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Original Research Article

Recent trends in the patterns of dyslipidemia and management strategy in newly diagnosed patients of type 2 diabetes mellitus-2

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ABSTRACT

Background: Objective of the study was to evaluate the patterns of dyslipidaemia in newly diagnosed type 2 diabetes mellitus-2 (T2DM) patients and to understand the initial management options utilised by the treating physician.
Methods: The real world, retrospective, observational REcent trends in the patterns of dyslipidemia and Management strategy in newly diAgnosed Patients of type 2 diabetes mellitus-2 (REMAP-2) study was conducted at various centers including hospitals, clinics, and health care institutes across India between Apr-2021 and Mar-2022. Clinicians at the respective center captured the data in REMAP-2 study data capture form. Dyslipidemia was considered as: total cholesterol >200 mg/dl, low density lipoprotein cholesterol (LDL-C) >100 mg/dl, high density lipoprotein cholesterol (HDL-C) <40 mg/dl, or triglyceride >150 mg/dl.
Results: Of 9605 newly diagnosed T2DM patients with dyslipidemia, 68.94% (n=6622) had mixed dyslipidemia. The mean age was 53.8 years. Majority of the patients were males (63.3%), had family history of diabetes (52.5%), physical activity category of 'not very active' or 'lightly active' (79.33%), and were overweight or obese (58.9%). About 25.9% of the patients were smokers. Hypertension (72.33%) was the most common comorbidity followed by coronary artery disease (23.44%). The mean glycated hemoglobin (HbA1c) was 8.3%. The most commonly prescribed antidiabetic medication was metformin (87.71%), while lipid lowering therapy was atorvastatin (77.79%).
Conclusions: This study on newly diagnosed T2DM patients with dyslipidemia found that majority of the patients had hypertriglyceridemia, family history of diabetes and were physically inactive. More than half of T2DM patients were either overweight or obese. More than 2/3rd of the patients had mixed dyslipidemia. Statins were prescribed to the majority of these patients and atorvastatin was the most commonly prescribed statin in Indian T2DM patients with dyslipidemia.

Keywords: Diabetes mellitus, Newly diagnosed, Dyslipidemia

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is associated with a considerably increased risk of premature atherosclerosis, particularly coronary heart disease (CHD) and peripheral arterial disease.[1,2] Diabetes is considered to confer at least a twofold excess risk for cardiovascular diseases (CVD), independently from other conventional risk factors.[3,4] In T2DM patients, there is often an elevated cardiovascular risk for several years before biochemical hyperglycaemia begins. Obesity and insulin resistance, combined with hypertension and dyslipidaemia, commonly referred to as metabolic syndrome, are also present during this period.[5] Intensive glycaemic control has essentially failed to significantly improve cardiovascular outcomes in clinical trials.[3]

Dyslipidaemia is common in diabetes and there is convincing evidence that cholesterol lowering improves cardiovascular outcomes, even in patients with

unremarkable lipid profiles.[2,6] The lipid changes associated with diabetes mellitus are attributed to increased free fatty acid flux secondary to insulin resistance and aggravated by increased inflammatory adipokines.[7] Low density lipoprotein cholesterol (LDL-C) in patients with diabetes underestimates the atherogenic contribution of triglyceride-rich particles, and non-high density lipoprotein (HDL) cholesterol is a good measure of atherogenicity in diabetes.[8] The availability of several lipid-lowering drugs and nutritional supplements offers novel and effective options for achieving target lipid levels in people with diabetes.[9]

Most practice guidelines recommend statins as first-line therapy for dyslipidemia.[10] The use of combination of statins with fibrates or nicotinic acid in reducing cardiovascular events is inconclusive.[11] It is vital to understand the demographic profile, pattern of dyslipidaemia and initial management approach in T2DM patients with abnormal lipid profiles. This analysis will assist in optimizing the management strategies for dyslipidaemia in T2DM patients. The present retrospective observational study was designed to evaluate the patterns of dyslipidaemia in newly diagnosed T2DM patients, to evaluate the glycaemic status of the patients and the initial management options utilised by the treating physician.

