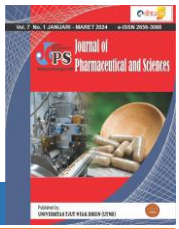
Journal of Pharmaceutical and Sciences
Electronic ISSN: 2656-3088 DOI: https://doi.org/10.36490/journal-jps.com
Homepage: https://journal-jps.com
ORIGINAL ARTICLE JPS. 2026, 9(3), 2184-2193



Effect of Atorvastatin Therapy on Blood Glucose Levels in Hospitalized Patients with Ischemic Stroke and Diabetes Mellitus

Pengaruh Terapi Atorvastatin terhadap Kadar Glukosa Darah pada Pasien Stroke Iskemik dengan Diabetes Melitus yang Dirawat di Rumah Sakit

Dwi Evi Diyan Sari [a]*, Erni Anika Sari [a], Faizatul Fitria [b], Hariyani [a], Krisogonus Ephriono Seran [a], Shofiatul Fajriyah [a], Yogi Bhakti Marhenta [a], Alissya Okta Nanda Agustina [c]

[a] Department of Clinical and Community Pharmacy, Faculty of Pharmacy, Institut Ilmu Kesehatan Bhakti Wiyata, Kediri, East Java, Indonesia.
[b] D3 Midwifery Study Program, Faculty of Health, Institut Ilmu Kesehatan Bhakti Wiyata, Kediri, East Java, Indonesia.
[c] Undergraduate Student, Faculty of Pharmacy, Institut Ilmu Kesehatan Bhakti Wiyata, Kediri, East Java, Indonesia.

*Corresponding Authors: dwi.evi@iik.ac.id

Abstract

Background: The use of atorvastatin in patients with stroke as a primary preventive therapy may be associated with an increased risk of elevated blood glucose levels. This study aimed to evaluate the effect of atorvastatin on changes in blood glucose levels in patients with ischemic stroke. **Methods:** An analytical observational study with a retrospective design was conducted among 28 hospitalized patients with ischemic stroke at Bhayangkara Hospital, Kediri City, from March to April 2024. Inclusion criteria comprised patients aged >15 years, with a history of diabetes mellitus, receiving atorvastatin therapy, and having available blood glucose data before and three days after treatment initiation. Data were analyzed using the Shapiro–Wilk test to assess normality and the paired sample t-test to evaluate changes in blood glucose levels. **Results:** A total of 64,29% of patients experienced an increase in blood glucose levels; however, statistical analysis demonstrated no significant difference between blood glucose levels before and after atorvastatin administration (231.64 ± 99.039 vs 231.50 ± 61.425 mg/dL; Δ = −0.14 mg/dL; p= 0.993). **Conclusion:** Atorvastatin therapy was not associated with statistically significant changes in random blood glucose levels. However, the high proportion of patients with increased blood glucose warrants further prospective investigation.

Keywords: Atorvastatin; diabetes mellitus; adverse effects; blood glucose; ischemic stroke.

Abstrak

Latar belakang: Penggunaan atorvastatin pada pasien stroke sebagai pencegahan primer dapat berisiko meningkatkan glukosa darah. Penelitian ini bertujuan menilai pengaruh atorvastatin terhadap perubahan kadar gula darah pada pasien stroke iskemik. **Metode**:Penelitian observasional analitik dengan desain retrospektif dilakukan pada 28 pasien stroke iskemik rawat inap di RS Bhayangkara Kota Kediri periode Maret–April 2024. Kriteria inklusi meliputi pasien berusia >15 tahun, memiliki riwayat diabetes melitus, menerima atorvastatin, serta memiliki data kadar gula darah sebelum dan 3 hari setelah terapi. Data dianalisis menggunakan uji *Shapiro–Wilk* untuk menilai normalitas dan uji *paired sample t-test* untuk menilai perubahan gula darah. **Hasil:** Sebanyak 64,29% pasien mengalami peningkatan gula darah, tetapi analisis statistik menunjukkan tidak terdapat perbedaan signifikan antara kadar gula darah sebelum dan sesudah pemberian atorvastatin (231,64 ± 99,039 vs 231,50 ± 61,425 mg/dL; Δ = –0,14 mg/dL; p = 0,993). **Kesimpulan:** Terapi atorvastatin tidak menunjukkan hubungan yang bermakna secara statistik terhadap perubahan kadar glukosa darah acak. Meskipun demikian, tingginya proporsi pasien yang mengalami peningkatan kadar glukosa darah mengindikasikan perlunya penelitian prospektif dengan jumlah sampel yang lebih besar untuk mengonfirmasi temuan ini.

Kata kunci: Atorvastatin, diabetes melitus, efek samping, gula darah, stroke iskemik.

Article History:
Received: 11/03/2026,
Revised: 16/07/2026
Accepted: 16/07/2026,
Available Online: 22/07/2026.

QR access this Article

https://doi.org/10.36490/journal-jps.com.v9i3.1481

Introduction

Ischemic stroke is a medical emergency characterized by the sudden onset of neurological deficits resulting from reduced cerebral blood flow, leading to brain tissue damage or infarction [1]. This condition represents serius global health problem and ranks as the second leading cause of death worldwide [2,3]. In 2021, ischemic stroke was reported to cause approximately 3.6 million deaths globally [4,5]. Its prevalence varies across regions, with a global age-standardized prevalence rate (ASPR) reported at 1,240.263 per 100,000 population in 2019, while lower rates reported in Europe [3]. These figures continue to increase, particularly in low- and middle-income countries, which account for approximately 87% of stroke-related deaths and 89% of global disability-adjusted life years (DALYs) [6]. In Indonesia, stroke contributes to 15.4% of all deaths among individuals aged over five years [7]. Beyond its clinical impact, stroke imposes a substantial economic burden, including direct medical costs, productivity loss, and long-term care needs [8,9]. These findings highlight the importance of secondary prevention and long-term management strategies to reduce recurrence rates and improve patient clinical outcomes.

