Assessment of Low-Density Lipoprotein Cholesterol (LDL-C) Goal Achievement Rate among Type 2 Diabetic Patients in Security Forces Hospital Diabetic Center, Riyadh, Saudi Arabia

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Abstract

Background: Diabetes mellitus is a cardiovascular risk equivalent and associated with a higher risk of cardiovascular mortality comparing with general population. Small low-density lipoprotein cholesterol (LDL-C) particle size, which is highly atherogenic, is significantly associated with progression of coronary artery disease. American Diabetes Association (ADA) and National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III recommend aggressive dyslipidemia management in diabetic patients with a primary of LDL-C level < 100 mg/dL (<2.6 mmol/L).

Objective: To determine the achievement rate of LDL-C goal in type 2 diabetic patients in Saudi visiting the Diabetic Center at primary care department in Security Forces Hospital, Riyadh, Saudi Arabia, according to the ADA and NCEP (ATP III) guidelines and to assess the physicians' treatment prescribing pattern to achieve that goal.

Materials and Methods: After the Hospital Research Committee approval, the descriptive chart review study was conducted over 1,270 diabetic patients registered in Diabetic Center from January 1, 2013 to December 31, 2013. The data were extracted by Information Technology department using computerized system and analyzed by SAS/STAT software with appropriate analytical tests.

Result: The LDL-C goal achievement rate was 47.95%. About 95.5% of diabetic patients were using statin therapy, but 51.77% among them were out of goal and reached the maximum statin dose of 60 mg by only 2.74%. Despite being out of target, 75.99% had no change in dose, 5.83% had decreased the dose although they were still out of goal, and 18.18% only had increased the dose.

Conclusion: About half the number of patients (47.953%) achieved the LDL-C goal, and, as a result of physicians' treatment prescribing pattern, there is inappropriate statin titrating and dosing to achieve the goal.

KEY WORDS: Low-density lipoprotein cholesterol (LDL-C), type 2 diabetes mellitus, control, Saudi Arabia

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Introduction

According to the National Cholesterol Education Program (NCEP) Guideline and the UK Prospective Diabetes Study (UKPDS), low-density lipoprotein cholesterol (LDL-C) was found to be a causative and strongest independent predictor of cardiovascular disease (CVD). On the basis of this, there are many current international guidelines advocating

LDL-C < 100 mg/dL as the primary target for the management of dyslipidemia in patients with type 2 diabetes.[1–4]

Dyslipidemia is one of the modifiable CVD risk factor, but it unfortunately remains largely uncontrolled in patients with type 2 DM.[3] It should be managed aggressively as recommended by both the NCEP and American Diabetic Association (ADA) to achieve the LDL-C goal and improve long-term cardiovascular outcomes.[1,5] About half the number of the patients with type 2 diabetes mellitus (DM) exhibit dyslipidemia. This dyslipidemia is associated with highly atherogenic small LDL-C particle size, which is significantly associated with the progression of coronary artery disease.[3,6] The prevalence of DM was found to be 23.7% in Kingdom of Saudi Arabia (KSA) in 2004 in one of the studies done by Al-Nozha et al,[7] while the prevalence of high LDL-C according to Adult Treatment Panel (ATP) III guidelines among 507 diabetic patients was 77.1% according to the study done by Habib in 2006.[8]

There are different studies available, which show that this dyslipidemia can be controlled by statins. One such study done by Waters et al.[9] in L-TAP2 (Lipid Treatment Assessment Project 2) showed that, among people treated with statins, 67% reached NCEP LDL-C goal in the high-risk group that included diabetic patients. Goal achievement found to be quiet low (38%) in REALITY-Asia study for diabetes subgroup without CVD[10] and quiet high (87.4%) in CEPHUS study.[11] In a national study done by Guzu et al.,[12] it resulted in low LDL-C goal achievement among diabetic patients by 27.6%. However, Andrews et al.[13] in ACCESS demonstrated that it is possible to achieve NCEP targets in 80% or more of people with aggressive statin treatment.

So, this study was planned with the aim of decreasing the cardiovascular risk in diabetic patients, to determine the achievement rate of LDL-C goal among them according to the ADA and NCEP (ATP III) guidelines, and to address the physicians' treatment prescribing pattern for those patients with uncontrolled LDL-C.

