

## **Control of Diabetic Dyslipidemia in Primary and Hospital Health Care - Analytical Study**

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### **Abstract**

**Introduction:** Diabetic dyslipidemia holds an important impact in cardiovascular morbidity and mortality in patients with diabetes. It is essential to study all factors associated with the management of this condition, where the intensity of a statin represents a crucial criteria. There were no studies that compared different levels of care in the management of diabetic dyslipidemia.

**Objective:** Compare and evaluate the association between the control of diabetic dyslipidemia and the intensity of the statin prescribed by both institutions.

**Methods:** Analytic, cross-sectional study. Sample: diabetic patients with dyslipidemia from USF Almedina (n = 52) and from the diabetes department in CHTMAD. Review of medical records (September 2015 to April 2016). Exclusion criteria: medical appointment or lipid profile  $\geq$  12 months. Statistical analysis: significance level 5%; SPSS v19.0.

**Results:** No significant differences were observed between the two different health care settings and management of diabetic dyslipidemia or with regard to statin intensity applied to the subjects. A very high cardiovascular risk profile in a diabetic patient decreases its chance of attaining proper lipid level control.

Should read.

**Conclusion:** The level of care does not seem to have impact in the management of dyslipidemia, emphasizing the need of establishing joint strategies for improving lipid control.

**Keywords:** *Diabetic Dyslipidemia; Triglycerides (TG); High-Density Lipoprotein (HDL-C); Low-Density Lipoprotein (LDL-C)*

### **Introduction**

Atherogenic dyslipidemia, characterized by an increase in the concentration of triglycerides (TG), a decrease in high-density lipoprotein (HDL-C) and the presence of small and dense low-density lipoprotein (LDL-C) particles, has a crucial impact on morbidity and mortality of the patient with diabetes mellitus (DM). Although they are quantitatively minor lipid changes, there is a need for therapeutic intervention in diabetics to reduce their high cardiovascular risk [1].

LDL-C levels are generally similar to those of the general population, however, "similar to the general population" is different from "adequate levels". According to the results of the Framingham study, which were similar to the UKPDS study, 9% of men and 15% of women

had hypercholesterolemia (similar prevalences in the general population - 11 and 16% respectively) [1-3]. In Portugal, the PREVADIAB study revealed that > 85% of diabetics have LDL-C > 100 mg/dl and the DYSIS study identified 62% of diabetics treated with statins with LDL-C > 100 mg/dL [4,5]. These data reveal the importance of this health problem as well as the difficulty in controlling diabetic-dyslipidemia.

Stratification of cardiovascular risk (CVR) is essential to define the target values, however in the patient with DM2 this stratification is simplified by the fact that these are considered in a high risk category and patients with DM and with one or more cardiovascular risk factors (FRCV) have very high CVR, and therefore have more stringent therapeutic targets [6].

LDL-C reduction continues to be the main target of lipid-lowering and cardiovascular therapy, and secondary targets (total cholesterol, HDL and TG) should be corrected after reaching LDL (except for TG > 500 mg/dl).

The General Directorate of Health recommends a target value of LDL-C < 70 mg/dl or its reduction  $\geq 50\%$  in diabetics at very high cardiovascular risk (CVR) and an LDL-c value < 100 mg/dl in patients classified with high RCV [7].

Statin potency is considered the main criterion for choosing statins. The statin decision to use is one of the most important “steps” to approach diabetic dyslipidemia taking into account therapeutic targets. Although it is possible to think that “little” is better than “nothing”, the truth is that in this case “little” can be “nothing”. Some studies that have assessed the impact of LDL-C reduction on CVR have shown that low-potency statins promote a small reduction in LDL-C and therefore have no impact on RCV reduction [8-10].

The American Diabetes Association (ADA) recommends the use of high-potency statins (atorvastatin 40 - 80 mg or rosuvastatin 20 - 40 mg) in diabetics with CVRD or cardiovascular disease (CVD). In those intolerant to high doses of statin or who have suffered recent acute myocardial infarction and have LDL-C  $\geq 50$  mg/dl, the ADA also recommends the statin/ezetimibe association [11].

The inability to reach the target LDL-C values affects the occurrence of potentially preventable vascular events. Although several studies have been carried out on the referred health problem, which explain the difficulty in controlling diabetic dyslipidemia, the researched literature did not identify studies comparing lipid changes in patients with DM at different levels of health care: primary (CSP) and hospital (CSH). In addition, given that several studies have invoked the hypothesis that statin potency is an essential factor in reaching the target LDL-C values, this study is even more important as it evaluates factors that may be associated with the control of dyslipidemia, namely statin potency.