Comprehensive management of ischemic stroke should begin with primary prevention focused on the control of modifiable cardiovascular risk factors, including dyslipidemia, hypertension, and diabetes mellitus [10]. Dyslipidemia plays a central role in the development of atherosclerosis, which contributes to increased risk of ischemic stroke [11]. Statins are recommended as first-line pharmacological agents to reduce atherosclerotic cardiovascular disease (ASCVD) events due to their proven efficacy, safety, and cost-effectiveness. By inhibiting β-hydroxy β-methylglutaryl–coenzyme A (HMG-CoA) reductase, statins reduce hepatic cholesterol synthesis, which subsequently increases the transcription of low-density lipoprotein receptor (LDLR) [12]. Among the various types of statins, atorvastatin is one of the most widely used due to its high effectiveness in reducing recurrent stroke events. The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial demonstrated that high-dose atorvastatin (80 mg/day) significantly reduced the risk of recurrent stroke in patients with a history of stroke or transient ischemic attack (TIA) [13,14]. Patients receiving atorvastatin have also been reported to achieve better final values of total cholesterol (TC), HDL, and triglycerides (TG) compared with those receiving simvastatin [15]. Despite its proven benefits, long-term statin therapy may be associated with potential adverse effects.

Commonly reported adverse effects include myopathy [16], elevated liver enzymes [17,18], and mild gastrointestinal complaints [19]. In recent years, attention has also been directed toward the metabolic effects of statins on glucose regulation. Several studies have reported that statin therapy, including atorvastatin, may increase the risk of new-onset diabetes mellitus (NODM) [20], increase diabetes risk [21], and affect insulin resistance and secretion [22]. The exact mechanisms underlying statin induced hyperglycemia remain unclear. Several hypotheses suggest mitochondrial dysfunction leading to reduced adenosine triphosphate (ATP) production and increased oxidative stress, which may affect glucose metabolism [16,23], inhibition of isoprenoid metabolite synthesis, which important for cellular function and may lead to insulin resistance [24,25], and the tissue inflammation and oxidative stress, which further contribute to insulin resistance [26].

The association between statin use and alterations in blood glucose levels remains controversial. Several studies report that statins have diabetogenic effects, potentially increasing the risk of type 2 diabetes mellitus. This effect is thought to be related to the potency and dosage of the statins used [27–30]. In individuals without a history of diabetes, fasting plasma glucose (FPG) increase from 98 mg/dL to 105 mg/dL after statin therapy, whereas in patients with diabetes, the increase occurred from 102 mg/dL to 141 mg/dL [31]. Approximately 55.9% of statin users experienced diabetes progression compared with 48.0% in the comparator group, with an odds ratio of 1.37 (95% CI 1.35–1.40) [32]. A meta-analysis by Erqou et al. reported that statin users

Electronic ISSN : 2656-3088
Homepage: https://www.journal-jps.com

experienced an increase in Hemoglobin A1c (HbA1c) of 0.12% compared with the control groups [33]. Another study demonstrated that hypertensive patients receiving statins had higher HbA1c levels compared with non-users [34]. In addition, the intensity of statin therapy influences HbA1c levels, with moderate- and high-intensity therapy showing greater increases compared with low-intensity therapy [35]. Another study among patients with diabetes mellitus also reported that simvastatin use was significantly associated with increased blood glucose levels, with an odds ratio (OR) of 3.3 [36]. Most previous studies have been conducted in general populations or in non-stroke cardiovascular patients, while data regarding the impact of statins on blood glucose levels in ischemic stroke patients remain limited. In fact, patients with ischemic stroke generally require statin therapy as part of secondary prevention, and glycemic changes in this population may potentially affect clinical outcomes and recovery processes. Therefore, this study aimed to analyze the effect of atorvastatin on blood glucose levels in patients with ischemic stroke at Bhayangkara Hospital.

Method

Study Design

Data were obtained from the medical records of hospitalized patients with ischemic stroke at Bhayangkara Hospital, Kediri, Indonesia, between January and June 2024. A retrospective design was selected because the study aimed to evaluate changes in blood glucose levels using routinely collected clinical data from hospitalized patients without influencing treatment decisions or patient management.

Population and Sample

The study population consisted of all ischemic stroke patients hospitalized at Bhayangkara Hospital during the study period. A total of 305 patients with ischemic stroke were screened during the study period. Consecutive sampling was applied, and all patients who fulfilled the predefined inclusion and exclusion criteria were included. Of the 305 patients screened, 28 met the eligibility criteria and were included in the final analysis.

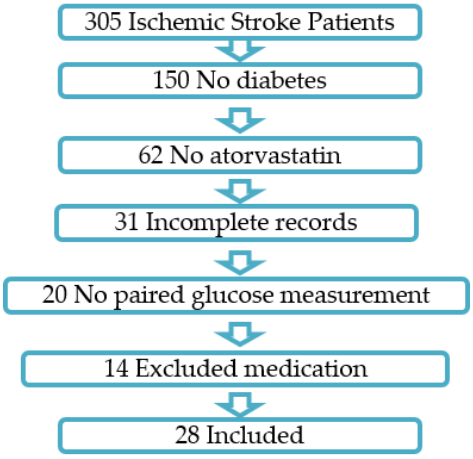


Figure 1. Flowchart of patient selection

This study was approved by the Health Research Ethics Committee of, Institut Ilmu Kesehatan Bhakti Wiyata (Approval No. 943/F/EP/II/2025). Because of the retrospective design and the use of anonymized medical records, the requirement for informed consent was waived by the Ethics Committee.

Inclusion and Exclusion Criteria

The inclusion criteria consisted of ischemic stroke patients aged >15 years, with or without complications, with a documented history of diabetes mellitus, who received statin therapy, and had available random blood glucose measurements before and three days after treatment initiation. Patients who died during hospitalization were also included, provided that at least two blood glucose measurements were available. Exclusion criteria were patients with incomplete medical records, unavailable paired blood glucose measurements, and patients receiving concomitant medications known to affect blood glucose levels, such as systemic corticosteroids, thiazide diuretics, atypical antipsychotics [21,37].

