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Original Research Article

Examining Blood Sugar Levels in Statin-Naive Diabetic Patients: A Cross-Sectional Study

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Abstract:

Background: Diabetes mellitus is a chronic disorder marked by hyperglycemia due to insulin defects. Managing blood sugar is crucial to prevent complications like cardiovascular disease and neuropathy. The study investigated glycemic status and side effects in statin-naive diabetic patients, highlighting the impact of statin therapy on blood glucose levels and adverse reactions.

Methods: The study involved 100 participants aged over 30 who were prescribed statins for at least 12 months and had fasting blood glucose levels below 100 mg/dl at the commencement of statin therapy. Data on demographics, clinical characteristics, medication histories, and blood glucose levels were collected using standardized forms. Statistical analyses were performed using SPSS version 23.

Results: Participants had a mean age of 52.6 years (± 8.4), with 45% females and 55% males. Family history included 68% with cardiovascular disease and 32% with diabetes. During the study, 28% developed NODM and 20% were diagnosed with prediabetes. Mean fasting blood glucose was 130.4 mg/dl (± 15.2) for NODM and 105.8 mg/dl (± 8.9) for prediabetes. Adverse effects were reported by 15%, mainly muscle pain (8%). Significant predictors of NODM were family history of diabetes ($\chi^2 = 12.34$, $p < 0.05$), age (OR = 1.08, $p < 0.05$), and family history of diabetes (OR = 2.34, $p < 0.05$).

Conclusion: The study highlights the significant impact of statin therapy on blood glucose levels in statin-naive diabetic patients. Patients with a family history of diabetes are at a higher risk of developing NODM when on statins.

Recommendations: Clinicians should monitor blood glucose levels closely in statin-naive diabetic patients, especially those with a family history of diabetes. Further research is needed to explore the mechanisms by which statins influence glycemic control.

Keywords: Diabetes Mellitus, Statin Therapy, Blood Glucose Levels, New-Onset Diabetes Mellitus, Glycemic Control.

Introduction

Diabetes mellitus, a chronic metabolic disorder characterized by hyperglycemia, results from defects in insulin secretion, insulin action, or both. The management of blood sugar levels in diabetic patients is crucial to preventing complications such as cardiovascular disease, neuropathy, nephropathy, and retinopathy. Statins, widely prescribed for their cholesterol-lowering effects, also influence blood sugar levels, making it imperative to understand their impact on diabetic patients who have not yet been treated with these drugs [1].

In the context of diabetes management, blood sugar regulation involves maintaining glucose levels within a target range to minimize the risk of both short-term and long-term complications. For statin-naive diabetic patients, managing blood sugar levels involves a multifaceted approach, including lifestyle modifications, dietary changes, and pharmacotherapy aimed at improving insulin sensitivity and secretion [2]. Statin-naive patients are those who have not been exposed to statins, thus providing a clear perspective on blood sugar regulation without the confounding effects of these medications.

The relationship between blood sugar levels and statin use in diabetic patients has been a subject of extensive research. Statins, while effective in reducing cardiovascular risk, have been associated with an increased risk of new-onset diabetes and

alterations in glycemic control among existing diabetic patients. This dual effect underscores the importance of monitoring blood sugar levels in statin-naive diabetic patients before and after the initiation of statin therapy [3].

The mechanisms by which statins influence blood sugar levels include the potential impairment of pancreatic β-cell function and increased insulin resistance. Research indicates that the differential impact of various statins on glucose metabolism may be dose-dependent, with higher doses posing a greater risk of dysglycemia [4]. Furthermore, the baseline characteristics of diabetic patients, such as the duration of diabetes, HbA1c levels, and existing comorbidities, play a crucial role in determining the extent to which statins affect blood sugar levels.

Understanding blood sugar regulation in statin-naive diabetic patients is essential for clinicians to tailor individualized treatment plans that optimize both glycemic control and cardiovascular outcomes. The interplay between lipid-lowering therapy and glucose metabolism requires careful consideration of the benefits and risks associated with statin use. By focusing on statin-naive patients, researchers and healthcare providers can better assess the true impact of statins on blood sugar levels, thereby improving the overall management of diabetes.

Managing blood sugar levels in statin-naive diabetic patients is a critical aspect of diabetes care. It involves understanding the complex interactions between various treatment modalities and their effects on glycemic control. This knowledge is vital for developing effective strategies to optimize the health outcomes of diabetic patients while mitigating potential adverse effects associated with statin therapy.

The aim of the study was to investigate the glycemic status and assess the side-effect profile in statin-naive diabetic patients, providing insights into the potential impact of statin therapy on blood glucose levels and adverse reactions in this population.

Methodology

Study Design: A cross-sectional approach.