### Aim of the Study

1. Compare the control of diabetic dyslipidemia in two healthcare institutions: USF Almedina (CSP) and CHTMAD (CSH).
2. Comparison of care institutions in relation to the potency of statins.
3. Assess the association between the control of diabetic dyslipidemia and the potency of the instituted statin.

### Materials and Methods

Cross-sectional analytical study evaluating the control of diabetic dyslipidemia using the registration of serum LDL-C in 2 health care institutions (Diabetology consultation at USF Almedina and Centro Hospitalar de Trás-os-Montes and Alto Douro) them together. This study included patients diagnosed with DM and dyslipidemia followed at the referred institutions and who resulted from the selection of 1 representative and random sample from the USF Almedina (n = 60) and 1 representative and convenience sample from the CHTMAD diabetology consultation (n = 52). Patients with follow-up appointments and with lipid profile assessment for more than 12 months were excluded.

Data collection was carried out between September 2015 and April 2016.

The computerized clinical processes were consulted in the SClinico® computer module to collect the variables. The information medium used was the Microsoft Excel database “BDDD - Diabetes and Dyslipidemia Database”.

Information about the following variables was collected: age; genre; presence of CVRF (LDL-C > 100 mg/dl, HTN, smoking, overweight, obesity); presence of CVD (event CV, SCA); RCV classification (high, very high); statin potency instituted (none, low, moderate and high); serum levels of LDL-C (mg/dl) and HbA1c (%) (last value recorded in the last 12 months).

The following hypotheses were put forward to be analyzed: H0.1 - The control of diabetic dyslipidemia is independent of where the provision of health care (primary or hospital) takes place; H0.2 - The control of diabetic dyslipidemia in CSP and CSH is independent of the potency of the instituted statin. H0.3 - The potency of the statin instituted is independent of where the provision of health care (primary or hospital) occurs.

### Statistical analysis

Quantitative variables were summarized using descriptive statistics, namely mean, median, standard deviation, minimum and maximum. Qualitative variables were summarized by calculating absolute (n) and relative (%) frequencies.

The statistical analysis of the data was conducted through frequency tables for qualitative variables and tables with descriptive statistics for quantitative variables.

The comparisons between patients followed in CSH versus CSP in relation to categorical variables were made using the chi-square test (QQ) or Fisher’s exact test (FS) when the expected frequencies were low.

The comparison between patients followed in CSH versus CSP vis-à-vis quantitative variables was analyzed using the Mann-Whitney (MW) non-parametric test since there was no assumption of normality in at least one of the groups.

The correlation between the LDL-C value and the statin potency was assessed using Spearman’s correlation coefficient.

The results of the multiple logistic regression analysis for the control of diabetic dyslipidemia were presented using odds ratios (OR) and respective 95% confidence intervals. For the initial model, the variables institution, statin potency and those that were statistically significant in the comparative bivariate analysis of the institutions were included. The optimized model presents only the variables with a statistically significant OR.

The statistical tests were carried out bilaterally considering a 5% significance level.

The statistical analysis was performed using the statistical program SPSS v19.0.

## Results

### Sample characterization

This study included 112 participants with diabetes and dyslipidemia. According to table 1, approximately 54% were female and had an average age of  $65.3 \pm 8.9$  years. Approximately 17% of patients had CVRF and CVD, 95.5% had a very high cardiovascular risk and 7.1% were on high-potency statins.

Variables	Total (n = 112)	
<b>Gender, n (%)</b>		
Male	52	46,4%
Female	60	53,6%
<b>Moderate</b>		
CSH	52	46,4%
CSP	60	53,6%
<b>Age (years)</b>		
Mean	65,27	
Standard deviation	11,39	
Minimum	31	
Maximum	90	
<b>FRCV/DCV, n (%)</b>		
Without FRCV or DVC	4	3,6%
With FRCV	89	79,5%
With FRCV	19	17,0%
<b>Cardiovascular risk, n (%)</b>		
High	5	4,5%
Very high	107	95,5%
<b>PStatin potency, n (%)</b>		
None	32	28,6%
Low	5	4,5%
Moderate	67	59,8%
High	8	7,1%
<b>LDL C (mg/dl)</b>		
Average	92,65	
Median age (years)	89,30	
Standard deviation	26,86	
Minimum	29,0	
Maximum	170,0	
<b>HbA1c (%)</b>		
Average	7,00	
Median	6,75	
Standard deviation	1,20	
Minimum	5,1	
Maximum	11,6	
<b>Control of diabetic dyslipidemia (%)</b>		
No	89	79,5%
Yes	23	20,5%

**Table 1:** Characterization of the sample.

The average LDL-C was 92.5 mg/dl (range 29 mg/dl to 170 mg/dl) and the average HbA1c was 7% (range: 5.1% to 11.6%).