Electronic ISSN : 2656-3088
Homepage: https://www.journal-jps.com

Study Variables

The independent variable in this study was atorvastatin therapy in patients with ischemic stroke and diabetes mellitus. The dependent variable was the change in random blood glucose levels during hospitalization. The change in blood glucose level was defined as the difference between the random blood glucose level (mg/dL) measured before atorvastatin therapy and the random blood glucose level (mg/dL) measured after atorvastatin therapy during hospitalization. Blood glucose levels were expressed in mg/dL and analyzed as a continuous variable.

Data Collection

Data were collected from patients' medical records using a secondary data extraction form. The extracted variables included patient characteristics, atorvastatin dose, comorbidities, medical history, blood pressure, antidiabetic therapy, and blood glucose measurements before and three days after atorvastatin administration. The primary outcome was the change in random blood glucose levels before and three days after initiation of atorvastatin therapy. Atorvastatin doses were categorized as moderate-intensity (10–20 mg/day) or high-intensity (40 mg/day).

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version XXI. Data normality was assessed using the Shapiro–Wilk test. As the data were normally distributed, comparisons of random blood glucose levels before and after atorvastatin therapy were conducted using a paired-sample t-test. To adjust for potential confounding effects of baseline random blood glucose and antidiabetic therapy category, analysis of covariance (ANCOVA) was performed. A p-value < 0.05 was considered statistically significant.

Results and Discussion

Patient characteristics

Table 1. Baseline characteristics of ischemic stroke patients receiving atorvastatin

Variables	n	%
Sex		
Male	16	57.14
Female	12	42.86
		Mean ± SD
Age (years)		58.04 ± 9.197
Systolic blood pressure (mmHg)		151.75 ± 21.041
Diastolic blood pressure (mmHg)		86.68 ± 9.911
HbA1c (%) n=15		9.5±2.123

Among the 28 patients included in the study, most were male (57.14%). Previous studies have shown that women are less likely than men to be prescribed statins following ischemic stroke. For example, one study reported that 58.0% of women received statin therapy compared with 71.8% of men [38]. A study conducted in South Korea similarly demonstrated a predominance of male patients [39]. Multiple studies have consistently reported that women are generally less likely than men to receive statins prescribed across various clinical conditions, including cardiovascular disease and diabetes mellitus [40–45]. Moreover, women are less likely to receive high-intensity statin therapy and are more prone to discontinuing statin treatment because of perceived adverse effects or statin intolerance [41,43,46]. All patients included in this study had a documented history of diabetes mellitus according to the inclusion criteria. The mean systolic and diastolic blood pressures were 151.75 ± 21.04 mmHg and 86.68 ± 9.91 mmHg, respectively (Table 1), indicating that many patients presented with elevated blood pressure during hospitalization. Diabetes mellitus and hypertension are well-established risk factors for ischemic stroke and are associated with poorer neurological outcomes, increased disability, and delayed functional recovery, as reported in previous studies [39,47–50]. These metabolic conditions may also contribute to the variability in glycemic responses observed during statin therapy.

Regarding antidiabetic treatment (Table 2), insulin monotherapy was the most frequently used regimen (32%), followed by oral monotherapy (25%), oral–insulin combination therapy (25%), and oral combination therapy (18%). This pattern is consistent with current clinical practice in the acute management of ischemic stroke, where insulin is often preferred during hospitalization to achieve rapid glycemic control in patients

Electronic ISSN : 2656-3088
Homepage: https://www.journal-jps.com

with unstable metabolic status. Insulin therapy is frequently administered to hospitalized patients with acute ischemic stroke because it provides rapid glycemic control and possesses anti-inflammatory and neuroprotective properties that may attenuate ischemic brain injury [51]. In contrast, oral antidiabetic agents are typically prescribed for patients with more stable clinical conditions. The predominance of insulin therapy observed in the present study therefore likely reflects the acute clinical condition of the study population rather than differences in long-term diabetes management.

Antidiabetic Therapy

Table 2. Characteristics of therapy

Variables	**n**	**%**
Atorvastatin dose category		
Moderate-intensity statin	26	92.86
High-intensity statin	2	7.14
Antidiabetic therapy	**n**	**%**
Oral monotherapy	7	25
Insulin monotherapy	9	32
Oral-insulin combination	7	25
Oral combination	5	18

Changes in Blood Glucose Levels After Atorvastatin Therapy

Table 3. Summary of Adverse Events Related to Blood Glucose Changes

Category	**n**	**%**
Increased blood glucose	18	64.29
No increase in blood glucose	10	35.71
Total	28	100

