Available online **www.ijpras.com**

International Journal of Pharmaceutical Research & Allied Sciences, 2021, 10(2):35-41
https://doi.org/10.51847/Ib4osQuWE6

Original Article

ISSN : 2277-3657
CODEN(USA) : IJPRPM

Effect of Multidisciplinary Dyslipidemia Educational Program on Adherence to Guidelines Directed Medical Therapy in Saudi Arabia

Fakhr AlAyoubi[1], Ahmad Hayajneh[2], Samha AlAyoubi[3], Fayez El Shaer[4,5]*

[1]Department of Clinical Pharmacy Services, King Saud University Medical City, King Saud University, Riyadh, Saudi Arabia.
[2]Department of Nursing, King Fahad Cardiac Center, King Saud University, Riyadh, Saudi Arabia.
[3]Department of Basic Science Unit Cardiac, King Fahad Cardiac Center, King Saud University, Riyadh, Saudi Arabia.
[4]Department of Cardiac Science, King Fahad Cardiac Center, King Saud University, Riyadh, Saudi Arabia.
[5]National Heart Institute, Cairo, Egypt.

***Email:** felshaer@ksu.edu.sa*

ABSTRACT

A prospective cohort study was conducted. The practice in three clinics, cardiology, primary care, and endocrine, was assessed by data collection including demographic information, lipid profile (HDL, triglyceride, LDL, total cholesterol), and lipid-lowering drugs. All consecutive patients with hyperlipidemia were included. Extensive educational sessions have been implemented at the beginning of the study. Morisky score was assessed at the initial visit and months 3 and 9 to assess the medication adherence.
401 patients were included with a mean age of 60±13 years, 62 % were males. Evaluation of the prescription pattern of lipid-lowering drugs in outpatient pharmacy revealed 40 % of the hyperlipidemic patients were prescribed lipid-lowering drugs with only 15% was on proper dosing. Rosuvastatin was prescribed more in PCC (60%) while Atorvastatin was more in Cardiology (80%). Initially, the research team conducted a workshop with a campaign to educate the health care practitioners with the guidelines directed to medical therapy. Morisky score calculation was carried out at the beginning, and months 3 and 9. Morisky score was used to evaluate therapy adherence together with knowledge and motivation level. Morisky score initially was above 2 (low adherence) in 43% of the patients and 2 or less (moderate to high adherence) in 57%. Morisky score (above 2) was decreased to 29% from at the first visit (month 3) to 12 % in the last visit (month 9), which reflect on the effectiveness of the extensive education program which was given by the research teams at the beginning of the study.

Key words: *Hyperlipidemia, Guidelines, Statin products, Saudi Arabia, Adherence, Education program*

INTRODUCTION

Hyperlipidemia is abnormally elevated levels of lipids or lipoproteins in the blood [1, 2]. Blood contains three main types of lipid: LDL which is a bad constituent as it forms plaques at blood vessels [3], HDL is a good constituent as it removes LDL from the blood and TG comes from food and is stored in fat cells [4]. Hyperlipidemia may be defined as the enhancement of serum total cholesterol (TC) and/or triglyceride (TG) or decreased high-density lipoprotein (HDL) cholesterol with an increased low-density lipoprotein (LDL) [5].
High cholesterol causes atherosclerosis [6] with plaque formation leading to atherosclerotic cardiovascular disease, acute coronary syndromes, and cerebrovascular accidents [7].

HMG-CoA reductase inhibitors are the most important therapeutic options that reduce adverse cardiac events and mortality in those at high risk of cardiovascular disease [8]. Statins are the preferred treatment for patients with increased cholesterol in the blood [9]. Many clinical trials have shown that statins have been effective and well-tolerated [10] with a significant clinical effect on mortality and morbidity, rarely showed a negative effect on the liver, kidney, and joint systems during treatment, and there was no increase in the incidence of cancer [11].

Statins have three generations: the first generation is lovastatin and pravastatin with low potency which reduce coenzyme Q10 that is an essential mitochondrial redox component and endogenous antioxidant [12]. The second generation is atorvastatin and simvastatin; atorvastatin is well tolerated in the long-term treatment of dyslipidemia with a safety profile, best-selling as a medicine in the world, and has well-documented benefits for cardiovascular disease [13]. Simvastatin decreases serum cholesterol without clinically relevant effects on hormones as steroid hormones [14]. The third generation is Rosuvastatin with high potency against HMG-COA reductase [15].