Study Objectives
Primary Objectives
- To determine the achievement rate of LDL-C goal according to the ADA and NCEP (ATP III) guidelines among type 2 diabetic patients in Saudi visiting the Diabetic Center Clinics in Family Medicine Department at Security Forces Hospital, Riyadh, KSA.
- To assess the physicians' treatment prescribing pattern to achieve the LDL-C goal.

Secondary Objective
- To study the association between failure of LDL-C goal achievement and study variables.

Materials and Methods

Study Design and Setting
A descriptive observational study was conducted over the Diabetic Center at primary care department in Security Forces

Hospital, Riyadh, KSA, from January 1, 2013 to December 31, 2013. Security Forces Hospital is one of the major hospitals in Riyadh, which provide the health care for the Ministry of Interior employees and their families. The primary care department is the gate of the hospital and the first place to contact by the patients. Diabetic Center has a special system to ensure providing the recommended and appropriate care for type 2 diabetic patients.

Inclusion Criteria
1. All type 2 diabetic patients, both genders, aged ≥ 20 years.
2. Those with at least two lipid profile readings in the period from January 1, 2013 to December 31, 2013.
3. Eligible to get care and registered in Diabetic Center in primary care department.

Our criteria came out with 1,270 patients, and, because the study design is descriptive in nature, all of them were enrolled in the study.

Exclusion Criteria
1. Patients with other comorbidities apart from diabetes that affect lipid profile such as hypothyroidism, familial hypercholesterolemia, nephrotic syndrome, obstructive liver disease, and patients following renal transplantation.[14–16]
2. Those patients who cannot tolerate lipid-lowering agents such as patients with an active liver disease, cirrhosis or liver failure, and pregnant women in the same period of study were excluded.

Data Collection Tool
The patients' data in the medical record (MR-V) computerized program, which are used to monitor and follow up the patients through pharmacological and laboratory assessments, were taken and extracted by Information Technology via the computerized system, and the row data were received on excel sheet ready for analysis.

Study Variables and their Working Definition
- Demographic data: Patient's age, gender, and body mass index (BMI).
- DM: (Diagnosis based on ADA criteria), at least two readings of FBS ≥ 126 mg/dL (≥ 7 mmol/L), HbA1c ≥ 6.5% (48 mmol/mol), or OGTT 2h after 75g anhydrous glucose ≥ 200 mg/dL (≥ 11.1 mmol/L) and diabetes control if HbA1c < 7.[17]
- Lipid profile: According to NCEP and ATP III, LDL-C target for diabetic patients is < 100 mg/dL, high-density lipoprotein (HDL-C) target ≥ 40 mg/dL, triglycerides target <150 mg/dL, and total cholesterol target <200 mg/dL.[14]
- "The LDL-C goal achievement is considered if the last two consecutive readings with 3–6 months apart were both <100 mg/dL (<2.6 mmol/L)."
- Hypertension: According to the ADA, systolic blood pressure (SBP) ≥140 mmHg and diastolic blood pressure (DBP) ≥80 mmHg or patients taking antihypertensive treatment.[17]

- Using of lipid-lowering agents: atorvastatin, simvastatin (statins), gemfibrozil, or ezetimibe.
- Changing in the statin dose: On the basis of LDL-C reading, whether increase, decrease, or remain unchanged.
- Using of insulin or oral hypoglycemic agents.

Statistical Analysis

All statistical analysis was performed using SAS/STAT software. Continuous variables were expressed as mean ± standard deviation and categorical variables expressed as number and proportions (%). The statistically significant result was set at $p < 0.05$ by using Student's t-test for continuous variables and χ^2-tests for categorical variables, while multivariate logistic regression analysis was performed to identify the variables associated with failure of LDL-C goal achievement.

Ethical Consideration

After the Hospital Research Committee approval, this study was conducted without violating the privacy and confidentiality of the enrolled patients. So, all data were extracted without knowing the patients names and personal data.

Result

Clinical and Biochemical Characteristics of Subject

The mean age of patients was 57.69 ± 11.37 years. Male patients were 49.8%. On an average, the patients were obese with a mean BMI of 31.12 kg/m². The proportions of uncontrolled DM were 79.2%, cholesterol: 2.9%, triglycerides: 22.4%, HDL-C: 59.4%, SBP: 28.2%, and DBP: 16.2%. About half the number of the patients was using insulin (50.6%); about 95.5% were on the statin, and only 1% had combined lipid-lowering agents as shown in Table 1.