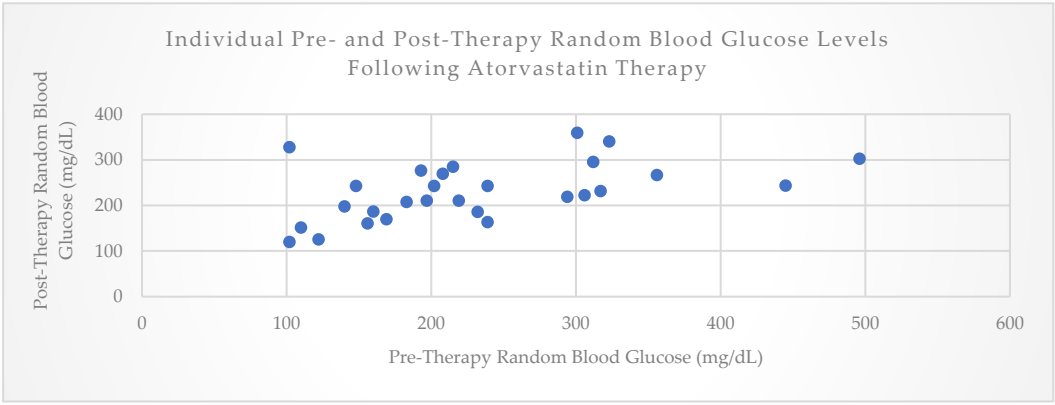


Figure 2. Individual Changes in Random Blood Glucose

Despite the absence of a statistically significant difference in mean blood glucose levels, approximately 64% of patients showed an increase in random blood glucose after atorvastatin therapy. This finding suggests that the potential for statin-associated hyperglycemia remains clinically relevant in populations with comorbid conditions, particularly diabetes mellitus and hypertension, which predominated in the study sample. From a physiological perspective, statins have been reported to influence glucose metabolism through multiple mechanisms, including effects on insulin secretion, adipokine regulation, the gut microbiota, oxidative stress, and gene expression [30,52–57]. These effects may vary depending on the type of statin used and individual patient characteristics. Therefore, the relatively high proportion of patients exhibiting increased blood glucose levels in this study may be influenced by a combination of the pharmacological effects of atorvastatin and pre-existing metabolic vulnerability to dysglycemia. In addition, variability in statin dose [35,58–61], duration of therapy [31], and statin type [28,62–64] may further contribute to interindividual differences in glycemic responses.

Electronic ISSN : 2656-3088
Homepage: https://www.journal-jps.com

Statistical Analysis of Blood Glucose Changes

Table 4. Paired-Sample t-Test Results for Blood Glucose Levels Before and After Atorvastatin Therapy

Blood glucose before (Mean ± SD)	Blood glucose after (Mean ± SD)	Δ Blood glucose (mg/dL)	P-value
231.64 ± 99.039	231.50 ± 61.425	-0.14	0.993

In this study, an increase in blood glucose levels was defined as a rise in random plasma glucose values after atorvastatin administration compared with pre-treatment levels, based on patients' medical records. This assessment was performed on an individual basis and, therefore was not necessarily reflected in changes in the population mean. Although most patients clinically (64,29%) experienced an increase in blood glucose levels following atorvastatin therapy, statistical analysis using a paired-sample t-test demonstrated no statistically significant difference in mean blood glucose levels before and after atorvastatin administration (Δ = −0.14 mg/dL, p = 0.993). A p-value of 0.993 indicates that no statistically significant difference was detected in the mean random blood glucose levels before and after atorvastatin therapy. However, the absence of statistical significance should not be interpreted as evidence that atorvastatin has no effect on glucose metabolism. Rather, the observed result may reflect substantial interindividual variability in glycemic response together with the relatively small sample size, which limited the statistical power to detect modest changes. This apparent discrepancy reflects substantial inter-individual variability in glycemic response, as illustrated in Figure 2. Although most patients experienced increases in random blood glucose following atorvastatin therapy, several individuals exhibited marked reductions in glucose levels, thereby offsetting the increases observed in others. Consequently, these opposing responses produced an overall mean change that was close to zero (Δ = −0.14 mg/dL). Such compensatory effects are commonly observed in heterogeneous clinical populations and may arise from differences in baseline glycemic status, adherence to antidiabetic therapy, dietary intake, concomitant medications, and individual metabolic susceptibility. This finding may be explained by substantial interindividual variability, as reflected by the wide standard deviation of baseline blood glucose levels (± 99 mg/dL). Such variability indicates marked metabolic heterogeneity and the presence of potential confounding factors, particularly the imbalance in atorvastatin dosing within the sample. The majority of patients (92.86%) received moderate-intensity statin therapy, whereas only 7.14% received high-intensity statin therapy; consequently, glycemic effects reported to be more pronounced at higher doses may not have been statistically detectable.

The absence of statistically significant changes in random blood glucose levels in this study is consistent with several previous studies that have distributed atorvastatin therapy in patients with cardiovascular disease or diabetes mellitus. Al-Bayyari et al. reported that atorvastatin can improve fasting blood glucose and HbA1c in both diabetic and non-diabetic patients, but the difference was not statistically significant ($p > 0.05$) [65]. Another study also showed that atorvastatin at a dose of 20 mg/day does not induce significant changes in fasting blood glucose (FBG) or hemoglobin A1c (HbA1c) levels in patients with ischemic stroke, whereas atorvastatin at 40 mg/day is associated with significant increases in both FBG and HbA1c [66]. Other studies have also reported that atorvastatin use is associated with an increased risk of new-onset diabetes mellitus, particularly at higher doses [67]. Meanwhile, another study reported that higher adherence and intensity of statin use were significantly associated with increased fasting glucose in non-diabetic individuals [28]. Another study found that atorvastatin use caused significant increases in insulin and Hba1C levels. These findings indicate a tendency toward insulin resistance and increased glycemia in patients with hypercholesterolemia [68].

Table 5. ANCOVA results for the effect of atorvastatin intensity on changes in random blood glucose levels

Source of variation	df	F	P-value
Atorvastatin intensity	1	0,296	0,591
Baseline random blood glucose	1	41,880	0,00
Antidiabetic therapy category	1	1,096	0,306

Analysis of covariance (ANCOVA) demonstrated that, after adjustment for baseline random blood glucose and antidiabetic therapy category, atorvastatin intensity was not significantly associated with changes in random blood glucose levels ($F = 0.296$, $p = 0.591$). In contrast, baseline random blood glucose was identified as a significant covariate influencing changes in random blood glucose levels ($F = 41.880$, $p < 0.001$), whereas the category of antidiabetic therapy was not significantly associated with glycemic changes ($F = 1.096$, $p =$

Electronic ISSN : 2656-3088
Homepage: https://www.journal-jps.com

0.306). These findings suggest that patients' baseline glycemic status had a greater influence on changes in blood glucose levels during hospitalization than atorvastatin intensity itself. Patients presenting with higher baseline blood glucose levels were more likely to experience greater glycemic variability during the acute phase of ischemic stroke, which may be attributable to physiological stress responses, inflammatory activation, and pre-existing metabolic disturbances. This interpretation is consistent with previous evidence highlighting the critical role of glycemic variability in acute ischemic stroke. Early glycemic variability has been associated with early neurological deterioration in patients with diabetes mellitus and acute ischemic stroke [69] and has also been identified as an independent predictor of mortality in patients with severe acute stroke [70]. Furthermore, another study demonstrated that high glycemic variability during the first 48 hours after stroke was independently associated with increased mortality, potentially through exacerbation of the inflammatory response characterized by elevated interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) levels [71,72]. In addition, admission hyperglycemia has been recognized as an independent predictor of poor clinical outcomes in patients with acute ischemic stroke [73]. Collectively, these findings support the importance of considering baseline glycemic status when interpreting changes in blood glucose levels during atorvastatin therapy.

