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The achievement of optimal low density lipoprotein level by patients with stable ischemic heart disease: A study in Ibn Al-Bitar cardiac center

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Abstract
Background: Intensive lipid-lowering therapy plays a crucial role in the secondary prevention of patients with acute coronary syndrome and stable ischemic heart disease. Guidelines recommend achieving a low-density lipoprotein cholesterol (LDL-C) level below 70 mg/dL as the primary treatment goal. Objectives: This study aimed to assess the frequency of LDL-C target value attainment and its predictors among patients with stable ischemic heart disease attending Ibn Al-Bitar Center for Cardiac Surgery.
Methods: A cross-sectional study was conducted from February 15th to August 15th, 2020, on a convenient sample of 300 patients with stable ischemic heart disease. Patients' demographic, clinical, and behavioral data were collected through interviews, along with medical record reviews. All participants had undergone a recent lipid analysis (within 30 days) and had been on statin therapy for at least 3 months.
Results: Among the 300 patients studied, 96.7% were receiving statin treatment, with 71.4% on high-intensity therapy. The mean LDL-C level was 68.13±25.007 mg/dL, with a mean atorvastatin-equivalent dose of 42.41±20.267 mg. Older age, male gender, absence of hypertension, stroke, and peripheral arterial disease, along with high-intensity statin therapy, were significantly associated with better LDL-C target attainment. Obese patients were less likely to reach the LDL-C target (67.2% vs. 30.2%).
Conclusion: The LDL-C target of <70 mg/dL was achieved by 66.3% of the patients. Significant predictors of reaching this target included older age, male gender, and absence of hypertension and stroke.

Keywords: Optimal, low density lipoprotein, stable ischemic heart disease, Ibn Al-Bitar cardiac center

Introduction
Hypercholesterolemia is a significant contributor to the development of atherosclerosis, leading to stable or unstable ischemic heart disease, with all-cause mortality increasing as LDL-C concentrations rise [1]. Elevated LDL-C levels are strongly associated with cardiovascular events across various populations, including patients with post-acute cardiovascular events, stable ischemic heart disease (SIHD), and even in those without established disease [2]. Evidence confirms that the retention of LDL-C and other cholesterol-rich apolipoprotein B (Apo B) lipoproteins within the arterial wall is the key initiating event in atherogenesis [3]. Studies have demonstrated that every 1 mmol/L reduction in LDL-C through statin therapy results in a 21% reduction in major vascular events [4]. The 2019 European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS) Guidelines, along with the 2018 American Heart Association (AHA) and American College of Cardiology (ACC) Guidelines, recommend a ≥50% LDL-C reduction from baseline and an absolute LDL-C target of <55 mg/dL (ESC/EAS) or <70 mg/dL (AHA/ACC) for very high-risk patients. Statins should be prescribed at the highest tolerated dose to achieve these goals [5, 6]. A meta-analysis of statin trials revealed a significant correlation between achieved LDL-C concentrations and reduced cardiovascular outcomes across various LDL-C levels [7]. Despite the widespread use of lipid-lowering therapy (LLT), many patients fail to reach the recommended targets. In the Dyslipidemia International Study (DYSIS), only 21.7% of very high-risk, statin-treated patients achieved an LDL-C level below 70 mg/dL, highlighting the

insufficiency of treatment potency to mitigate cardiovascular risk in these individuals [8]. Similarly, the Centralized Pan-Regional Surveys on the Under treatment of Hypercholesterolemia (CEPHEUS) found only 22.8% of patients reached the LDL-C target [9], with slightly better results observed among Asian patients (34.9%) [10]. Failure to meet dyslipidemia management goals can be attributed to several factors, including lack of follow-up, improper statin dose titration [11, 12], and most notably, poor adherence to treatment, even among patients at high cardiovascular risk [13]. The aim of study to assess frequency and predictors of low-density lipoprotein cholesterol (LDL-C) target value attainment among patients with stable ischemic heart disease.