METHODS

Study design

The real world, retrospective, cross-sectional, observational REMAP-2 (REcent trends in the patterns of dyslipidemia and Management strategy in newly diAgnosed Patients of type 2 diabetes mellitus-2) study was conducted at various centers including hospitals, clinics, and health care institutes across India between April 2021 and March 2022. The respective center physicians, diabetologists, endocrinologists and cardiologists collected the data retrospectively in the predesigned REMAP-2 study data capture form.

The details on patient's diagnosis, age, gender, dietary habit, level of physical activity, family history of T2DM, status of obesity, history of smoking, presenting complaints, comorbid conditions, stage of chronic kidney disease (CKD) if present, glycemic status [Glycated hemoglobin (HbA1c), fasting blood glucose (FBG), post-prandial blood glucose (PPBG)], lipid profiles, dietary advice, prescribed anti-diabetic drugs and lipid lowering drugs were captured from the medical records. Patients were selected based on treating physician's discretion, and no additional evaluations or investigations were performed during data capture in this real world, observational study. The dyslipidemia was defined if any of these four conditions were met: total cholesterol >200 mg/dl or LDL-C >100 mg/dl, or HDL-C <40 mg/dl or triglycerides (TG) >150 mg/dl. The mixed dyslipidemia was defined as TG >150 mg/dl, total LDL-C >100 mg/dl or HDL-C <40 mg/dl.

Outcomes

The study outcomes were the evaluation of proportion of T2DM patients with mixed dyslipidemia, smoking status, and family history with diabetic dyslipidemia, status of glycemic parameters, patterns of dyslipidemia in the patients, percentage of patients prescribed statin and fenofibrate therapies, percentage of patients on various antidiabetic medications as well as various types of the diet plan.

Sample size and statistical analysis

This was a real-world study and the patients' data was collected retrospectively without any predetermined sample size. There was no hypothesis tested in this study and the observations from patient's records only were analyzed. Descriptive statistics was used for demographic and baseline characteristics. Categorical variables were summarized with frequency and percentage, whereas count, mean, and standard deviation were presented for continuous variables. Statistical analyses were performed using Microsoft excel (IBM Corp., USA).

Ethics statement

This retrospective study protocol carried less than minimal risk according to the Indian council of medical research 'Ethical guidelines for biomedical research on human participants'.[12] The study was conducted after due approval from bio-smart independent ethics committee, Ahmedabad, India. This was a retrospective study without patient identifiers; hence, the informed consent of patients was not obtained. There was no confidentiality breach of the data during its analysis and interpretation.

RESULTS

A total of 9605 patients of newly diagnosed T2DM with dyslipidemia identified between April 2021 and March 2022 were included in this study. Table 1 provides the details on demographic profile of the patients. The patients had a mean age of 53.8 years, and majority of the patients were males (63.3%) while females constituted 36.7% of the study population. More than half of the patients were either overweight (39%, n=3743) or obese (19.9%, n=1908). A total 68.9% (n=6622) patients had mixed dyslipidemia. The triglyceride levels were found to be high (>150 mg/dl) in 85% (n=8190) of patients. The mean glycated hemoglobin (HbA1c) was 8.33% in newly diagnosed T2DM patients with dyslipidemia. Approximately one fourth (25.9%) of newly diagnosed T2DM patients were found to be smokers in this study and 43.54% of them consumed >10 cigarettes per day. Around 52.6 percentages patients had positive family history of diabetes. Most (79.33%) of the patients were not very physically active or lightly active. In the context of dietary pattern, majority (59.42%) of the patients were non-vegetarian.

Table 1: Baseline demography and disease characteristics (n=9605).

