

Dyslipidemia among People with Diabetes: Control and Pattern of Prescribing

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Objective: To evaluate lipid control and drugs used in the management of diabetic people with dyslipidemia.

Design: A retrospective clinical study.

Setting: NBB Dair Health Center.

Method: Copies of prescriptions for people with diabetes from 2 January 2011 to 30 April 2011 were retrieved. Prescriptions containing anti-lipid medications were screened. The charts of these patients were reviewed. Data collected include age, sex, lipid profile, drug used and its dose, compliance with liver enzymes monitoring and their levels and the use of combination drugs. In addition, the total number of visits made by the patients during 2010 was documented.

Result: Four hundred twenty-six patients were included in the study. Two hundred sixty (61%) were females. Two hundred fifty-five patients (59.8%) achieved LDL <2.6 (<100 mg/dL). Triglycerides target (<1.7; <150 mg/dL) was achieved in 247 (58%) patients. HDL target (>1; >40) was achieved in 297 (69.7%) patients; one hundred thirty-three patients (31.2%) achieved these three targets. Two hundred thirty-three patients (55%) were using either Pravastatin 20 mg or Simvastatin 20 mg. Four patients (0.94%) were on combination of statins and Bezafibrate. No significant gender difference in the level of control and statins doses was found.

Conclusion: The study revealed that the management of dyslipidemia among people with diabetes is suboptimal. Using moderate to high potency statins and/or combination is needed to increase the number of patients who meet guidelines recommendations.

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Diabetes mellitus is a common complex metabolic disorder, which has a significant impact on health, quality of life, life expectancy and healthcare system. It is a highly prevalent non-communicable disease worldwide especially in developing countries¹. The estimated prevalence in 2010 showed that five of the Gulf States, including Bahrain, were among the top ten countries.

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The prevalence in Bahrain is 15.4%, and it is expected to rise to 17.3% by the year 2030¹.

Cardiovascular disease (CVD) is the single most common cause of death worldwide. It is the main cause of morbidity and mortality in people with diabetes. The risk of death from CVD is more than twice that in patients without diabetes². Furthermore, studies have found that the contribution of diabetes to CVD has increased^{3,4}. Therefore, interventions to control cardiovascular risk factors associated with diabetes is important. According to a study, risk factors were increased concentrations of low-density lipoprotein cholesterol (LDL), decreased concentrations of high-density lipoprotein cholesterol (HDL), raised blood pressure, hyperglycemia and smoking⁵.

While intensive control of blood sugar had not resulted in significant reduction of cardiovascular events in recent large clinical trials and an increased mortality in one study, a linear relationship has been found between reduction of serum cholesterol, LDL and CVD⁶⁻¹¹. A meta-analysis of 14 trials found that major coronary events and stroke could be reduced by about one-fifth for each one mmol decrease in LDL cholesterol; this highlights the importance of dyslipidemia as a modifiable risk factor in these people¹¹.

Statins (3-hydroxy-3-methylglutaryl coenzyme-A reductase inhibitors) is one of the most useful and important drug group, which have been introduced in the nineteen-eighties of the last century. These drugs work primarily on LDL and to a lesser extent on HDL and triglycerides. The efficacy of these drugs to reduce major cardiovascular events have been found in both primary and secondary prevention trials, including those that were done exclusively in people with diabetes¹²⁻¹⁷. Despite that, many studies have found that management of dyslipidemia is far from optimal and tend to be worse in high-risk patients, such as those people with diabetes¹⁸⁻²⁴. Data about the management of this condition among people with diabetes at National Bank of Bahrain Health Center at Dair (NBB Dair) is lacking.

The aim of this study is to evaluate lipid control and pattern of drugs used in the management of diabetic patients with dyslipidemia.

METHOD

Copies of prescriptions for people with diabetes from 2 January 2011 to 30 April 2011 were retrieved. Prescriptions, which contained anti-lipid medications, were screened by the author. The charts of the patients were reviewed by the author.