Study Setting: The research took place at SCB Medical College, Cuttack, spanning from March 2019 to March 2020.

Participants: The study involved the recruitment of 100 individuals.

Inclusion and Exclusion Criteria: Inclusion criteria encompassed subjects of both genders, aged over 30, who had been prescribed statins for at least 12 months, and exhibited a fasting blood glucose level below 100 mg/dl upon commencing statin therapy. Exclusion criteria included pre-existing diabetes, the use of medications known to elevate blood glucose levels, and pregnancy or lactation.

Bias: Efforts were made to minimize bias by meticulously documenting detailed medical histories, with a focus on risk factors for metabolic syndrome and family medical backgrounds. Information regarding demographics, clinical characteristics, and medication histories was collected using standardized forms.

Variables: The primary objectives revolved around the incidence of NODM and prediabetes. Blood glucose levels were evaluated in all participants, with additional analyses conducted for those who developed diabetes. Adverse effects associated with statin usage were also documented.

Data Collection: Data collection procedures involved the use of standardized forms to systematically record demographic details, clinical characteristics, medication histories, and pertinent medical data. Blood glucose levels were measured for all participants, and further assessments were conducted for those diagnosed with diabetes. Any adverse effects linked to statin usage were also noted.

Statistical Analysis: Statistical analyses were carried out using SPSS version 23 and Excel software. Descriptive statistical methods were employed to analyze baseline characteristics, with continuous variables reported as mean ± standard deviation or median and interquartile range for skewed data. Categorical variables were presented as counts and percentages.

Ethical Considerations: The study protocol was approved by the Ethics Committee and written informed consent was received from all the participants.

Result

Table 1: Socio-Demographic Characteristics of Participants

Characteristic	Values
Mean Age (years)	52.6 (8.4)
Gender	
Female	45%
Male	55%
Education Level	
High School	25%

College	45%
Graduate	30%
Employment Status	
Employed	60%
Unemployed	20%
Retired	20%
Marital Status	
Married	70%
Single	20%
Divorced	10%

Of the 100 participants enrolled in the study, the mean age was 52.6 years (± 8.4), with 45% being female and 55% male. The majority of participants (68%) had a family history of cardiovascular disease, while 32% reported a family history of diabetes.

Table 2: Clinical Characteristics of Participants

Characteristic	Values
Family History of Diabetes	32%
Family History of CVD	68%
Mean Duration of Statin Use (years)	3.5 (1.2)
Mean (SD)	
Prediabetes	20%
New-Onset Diabetes Mellitus (NODM)	28%

Among the participants, 28% (n = 28) developed NODM during the study period, while 20% (n = 20) were diagnosed with prediabetes. The mean fasting blood glucose level for those diagnosed with NODM was 130.4 mg/dl (± 15.2), whereas for those with prediabetes, it was 105.8 mg/dl (± 8.9).

Insulin levels were measured in all participants who developed diabetes. The mean fasting insulin level among these individuals was 18.6 μU/ml (± 6.3).

Of the total participants, 15% (n = 15) reported adverse effects related to statin use. The most commonly reported side effect was muscle pain (8%), followed by gastrointestinal discomfort (5%) and headache (2%).

Table 3: Side-Effect Profile of Patients on Statins

Side Effect	Values
Muscle Pain	8%
Gastrointestinal Discomfort	5%
Headache	2%

A Chi-square test was conducted to assess the association between family history of diabetes and the development of NODM. The analysis revealed a significant association ($\chi^2 = 12.34$, $p < 0.05$), indicating that participants with a family history of diabetes were more likely to develop NODM.

Furthermore, an independent samples t-test was performed to compare the mean fasting blood glucose levels between participants with NODM and those with prediabetes. The analysis showed a significant difference between the two groups ($t = 4.76$, $p < 0.001$), with participants diagnosed with NODM having significantly higher blood glucose levels compared to those with prediabetes.

Additionally, logistic regression analysis was conducted to identify predictors of NODM development. Variables such as age, gender, family history of diabetes, and duration of statin use were included in the model. The results revealed that age (OR = 1.08, 95% CI [1.02-1.15], $p < 0.05$) and family history of diabetes (OR = 2.34, 95% CI [1.12-4.89], $p < 0.05$) were significant predictors of NODM development, while gender and duration of statin use did not significantly predict NODM.

Discussion

The study included 100 participants with a mean age of 52.6 years (± 8.4), consisting of 45% females and 55% males. Regarding education, 25% had a high school education, 45% had attended college, and 30% were graduates. Sixty percent were employed, 20% were unemployed, and 20% were retired. Maritally, 70% were married, 20% were single, and 10% were divorced.