Achievement Rate of LDL-C Goal

The LDL-C goal achievement among type 2 diabetic patients in Saudi visiting the Diabetic Center in Family Medicine department at Security Forces Hospital, Riyadh, KSA was 47.95% as shown in the [Figure 1].

Physicians' Treatment Prescribing Pattern

Among patients who were using statin (95.5%), there was 51.77% who had uncontrolled LDL-C, 75.99% of them who had no change in statin dose, while 18.18% who only had increased it and 5.83% who had decreased the dose although they were still uncontrolled as shown in [Figure 2]. The maximum dose reached for those not achieving the LDL-C goal was 60 mg of statin by only 2.74%, and most of them were on 10 mg (29.16%) and 20 mg (40.82%) of statin as shown in [Figure 3]. Among patients on the statin, 48.23% had controlled LDL-C, 89.42% of them remained on the same dose, while the dose was increased in 6.54% and decreased in 4.04% as shown in [Figure 2]. Only 0.58% of patients
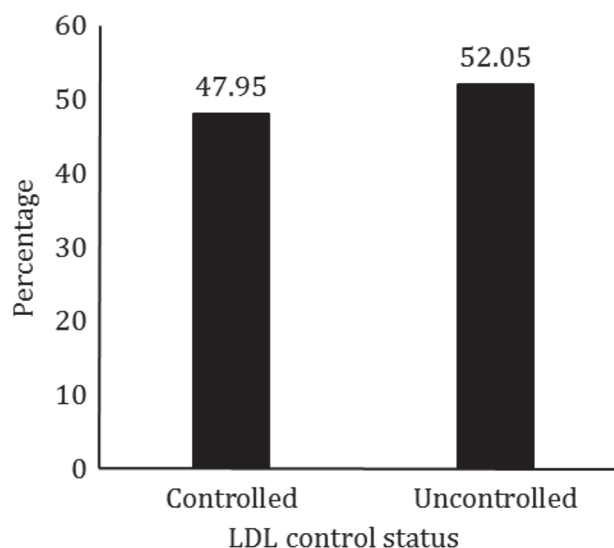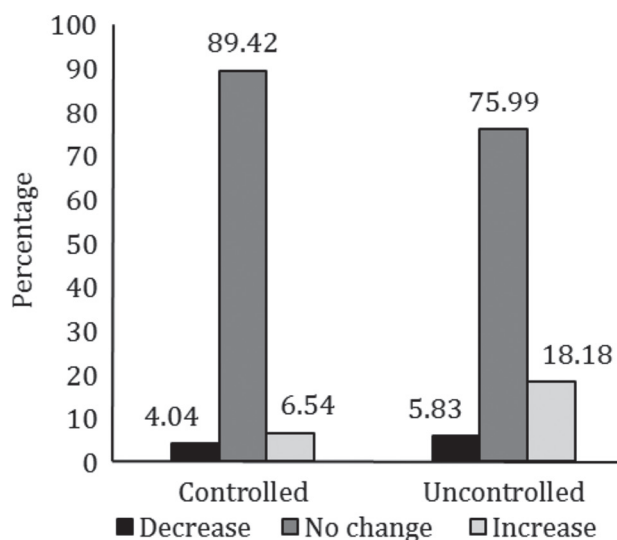

Figure 1: Achievement rate of LDL-C.

Figure 2: Changing rate in statin dose among controlled and uncontrolled LDL-C patients.

achieving the LDL-C goal reached the 60 mg of statin, and most of them were controlled on 10 mg (41.73%) and 20 mg (43.46%) of statin dose as shown in [Figure 3].

Association between Uncontrolled LDL-C with Study Variables

The controlling status of LDL-C as shown in Tables 2 and 3 is affected by:

- Age: Among diabetic patients with uncontrolled LDL-C, the mean age was 58.75±11.41 years comparing with 56.72 ± 11.25 years in controlled LDL-C [(odds ratio (OR): 1.01, $p = 0.001$].
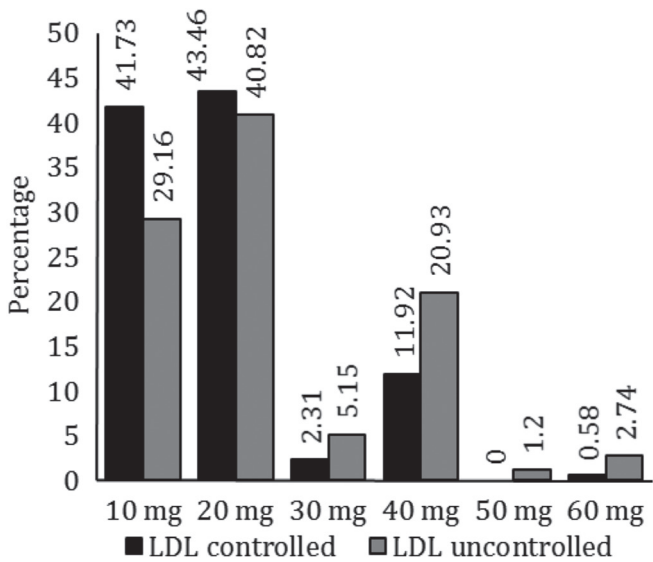
Figure 3: The rate of statin doses reached among controlled and uncontrolled LDL-C patients.

- Insulin usage: About 54.9% of diabetic patients on insulin showed uncontrolled LDL-C (OR: 1.261, *p* = 0.040).
- Changing of statin dose: About 61.82% in total dose decrement were uncontrolled, 48.79% for those with no dose change were uncontrolled, while 75.71% in total dose increment were out of goal (OR: 3.272, *p* <0.001).
- Diabetes status: For uncontrolled diabetic patients, about 54.74% were out of LDL-C goal and 41.83% out of goal, although they were with controlled diabetes (OR: 1.682, *p* <0.001).
- Cholesterol status: In diabetic patients with control of cholesterol, about half the number of them (50.61%) were out of LDL-C, and all of the patients (100%) were out of LDL-C goal if the cholesterol was uncontrolled (OR: 37.19, *p* < 0.001).
- The gender, BMI, using of statin, triglyceride control status, the level of HDL, and hypertension did not affect the controlling status of LDL-C and showed insignificant *p* value for all as shown in Tables 2 and 3. With logistic regression analysis in Table 4, LDL-C being out of goal is shown to be highly associated with dose increment of statin, uncontrolled diabetes, and while in advance age with OR/ *p* (3.05/<0.001, 1.65/0.001, and 1.02/0.002), respectively.

Table 1: Clinical and biochemical characteristics

Variable	Level	N = 1,270	%
Age	Mean ± SD	57.69 ± 11.37	–
BMI	Mean ± SD	31.12 ± 4.26	–
Gender	Female	638	50.2
	Male	632	49.8
Insulin	No	627	49.4
	Yes	643	50.6
Statin	No	57	4.5
	Yes	1,213	95.5
Combined lipid-lowering agents	No	1,285	99
	Yes	12	1
Dose	Decrease	55	5
	No change	908	82.3
	Increase	140	12.7
Diabetes mellitus	Controlled	263	20.8
	Uncontrolled	1,007	79.2
Cholesterol	Controlled	1233	97.1
	Uncontrolled	37	2.9
Triglyceride	Controlled	985	77.6
	Uncontrolled	285	22.4
HDL-C	Controlled	516	40.6
	Uncontrolled	754	59.4
Systolic blood pressure	Controlled	910	71.8
	Uncontrolled	358	28.2
Diastolic blood pressure	Controlled	1063	83.8
	Uncontrolled	205	16.2

