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Evaluation of Drug Utilization and Dose Intensity Pattern in Dyslipidemic Patients with Type 2 Diabetes Mellitus

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Abstract

Dyslipidemia can increase the risk of cardiovascular disease in individuals with metabolic diseases. Patients may have to take multiple medications simultaneously, leading to polypharmacy. A retrospective study was conducted to evaluate drug utilization and dose intensity patterns in dyslipidemic patients with type 2 diabetes mellitus over an 8-month period at a tertiary care hospital. The study included the case sheets of patients diagnosed with dyslipidemia and type 2 diabetes. The required data for the study were collected from the patient's case sheets from the Medical Records Department (from June 2015 to May 2020). The data were documented using MS Excel 2013 and analyzed descriptively using SPSS software version 20. Among the 384 study population, 53% were males and 47% were females, with an age group of 45 to 59 years. Metformin and glimepiride were the most commonly prescribed oral hypoglycemic agents, while glibenclamide was the least prescribed. Atorvastatin was the most prescribed hypolipidemic agent. The combination of atorvastatin and fenofibrate was the most preferred combination therapy. The most frequently prescribed hypoglycemic and hypolipidemic agents were metformin and atorvastatin, respectively. Dyslipidemic patients with diabetes mellitus require the administration of multiple medications. It is crucial to monitor medication adherence and medication-related problems among these populations.

Keywords
- drug utilization
- dyslipidemia
- type 2 diabetes mellitus
- medication adherence

Introduction

Dyslipidemia is irregularities in lipid levels, including cholesterol, low-density lipoprotein cholesterol (LDL-C), triglycerides, and high-density lipoprotein (HDL).[1] Cholesterol is a fatty substance synthesized in the liver and obtained from fatty foods like oil, meat, and cheese, which is essential for the body's systematic functioning. Dyslipidemia is characterized by an excess of LDL, triglycerides, total cholesterol, and a deficient in HDL, leading to an abnormal lipid profile. Hyperlipidemia is the term used to describe the metabolic disorder of these lipoproteins. A slight increase in LDL is a warning sign of cardiovascular disease (CVD). Therefore, dyslipidemia is a significant contributor to CVD, along with type 2 diabetes mellitus (T2DM).[2–4] Recent research indicates that the prevalence of high cholesterol is

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approximately 25 to 30% in urban areas and 15 to 20% in rural areas, which is lower than in high-income countries.[5] According to a 2008 report by the World Health Organization (WHO), Europe (53.7%) and America (47.7%) exhibit the highest prevalence of hypercholesterolemia in adults, followed by South East Asia (30.3%). Africa, on the other hand, shows a comparatively lower prevalence (23.1%).[6] According to the WHO reports from 2019, 17.9 million people died due to CVD, accounting for approximately 32% of all global deaths.[7]

Statins are the most commonly recommended drugs for managing dyslipidemia and hypercholesterolemia in patients with T2DM, as they can prevent or serve as prophylaxis for CVD.[3] Statins are classified as high intensity and low intensity. High-intensity statin therapy is more commonly used. Other drugs used in the management of dyslipidemia include fibrates such as fenofibrate, bezafibrate, ciprofibrate, and gemfibrozil, and drugs that specifically reduce the intestinal absorption of phytosterols and dietary cholesterol, such as cholestyramine, colesevelam, colestipol, and ezetimibe. Niacin, also known as vitamin B3, PP, or nicotinic acid, substantially increases HDL levels while lowering very LDL (VLDL) levels.[8]

Insulin is widely used to treat diabetes, with approximately 4 out of 10 patients in India using it. South India shows a higher prevalence of dyslipidemia with diabetes compared to North India.[9] Therefore, we intend to analyze the drug utilization and dose intensity pattern of dyslipidemia drugs in patients with diabetes mellitus.

Methodology

Study Design

A retrospective study was carried out for a period of 8 months, from September 2021 to May 2022, in the general medicine department of a tertiary care hospital. The study included case sheets of 384 patients. The data needed for the study were collected from the patient's case sheets obtained from the Medical Records Department (from June 2015 to May 2020). The study was initiated after getting permission from the Institutional Ethics Committee (Ref No: NGSMIPS/IEC/11/2021).