Method

A cross-sectional study with analytic elements was conducted from February 15th to August 15th, 2020, to assess the attainment of LDL-C target values among patients with stable ischemic heart disease (SIHD) attending the cardiac outpatient clinic at Ibn Al-Bitar Center for Cardiac Surgery in Baghdad. A convenient sample of 300 patients was included in the study. Patients were selected from those attending the clinic during the data collection period, between February 15th and May 31st. The sample size was calculated using the sample size equation, yielding 246 patients with an additional 15% added to account for non-responses, resulting in a final sample size of 300. Inclusion criteria included patients aged 18 years or older with SIHD, diagnosed by their cardiologist based on procedures like coronary angiography (stenosis > 50%), cardiac computed tomography (stenosis > 50%), or a history of percutaneous cardiac intervention or coronary artery bypass graft surgery. Patients had to have been on statin therapy for at least 3 months and have a recent serum lipid analysis (within the past 30 days). Exclusion criteria included recent acute ischemic events (within the past 3 months), chronic renal failure on dialysis, severe heart failure, triglyceride levels over 250 mg/dL, chronic inflammatory disease, and familial hypercholesterolemia. Data were collected through direct patient interviews and medical record reviews, using a structured questionnaire. The information collected included demographic, clinical, and behavioral characteristics such as age, gender, hypertension, diabetes, smoking status, sedentary lifestyle, and family history of coronary heart disease and stroke. Measurements of BMI and waist circumference were also taken. Data were analyzed using SPSS version 23, with results expressed as mean ± standard deviation. Logistic regression analysis was applied to determine the effect of independent predictors on the likelihood of achieving the LDL-C target (<70 mg/dL). A significance level of $p \leq 0.05$ was used.

Results

Three hundred patients were included in this study (62%) were male. The mean age was 60.95±8.530 SD. The number of male patients above 55 years and female patients above 65 years was 201 (67%). Most of the patients had the sedentary lifestyle (77%) and central obesity (77.7%). Diabetes mellitus type II and hypertension also were common (56.3%) (71.7%) respectively (Table 1).

Table 1: The distribution of study sample according to socio-demographic characteristic and clinical variables.

Variable		Frequency N=300	Percentage %
Age	M[1]<55 or F[2]<65	99	33
	M≥55 or F≥65	201	67
gender	Male	186	62
	Female	114	31
Family hx. of IHD	Yes	32	10.7
	No	268	89.3
Smoking	Yes	66	22
	No	234	78
Sedentary lifestyle	Yes	231	77
	No	69	23
Hypertension	Yes	215	71.7
	No	85	28.3
Diabetes	Yes	169	56.3
	No	131	43.7
Stroke	Yes	76	25
	No	224	75
PAD[3]	Yes	13	4.3
	No	287	95.7
BMI[4]	Yes	128	42.7
	No	172	57.3
Central obesity	Yes	233	77.7
	No	67	22.3

[1]Male [2]Female [3] peripheral arterial disease [4] Body mass index

The mean level of LDL for the SIHD cohort treated patients with LLT was 68.13±25.007 mg/dL. The optimum LDL level (<70mg/dl) was found in 199 patients (66.3%) while the non-optimum level of LDL (>70mg/dl) was found in 101 patients (33.7%). (figure 1).

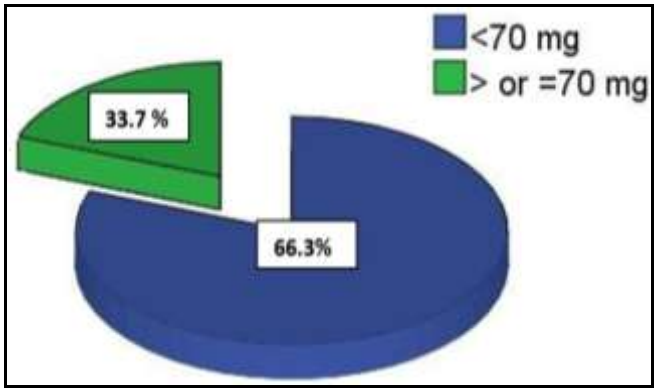

Fig 1: Classification of the participants according to optimum LDL level.