Parameters	
Age (Years), mean ± SD	53.8±10.36
Gender, N (%)	
Men	6081 (63.3)
Women	3524 (36.7)
Weight (kg), mean ± SD	75.23±12.09
BMI (kg/m^2)	27.6
Weight status, N (%)	
Underweight	318 (3.30)
Normal BMI (Kg/m^2)	3636 (37.9)
Overweight	3743 (39.0)
Obese	1908 (19.9)
Lipid parameters, (mg/dl), N (%)	
Total cholesterol >200	7307 (76.07)
LDL-C >100	8181 (85.17)
HDL-C <40	3735 (38.89)
TG >150	8190 (85.27)
Glycaemic parameter, mean (SD)*	
HbA1c%	8.33 (1.34)
FBG in mg/dl	173 (43.05)
PPBG in mg/dl	255.33 (65.70)
Smoking history, N (%)	
Yes	2495 (25.98)
<1/day	41 (1.6)
1-5/day	610 (24.45)
6-10/day	671 (26.89)
>10/day	1085 (43.49)
No	7110 (74.0)
Family history of diabetes present, N (%)	5052 (52.6)
Dietary pattern, N (%)†	
Non-vegetarian	5171 (59.42)
Vegetarian	3531 (40.58)
Physical activity, N (%)#	
Not very active	2913 (32.51)
Lightly active	4195 (46.82)
Active	1695 (18.92)
Very active	157 (1.75)

*Data from 9405 patients; †Data from 8702 patients; #Data from 8960 patients. FBG, fasting blood glucose, HbA1c, glycated hemoglobin, HDL-C, high density lipoprotein cholesterol, LDL-C, low density lipoprotein cholesterol, PPBG, post-prandial blood glucose, TG, triglyceride. Data on the number of cigarettes per day was not available for 88 patients.

More than half (58.9%) of T2DM patients were either overweight (39%, n=3743) or obese (19.9%, n=1908). Hypertension (72.39%) was the most common comorbidity followed by coronary artery disease (23.46%) in patients of newly diagnosed T2DM with dyslipidemia (Table 2).

The coexisting hypertension and dyslipidemia known as 'lipitension' was found in 72.39% of patients.

Table 2: Proportion of patients with comorbidities in T2DM with dyslipidemia.

Comorbidity	Frequency (%)
Hypertension	6947 (72.33)
Coronary artery disease	2251 (23.44)
Heart failure	421 (4.38)
Chronic kidney disease	7 (0.07)
Hypothyroid	4 (0.04)
Cancer	1 (0.01)
Metabolic syndrome	1 (0.01)

Medical therapy

Statin therapy was used in 94.7% (n=9101) patients, of which atorvastatin was the most (77.69%) preferred statin therapy (Figure 1). Fenofibrate therapy was prescribed in 26.40% of mixed dyslipidemia patients.

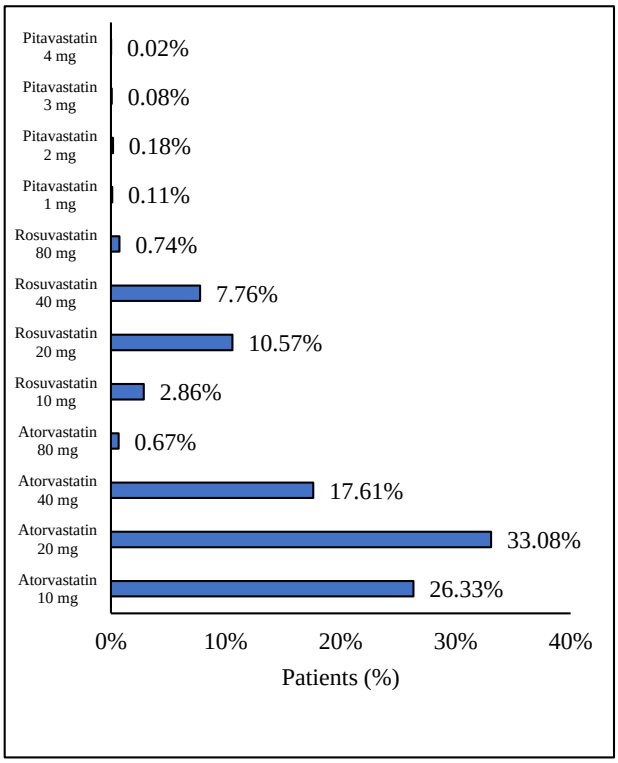

Figure 1: Prescribed statin therapy in newly diagnosed T2DM patients with dyslipidaemia, (n=9101).