Sample Size

At 5% level of significance, the anticipated proportion of 0.5, and margin of error of 5% (0.05), the sample size was calculated as 384. The sample size was calculated using the software nMaster version 2.0.

Study Population

The study included case sheets of inpatients of either gender above 18 years diagnosed with dyslipidemia with T2DM admitted to the general medicine department. Patients referred to another department, incomplete case records, dyslipidemia drugs used for other treatments, and pregnant women were excluded from the study.

Data Collection

The data were collected from medical records. Disease-related information, such as complications, and treatment-related information, including different classes of medications, medications per prescription, and dose, dosage form, and route of administration of the drugs, were extracted from the medical records. Two investigators to ensure the accuracy of the collected data performed the data extraction.

Statistical Analysis

The data were analyzed using the Kolmogorov test, which showed that the data were not normally distributed. Chi-square test was used to analyze the data using SPSS software version 20.0.

Results

In the study, a total of 384 patient records were included from the Medical Records Department. The files were screened using the International Classification of Diseases 10th Revision coding in the Medical Records Department software.

Age and Gender-Wise Distribution of the Study Population

Among the 384 patients, 204 were males (53%) and 179 were females (47%). The age distribution is as follows, 5 patients aged 18 to 29 years, 38 patients aged 30 to 34 years, the greatest number of patients (182) was in the age range of 45 to 59 years, 143 patients were aged 60 to 74 years, and 16 patients were aged 75 years or older.

Drug Utilization Pattern of Oral Hypoglycemic Agents

The most commonly prescribed hypoglycemic agent was metformin from the biguanide class, followed by glimepiride from the sulfonylureas class. The least prescribed drug was glibenclamide, also from the sulfonylureas class. Metformin was the most commonly prescribed oral antidiabetic agent, with a defined daily dose (DDD)/100 bed days of 0.0654 (►**Tables 1** and **2**).

Human insulin was the most preferred insulin, accounting for 26.04% of prescriptions, while insulin aspart was the least prescribed at 1.04%. The average DDD/100 bed days of insulin usage was 0.0264.

Lipid Profile of the Study Population

The median cholesterol levels (216 mg/dL) in males and females of the study population were the same, and no significant difference was observed between them (p: 0.925), but a significant difference was observed in the VLDL level (p: 0.034) (►**Table 3**).

In a comparison of lipid profiles across different age groups, significant differences were observed in the VLDL level when comparing the age groups of 30 to 44/60 to 74 (p: 0.031), 30 to 44/≥ 75 (p: 0.002), 45 to 59/60 to 74 (p: 0.000), 45 to 59/≥ 75 (p: 0.000), and 60 to 74/≥ 75 (p: 0.001). Similarly, a significant difference was observed in the total cholesterol levels between the age groups 45 to 59/60 to 74 (p: 0.011) and 45 to 59/≥ 75 (p: 0.032) (►**Table 4**).

Table 1 Prescription pattern of antidiabetic agents

Class of drugs	Name of drug	Frequency (*n*)	Percentage (%)
Biguanides	Metformin	197	51.30
Sulphonylureas	Glimepiride	79	20.57
	Gliclazide	5	1.30
	Glipizide	5	1.30
	Glibenclamide	8	9.37
Alpha glucosidase inhibitor	Voglibose	36	8.33
DPP4 Inhibitors	Teneligliptin	30	7.81
	Vildagliptin	7	1.82
Thiazolidinediones	Pioglitazone	17	4.42
Insulin	Human insulin	223	58.07
	Insulin aspart	8	2.08
	Insulin glargine	43	11.19