Two hundred ninety patients (96.7%) were taking statin treatment. Atorvastatin was used by 181 (62.4%). The mean of atorvastatin equivalent dose was 42.41±20.267. The High Intensity Statin Therapy was used by 207patients (71.4%). (Table 2)

Table 2: The distribution of study sample according to treatment modalities:

Variable		Frequency N	Percent %
Patients on statin Tx.	Yes	290 (300)	96.7
	No	10 (300)	3.3
Statin type	Atorvastatin	181(290)	62.4
	Rosuvastatin	109 (290)	37.6
Combination of Tx.	Statin + Ezetimibe	5 (290)	1.7
	Statin+other[1]	27 (290)	9.3
Atorvastatin equivalent dose	Mean ± SD	42.41±20.267	
Intensity Statin Therapy	High	207 (290)	71.4
	Moderate	83 (290)	28.6

[1]Fenofibrate or omega 3

One hundred fifty-four (77.3%) of patients were above 55 years for males and above 65 years for females attain target LDL-C value with significant P value, also, Male gender has higher target value attainment than female gender, (p value= 0.0000). Patients with no hypertension, stroke or PAD were significantly reaching target level of LDL-C more than those patients with these co- morbidities. Most of the obese patients (67.2%) were significantly not reaching target LDL-C Compared with non-obese patients who were better in reaching optimum target level of LDL-C. (Table 3).

Table 3: Relationship of optimum LDL-C Level with socio-demographic and clinical variables.

Variable		<70		≥70		P value
		N	%	N	%	
Age	M[1]<55 or F[2]<65	45	22.7	54	53.4	0.000[4]
	M≥55 or F≥65	154	77.3	47	46.6	
Gender	Male	158	79.3	28	37.9	0.000[4]
	Female	41	20.7	73	62.1	
Family hx.	Yes	20	5	12	12.1	0.627
	No	179	95	89	87.9	
Smoking	Yes	45	22.6	21	20.7	0.719
	No	154	77.4	80	79.3	
Sedentary lifestyle	Yes	157	78.9	74	67.2	0.341
	No	42	21.1	27	32.8	
Hypertension	Yes	123	62	92	91	0.000[4]
	No	76	38	9	9	
Diabetes	Yes	110	55.4	59	58.6	0.604
	No	89	44.6	42	41.4	
Stroke	Yes	15	7.4	61	60.3	0.000[4]
	No	184	92.6	40	39.7	
PAD[3]	Yes	5	2.5	8	8.6	0.038[4]
	No	194	97.5	93	91.4	
BMI	Obese	60	30.2	68	67.2	0.000[4]
	Non-obese	139	69.8	33	32.8	
Central obesity	Yes	160	80.6	73	72.4	0.110
	No	39	19.4	28	27.6	

[1]Male [2]Female [3]peripheral arterial disease [4]statistically significant result

Patients who significantly reached the LDL target; 99% of them are on statin therapy. Patients on high intensity level of statin therapy significantly attained the target level of LDL More than those on moderate intensity level of statin (76.7% vs 23.3% respectively). (Table 4).

Table 4: The Relationship of optimal LDL target level with treatment modality:

Variable		LDL level				P value
		<70		>70		
		N	%	N	%	
Patients on statin Tx.	Yes	197 (199)	99	93 (101)	92	0.003[1]
	No	2 (199)	1	8 (101)	8	
Statin type	Atorvastatin	125 (197)	63.3	56 (93)	60	0.595
	Rosuvastatin	72 (197)	36.7	37 (93)	40	
Combination of Tx.	Statin+ Ezetimibe	4 (197)	2.5	1 (93)	0.99	0.637
	Statin+others[2]	17 (197)	8.5	10 (93)	10	
Atorvastatin equivalent dose	Mean	41.42		47.20		0.154
	SD	18.468		27.033		
Statin dose intensity	High	151 (197)	76.7	56 (93)	60	0.004[1]
	Moderate	46 (197)	23.3	37 (93)	40	

1statistically significant result[2]Fenofibrate or omega 3

We used the binary logistic regression analysis to know the significant predictors of reaching optimum target LDL (<70 mg/dl). After using Chi-square to test the association of optimum LDL with other variables included in the study, we entered the significant variables (age, gender, hypertension, stroke, PAD, obesity and statin dose intensity) for the binary logistic regression test to know the significant predictors of reaching optimum LDL. We found that:

- Older age (AOR=0.288, 95% CI 0.087-0.953, P=0.041)
- Male gender (AOR=12.595, 95% CI 2.577-61.560, P=0.002)
- Not hypertensive (AOR=5.935, 95% CI 1.177-29.936, P=0.031)
- Having no stroke (AOR= 138.160, 95% CI 28.376-672.680, P=0.000), had the higher target level attainment with significant P value. (Table 5).