Patients were included in the study if they met the following criteria: full lipid profile (total cholesterol, LDL, HDL and triglycerides) is available during the year 2010 or 2011, and if the patient attended at least three diabetes-related visits during 2010. Data collected include age, sex, lipid profile, drug used and its dose, compliance with liver enzymes monitoring and their levels and the use of drug combination. In addition, the total number of visits (diabetes and non-diabetes related) made by the patients during 2010 was documented. The number of visits was available for 313 patients only. The definition of control of lipid profile components was used in this study is according to National Cholesterol Educational Program Adult Treatment Panel III (NCEP ATP III) and American Diabetes Association (ADA) recommendations²⁵⁻²⁷.

Data were analyzed by using the Epi-info Program (version 3.5.1). Chi-squared test was used to assess gender difference in the level of control, types and dose of statins used and the number of visits. P value of 0.05 or less was considered statistically significant.

RESULT

Five hundred eleven prescriptions were retrieved. Four hundred twenty-six patients met inclusion criteria and their data were analyzed. All patients, except one, were type 2. Two hundred sixty patients (61%) were females. One hundred fifty-six (36.6%) patients were ≥ 60 years. Distribution of the total sample according to age and sex is presented in table 1.

Table1: Sample Distribution by Age Group and Sex

Age Group (years)	Males (number and percentage)	Females (number and percentage)	Total
< 40	4 (2.4)	10 (3.8)	14 (3.3)
40 - 49	37 (22.3)	48 (18.5)	85 (20)
50 - 59	66 (39.8)	105 (40.4)	171 (40.1)
≥ 60	59 (35.5)	97 (37.3)	156 (36.6)
Total	166 (100)	260 (100)	426 (100)

P=0.688

No statistical gender difference in age distribution was found, see table 1. Two hundred fifty-five (59.8%) and two hundred forty-seven (58%) achieved LDL and triglycerides targets, respectively. Ten patients (2.3%) have ischemic heart disease; six achieved LDL <2.6 mmol/L, three achieved LDL <1.8 mmol/L (<70 mg/dL).

Two hundred ninety-seven (69.7%) patients had achieved HDL target. ADA HDL target for females (>1.3 mmol/L, >50 mg/dL) was achieved in 116 (116/260; 44.6%). The targets for LDL, HDL and triglycerides combined (Optimal Lipid Profile; OLP) were achieved in 133 (31.2 %) patients. Distribution of lipid profile according to age and sex is presented in table 2.

Table 2: Lipid Control by Age and Sex

Age (years)	Females (number and percentage)	Males	Total	P value
LDL (<2.6 mmol/L, <100 mg/dL)				
< 40	6 (3.8)	2 (2)	8 (3.1)	
40 - 49	34 (21.7)	19 (19.4)	53 (20.8)	
50 - 59	61 (38.8)	43 (43.9)	104 (40.8)	0.765
≥ 60	56 (35.7)	34 (34.7)	90 (35.3)	
Total	157 (100)	98 (100)	255 (100)	
HDL (>1 mmol/L, > 40 mg/dL)				
< 40	7 (2.6)	2 (2)	9 (2.4)	
40 - 49	35 (17.9)	22 (21.6)	57 (19.2)	
50 - 59	82 (42.1)	41 (40.2)	123 (41.4)	0.772
≥ 60	73 (37.4)	37 (36.3)	110 (37)	
Total	195 (100)	102 (100)	297 (100)	
Triglycerides (<1.7 mmol/L, <150 mg/dL)				
< 40	7 (4.5)	2 (2.2)	9 (3.6)	
40 - 49	27 (17.4)	16 (17.4)	43 (17.4)	
50 - 59	57 (36.8)	33 (35.9)	90 (36.5)	0.794
≥ 60	64 (41.3)	41 (44.5)	105 (42.5)	
Total	155 (100)	92 (100)	247 (100)	
Optimal Lipid Profile (OLP)				
< 40	2 (2.4)	2 (4)	4 (3)	
40 - 49	18 (21.7)	9 (18)	27 (20.3)	
50 - 59	28 (33.7)	20 (40)	48 (36.1)	0.815
≥ 60	35 (42.2)	19 (38)	54 (40.6)	
Total	83 (100)	50 (100)	133 (100)	

The table reveals was no significant gender difference in the level of control of lipid profile components, including those who achieved OLP.

Forty-six patients (46/255; 18%) with controlled LDL cholesterol had triglycerides >2.25 mmol/L (>200 mg/dL). Twenty-eight (58.3%) of these patients (11 males and 17 females) had uncontrolled non-HDL cholesterol (>3.36 mmol/L; >130 mg/dL).