A small difference in molecular compositions pharmacodynamics and in human physiology can substantially alter the overall effectiveness of the drug [10].

A risk score is used to assess the risk of hyperlipidemia. 4 groups are considered as very high and high-risk scores, which necessitates high-intensity statin therapy, including any form of clinical ASCVD, patients with primary LDL-C levels of ≥190 mg/DL, diabetics aged 40-75 years with LDL-C levels of 70-189 mg/DL and non-diabetics aged 40-75 years with an estimated 10-year ASCVD risk ≥ 7.5% [4].

This is a prospective cohort study intended to observe the prescribing patterns and doses of anti-hyperlipidemias (Atorvastatin, Rosuvastatin, and Simvastatin) also assess adherence using the Morisky score.

MATERIALS AND METHODS

A prospective cohort study was carried out in KKUH, including three clinics, Primary Care Clinic (PCC), cardiology clinic, and endocrinology clinics. All patients diagnosed with hyperlipidemia more than 18 years old from December 2018 until December 2019 followed in KKUH outpatients' clinics were included in the study. Demographic, lipid profile, and lipid-lowering drugs were collected.

The research team conducted a hand-on training and workshops campaign to educate the health care practitioners providing the data of guidelines directed medical therapy and Morisky score calculation (0 = high adherence, 1-2 = medium adherence, >2 = low adherence). Assessment of prescribing pattern and patient adherence was carried out before the study and during follow-up in months 3 and 9.

RESULTS AND DISCUSSION

Evaluation of the prescription pattern to lipid-lowering drugs in outpatient pharmacy revealed only 40 % of the hyperlipidemic patients were prescribed lipid-lowering drugs, 60 % of the patients were overlooked and misdiagnosed with only 15% of the prescribed group on proper dosing.

401 patients were included, 62% were males (249) and 38% are females (152). The mean age was 66 ±5 years, 52% more than 60 years (207) patient, 28% in the range is from 50 to 60 (114) patients, 14% in the range of 40 to 50 (54), 24% in the range between 30 and 40 and 2% less than 30 years (9). 97% were Saudi, DM was found 77 %, HTN was 71 %, smoking 14%, ACS 35%, PAD 1%, CVA 4%, a mean ASCVD score was 9.6 %. 51% were followed in PCC by (204), 48% in Cardiology clinic, (193) patients, and 2% followed by endocrinology clinic (8) **(Table 1)**.

The most-prescribed cholesterol-lowering in the cardiology clinic was 40mg atorvastatin (108), followed by 20mg atorvastatin (48), and 80mg atorvastatin (10). The most prescribed lipid-lowering drugs in the PCC clinic were 20mg atorvastatin (60), they were 10mg atorvastatin (32) 20mg simvastatin (28), and 40mg atorvastatin (25). In endocrinology clinics 10 mg atorvastatin (2) patients, 20 mg atorvastatin (2) patients, 20 mg simvastatin (2) patients, and 10 mg Rosuvastatin (2) patients. Rosuvastatin was used by 5 patients in (10 mg) and 6 patients (20mg) in PCC **(Figures 1 and 2)**.

Table 1. Epidemiology of patients

No. of patients	401
Age, mean(SD)	60(12.8)
Sex,(male%)	62
Diabetic,%	77

Hypertensive,%	71
ACS,%	35
MI,%	7
Stroke,%	4
CVA/TIA,%	3
PAD,%	1
Smoking,%	14
Family history of MI,%	14
Family history of dyslipidemia,%	51
On Statin,%	89