Table 2: LDL-C control status in study variables

Covariate	Statistic	Level	LDL-C control status		p^*
			Controlled, $N = 609$	Uncontrolled, $N = 661$	
Age	Mean ± SD	–	56.72 ± 11.25	58.75 ± 11.41	**0.001**
BMI	Mean ± SD	–	31.27 ± 4.23	30.99 ± 4.92	0.245
Insulin	N (%)	No	319 (50.88)	308 (49.12)	**0.040**
	N (%)	Yes	290 (45.1)	353 (54.9)	
Statin	N (%)	No	24 (42.11)	33 (57.89)	0.367
	N (%)	Yes	585 (48.23)	628 (51.77)	
Dose	N (%)	Decrease	21 (38.18)	34 (61.82)	**<0.001**
	N (%)	No change	465 (51.21)	443 (48.79)	
	N (%)	Increase	34 (24.29)	106 (75.71)	
Diabetes mellitus	N (%)	Controlled	153 (58.17)	110 (41.83)	**<0.001**
	N (%)	Uncontrolled	454 (45.26)	549 (54.74)	
Cholesterol	N (%)	Controlled	609 (49.39)	624 (50.61)	**<0.001**
	N (%)	Uncontrolled	0 (0)	37 (100)	
Triglyceride	N (%)	Controlled	478 (48.53)	507 (51.47)	0.446
	N (%)	Uncontrolled	131 (45.96)	154 (54.04)	
HDL-C	N (%)	Controlled	253 (50.97)	263 (49.03)	0.525
	N (%)	Uncontrolled	356 (47.21)	398 (52.79)	
Systolic blood pressure	N (%)	Controlled	440 (48.35)	470 (51.65)	0.648
	N (%)	Uncontrolled	169 (46.94)	191 (53.06)	
Diastolic blood pressure	N (%)	Controlled	509 (47.83)	555 (52.17)	0.795
	N (%)	Uncontrolled	100 (48.55)	106 (51.45)	

*p value is calculated by t-test for numerical covariates and χ^2-test for categorical covariates.

Table 3: The association between uncontrolled LDL-C and study variables

Covariate	Level	Odds ratio	95%CI	p^*
Age	Increase	1.01	1.006–1.03	**0.001**
BMI	–	0.985	0.960–1.011	0.245
Insulin	Yes	1.261	1.011–1.572	**0.040**
	No	–	–	–
Statin	Yes	0.781	0.456–1.337	0.367
	No	–	–	0.063
Dose	Decrease	1.699	0.971–2.973	**<0.001**
	Increase	3.272	2.177–4.919	–
	No change	–	–	–
Diabetes mellitus	Uncontrolled	1.682	1.278–2.214	**<0.001**
	Controlled	–	–	–
Cholesterol	Uncontrolled	73.19	4.48–1194.67	**<0.001**
	Controlled	–	–	–
Triglyceride	Uncontrolled	1.108	0.851–1.443	0.446
	Controlled	–	–	–
HDL-C	Uncontrolled	1.075	0.860–1.346	0.525
	Controlled	–	–	–
Systolic blood pressure	Uncontrolled	1.059	0.829–1.353	0.648
	Controlled	–	–	–
Diastolic blood pressure	Uncontrolled	0.961	0.713–1.296	0.795
	Controlled	–	–	–

*p value is calculated by t-test for numerical covariates and χ^2-test for categorical covariates.

Table 4: The association between uncontrolled LDL-C and study variables after logistic regression analysis

Covariate	Level	Odds ratio	95%CI	p*
Dose	Increase	3.05	2.02–4.60	<0.001
Diabetes	Uncontrolled	1.65	1.22–2.23	0.001
Age	Increase	1.02	1.01–1.04	0.002

*p value is calculated by logistic regression analysis.

Discussion

On the basis of ADA and NCEP (ATP III) recommendation, about half the number of our diabetic patients (47.95%) achieved the LDL-C < 100 mg/dL (<2.6 mmol/L), and this rate of achievement is reasonable worldwide because of the difficulty to achieve this goal in most of the diabetic patients as seen in most of the studies. Our achievement rate is exceeding that in national study conducted at Al Kharj military hospital, where the LDL-C goal attained by 27.6% only in diabetic patients.[12] In comparison to international study, the achievement rate in (L-TAP 2) in high-risk group was 67%, which includes patients from the United States, Canada, Spain, Netherlands, France, Taiwan, Korea, Brazil, and Mexico.[9]

In the latest NHANES study, the LDL-C goal achievement among diabetic patients in the United States was improved from 29.7% to 54.4%.[18] The EUROASPIRE I and II surveys showed two-thirds of the diabetes subgroup taking lipid-lowering agents, and only 32.4% achieved the LDL-C goal.[19] Surprisingly, 87.4% of diabetic patients attained their LDL-C goals in CEPHUS study.[11] So, our goal achievement rate for LDL-C is reasonable in comparison to the worldwide and local studies.