Clinically, 32% had a family history of diabetes, while 68% had a family history of cardiovascular disease. The mean duration of statin use was 3.5 years (± 1.2). Twenty-eight percent of participants developed NODM, and 20% were diagnosed with prediabetes. The mean fasting blood glucose level for NODM was 130.4 mg/dl (± 15.2), and for prediabetes, it was 105.8 mg/dl (± 8.9). Insulin

levels among those with diabetes had a mean of 18.6 μU/ml (± 6.3). Fifteen percent reported adverse effects related to statin use, with the most common being muscle pain (8%).

In this study, the side-effect profile of patients on statins was evaluated. Among 100 participants, a minority experienced adverse effects related to statin use, with muscle pain being the most common (8%). Gastrointestinal discomfort was reported by 5%, and headache by 2%. No other specific side effects were noted. Overall, the incidence of statin-associated side effects in this cohort was relatively low.

Statistical analyses revealed significant associations between family history of diabetes and NODM development ($\chi^2 = 12.34$, $p < 0.05$), suggesting a higher likelihood of NODM among participants with a family history of diabetes. Additionally, participants diagnosed with NODM had significantly higher fasting blood glucose levels compared to those with prediabetes ($t = 4.76$, $p < 0.001$). Logistic regression analysis identified age (OR = 1.08, 95% CI [1.02-1.15], $p < 0.05$) and family history of diabetes (OR = 2.34, 95% CI [1.12-4.89], $p < 0.05$) as significant predictors of NODM development, highlighting the influence of these factors on diabetes onset, independent of gender and duration of statin use.

A study revealed that early initiation of statin therapy in statin-naive patients admitted with acute coronary syndromes (ACS) significantly lowered the incidence of in-hospital hyperglycemia. The adjusted odds ratio (OR) for developing hyperglycemia was 0.61 (95% CI 0.46-0.80; $p < 0.001$), and the need for insulin therapy was also reduced (adjusted OR = 0.56, 95% CI 0.41-0.76; $p < 0.001$) [5].

In another study, continuous glucose monitoring was used to determine glycemic profiles in drug-naive type 2 diabetes patients. The study found that to improve HbA1c levels, the average glucose level needs to be improved. Specifically, for patients with HbA1c < 7.0%, it is important to improve blood glucose levels after breakfast and before lunch. For those with HbA1c ≥ 8.0%, better control is needed after lunch and before dinner [6].

A study compared lipid profiles and other biochemical markers among type 2 diabetes patients on different durations of statin therapy. It found significant reductions in total cholesterol and LDL-c among long-term statin users, but no significant differences in liver enzyme levels or fasting blood glucose across the groups [7].

Furthermore, a study assessed how glycemic control impacts hemostatic regulation proteins in type 2 diabetes patients. Poorly-managed diabetes was associated with significantly lower levels and activity of protein C, protein S, and antithrombin III. In contrast, statin use was linked to higher levels and activity of these proteins, especially in well-managed diabetes patients [8].

In a study, researchers found that long-term statin therapy significantly increased fasting blood sugar (FBS), post-prandial blood sugar (PPBS), and HbA1c levels in type 2 diabetes patients. This highlights the need for careful glucose monitoring in patients on statin therapy [9].

A study found a significant increase in fasting blood glucose and HbA1c levels following statin intake. This suggests an association between statin use and elevated blood glucose levels in this population [10].

In a study, metformin monotherapy significantly improved lipid profiles in statin-naive individuals with newly diagnosed type 2 diabetes. Improvements were seen in LDL-C, TG, and HDL-C levels, indicating metformin's beneficial effects on lipid metabolism [11].

A study explored the risk of NODM and hyperglycemia in patients on statins. The study found a mild-to-moderate risk of developing diabetes, with atorvastatin being the most commonly prescribed statin associated with this risk [12].

A study reviewed how diabetes affects the pharmacokinetics and pharmacodynamics of statins, altering their effectiveness and side effect profile. The study emphasized the need for more clinical research to better understand these interactions [13].

A study compared blood glucose profiles between East Asian and Caucasian patients inadequately controlled on oral medications. The study underscored the importance of individualized therapy based on patient demographics and glycemic profiles [14].

Conclusion

The study demonstrates that statin therapy significantly impacts blood glucose levels in statin-naive diabetic patients, with a considerable proportion developing NODM and prediabetes. Key predictors of NODM included age and a family history of diabetes. These findings underscore the necessity for clinicians to closely monitor blood glucose levels in diabetic patients initiating statin therapy, particularly those with a family history of diabetes. Enhanced vigilance and individualized treatment plans are essential to mitigate potential adverse effects and optimize patient outcomes.

Limitations: The limitations of this study include a small sample population who were included in this

study. Furthermore, the lack of comparison group also poses a limitation for this study's findings.

Recommendation: Clinicians should monitor blood glucose levels closely in statin-naive diabetic patients, especially those with a family history of diabetes. Further research is needed to explore the mechanisms by which statins influence glycemic control.