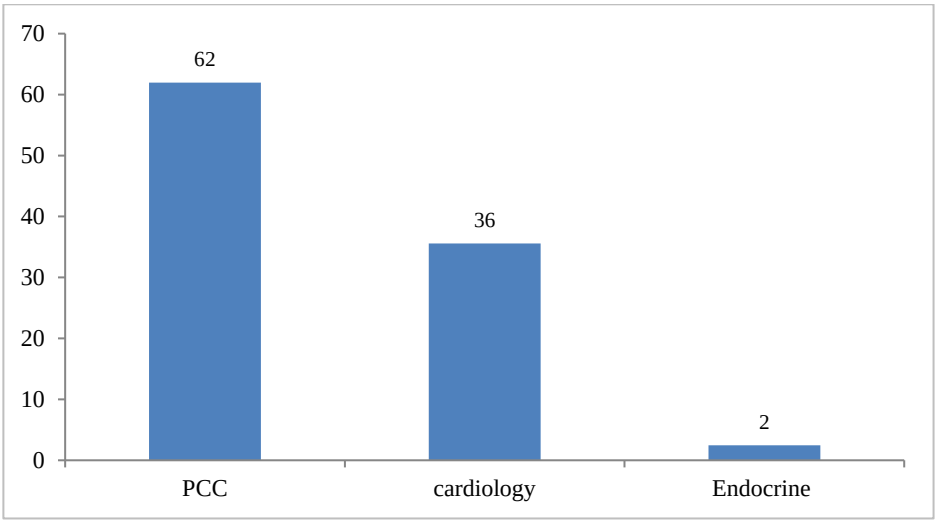

Figure 1. Percentage of patients visiting per clinic

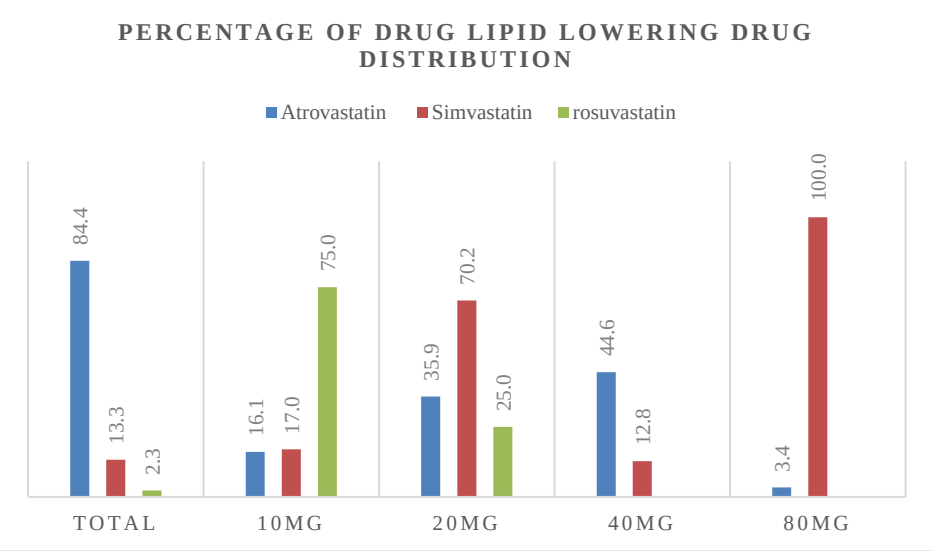

Figure 2. Drug lipid percentage lowering drug distribution

At baseline, the mean of baseline total cholesterol was 5.4, LDL 2.5, HDL 1, TG 2.4 **(Figure 3)**. In month three, the total cholesterol level was 4.8 in PCC, 3.6 in cardiology, and 3.7 in endocrine clinics. The average LDL level in Cardiology by 1.96 mmol and followed by 1.9 in endocrinology clinics and 1.8 in PCC clinics. HDL level was 1.91 in cardiology clinics followed by 1.2 in endocrinology clinics and 1.1 in PCC clinics. Triglyceride levels were 3.7 in PCC, 1.8 in cardiology, and 1.3 in endocrinology clinics **(Figure 4)**.