Anti-diabetic medications

Metformin (87.71%) was the most commonly prescribed antidiabetic agent in T2DM patients with dyslipidaemia followed by dipeptidyl peptidase 4 inhibitors (DPP4i, 60.03%) and sodium-glucose cotransporter 2 inhibitor (SGLT2i, 45.84%) (Figure 2).

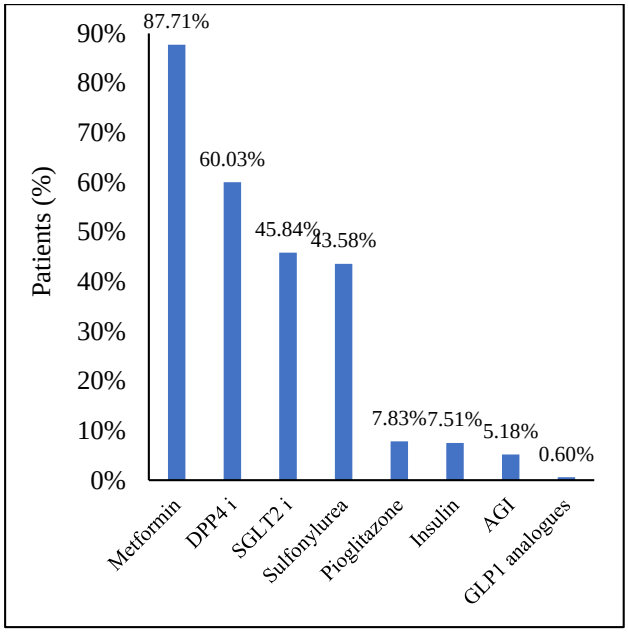

Figure 2: Prescribed antidiabetic medications, (n=9605).

AGI: α-glucosidase inhibitor; DPP4i: dipeptidyl peptidase 4 inhibitors; GLP1: glucagon-like peptide 1; SGLT2i: sodium-glucose cotransporter 2 inhibitor.

DISCUSSION

Dyslipidaemia is highly prevalent in patients with T2DM and is one of the major risk factors for CVDs in these patients.[13,14] The present observational study was conducted on 9605 newly diagnosed T2DM patients with dyslipidaemia at various centres across India between 2021 and 2022.

The mean age of the newly diagnosed T2DM patients in this study was 53.8 years, which was lower than another Indian study wherein about 50% of the patients with dyslipidaemia were greater than 55 years.[15] Almost half of newly diagnosed T2DM patients had positive family history for T2DM. Hypertension was widely prevalent in newly diagnosed patients of T2DM with dyslipidaemia. A remarkably high prevalence of hypertension was noted (72.33%) in the present study. Epidemiological studies have established that prevalence of hypertension is associated with increase in blood lipid levels.[16] This could be due to common pathophysiological aetiologies, resulting in dysregulation of adipocytokine release from adipose tissue and changes in arterial properties.[17]

Smoking is considered as a risk factor associating diabetes and dyslipidaemia. In the present study, 25.9% patients were found to be smokers. These results are comparable to one of the recently published systematic review and meta-analysis, which showed the global mean prevalence of tobacco use in T2DM patients as 20.81%.[18] Studies have shown that intensity of smoking is associated with small but significant increases in LDL-C and decreases in HDL-C.[19] In the present study, out of 2495 patients who had positive history of smoking, 43.49% consumed >10 cigarettes per day.

In one study of inheritance on T2DM in western Indian population, 58% patients showed family history of the disease.[20] About 52.6% patients had positive family history of diabetes in our study.

