Lipid Control and Factors Associated with LDL-C Control among Patients with Type 2 Diabetes Mellitus on Statins in Western Kenya

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Abstract

Background: Dyslipidemia is the presence of abnormal blood lipid parameters, characterized by increased LDL-C, triglycerides, and total cholesterol but reduced HDL-C. It is a common finding in patients with T2DM, occurring at a prevalence rate of between 70% and 85%, and promotes the development of long-term cardiovascular complications, which are the leading cause of mortality in this population. Statins are the first-line drugs, but lipid control varies from patient to patient despite being widely used.

Objective: To assess lipid control and the factors associated with LDL-C control in patients with type 2 DM who are on statins at a national referral hospital in Western Kenya.

Methods: A retrospective study on 211 patients with type 2 DM who had been on a statin for at least three months. Data was obtained from patient records and lipid measures categorized as controlled or uncontrolled based on the Kenya National Guidelines for the Management of Diabetes Mellitus, 2018. Chi-square and Fischer's exact test determined the association between variables. A multivariate logistic regression model was fit for variables significant at the bivariate level, and a P value of <0.05 was considered significant.

Results: Most (99%) were on a single lipid-lowering drug, mainly atorvastatin, and 92% were on moderate-intensity dosing. Regarding lipid control, 50.3% had uncontrolled LDL-C, 30% had uncontrolled HDL-C, and 47% had uncontrolled triglyceride levels. Being on a high-intensity statin increased the likelihood of LDL-C control compared to moderate-intensity dosing (OR 8.57 [95% CI 4.3-16.9, P<0.001]).

Conclusion: LDL-C was the most poorly controlled parameter. Patients on high-intensity statins had better LDL-C control; therefore, high-intensity statin therapy should be initiated in diabetic patients who do not achieve their LDL-C targets.

Index Terms- dyslipidemia, lipid control, statins, statin intensity, type 2 diabetes mellitus

I. INTRODUCTION

Dyslipidemia is a major modifiable risk factor for atherosclerotic cardiovascular disease, which is the leading cause of mortality in patients with T2DM, accounting for about 80% of deaths in this group of patients globally (Huang et al., 2017). Managing dyslipidemia is, therefore, a cornerstone intervention in the overall management of DM to reduce the risk of cardiovascular disease. Statins are the first-line hypolipidemic drugs recommended for managing dyslipidemia and have been shown to modify lipid levels favorably with a consequent reduction in cardiovascular events such as acute coronary disease and stroke (Colhoun et al., 2004).

Despite the widely established benefit of statin use, studies show that there is considerable interpatient variability in lipid reduction among statin-treated patients, and lipid control is sub-optimal in many cases globally (Gitt et al., 2016). Achievement of set targets is one strategy in assessing lipid control, and failure to achieve these targets may leave patients at risk of ASCVD despite their being on treatment. Consequently, the Kenya national guidelines for the management of diabetes mellitus 2018 (National Diabetes Control Program, 2018), recommends lipid targets for patients with type 2 DM for cardiovascular risk reduction. These targets are an LDL-C level of <2.6 mmol/L and < 1.8 mmol/L in patients with existing ASCVD, triglycerides < 1.7mmol/L and HDL-C >1.0 mmol/l for males and >1.2 mmol/L for females. However, there is not much data on how well dyslipidemia is controlled based on these targets or factors associated with LDL-C control, which is this population's most significant predictor of cardiovascular disease.

II. METHODOLOGY

The study was conducted at The Moi Teaching and Referral Hospital (MTRH) diabetes outpatient clinic in Western Kenya. Adult patients with type 2 diabetes mellitus were recruited if they had a lipid profile measurement not exceeding 12 months at the time of data collection and had used a statin for at least three months when the lipid measurement was taken. Their demographic and clinical data was obtained from their records, and the lipid measures were categorized as controlled or

uncontrolled based on the Kenya National Guidelines for Diabetes Management, 2018 (National Diabetes Control Program, 2018). Approval to conduct the study was obtained from the Moi University/MTRH Institutional Research and Ethics Committee and the National Commission for Science Technology and Innovation (NACOSTI).

III. STUDY FINDINGS

A. Demographic and Clinical Characteristics

Of the 211 participants enrolled, 56.4 % were female. The majority were aged above 50 years (93.4%), with a median age of 65 (IQR 59-72). Hypertension was the most prevalent comorbidity, occurring in 82.4% of participants; 16% had chronic kidney disease, and 10 (5%) had documented pre-existing ASCVD. HbA1c was poorly controlled, with 78% of participants having values above 7%. The mean HbA1c was 8.8 (SD 2.2). About half (46.5%) of patients had diabetes for longer than ten years. Over 50% were overweight or obese, and the mean BMI was 25.6 (SD 3.3).

Atorvastatin was used by 94.8% of participants, and 99% were on monotherapy lipid lowering with a statin. 92% were on a moderate-intensity statin, 7.6% were on high-intensity, and the median duration of statin use was 17 months IQR (9-36).

B. Lipid control

Mean lipid values were 2.7 ±1.07 mmol/L, 1.17±0.36 mmol/L, and 1.8±0.85 mmol/L for LDL-C, HDL-C, and triglycerides, respectively. Only 49.7% of the participants attained LDL-C targets, about 70% attained HDL-C targets, and 52.6% attained triglyceride targets. The overall proportion of dyslipidemia (at least one parameter outside the target) was 95.7%.