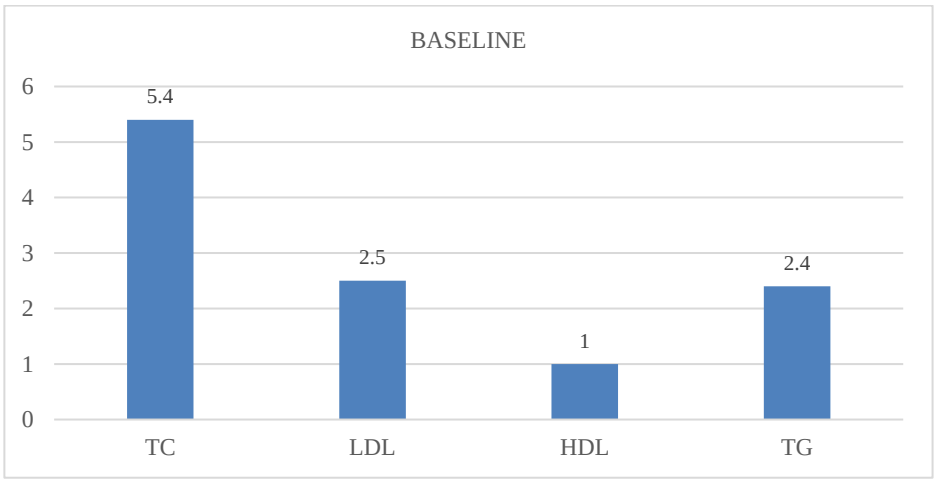

Figure 3. Baseline

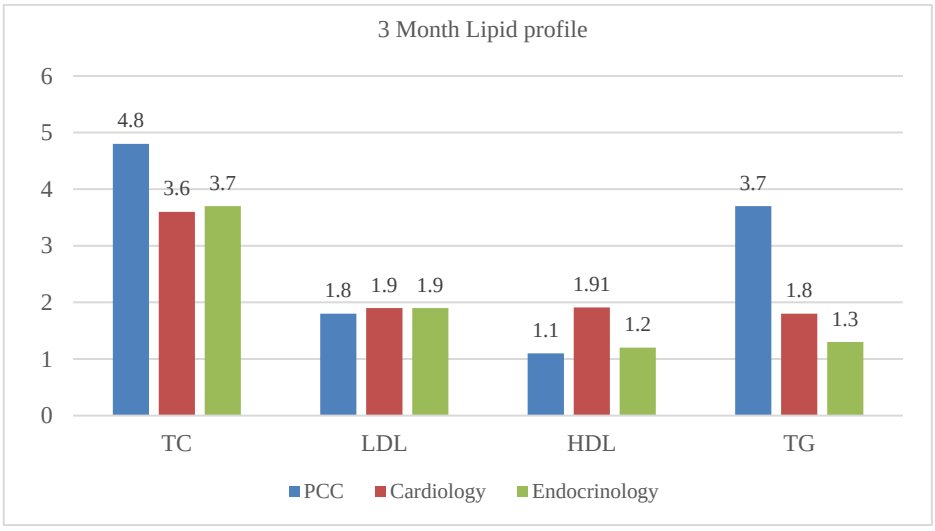

Figure 4. Lipid profile after 3 Month

In month 9, the total cholesterol level was 3.6 in cardiology clinics, 4.4 in endocrinology clinics, and 4.3 in PPC clinics. The average LDL is 3.08 mmol in PCC, 2.71 in both cardiology and endocrinology clinics. HDL average level was 1.8 mmol in a cardiology clinic and 1.3 in endocrinology and PCC clinics. Triglycerides levels are, 2.4 in cardiology, 1.7 in endocrinology and 2.4 in PCC. Triglyceride is getting higher in PCC and endocrinology clinics **(Figure 5)**.

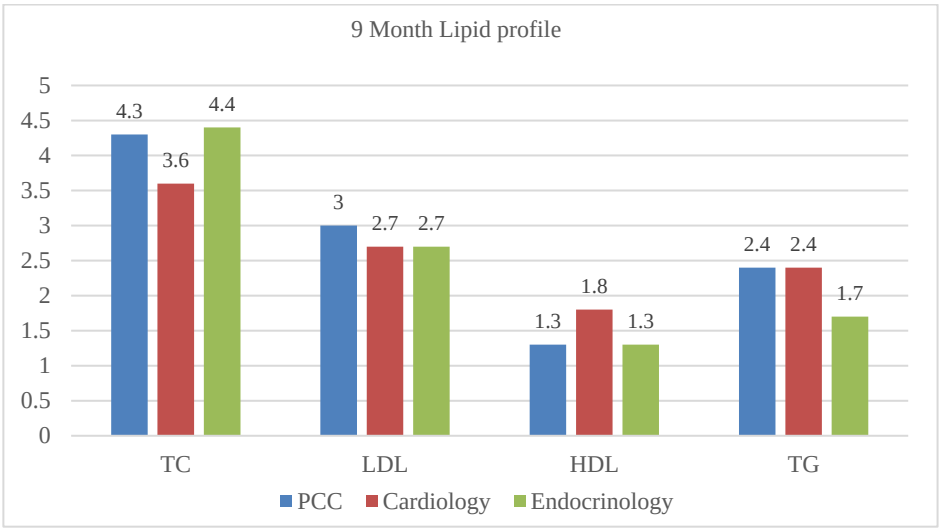

Figure 5. Lipid profile after 9 Month

The morisky score was initially above 2 in 43 % of the patients, 1-2 was 31 % and = 0 was 26%. In month 3, Morisky score above 2 decreased to 29%, 1-2 to 27%, and = 0 increased to 44%, also, the Morisky score in 9 months above 2 decreases to 12 %, 1-2 to 26% and = 0 increased to 62 %, which reflect on the effectiveness of the extensive education program which was given by the research teams at the beginning of the study **(Figure 6)**.