Nevertheless, the absence of a significant association between atorvastatin intensity and changes in blood glucose levels in the present study should be interpreted with caution, as only two patients received high-intensity atorvastatin therapy. This marked imbalance in treatment groups may have reduced the statistical power to detect dose-related differences in glycemic response. Consequently, the findings of this study primarily reflect the short-term glycemic effects of moderate-intensity atorvastatin therapy rather than those of high-intensity treatment. Therefore, larger prospective studies with a more balanced distribution of atorvastatin intensity are warranted to further clarify the relationship between atorvastatin intensity and changes in blood glucose levels.

Conclusions

Atorvastatin therapy was not associated with a statistically significant changes in random blood glucose levels in this study. However, the relatively high proportion of patients who experienced increased blood glucose levels warrants further investigation in larger prospective studies.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Acknowledgment

The authors express their sincere gratitude to all individuals and institutions that provided support for the conduct of this study.

References

[1] Prabhakaran S, Gonzalez NR, Zachrison KS, Adeoye O, Alexandrov AW, Ansari SA, et al. 2026 Guideline for the Early Management of Patients With Acute Ischemic Stroke: A Guideline From the American Heart Association/American Stroke Association. Stroke 2026. https://doi.org/10.1161/STR.0000000000000513.

[2] Coculescu BI, Stocheci CM, Ripszky Totan A, Coculescu EC. A statistical analysis of acute ischemic stroke before and during the COVID-19 pandemic. Rom J Med Pract 2022;17:41–6. https://doi.org/10.37897/RJMP.2022.1.7.

[3] Zhang L, Lu H, Yang C. Global, regional, and national burden of stroke from 1990 to 2019: A temporal trend analysis based on the Global Burden of Disease Study 2019. Int J Stroke 2024;19:686–94. https://doi.org/10.1177/17474930241246955.

[4] Hou S, Zhang Y, Xia Y, Liu Y, Deng X, Wang W, et al. Global, regional, and national epidemiology of ischemic stroke from 1990 to 2021. Eur J Neurol 2024;31. https://doi.org/10.1111/ene.16481.

[5] Li X yu, Kong X meng, Yang C hao, Cheng Z feng, Lv J jie, Guo H, et al. Global, regional, and national burden of ischemic stroke, 1990–2021: an analysis of data from the global burden of disease study 2021. EClinicalMedicine 2024;75:102758. https://doi.org/10.1016/j.eclinm.2024.102758.

[6] Feigin VL, Brainin M, Norrving B, Martins SO, Pandian J, Lindsay P, et al. World Stroke Organization: Global