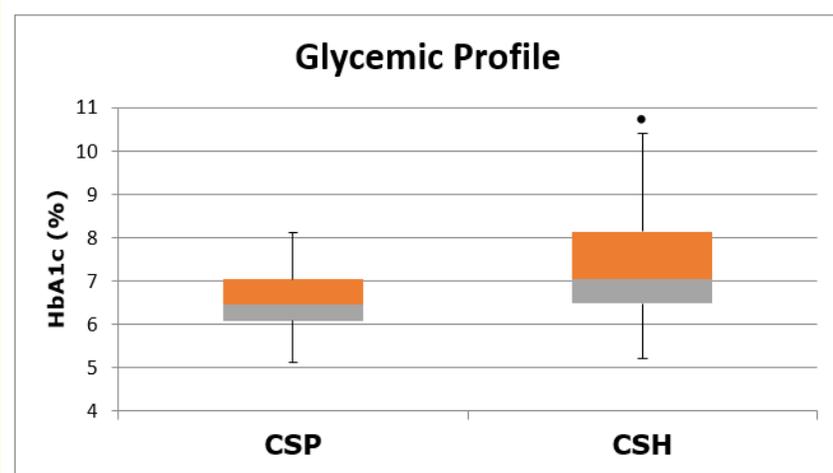
It was found that 20.5% of patients had controlled diabetic dyslipidemia.

**Patients followed in CSP versus CSH**

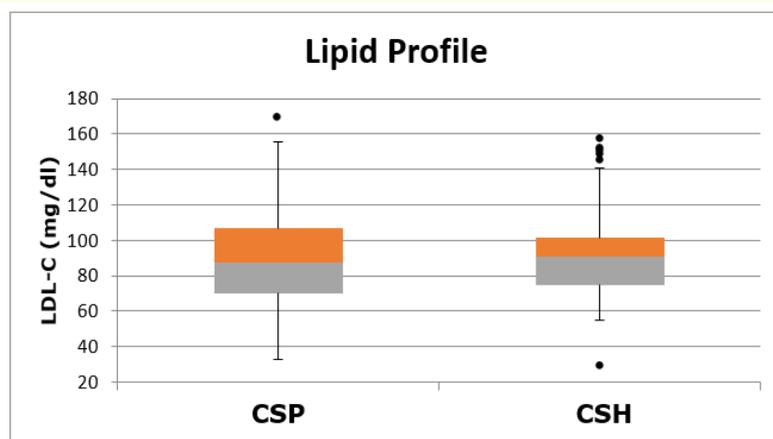
Patients followed on CSH were compared with patients followed on CSP (Table 2). The proportion of patients with very high cardiovascular risk was found to be higher in the group of patients followed in CSP than in patients followed in CSH (100% versus 90.4%, p = 0.019). The median value of HbA1c is higher in patients followed in CSH compared to patients followed in CSP (7.1% versus 6.5%, p = 0.001) (Figure 1). A greater proportion of patients with controlled diabetic dyslipidemia (17.3% versus 23.3%, p = 0.431) and a lower LDL-C mean (91.25 ± 26.97 mg/dl versus 94.27 ± 26.92 mg/dl, p = 0.604) (Figure 2) in patients followed in CSP, although in both cases without statistical significance. The potency of the instituted statin was also not significantly associated with any of the institutions.

	CSH		CSP		p-value
	(n = 52)		(n = 60)		
<b>Cardiovascular risk, n (%)</b>					
High	5	9,6%	0	0,0%	FS: 0,019
Very high	47	90,4%	60	100,0%	
<b>Statin potency, n (%)</b>					
None	16	30,8%	16	26,7%	
Low	3	5,8%	2	3,3%	
Moderate	29	55,8%	38	63,3%	
High	4	7,7%	4	6,7%	
<b>Average</b>	1,40		1,50		
Median	2,00		2,00		MW: 0,612
Standard deviation	1,015		,966		
<b>LDL C (mg/dl)</b>					
Average	94,27		91,25		
Median	91,00		87,20		MW:0,604
Standard deviation	26,91		26,97		
<b>HbA1c (%)</b>					
Average	7,37		6,68		
Median	7,05		6,45		MW:0,001
Standard deviation	1,27		1,05		
<b>Control of diabetic dyslipidemia (%)</b>					
No	43	82,7%	46	76,7%	QQ:0,431
Yes	9	17,3%	14	23,3%	

**TABLE 2:** PATIENTS FOLLOWED AT THE PHC VERSUS THOSE FOLLOWED AT THE PHC.



**Figure 1:** Comparison of the distribution of the glycemic profile (HbA1c) in the two institutions studied. CSP - Primary Health Care; CSH - Hospital Health Care.



