93	0.175
Leptin (ng/mL)	−2.07 ± 2.16	−3.42 ± 2.24	<0.001*

Multivariate linear regression analysis demonstrated that statin type remained an independent predictor of biomarker change after adjustment for age, sex, and body mass index. Rosuvastatin was independently associated with a significantly greater reduction in hs-CRP (B = 17.32, $p = 0.015$) and leptin (B = 1.28, $p < 0.001$), whereas the difference in adiponectin change between the two statins was not statistically significant ($p = 0.200$) (Table 3).

Table 3. Multivariate Regression Analysis for Biomarker Changes

Dependent Variable	B	SE	p-value
hs-CRP change	17.32	7.03	0.015*
Adiponectin change	−0.15	0.12	0.200
Leptin change	1.28	0.32	<0.001*

DISCUSSION

The present randomized comparative study evaluated the differential effects of atorvastatin and rosuvastatin on inflammatory biomarker hs-CRP and adipokines, namely adiponectin and leptin, in patients with type 2 diabetes mellitus and dyslipidemia. The key finding of this study is that although both statins significantly improved inflammatory and adipokine profiles over six months, rosuvastatin consistently produced a greater magnitude of benefit, particularly in reducing hs-CRP and leptin levels, indicating superior pleiotropic anti-inflammatory and adipokine-modulating effects.

In the present study, baseline hs-CRP levels were comparable between the atorvastatin and rosuvastatin groups, ensuring a similar inflammatory status at study initiation. After six months of therapy, both statins resulted in highly significant

intragroup reductions in hs-CRP, confirming the well-recognized anti-inflammatory properties of statins. However, the reduction in hs-CRP was significantly greater with rosuvastatin. This observation is consistent with the findings of Werida et al. [14], who reported a greater percentage reduction in hs-CRP with rosuvastatin compared to atorvastatin in dyslipidemic patients. Similarly, Anagnostis et al. [15] demonstrated that rosuvastatin exerted stronger anti-inflammatory effects along with improvements in insulin sensitivity indices. A meta-analysis by Chruściel et al. [16] further supports these findings, showing that statin therapy significantly reduces hs-CRP levels, with higher-potency statins producing more pronounced effects independent of lipid lowering. Collectively, these studies support the superior anti-inflammatory efficacy of rosuvastatin observed in the present study.

Adiponectin levels increased significantly in both treatment groups, indicating improved adipose tissue function and attenuation of metabolic inflammation. Notably, rosuvastatin produced a significantly greater increase in adiponectin levels compared to atorvastatin at follow-up. Adiponectin is a protective adipokine with anti-inflammatory, insulin-sensitizing, and anti-atherogenic properties, and reduced levels are commonly associated with increased cardiovascular risk in patients with type 2 diabetes mellitus. The greater adiponectin elevation observed with rosuvastatin is in agreement with Werida et al. [14], who reported a markedly higher rise in adiponectin levels with rosuvastatin than with atorvastatin. Chruściel et al. [16], in a comprehensive meta-analysis of randomized controlled trials, demonstrated that statin therapy significantly increases adiponectin concentrations, particularly with longer treatment duration and greater statin potency. Anagnostis et al. [78] [15] also observed that rosuvastatin improved insulin sensitivity despite modest short-term adipokine changes, suggesting a broader metabolic advantage. These findings collectively support the enhanced adiponectin-stimulating effect of rosuvastatin demonstrated in the present study.

With respect to leptin, both atorvastatin and rosuvastatin significantly reduced circulating leptin levels after six months of therapy, reflecting improvement in adipokine dysregulation and attenuation of pro-inflammatory signaling. However, the reduction in leptin was significantly greater in the rosuvastatin group, despite higher baseline leptin levels in this cohort. Elevated leptin levels are associated with leptin resistance, chronic inflammation, endothelial dysfunction, and increased cardiovascular risk. The greater leptin reduction observed with rosuvastatin aligns with the findings of Werida et al. [14], who reported a more pronounced decline in leptin levels with rosuvastatin compared to atorvastatin. Chruściel et al. [16] further demonstrated that statins exert pleiotropic metabolic effects by increasing adiponectin while simultaneously reducing pro-inflammatory adipokines such as leptin. These observations suggest that rosuvastatin more effectively improves adipokine balance, thereby contributing to reduced inflammatory burden.

Analysis of mean changes in biomarkers further reinforced these findings. In the present study, rosuvastatin produced significantly greater reductions in hs-CRP and leptin compared to atorvastatin, while the increase in adiponectin, although numerically higher, did not reach statistical significance. This pattern is consistent with previous comparative studies indicating that rosuvastatin exerts stronger effects on pro-inflammatory markers, whereas both statins similarly enhance protective adipokines [14,15,16].

Importantly, multivariate regression analysis demonstrated that statin type remained an independent predictor of changes in hs-CRP and leptin after adjustment for age, sex, and body mass index. This finding indicates that the observed differences are attributable to intrinsic pharmacological properties rather than demographic or anthropometric confounders. Similar conclusions were reported by Anagnostis et al. [15] and supported by meta-analytic data from Chruściel et al. [16], emphasizing the role of statin potency and molecular characteristics in mediating pleiotropic effects.

From a mechanistic perspective, rosuvastatin's superior efficacy may be related to its higher affinity for HMG-CoA reductase, greater hepatoselectivity, hydrophilic nature, and longer plasma half-life, which collectively enhance endothelial function, reduce oxidative stress, and modulate adipocyte-derived cytokine secretion. These properties likely underlie the greater reductions in hs-CRP and leptin and the enhanced adiponectin response observed in the present study.

In conclusion, the present study demonstrates that while both atorvastatin and rosuvastatin significantly improve inflammatory and adipokine profiles in patients with type 2 diabetes mellitus and dyslipidemia, rosuvastatin exerts superior pleiotropic effects, characterized by greater reductions in hs-CRP and leptin and a more pronounced increase in adiponectin. These findings, consistent with existing literature [14,15,16], support the preferential use of rosuvastatin in patients with heightened inflammatory and cardiometabolic risk.

CONCLUSION

In conclusion, the present study demonstrates that both atorvastatin and rosuvastatin significantly improve inflammatory status and adipokine profiles in patients with type 2 diabetes mellitus and dyslipidemia, as evidenced by marked reductions in hs-CRP and leptin levels and significant increases in adiponectin over six months of therapy. However, rosuvastatin consistently exhibited superior pleiotropic effects, producing greater reductions in hs-CRP and leptin and a more pronounced increase in adiponectin, even after adjustment for age, sex, and body mass index. These findings highlight rosuvastatin's stronger anti-inflammatory and adipokine-modulating properties, which may offer additional cardiometabolic benefit in patients with heightened inflammatory burden. While both statins remain effective and well

tolerated, rosuvastatin may be preferred in individuals with type 2 diabetes mellitus and dyslipidemia where targeting inflammation and adipose tissue dysfunction is of particular clinical importance, although longer-term studies are needed to confirm whether these biochemical advantages translate into improved cardiovascular outcomes.

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