Table 5: Binary logistic regression analysis (AOR with 95% CI) for variables related to ischemic heart disease regarding optimum LDL level.

Variable	SE coefficient	AOR	95% CI	P value
Age	0.611	0.288	0.087-0.953	0.041
Gender	0.810	12.595	2.577-61.560	0.002
Hypertension	0.826	5.935	1.177-29.936	0.031
Stroke	0.808	138.160	28.376-672.680	0.000
PAD	1.123	2.214	0.245-20.001	0.479
BMI	0.526	2.579	0.920-7.230	0.072
Statin dose intensity	0.575	0.934	0.303-2.882	0.905

Discussion

The current guidelines recommend statin therapy for patients with stable ischemic heart disease (SIHD) to reduce cardiovascular risk [5, 6]. Clinical evidence from randomized controlled trials and meta-analyses indicates that the benefits of statin therapy are dependent on both the intensity of treatment and the degree of LDL-C reduction achieved [14]. Despite this, international guidelines differ in their approaches, with some focusing on statin intensity [5] and others emphasizing LDL-C targets, specifically below 70 mg/dL [6]. In this study, 77% of the participants had a sedentary lifestyle, with high prevalences of type 2 diabetes (56.3%) and hypertension (71.7%). These characteristics were comparable to those in similar studies conducted in Thailand, Belgium, and Saudi Arabia [15-17]. Obesity (BMI >30) was common (42.7%), though lower than in the Saudi study (58.8%) [17], while central obesity was present in 77.7% of patients. Central obesity has been shown to pose a higher risk for coronary heart disease (CHD) than general obesity [18]. The mean LDL-C level in this cohort was 68.13±25.007 mg/dL, which is lower than levels reported in studies from France, Thailand, and Saudi Arabia [15, 17, 19], where the mean LDL-C was higher (87.4–94.9 mg/dL). The relatively better LDL-C control in our study is likely attributable to the fact that patients were treated at a tertiary cardiac center, with close monitoring and frequent follow-up by interventional cardiologists. Additionally, the availability of free lipid-lowering therapy (LLT) and patient education programs at the center may have contributed to better adherence to treatment. In this study, 66.3% of patients achieved the LDL-C target of <70 mg/dL, compared to lower attainment rates in other countries, such as Saudi Arabia (24.8%) [17] and the Asia-Pacific region (32.6%) [10]. The reasons for this disparity may include more frequent follow-up and better titration of statin doses in our study population. In Belgium, only 40.6% of SIHD patients achieved the LDL-C target, despite the widespread use of LLT [16]. Regarding treatment, 96.7% of patients in our study were on statin therapy, with atorvastatin being the most commonly used (62.4%), followed by rosuvastatin (37.6%). This finding is comparable to studies from France and Saudi Arabia, where atorvastatin was also the most frequently prescribed statin [17, 19]. Only 1.7% of patients were on a combination of statins and ezetimibe, a figure lower than those reported in other studies [10, 17], likely due to the high cost and limited availability of ezetimibe. The mean atorvastatin-equivalent dose in our study was 42.41±20.267 mg/day, higher than in other studies [10, 17], which may explain the higher proportion of patients achieving the LDL-C target. High-intensity statin therapy was used by 71.4% of patients, which is higher than the rate reported in a French study (56.8%) [19]. This variation could be due to differences in patient populations, geographical factors, and follow-up durations. We found that older age, male gender, absence of hypertension, and stroke were significant predictors of achieving the LDL-C target. These results align with those from studies in Thailand [15] and Korea [20], which also found that older patients and men were more likely to reach LDL-C goals. The frequent physician visits and better awareness among older patients may explain this finding. However, other studies, such as those from France [21] and Korea [20], found that older age was associated with a lower likelihood of LDL-C target attainment. The discrepancy in findings across studies regarding predictors such as obesity, peripheral arterial disease (PAD), and diabetes highlights the variability in study populations, design, and the prevalence of comorbidities.

Conclusion

It was found most of our patients followed sedentary lifestyle pattern and had central obesity. The main predictors of LDL-C target attainment which founded in this study were male gender and old age group. The majority of the SIHD patients used statin therapy, and 66.3%of them reached the LDL-C target >70 mg/dl.

Conflict of Interest

Not available

Financial Support

Not available

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