Electronic ISSN : 2656-3088
Homepage: https://www.journal-jps.com

Stroke Fact Sheet 2025. Int J Stroke 2025;20:132–44. https://doi.org/10.1177/17474930241308142.
[7] Kusuma Y, Venketasubramanian N, Kiemas LS, Misbach J. Burden of Stroke in Indonesia. Int J Stroke 2009;4:379–80. https://doi.org/10.1111/J.1747-4949.2009.00326.X.
[8] Volpi JJ, Kasner SE, Neervoort J, Wolters LF, Louwsma T, Marti AK, et al. The annual economic burden of patent foramen ovale-associated stroke in the United States. J Stroke Cerebrovasc Dis 2025;34:108319. https://doi.org/10.1016/J.Jstrokecerebrovasdis.2025.108319.
[9] Wang J, Chen M, Yang J. Impact of DRG Reform Policies on Hospitalization Costs of Stroke Patients in Western China: Wisdom from Traditional Chinese Medicine. Risk Manag Healthc Policy 2025;18:2401–11. https://doi.org/10.2147/RMHP.S525667.
[10] Ministry of Health of the Republic of Indonesia. Keputusan Menteri Kesehatan Republik Indonesia Nomor HK.01.07/MENKES/394/2019 Tentang Pedoman Nasional Pelayanan Kedokteran Tata Laksana Stroke. 2019.
[11] Ciplak S, Adiguzel A, Deniz YZ, Aba M, Ozturk U. The Role of the Low-Density Lipoprotein/High-Density Lipoprotein Cholesterol Ratio as an Atherogenic Risk Factor in Young Adults with Ischemic Stroke: A Case—Control Study. Brain Sci 2023, Vol 13, Page 1180 2023;13:1180. https://doi.org/10.3390/BRAINSCI13081180.
[12] McPherson R, Adreak N, Sharma A. Medications for Lipid Control: Statins vs Newer Drugs. Can J Cardiol 2024;40:S26–34. https://doi.org/10.1016/j.cjca.2024.05.004.
[13] Welch KM. Review of the SPARCL trial and its subanalyses. Curr Atheroscler Rep 2009;11:315–21. https://doi.org/10.1007/s11883-009-0048-0.
[14] Sanossian N, Ovbiagele B. Drug Insight: translating evidence on statin therapy into clinical benefits. Nat Clin Pract Neurol 2008;4:43–9. https://doi.org/10.1038/ncpneuro0705.
[15] Latif WD, Aswad M, Bahar MA. Perbandingan Efektivitas Klinik Simvastatin dan Atorvastatin Terhadap Profil Lipid Darah: Studi Kasus di Rumah Sakit Universitas Hasanuddin. J Sains Farm Klin 2022;9:34. https://doi.org/10.25077/jsfk.9.1.34-41.2022.
[16] Zakyrjanova GF, Matigorova VA, Kuznetsova EA, Dmitrieva SA, Tyapkina O V., Tsentsevitsky AN, et al. Key genes and processes affected by atorvastatin treatment in mouse diaphragm muscle. Arch Toxicol 2025;99:2877–901. https://doi.org/10.1007/s00204-025-04056-6.
[17] Sreenivasan A, KS L, Vijayan M, G Pai P. Atorvastatin induced liver injury: A Case Series. Res J Pharm Technol 2022:3507–10. https://doi.org/10.52711/0974-360X.2022.00588.
[18] A Shoiab A, Gardouh A, Khwaldeh A, Alsarhan A. The Comparison Between the Effect of Atorvastatin and Nanoparticle Atorvastatin on Rat Liver. Biomed Pharmacol J 2023;16:237–41. https://doi.org/10.13005/bpj/2605.
[19] Soliemanabad SK, Rasouli K, Zakariaei Z, Soleymani M, Aliabadi PK. Rhabdomyolysis due to warfarin and atorvastatin combination therapy in a patient with ischemic heart disease: (A drug interaction). Ann Med Surg 2022;75. https://doi.org/10.1016/j.amsu.2022.103384.
[20] Putra MAP, Muhamad GS, Hendarti HF, Bhaskoro MFA, Kalaij GI. Risiko Diabetes Onset Baru pada Pemberian Terapi Statin: Kajian Literatur Populasi Asia. J Kesehat Tambusai 2023;4:4229–35. https://doi.org/https://doi.org/10.31004/jkt.v4i3.18719.
[21] Widiarti W, Saputra PBT, Savitri CG, Putranto JNE, Alkaff FF. The impact of cardiovascular drugs on hyperglycemia and diabetes: a review of 'unspoken'' side effects.' Hell J Cardiol 2025;83:71–7. https://doi.org/10.1016/j.hjc.2024.09.007.
[22] Abbasi F, Lamendola C, Harris CS, Harris V, Tsai M-S, Tripathi P, et al. Statins Are Associated With Increased Insulin Resistance and Secretion. Arterioscler Thromb Vasc Biol 2021;41:2786–97. https://doi.org/10.1161/ATVBAHA.121.316159.
[23] Sirvent P, Fabre O, Bordenave S, Hillaire-Buys D, Raynaud De Mauverger E, Lacampagne A, et al. Muscle mitochondrial metabolism and calcium signaling impairment in patients treated with statins. Toxicol Appl Pharmacol 2012;259:263–8. https://doi.org/10.1016/j.taap.2012.01.008.
[24] Han KH. Functional Implications of HMG-CoA Reductase Inhibition on Glucose Metabolism. Korean Circ J 2018;48:951. https://doi.org/10.4070/kcj.2018.0307.
[25] Wang L, Zheng Z, Zhu L, Meng L, Liu H, Wang K, et al. Geranylgeranyl pyrophosphate depletion by statins compromises skeletal muscle insulin sensitivity. J Cachexia Sarcopenia Muscle 2022;13:2697–711. https://doi.org/10.1002/jcsm.13061.
[26] Kamisah Y, Nordin AH, Harafinova H-S, Nordin ML, Nurhidayah M, Muhammad NA, et al. Statin-associated new-onset diabetes mellitus and insulin resistance: a 30-year bibliometric study (1992-2022). Biomed Res Ther 2023;10:6035–48. https://doi.org/10.15419/bmrat.v10i11.845.
[27] Cybulska B, Kłosiewicz-Latoszek L. How do we know that statins are diabetogenic, and why? Is it an important issue in the clinical practice? Kardiol Pol 2018;76:1217–23. https://doi.org/10.5603/KP.a2018.0150.
[28] Kim J, Lee HS, Lee K-Y. Effect of statins on fasting glucose in non-diabetic individuals: nationwide population-based health examination in Korea. Cardiovasc Diabetol 2018;17:155. https://doi.org/10.1186/s12933-018-0799-4.
[29] Maki KC, Ridker PM, Brown WV, Grundy SM, Sattar N. An assessment by the Statin Diabetes Safety Task Force: 2014 update. J Clin Lipidol 2014;8:S17–29. https://doi.org/10.1016/j.jacl.2014.02.012.
[30] Liu Y, Shen Y, Guo T, Parnell LD, Westerman KE, Smith CE, et al. Statin Use Associates With Risk of Type 2 Diabetes via Epigenetic Patterns at ABCG1. Front Genet 2020;11. https://doi.org/10.3389/fgene.2020.00622.