Table 2 DDD/100 bed days of antidiabetic agents

Drug name	Dose	Route of administration	ATC code	DDD	DDD/100 bed days
Metformin	500 mg	Oral	A10BA02	2000 mg	0.0654
Glimepiride	2 mg	Oral	A10BB12	2 mg	0.0131
Gliclazide	30 mg	Oral	A10BB09	60 mg	0.0008
Glipizide	5 mg	Oral	A10BB07	10 mg	0.0006
Glibenclamide	5 mg	Oral	A10BB01	10 mg	0.0009
Voglibose	0.3 mg	Oral	A10BF03	0.6 mg	0.0034
Teneligliptin	20 mg	Oral	A10BH08	20 mg	0.0049
Insulin (human)	As per sliding scale	Subcutaneous	A10AB01	40 units	0.0647
Insulin aspart	As per sliding scale	Subcutaneous	A10AD05	40 units	0.0023
Insulin glargine	As per sliding scale	Subcutaneous	A10AE04	40 units	0.0124

Abbreviations: ATC, Anatomical Therapeutic Chemical; DDD, defined daily dose.

Table 3 Comparison based on gender and lipid profile

	Male		Female		
	Median	IQR	Median	IQR	*p*-Value
Cholesterol	216.00	(177–242)	216	(178.5–244.5)	0.925
Triglyceride	175.0	(131.0–220)	180	(131.5–236.5)	0.255
HDL	129	(100–177.30)	137.00	(97.5–181.5)	0.824
LDL	39.00	(32–49)	39.70	(30.20–49.0)	0.901
VLDL	32	(22.40–41.20)	35	(24.7–47.10)	0.034

Abbreviations: HDL, high-density lipoprotein; IQR, interquartile range; LDL, low-density lipoprotein; VLDL, very low-density lipoprotein.

Dose Intensity Pattern in Hypolipidemic Agents

Among statins, atorvastatin was prescribed at a low-intensity dose in 40.62% of cases, followed by rosuvastatin at a low-intensity dose in 10.41% of cases, simvastatin at a low-intensity dose in 2.60% of cases, and pitavastatin at moderate and high-intensity doses in 1.30% of cases. Fibrates, specifically fenofibrate, were prescribed at moderate and high-intensity doses in 1.56% of cases. Additionally, aspirin, an anticoagulant, was prescribed at moderate and high-intensity doses in 7.55% of cases, while clopidogrel, an antiplatelet drug, was prescribed at moderate and high-intensity doses in 6.51% of cases (►**Table 5**)

Drug Utilization Pattern of Dyslipidemic Agents

The most prescribed drug for dyslipidemia was atorvastatin, a statin, accounting for 40.62% of prescriptions. The least

Table 4 Comparison based on age group and lipid profile

Age group	Cholesterol		Triglyceride		VLDL	
	U	*p*-Value	U	*p*-Value	U	*p*-Value
30–44/45–59	3715.0	0.606	3708.0	0.593	3879.0	0.929
30–44/60–74	2742.50	0.283	2706.50	0.234	2408.50	0.031
30–44/≥ 75	275.0	0.138	242.50	0.083	158.0	0.002
45–59/60–74	10876.0	0.011	10723.50	0.006	11710.50	0.000
45–59/≥ 75	983.50	0.032	866.0	0.007	412.50	0.000
60–74/≥ 75	979.0	0.345	888.50	0.143	567.0	0.001

Abbreviation: VLDL, very low-density lipoprotein.

Table 5 Medication approach and dose intensity pattern of hypolipidemic agents

Class of drug	Name of drugs	Intensity of dose	Frequency	Percentage (%)
Statins	Atorvastatin	Low intensity	156	40.62
	Rosuvastatin	Low intensity	40	10.41
	Simvastatin	Low intensity	10	2.60
	Pitavastatin	Moderate and high intensity	5	1.30
Fibrates	Fenofibrate	Moderate and high intensity	6	1.56
Anticoagulant	Aspirin	Moderate and high intensity	29	7.55
Antiplatelet	Clopidogrel	Moderate and high intensity	25	6.51