C. Factors associated with LDL-C control

Bivariate analysis using the Chi-square test and Fischer's Exact test found that age, gender, duration of diabetes, HbA1c, patient's BMI, presence of existing ASCVD, type of statin used, and the intensity category were associated with LDL-C control (P <0.05). These were subjected to a multivariate logistic regression to explore independent association and results presented in Table 1.

Younger age (40-49 years) was associated with increased odds of achieving control, while age above 65 had decreased odds. High-intensity statins had an 8.57 (95% CI [4.3-16.9] P <0.0001) higher odds of achieving control compared to moderate-intensity dosing.

Table 1: Multivariate logistic regression of factors associated with LDL control

Variable	Adjusted OR	95% CI	P value
Age in years			
40-49	5.04	2.0-12.6	<0.001
50-64	1.56	0.78-3.12	0.22
≥65	0.20	0.11-0.32	<0.001
Duration of DM in years			
1-4	1.3	0.5-3.7	0.6
4-9	0.96	0.4-2.3	0.9
≥10	1.06	0.6-2.0	0.99
HbA1c <7%	1.01	0.6-1.6	0.96
BMI			
Underweight	0.93	0.3-2.9	0.9
Overweight	1.01	0.4-2.5	0.99
Obese	1.1	0.6-2.0	0.7
Presence of ASCVD (Yes)	1.8	0.6-5.0	0.25
Type of statin (Rosuvastatin)	1.45	0.6-3.7	0.42
Dosing			
High Intensity	8.57	4.3-16.9	<0.001
Low intensity	1.82	0.1-3.45	0.11

IV. DISCUSSION

This study determined the proportion of patients with type 2 DM who achieved desired lipid control while on hypolipidemic agents and factors associated with LDL-C control. The main findings were that nearly 96% of the patients did not achieve their target blood level of one or more lipid parameters (as defined by the Kenya Guidelines) and that less than half of patients (49.7%) reached the prescribed LDL-C goals despite statin use. This was similar to the study in South Africa by Daya et al., 2017, where the overall prevalence of dyslipidemia was 93.5%, and LDL-C

target attainment was less than 30% despite treatment with simvastatin for all patients (Daya et al., 2017). We obtained results similar to those of other studies in the other individual parameters, with a study in Portugal similarly finding a high proportion of HDL-C target attainment of 64.2% (Monteiro & Palma, 2016) and DYSIS Egypt reported a 62.9% proportion (Eltriby et al., 2013) which were both comparable to 69.6% in this study.

The findings that the use of high-intensity statins was positively and significantly associated with LDL-C control compared to moderate intensity are comparable to a Swedish study (Mazhar et al., 2022) and a Belgian study (Hermans et al., 2020). Indeed, this is the intention of the guidelines referenced, which were mainly informed by studies from North America and Western Europe. However, it is of note that The International Cholesterol Management Practice Study (ICLPS) that was conducted across 18 countries in 5 continents outside Western Europe, including 2 African countries, found that a higher intensity statin was associated with a 1.4-fold lower likelihood of achieving targets (Danchin et al., 2018). Statin intolerance, similarly associated with non-achievement of LDL-C goals, may indirectly explain this.

Higher statin dosing is often associated with increased incidences of intolerance due to adverse effects and may often compromise adherence. Muscle-related adverse effects are the most commonly observed but are usually mild and exacerbated by drug-drug interactions, increasing age, genetic factors, and higher dosing (Newman et al., 2019). In this study, age above 65 predicted poor LDL-C control, which may necessitate higher statin dosing in this population. However, increasing the dose in this age group must balance adverse effects and efficacy risks. A retrospective study in Denmark suggested that low or moderate-intensity statins in patients older than 75 years had more significant LDL-C reduction compared to patients less than 50 years of age, and high-intensity statins achieved a similar reduction (Corn et al., 2023). Further research in this study setting may be necessary to evaluate the relationship between statin intensity and adverse effect incidence, especially in older patients above 65. This can guide potential risks that can be weighed against the potential benefit of LDL-C control.

In addition, other lipid-lowering strategies may be considered, such as additional lipid-lowering drugs, reinforcing lifestyle modifications, and increasing medication adherence. The use of an additional class of lipid-lowering drugs to statins has been associated with increased rates of achieving LDL-C targets (Cannon et al., 2015). The majority of guidelines recommend adding a non-statin drug where treatment targets cannot be achieved with statins. Ezetimibe is recommended by both ACC/AHA and ESC guidelines as additional therapy and maybe a reasonably effective option for increasing the statin dose (Arnett et al., 2019) (Cosentino et al., 2020). Kenyan guidelines indicate that fibrates and niacin can be additional options to statins for hypertriglyceridemia (National Diabetes Control Program, 2018). However, adding another drug would need to consider other factors, such as cost and the influence of an additional drug on the existing treatment dynamics. This can be compared to the cost of a higher statin dose and the potential hazard of not achieving LDL-C targets.

V. CONCLUSION

The occurrence of dyslipidemia in this study was high (96%), with LDL-C being the most poorly controlled lipid parameter. Using a high-intensity statin significantly increased the odds of achieving LDL-C control. Intensification of therapy by increasing the statin intensity used or adding other lipid-lowering drugs, as recommended by most guidelines, should be actuated in diabetic patients who do not achieve their LDL-C targets.

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