Electronic ISSN : 2656-3088
Homepage: https://www.journal-jps.com

[31] Sukhija R, Prayaga S, Marashdeh M, Bursac Z, Kakar P, Bansal D, et al. Effect of Statins on Fasting Plasma Glucose in Diabetic and Nondiabetic Patients. J Investig Med 2009;57:495–9. https://doi.org/10.2310/JIM.0b013e318197ec8b.
[32] Mansi IA, Chansard M, Lingvay I, Zhang S, Halm EA, Alvarez CA. Association of Statin Therapy Initiation With Diabetes Progression. JAMA Intern Med 2021;181:1562. https://doi.org/10.1001/jamainternmed.2021.5714.
[33] Erqou S, Lee CC, Adler AI. Statins and glycaemic control in individuals with diabetes: a systematic review and meta-analysis. Diabetologia 2014;57:2444–52. https://doi.org/10.1007/s00125-014-3374-x.
[34] Liew SM, Lee PY, Hanafi NS, Ng CJ, Wong SSL, Chia YC, et al. Statins use is associated with poorer glycaemic control in a cohort of hypertensive patients with diabetes and without diabetes. Diabetol Metab Syndr 2014;6:53. https://doi.org/10.1186/1758-5996-6-53.
[35] Davis TME, Badshah I, Chubb SAP, Davis WA. Dose–response relationship between statin therapy and glycaemia in community-based patients with type 2 diabetes: the <scp>F</scp> remantle <scp>D</scp> iabetes <scp>S</scp> tudy. Diabetes, Obes Metab 2016;18:1143–6. https://doi.org/10.1111/dom.12710.
[36] Wandira E, Simamora S, Rulianti MR. Hubungan Penggunaan Obat Simvastatin Dengan Kadar Gula Darah Penderita Diabetes Mellitus Di Rs B hayangkara Palembang. Sel J Penelit Kesehat 2021;8:1–14. https://doi.org/10.22435/sel.v8i1.4705.
[37] Heurtebize M-A, Faillie J-L. Drug-induced hyperglycemia and diabetes. Therapies 2024;79:221–38. https://doi.org/10.1016/j.therap.2023.09.010.
[38] Mansoor H, Manion D, Kucharska-Newton A, Delcher C, Lo-Ciganic W-H, Jicha GA, et al. Sex Differences in Prescription Patterns and Medication Adherence to Guideline-Directed Medical Therapy Among Patients With Ischemic Stroke. Stroke 2025;56:318–25. https://doi.org/10.1161/Strokeaha.124.048058.
[39] Kim JT, Lee JS, Kim H, Kim BJ, Kang J, Lee KJ, et al. Comparative Effectiveness of Rosuvastatin Versus Atorvastatin in Acute Ischemic Stroke Treatment. J Am Hear Assoc 2025;14:38080. https://doi.org/10.1161/JAHA.124.038080..
[40] Zhang H, Plutzky J, Shubina M, Turchin A. Drivers of the Sex Disparity in Statin Therapy in Patients with Coronary Artery Disease: A Cohort Study. PLoS One 2016;11:e0155228. https://doi.org/10.1371/journal.pone.0155228.
[41] Witting C, Azizi Z, Gomez SE, Zammit A, Sarraju A, Ngo S, et al. Natural language processing to identify reasons for sex disparity in statin prescriptions. Am J Prev Cardiol 2023;14:100496. https://doi.org/10.1016/j.ajpc.2023.100496.
[42] Kiss PAJ, Uijl A, de Boer AR, Duk TCX, Grobbee DE, Hollander M, et al. Sex differences in the intensity of statin prescriptions at initiation in a primary care setting. Heart 2024;110:981–7. https://doi.org/10.1136/heartjnl-2023-323722.
[43] Nanna MG, Wang TY, Xiang Q, Goldberg AC, Robinson JG, Roger VL, et al. Sex Differences in the Use of Statins in Community Practice. Circ Cardiovasc Qual Outcomes 2019;12. https://doi.org/10.1161/Circoutcomes.118.005562.
[44] Gamboa CM, Colantonio LD, Brown TM, Carson AP, Safford MM. Race-Sex Differences in Statin Use and Low-Density Lipoprotein Cholesterol Control Among People With Diabetes Mellitus in the Reasons for Geographic and Racial Differences in Stroke Study. J Am Heart Assoc 2017;6. https://doi.org/10.1161/Jaha.116.004264.
[45] Virani SS, Woodard LD, Ramsey DJ, Urech TH, Akeroyd JM, Shah T, et al. Gender Disparities in Evidence-Based Statin Therapy in Patients With Cardiovascular Disease. Am J Cardiol 2015;115:21–6. https://doi.org/10.1016/j.amjcard.2014.09.041.
[46] Muck MA, Baessler A. Schlagen Frauenherzen anders? – Geschlechterunterschiede im Lipidmanagement. J Für Endokrinol Diabetol Und Stoffwechsel 2025;18:23–9. https://doi.org/10.1007/s41969-025-00263-9.
[47] Wu Y, Zheng H, Hu S, Chen X, Chen Y, Liu J, et al. The impact of metabolic diseases and their comorbidities for stroke in a middle-income area of China: a case-control study. Int J Neurosci 2023;133:1055–63. https://doi.org/10.1080/00207454.2022.2042692.
[48] Anwar MMU, Jahan SMS, Afrin S, Hossain MZ. Diabetic and Non-diabetic Subjects with Ischemic Stroke: Risk Factors, Stroke Topography and Hospital Outcome. J Med 2017;18:75–9. https://doi.org/10.3329/jom.v18i2.33684.
[49] Amory CF, Weinberger J. Cerebrovascular Disease. Textb. Diabetes, Wiley; 2017, p. 673–82. https://doi.org/10.1002/9781118924853.ch46.
[50] Qian Y, Chopp M, Chen J. Emerging role of microRNAs in ischemic stroke with comorbidities. Exp Neurol 2020;331:113382. https://doi.org/10.1016/j.expneurol.2020.113382.
[51] Paolino AS, Garner KM. Effects of Hyperglycemia on Neurologic Outcome in Stroke Patients. J Neurosci Nurs 2005;37:130–5. https://doi.org/10.1097/01376517-200506000-00002.
[52] Chan DC, Pang J, Watts GF. Pathogenesis and Management of the Diabetogenic Effect of Statins: a Role for Adiponectin and Coenzyme Q10? Curr Atheroscler Rep 2015;17:472. https://doi.org/10.1007/s11883-014-0472-7.
[53] Sunjaya A, Sunjaya A, Halim S, Ferdinal F. Risk and Benefits of Statins in Glucose Control Management of Type II Diabetes. Int J Angiol 2018;27:121–31. https://doi.org/10.1055/s-0036-1572523.
[54] Nakata M, Nagasaka S, Kusaka I, Matsuoka H, Ishibashi S, Yada T. Effects of statins on the adipocyte maturation and expression of glucose transporter 4 (SLC2A4): implications in glycaemic control. Diabetologia 2006;49:1881–92. https://doi.org/10.1007/s00125-006-0269-5.
[55] S. Kostapanos M, L. Liamis G, J. Milionis H, S. Elisaf M. Do Statins Beneficially or Adversely Affect Glucose Homeostasis? Curr Vasc Pharmacol 2010;8:612–31. https://doi.org/10.2174/157016110792006879.
[56] She J, Tuerhongjiang G, Guo M, Liu J, Hao X, Guo L, et al. Statins aggravate insulin resistance through reduced

Electronic ISSN : 2656-3088
Homepage: https://www.journal-jps.com

blood glucagon-like peptide-1 levels in a microbiota-dependent manner. Cell Metab 2024;36:408-421.e5. https://doi.org/10.1016/j.cmet.2023.12.027.