Table 6 DDD/100 bed days of hypolipidemic agents

Drug name	Dose	Route of administration	ATC code	DDD	DDD/100 bed days
Atorvastatin	40 mg	Oral	C10AA05	20 mg	0.0513
Rosuvastatin	10 mg	Oral	C10AA07	10 mg	0.0066
Simvastatin	10 mg	Oral	C10AA01	30 mg	0.0016
Pitavastatin	2 mg	Oral	C10AA08	2 mg	0.0008
Fenofibrate	160 mg	Oral	C10AB05	200 mg	0.0007
Aspirin	75 mg	Oral	B01AC06	1 tablet independent of tablet strength	0.0048
Clopidogrel	75 mg	Oral	B01AC04	75 mg	0.0041

Abbreviations: ATC, Anatomical Therapeutic Chemical; DDD, defined daily dose.

prescribed statin was pitavastatin, at 1.30%. The combination of atorvastatin and fenofibrate was the most preferred, accounting for 22.65% of prescriptions, while the combination of aspirin, rosuvastatin, and clopidogrel was the least prescribed, accounting for only 1.56% of prescriptions The most frequently prescribed hypolipidemic medication in our study was the combination of atorvastatin with a DDD/100 bed days of 0.0513 (►**Table 6**).

Discussion

The current study analyzed 384 patients' case sheets to determine the characteristics and treatment patterns of individuals with dyslipidemia. A similar pattern was observed in the study conducted by Gazzaz et al[10] and Elnaem et al.[7]

The research revealed a higher prevalence of the disease among males compared to females, which is similar to the findings of Mehta et al.[11] However, it is important to note that the prevalence of the disease can vary depending on the geographical location. Furthermore, the study found a higher prevalence in the age group between 45 and 59, which aligns with the results reported by Gazzaz et al.[10]

Metformin was the most commonly prescribed oral antidiabetic agent, with a DDD/100 bed days of 0.0654, consistent with the findings of the study conducted by Poonam et al[12] and Hannan et al.[13] Among the study population, the most frequently prescribed combination therapy was metformin with glimepiride (17.44%). This finding is similar to the study by Dada et al[14] which reported that biguanides and sulphonylureas were the most frequently prescribed agents (32.8%).

Atorvastatin was the most commonly prescribed drug (40.62%) for patients with hyperlipidemia, consistent with the findings of Raja et al.[15] However, it is important to note that the overall utilization of hypolipidemic medication was relatively low. The most frequently prescribed hypolipidemic medication in our study was the combination of atorvastatin with a DDD/100 bed days of 0.0513. Nevertheless, the Raja et al[15] study reported that atorvastatin along with aspirin was the most frequently prescribed likely due to the presence of comorbid conditions in those patients.

The study found a significant relationship between VLDL levels and gender (p-value 0.034). In contrast, Shahwan et al[16] reported a significant difference in HDL cholesterol (HDL-C). Furthermore, we observed significant variations in cholesterol and triglyceride levels among the age group of 45 to 59 years (p-value 0.026 for cholesterol and p-value 0.007 for triglycerides). Conversely, a study conducted in China by Wei et al[17] reported higher incidences of LDL, total cholesterol, and non-HDL-C in nonelderly patients (< 60 years).

Strength and Limitations

The strength of the study is that we analyzed the medication approach of both antidiabetic and hypolipidemic agents in dyslipidemic patients with diabetes mellitus. However, there were some limitations to the study, including the retrospective design, the limited sample size, and the short duration of the study. Additionally, we did not evaluate the effectiveness of the therapy, which could be done in a larger prospective study over a longer period of time.

Conclusion

Metformin and glimepiride were the predominant oral hypoglycemic agents prescribed, while human insulin was the preferred option for insulin therapy. Atorvastatin was identified as the most commonly prescribed medication for managing dyslipidemia, often administered at lower dose intensities. The combination of atorvastatin and fenofibrate was frequently prescribed. These findings offer crucial insights to health care professionals, to provide precise treatment approaches for patients.

Ethical Approval

The study was approved by the Institutional Ethics Committee, NGSM Institute of Pharmaceutical Sciences, Nitte (Deemed to be University), Karnataka, India (Ref No: NGSMIPS/IEC/11/2021).

Conflict of Interest

None declared.

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