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List of abbreviations:

DM - Diabetes Mellitus

CVD - Cardiovascular Disease

NODM - New-Onset Diabetes Mellitus

OR - Odds Ratio

CI - Confidence Interval

ACS - Acute Coronary Syndromes

HbA1c - Hemoglobin A1c

LDL-c - Low-Density Lipoprotein Cholesterol

TG - Triglycerides

HDL-C - High-Density Lipoprotein Cholesterol

FBS - Fasting Blood Sugar

PPBS - Post-Prandial Blood Sugar

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References

1. Cai, C., Wen, Z., & Li, L. The relationship between ApoE gene polymorphism and the efficacy of statins controlling hyperlipidemia. American journal of translational research, 2021;13(6): 6772-6777.
2. Hori, E., Kikuchi, C., Imaeda, K., Okayama, N., Suzuki, T., & Matsunaga, T. [Effect of Statins on Glycemic Status and Plasma Adiponectin Concentrations in Patients with Type 2 Diabetes Mellitus and Hypercholesterolemia]. Yakugaku zasshi: Journal of the Pharmaceutical Society of Japan, 2019; 139(5): 807-815.
3. Maini, J., Rehan, H., Yadav, M., & Gupta, L. Exploring the role of adipsin in statin-induced glucose intolerance: a prospective open label study. Drug Metabolism and Personalized Therapy, 2020;35.
4. Mansi, I., Chansard, M., Lingvay, I., Zhang, S., Halm, E., & Alvarez, C. Association of Statin Therapy Initiation with Diabetes Progression: A Retrospective Matched-Cohort Study. JAMA internal medicine. 2021.
5. Furtado, R., Genestreti, P., Dalçóquio, T., Baracioli, L., Lima, F., Franci, A., Giraldez, R., Menezes, F. R., Ferrari, A. G., Lima, V., Pereira, C. A. C., Nakashima, C. A. K., Salsoso, R., Godoy, L. C., & Nicolau, J. Association between statin therapy and lower incidence of hyperglycemia in patients hospitalized with acute coronary syndromes. Arquivos Brasileiros de Cardiologia, 2021;116(2): 285-294.
6. Mori, H., Okada, Y., Kawaguchi, M., Otsuka, T., Miyazaki, M., Sonoda, S., Sugai, K., Uemura, F., Tanaka, K., Hajime, M., Kurozumi, A., Narisawa, M., Torimoto, K., & Tanaka, Y. Glycemic profiling in patients with drug-naïve type 2 diabetes by continuous glucose monitoring. Journal of UOEH, 2018; 40(4): 287-297.
7. Habte, M. L., Melka, D. S., Degef, M., Menon, M., Yifter, H., & Feyisa, T. O. Comparison of lipid profile, liver enzymes, creatine kinase, and lactate dehydrogenase among type II diabetes mellitus patients on statin therapy. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, 2020;13: 763-773.
8. Addai-Mensah, O., Annani-Akollor, M., Nsafoah, F., Fondjo, L., Owiredu, E., Danquah, K. O., Duneeh, R., & Amponsah, F. A. Effect of poor glycaemic control on plasma levels and activity of protein C, protein S, and antithrombin III in type 2 diabetes mellitus. PLoS ONE, 2019; 14.
9. Jyothi, P. D., Sri Durga, P., Veena, Y., & Afsari, S. Analyzing the impact of statins use in type 2 diabetes mellitus patients at a tertiary care hospital in Andhra Pradesh. Asian Journal of Pharmaceutical and Clinical Research. 2020.
10. Chamsine, N., Mhanna, R., Hallit, S., Salameh, P., Malaeb, B., Hallit, R., & Malaeb, D. A retrospective study on the impact of statins on blood glucose levels in Lebanese controlled type two diabetic patients. Medical Research Archives, 2019; 7.
11. Lin, S. H., Cheng, P. C., Tu, S., Hsu, S., Cheng, Y. C., & Liu, Y. Effect of metformin monotherapy on serum lipid profile in statin-naïve individuals with newly diagnosed type 2 diabetes mellitus: A cohort study. Peer J, 2018;6.
12. 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 Journal of Pharmacology, 2018;50: 320-325.
13. Mashayekhi-Sardoo, H., Atkin, S., Montecucco, F., & Sahebkar, A. Potential alteration of statin-related pharmacological features in

diabetes mellitus. BioMed Research International, 2021.
14. Zhang, X., Li, P., Hou, J., & Ji, L. Blood glucose profiles in East Asian and Caucasian injection-naive patients with type 2 diabetes inadequately controlled on oral medication: A pooled analysis. Diabetes/Metabolism Research and Reviews, 2018;34.