Patients who had one or more lipid parameters (TG, total cholesterol, HDL-C or LDL-C) outside the normal range were considered to have dyslipidaemia in this study. The proportion of patients with total cholesterol >200 mg/dl was 76.07%, LDL-C >100 mg/dl was 85.17%, HDL-C <40 mg/dl was 38.89% and TG >150 mg/dl was 85.27%. More than half (68.94%) of the patients had mixed type of dyslipidaemia. The raised serum TG level along with other features of metabolic syndrome or CHD are indicative of the development of T2DM, and remain the predictor of CHD risk.[21] TGs are positively correlated with cholesterol, obesity, glucose intolerance, cigarette smoking, and hyperuricemia, and are negatively correlated with HDL cholesterol.[12,22] Diabetes leads to impaired reverse cholesterol transport through both reduced HDL concentrations and HDL dysfunction.[23] Low HDL cholesterol appears to be of greater importance in patients at high cardiometabolic risk and is amongst the factors that currently favour a decision to further reduce LDL-C levels.[13]

In the management of diabetic dyslipidaemia, lifestyle modifications are the first-line intervention, which include weight loss, dietary modification, and aerobic exercise.[23] Obesity increases insulin resistance and is associated with increased TGs and LDL-C, and decreased HDL-C.[24] In the present study 39% of the patients were overweight while 19.9% were obese with 40.58% of patients following vegetarian and 59.42% following non-vegetarian food habits. Weight loss is known to be associated with improvements in lipids and other cardiovascular risk factors including the incidence of T2DM and thus should be encouraged in overweight/obese patients with diabetes.[25]

Metformin decreases serum TGs in addition to improving insulin resistance.[26] Metformin therapy appreciably improves dyslipidaemia in people with T2DM and its lipid-modifying effect may be attributable to insulin sensitization, reduction of irreversibly glycated LDL-C, and weight loss.[27] In the present study population, 87.71% of the patients were prescribed metformin, which is in line with the guideline recommendation as first line therapy in all diabetics except patients with chronic kidney disease (CKD), followed by DPP4i (60.03%) and SGLT2i (45.84%). Statins inhibit 3-hydroxy-3-methylglutaryl-coenzyme A reductase, the rate-limiting enzyme in cholesterol biosynthesis and several trials have evidenced that lowering serum cholesterol with statins decreases the risk of CHD.[28,29] Statins reduce the risk of cardiovascular events in a dose-dependent fashion, higher dose of statins are associated with a greater lowering of cardiovascular

events.[30] In the present study, atorvastatin (77.69%) was the most commonly prescribed statin in Indian T2DM patients with dyslipidaemia. It was prescribed in different doses 10 mg (26.33%), 20 mg (33.08%), 40 mg (17.61%), 80 mg (0.67%) while rosuvastatin 5 mg (2. 86%), 10 mg (10.57%), 20 mg (7.76%), 40 mg (0.74%) was prescribed to 21.9% of the patients. Fibrates act as peroxisome proliferator-activated receptor (PPAR)-a agonists to reduce triglycerides and modestly increase HDL cholesterol but also affect multiple pathways linked to the retinoid-X receptor.[31] In the present study, 26.40% patients with mixed dyslipidaemia were prescribed fenofibrate therapy.

The interpretation of the current study findings requires consideration in view of certain limitations, which include missing data, and potential inconsistency in data entry as multiple study centres were involved.

CONCLUSION

This study found that in newly diagnosed T2DM patients with dyslipidemia, majority of the patients were physically inactive, had family history of diabetes and hypertriglyceridemia. More than half of T2DM patients were either overweight or obese. Hypertension was the most common comorbidity. More than 2/3rd of the patients was of mixed dyslipidaemia. Statins were prescribed to majority of these patients and atorvastatin was the most commonly prescribed statin in Indian T2DM patients with dyslipidaemia.

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Ethical approval: The study was approved by the Independent Bio-smart Ethics Committee, Ahmedabad, India

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