[57] Huptas S, Geiss H-C, Otto C, Parhofer KG. Effect of Atorvastatin (10 mg/day) on Glucose Metabolism in Patients With the Metabolic Syndrome. Am J Cardiol 2006;98:66–9. https://doi.org/10.1016/j.amjcard.2006.01.055.

[58] Bell DSH, DiNicolantonio JJ, O'Keefe JH. Is statin-induced diabetes clinically relevant? A comprehensive review of the literature. Diabetes, Obes Metab 2014;16:689–94. https://doi.org/10.1111/dom.12254.

[59] Bang CN, Okin PM. Statin Treatment, New-Onset Diabetes, and Other Adverse Effects: A Systematic Review. Curr Cardiol Rep 2014;16:461. https://doi.org/10.1007/s11886-013-0461-4.

[60] Rocco MB. Statins and diabetes risk: Fact, fiction, and clinical implications. Cleve Clin J Med 2012;79:883–93. https://doi.org/10.3949/ccjm.79a.12091.

[61] Thomson S, Chogtu B, Shetty R, Devasia T. Analysis of glycemic status in diabetes-naïve patients on statins: A hospital-based cross-sectional study. Indian J Pharmacol 2018;50:320. https://doi.org/10.4103/ijp.IJP_132_18.

[62] Rius Tarruella J, Millán Núñez-Cortés J, Pedro-Botet J, Pintó Sala X. La diabetogenicidad de las estatinas: ¿son todas iguales? Estado de la cuestión. Clínica e Investig En Arterioscler 2015;27:148–58. https://doi.org/10.1016/j.arteri.2015.02.001.

[63] Abboud N, Makhous R. The effect of some statins on Glucose blood levels in experimental animals. Res J Pharm Technol 2022:2661–6. https://doi.org/10.52711/0974-360X.2022.00445.

[64] Arnaboldi L, Corsini A. Could changes in adiponectin drive the effect of statins on the risk of new-onset diabetes? The case of pitavastatin. Atheroscler Suppl 2015;16:1–27. https://doi.org/10.1016/S1567-5688(14)70002-9.

[65] Al-Bayyari N, Saadeh N, Hailat R, Al-Zeidaneen S. Assessment of Atorvastatin Effect on Body Weight and Blood Glucose Levels Among Diabetic and Non-Diabetic Patients. Rom J Diabetes Nutr Metab Dis 2017;24:255–62. https://doi.org/10.1515/rjdnmd-2017-0031.

[66] Deng Y, Zou W, Chen G, Shangguan S, Zhou F, Jiang W, et al. Comparative studies on the effects of different doses of atorvastatin combined with aspirin on inflammatory cytokines and carotid plaques in patients with ischemic cerebrovascular disease. Int J Neurosci 2019;129:1133–8. https://doi.org/10.1080/00207454.2019.1635592.

[67] Nalini R, Ramya JE, Karthick R. Evaluation of glycemic status among hypercholesterolemic patients on atorvastatin in a tertiary care hospital – A retrospective study. Indian J Pharmacol 2022;54:165–70. https://doi.org/10.4103/ijp.ijp_943_20.

[68] Koh KK, Quon MJ, Han SH, Lee Y, Kim SJ, Shin EK. Atorvastatin Causes Insulin Resistance and Increases Ambient Glycemia in Hypercholesterolemic Patients. J Am Coll Cardiol 2010;55:1209–16. https://doi.org/10.1016/j.jacc.2009.10.053.

[69] Hui J, Zhang J, Mao X, Li Z, Li X, Wang F, et al. The initial glycemic variability is associated with early neurological deterioration in diabetic patients with acute ischemic stroke. Neurol Sci 2018;39:1571–7. https://doi.org/10.1007/s10072-018-3463-6.

[70] Cai Y, Wang C, Di W, Li W, Liu J, Zhou S. Correlation between blood glucose variability and the risk of death in patients with severe acute stroke. Rev Neurol (Paris) 2020;176:582–6. https://doi.org/10.1016/j.neurol.2019.12.003.

[71] Gutiérrez-Zúñiga R, Alonso de Leciñana M, Delgado-Mederos R, Gállego-Cullere J, Rodríguez-Yáñez M, Martínez-Zabaleta M, et al. Más allá de la hiperglucemia: la variabilidad glucémica como factor pronóstico en el infarto cerebral agudo. Neurología 2023;38:150–8. https://doi.org/10.1016/j.nrl.2020.06.018.

[72] Cai Y, Zhang H, Li Q, Zhang P. Correlation Between Blood Glucose Variability and Early Therapeutic Effects After Intravenous Thrombolysis With Alteplase and Levels of Serum Inflammatory Factors in Patients With Acute Ischemic Stroke. Front Neurol 2022;13. https://doi.org/10.3389/fneur.2022.806013.

[73] Tambunan N, Prawesti AP, Nuraeni A. Hiperglikemia Pada Saat Masuk Rumah Sakit Sebagai Prediktor Sepsis Dan Penentu Hasil Klinis Pada Pasien Dewasa di ICU: Tinjauan Komprehensif. J Ners 2026;10:1761–9. https://doi.org/10.31004/jn.v10i1.54147.

Electronic ISSN : 2656-3088
Homepage: https://www.journal-jps.com