Statins were used in 415 patients (97.4%). Drugs used by the patients and dosages in relation to gender are presented in table 3.

Table 3: Relationship between Statins Used, Dosages and Sex

Drugs Used	Males	Females	Total	P value
	(number and percentage)			
Pravastatin (20 mg)	35 (21.1)	74 (28.5)	109 (25.6)	0.34
Pravastatin (40 mg)	9 (5.4)	12 (4.6)	21 (4.9)	
Simvastatin (20 mg)	51 (30.7)	75 (28.8)	126 (29.6)	0.36
Simvastatin (40 mg)	24 (14.6)	26 (10)	50 (11.7)	
Atorvastatin (10 mg)	8 (4.8)	7 (2.7)	15 (3.5)	0.41
Atorvastatin (20 mg)	14 (8.4)	26 (10)	40 (9.4)	
Atorvastatin (40 mg)	4 (2.4)	4 (1.5)	8 (1.9)	
Fluvastatin (80 mg)	16 (9.6)	28 (10.8)	44 (10.3)	NA*
Bezalip (400 mg)	4 (2.4)	7 (2.7)	11 (2.6)	NA
Others**	1 (0.6)	1 (0.4)	2 (0.5)	NA
Total	166 (100)	260 (100)	426 (100)	

*NA= Not Applicable **One on Simvastatin 10 mg and one on Rosuvastatin 10 mg

The table shows that more than half of the patients (235/426; 55.2%) were on either Pravastatin 20 mg or Simvastatin 20 mg. However, no significant gender difference in statins used across the doses range. Four patients (0.94%) were on combination therapy (statin + Bezalip).

Screening for Alanine Aminotransferase (ALT) was done for 401 (94.1%) patients. It was > 3 times the upper limit of normal in two patients (0.5%); one female patient was on Simvastatin 20 mg and the other was a male on Atorvastatin 20 mg.

The number of visits made by the patients during 2010 and the relationship between the number of visits and lipid profile control in both sexes is presented in table 4 and 5, respectively. The number of visits was available for 313 patients only.

Table 4: Number of Visits during the Year

Number of Visits	Females	Males	Total	P value
	(number and percentage)			
3 - 6	62 (31.5)	48 (41.4)	110 (35.1)	0.024
7 - 10	73 (37)	47 (40.5)	120 (38.3)	
11 - 14	38 (19.3)	17 (14.7)	55 (17.6)	
> = 15	24 (12.2)	4 (3.4)	28 (9)	
Total	197 (100)	116 (100)	313 (100)	

Table 5: Relationship between Number of Visits and Level of Control

Number of visits	Controlled LDL			P value	Controlled HDL			P value	Controlled Triglycerides			P value
	M	F	T		M	F	T		M	F	T	
3 - 6	27	37	64	0.7	31	52	83	0.63	25	30	55	0.35
7 - 10	30	49	79		33	61	94		25	47	72	
11 - 14	10	20	30		13	32	45		11	23	34	
>= 15	3	12	15		3	20	23		0	15	15	

M=Males, F=Females, T=Total

Eighty-three (26.6%) patients visited the health center more than 10 times during 2010, see table 4. It shows that females were more likely to attend the health center frequently than males ($p=0.024$). However, the number of visits did not affect the level of lipid control, see table 5.

DISCUSSION

The study showed that about 60% of the patients achieved LDL target. OLP was achieved in about one-third (31.2%). There was no statistically significant gender difference in the level of control. More than half of the patients (55.2%) were on either Pravastatin 20 mg or Simvastatin 20 mg. No statistical significant gender difference in the range of drug doses was found. The study also showed that combination therapy was used in less than one percent of the patients. Higher number of visits was significantly common among females, but this has not been found to affect the level of lipid control.

While there is a room for improving the level of LDL control, the result is similar to some studies and better than others including recent ones^{18-21,23,24}. This indicates that management of this condition remains suboptimal and highlights the need for more aggressive intervention. The reasons for suboptimal achievement in this study include the use of lower doses and low potency statins, underuse of drug combination and patients and physicians adherence.