**Figure 2:** Comparison of the distribution of the lipid profile (LDL-cholesterol) in the two institutions studied. CSP - Primary Health Care; CSH - Hospital Health Care.

### Statin potency versus dyslipidemia control

It was found that, in the total sample, there are more controlled patients when statins of higher potency (moderate or high) are used compared to not using or using low potency statins, although without statistical significance (69.6% versus 30, 4%,  $p = 0.766$ ) (Table 3).

	Dyslipidemic control				P value
	No		Yes		
	(n = 89)		(n = 23)		
<b>Sample total</b>					
Statin potency, n (%)					
None/low	30	33,7%	7	30,4%	QQ: 0,766
Moderate/high	59	66,3%	16	69,6%	

**Table 3:** Statin potency versus dyslipidemia control Dyslipidemic control.

The correlation analysis of statin potency with the LDL-C value was not statistically significant, neither for the total sample nor in the analysis by institution (Table 4).

	Spearman’s correlation coefficient	p Value
<b>Sample total</b>		
Statin potency versus	-0,084	0,378
<b>CSH</b>		
Statin potency versus	-0,143	0,313
<b>CSP</b>		
Statin potency versus	-0,035	0,789

**Table 4:** Statin potency versus LDL-C Spearman’s correlation coefficient p-value

**Logistic regression analysis for the control of dyslipidemia**

According to the model optimized for the control of dyslipidemia (Table 5), only the presence of very high cardiovascular risk (compared to high risk) decreases the probability that the patient will have control of dyslipidemia (OR = 0.153; 95% CI, 0.024 - 0.979, p = 0.047).

	Initial model			Optimized model		
	Odds Ratio	Value p	95% IC para	Odds Ratio	Value p	95% IC para
			Odds Ratio			Odds Ratio
<b>Institutions</b>						
CSP	Ref.					
CSH	0,510	0,228	[0,171; 1,522]			
Statin potency	1,161	0,556	[0,707; 1,904]			
<b>Cardiovascular risk</b>						
No	Ref.			Ref.		
Yes	0,102	0,027	[0,013; 0,766]	0,153	0,047	[0,024; 0,979]
HbA1c	0,937	0,770	[0,603; 1,454]			
Model p value				0,048		
Overall percentage				80,4%		

**Table 5:** Logistic regression analysis for the control of dyslipidemia initial.

### Discussion and Conclusion

The inability to reach the target LDL values has an impact on the occurrence of potentially preventable vascular events, and it is therefore essential to know and control diabetic dyslipidemia in order to reduce the associated morbidity and mortality.

The study revealed that, even with statins, most patients did not reach the recommended therapeutic objectives (79.5%). A high proportion of patients without lipid-lowering therapy (28.6%) was identified. However, it is even more worrying that even the majority of patients who were on statins were not able to reach the target values for LDL-C.

The presence of very high CVR (compared to high CVR) is a predictive factor for worse control of diabetic dyslipidemia.

Several studies [8-10] have suggested that the choice of statin potency may be a preponderant factor and that is why international recommendations have emerged that recommend treatment with high potency statins. Despite this, this study did not demonstrate better control of dyslipidemia or a decrease in LDL-C levels with higher-intensity statins, especially the low prescription of high-potency drugs in both institutions (7.1%).

This study has some limitations that may have an impact on the results obtained. Even though a representative sample of the populations in question was selected, it was small in size and specific to two institutions, not allowing the extrapolation of the results to the global population reality. In addition, the fact that the selection of one of the samples was for convenience may not represent the total population of the sample. The lack of statistical significance in some of the data discussed may be conditioned by the limitations inherent in this type of study. Being a cross-sectional study, it is not possible to evaluate long-term results, preventing an estimate and prospective calculations; as a cross-sectional and observational study, only the data recorded in the patients' clinical files were analyzed. Finally, no data were collected on the patients' lifestyle, including their eating habits, genetic predisposition to CVD, or even data on adherence to therapy that can be important and explain some of the results.

Although there are studies on these two levels of care that also show the difficult control of diabetic dyslipidemia, this study confirmed that it is not through the level of care that control of the health problem is different, thus emphasizing the need to create standards joint actions to improve the quality of intervention in the control of the lipid profile of patients with DM.

It is essential to continue to reassess the most appropriate therapeutic strategies for the treatment of diabetic dyslipidemia with a view to reducing morbidity and mortality associated with them. For this, prospective studies will be necessary so that, using a temporal sequence of observation, more categorical results and more comprehensive conclusions can be obtained about these studied hypotheses and about the factors that may be more associated with the control of diabetic dyslipidemia.

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### Conflict of Interests

The authors declare no conflict of interest.

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