In our study, it was found that 75.99% of patients had no dose change, 5.83% decreased the dose although they were still out of goal, and 18.18% only increased the dose. Similar findings were observed in OLIMPIC study in Greece.[20] A study done in England,[21] which found most patients who begin treatment with statin remained at the initial dose and had inappropriate dose titration, which led to failure to achieve LDL-C. Moreover, in REALITY-Asia study, the statin doses in 80% of cases were not up-titrated or switched to a different drug, despite being out of LDL-C goal, and 89% of the patients were taking low- or moderate-potency statins.[10]

Underutilization of lipid-lowering agents among diabetic patients is a worldwide problem. In our study, it was seen in about 4.5% of diabetic patients who were not treated with statin, 57.89% of them who were out of LDL-C goal and accounted of 33 patients but is a low percentage when compared with the recent NHANES study where 42.2% of diabetic patients were taking lipid-lowering agents and just 54.4% achieving the LDL-C goal.[18] Moreover, a recent evaluation of the pharmacological treatment of mixed dyslipidemia in diabetic patients from a large US-managed health-care plan found that > 40% received no lipid-lowering therapy despite being out of LDL-C goal.[22]

With aggressive treatment as recommended by the NCEP and ADA, the achievement rate of LDL-C will improve.[1,5] In the Diabetes Atorvastatin Lipid Intervention (DALI) study, intensive therapy with 80 mg atorvastatin was significantly (p < 0.001) more effective in lowering LDL-C (–52%) than atorvastatin 10 mg (41%).[23] The reason behind underutilization, inappropriate titrating, and dosing can be explained by physicians' concern about statin side effect as reported by Rzouq et al.[24] But, as Kuznik Mardekian reported that is false concern and not supported by current evidence from randomized trials and meta-analysis, which demonstrate the safety and tolerability of statin.[18]

Because of the presence of CVD, the minimum target of LDL-C in our diabetic patient that should be achieved is <100 mg/dL (2.6 mmol/L); that explains those out of goal may consider as very high-risk patients in the presence of CVD or CVD risk equivalents, which will lower the target to <70 mg/dL (<1.8 mmol/L) as recommended by ADA and NCEP (ATP III) guidelines.[4,14] This target is difficult to achieve, and about 25% would require more than to lipid-lowering agents at maximum doses to attain this goal as reported by Kennedy et al.[25] In our study, only 1% had combined lipid-lowering agents. Russell et al.[26] found there is no clear target for diabetic patients without CVD, and this result seems to be supported by Stones et al.[27] in new blood cholesterol guidelines, because there is no LDL-C target for diabetic patients and, moderate- to high-intensity statin should be started for diabetic patients from 40 to 75 years.

In our study, after logistic regression analysis, the association between uncontrolled LDL-C and statin dose increment could be explained by a good response of physicians to increase the dose but is not as needed to achieve the goal. Moreover, the short period of statin treatment after increasing the dose may be not enough to overcome the uncontrolled LDL-C.

While the association of uncontrolled LDL-C with advanced age was seen with Yan in REALITY Asia study, which found those with advancing age were highly associated with LDL-C goal achievement, it could be owing to many reasons such as different lifestyle and compliance to treatment.[28] Finally, the result of the association between uncontrolled DM and failure to achieve the LDL-C in our study is expected and supported by many of the studies as found with the same result in the study done by Hildemann et al.[29]

Strengths and Limitations

Major strengths of our study are the following:

We consider tackling the important topic with known burden on health and economic status, being the first study in KSA, which assess the physicians' prescribing treatment pattern for uncontrolled LDL-C and address the status of LDL-C among diabetic patients with good sample size.

The limitations of the study were:

Limited variables were studied owing to limitation of database; so, other variables affecting the LDL-C controlling status were not studied such as presence of CVD or CVD risk equivalent,

which lead to lower target of LDL-C among diabetic patients to < 70 mg/dL (<1.8 mmol/L) as recommended by ADA and NCEP (ATP III) guidelines,[12,22] family history of CVD, socio-economic status, education level, smoking, medical nutrition therapy, exercise, alcohol intake, compliance to lipid-lowering agents, and diabetic therapy.

Conclusion

About half of type 2 diabetic patients in Saudi (47.953%) visiting the Diabetic Center in Family Medicine Department at Security Forces Hospital, Riyadh, KSA, were achieving the LDL-C goal. There is inappropriate titrating-up of the statin to achieve the LDL-C goal as shown in the result of physicians' treatment prescribing pattern.

Recommendations

More aggressive treatment and adherence to ADA and NCEP (ATP III) guidelines, which need more continuous medical education and assessment, will impact with better goal achievement rate.

Acknowledgment

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