Table 3 shows that 55.2% of patients are using 20 mg of either Pravastatin or Simvastatin. The use of subtherapeutic or low potency statins is common and has been found in several studies^{22,28}. The desirable outcome found in most clinical trials resulted from lowering LDL by at least 30-40% from baseline level; this is found even in patients with (normal) LDL level at baseline¹². Hence, American Diabetes Association recommends lowering LDL by at least 30-40%²⁷. Indeed, other guidelines recommend 50% decrease^{29,30}.

Some studies have found that Pravastatin 20 mg will reduce LDL by around 25%, which is equivalent to less than 1.5 mmol/L³¹⁻³⁴. While Simvastatin can reduce LDL by around 35%, it is important to keep in mind that there is a difference between the efficacy of these drugs (as shown in clinical trials) and their effectiveness in real practice³¹⁻³³. Effectiveness is usually lower because it is affected by many factors, such as, adherence to and persistence with treatment. Further, it is known that there is a non-linear dose-response relationship for statins (i.e. doubling the dose will add about 6% additional effect)³¹. Therefore, using a low dose or a low potency statins is less likely to achieve the target in these patients. The use of moderate to high potency

statins based on baseline LDL and estimated CVD risk increase the percentage of patients who achieve the required targets and reduce cardiovascular morbidity/mortality^{35,36}.

The study showed that 18% of patients with controlled LDL cholesterol had triglycerides >2.25 (>200 mg/dL). About 60% of these patients had uncontrolled non-HDL. Non-HDL is the secondary target to be controlled after LDL according to NCEP guidelines. Indeed, it was found to be a stronger predictor of CVD than LDL^{37,38}. However, it has been found that achievement of this goal is suboptimal and achieved less frequently than LDL goal²⁰. This further emphasizes the importance of using higher potency statins.

OLP was achieved in less than one-third of the patients, see table 2. This indicates that a large number of patients have mixed dyslipidemia that warrants combination therapy as statins work primarily on LDL. A large study found that despite significant reduction of LDL and triglycerides, 50% continued to have suboptimal HDL after 3 years of follow-up³⁹. Achievement of OLP is important because it was found that patients who had OLP had significant reduction of cardiovascular events when compared to patients who had one or more lipid component not at target^{40,41}.

ACCORD study revealed that the combination of Simvastatin with Fenofibrate resulted in a reduction in the rates of the primary cardiovascular events in 17% of patients who had triglycerides ≥ 2.3 mmol/L (≥ 204 mg/dL) and HDL ≤ 0.9 mmol/L (≤ 34 mg/dL). This might support the use of combination and is consistent with NCEP ATP III guidelines in targeting non-HDL⁴². Unexpectedly, the use of combination was found to be very low, less than one percent in this study.

Adherence to and persistence with the use of statins remain poor and is similar to treatments of other chronic conditions, such as, hypertension⁴³. A study found that the adherence rate is 63% only⁴⁴. Another study found that persistence with statins dropped to 45% after 3 years of treatment⁴⁵. This can have a significant impact on the control rate. Different predictors of non-adherence have been mentioned⁴⁶. Adherence of healthcare providers to CVD guidelines is also suboptimal and needs to be improved⁴⁷.

The study showed that the rate of monitoring of liver enzymes is high (94.1%). Only two patients had high ALT, which is in accord with the established safety of these drugs as found in major trials¹²⁻¹⁴. Combination of statins with fenofibrate was also found to be safe⁴². Screening of other liver enzymes is not recommended because being non-specific to the liver; only ALT is specifically secreted by the liver⁴⁸. Indeed, the need for routine screening has been recently questioned⁴⁹.

In a previous study, gender difference (favoring females) was found in hypertension control and it was hypothesized that it could be related to the number of visits to the health center⁵⁰. This study showed that as the number of visits increases, females were more likely to visit the health center, but this was not found to influence the level of control, see table 4 and 5.

In this study, there was no significant gender difference in the level of control and drugs used. This is in contrast to other studies in which suboptimal control and treatment in females is a

consistent finding and has been speculated as one of the causes of higher mortality among them^{51,52}.

CONCLUSION

This study revealed that the management of dyslipidemia among people with diabetes is suboptimal. Using moderate to high potency statins and/or combination is needed to increase the number of patients who meet guidelines recommendations.

Potential Conflicts of Interest: No

Competing Interest: None, **Sponsorship:** None

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