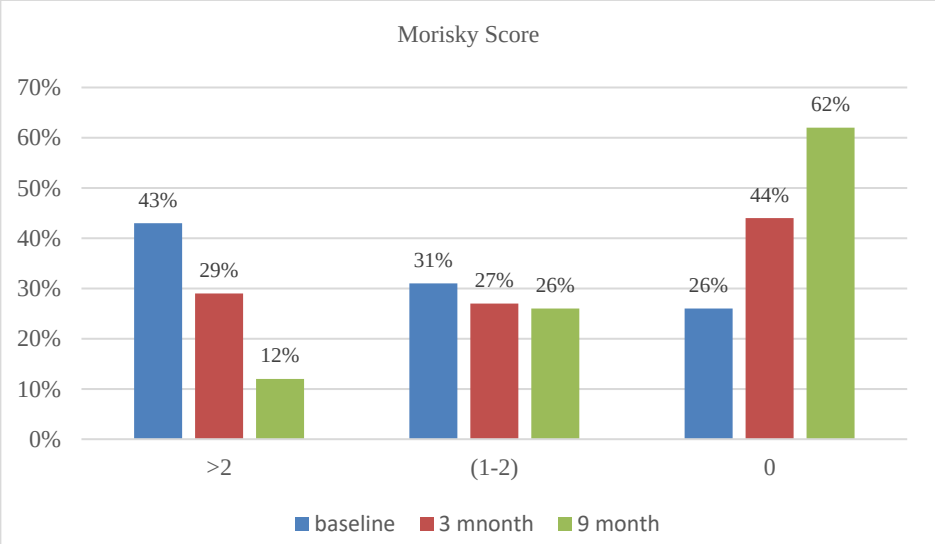

Figure 6. Morisky Score

45% (180) of patients were on atorvastatin 40 mg which was brand and replaced after 3 months of the study by generic which might be an explanation for the re-elevation of lipid profile in spite of good adherence.

ASCVD is a major cause of death in the KSA. Dyslipidemia has been considered an important risk factor in KSA. There is a direct relationship between LDL-C levels and ASCVD [11].

For many people, lifestyle changes are not enough to bring high cholesterol levels to a healthier level necessary for the reduction of cardiovascular risk. Lipid-lowering therapy is essential to do so. A 50% reduction in LDL and the guideline target is sometimes hard to achieve [4]. The cardiovascular events curve in favor of a greater reduction in LDL-C started to separate at about 4 months. Patients who did not achieve a 50% reduction in LDL and prescribed high-intensity statins had more favorable event curves than those who prescribed medium-intensity statins [10], "Unfortunately, a lot of studies document a significant treatment gap, with underuse of high-intensity statin therapy. There is a great need to involve the patients, caregivers, and communities to improve adherence to statin therapy [12].

Randomized trials have shown that lowering LDL-C post-MI reduces the risk for recurrent events. LDL lowering is a cornerstone of secondary prevention of cardiovascular disease [13].

Although Clinical Practice Guidelines (CPGs) developed by WHO improve patients' outcomes, some limitations affect their uptake and implementation by many payers and clinicians at the local level [14]. Lack of physician and patient motivation or education and misinformation on adverse effects are important contributing factors [15]. It was reported that physicians' awareness of the recommended LDL-C targets in patients with CAD is 40%, which is considered a gap between actual practice and decision making, and scientific evidence-based knowledge [16].

This is a prospective cohort study intended to observe the prescribing patterns and doses of anti-hyperlipidemias (Atorvastatin, Rosuvastatin, and Simvastatin) also, assess adherence using the Morisky score [17]. The physician's and patient compliance in prescribing statins according to the guidelines directed medical therapy was assessed and evaluated [18].

In patients with or at risk of coronary heart diseases, statins effectively lower LDL-cholesterol and reduce the risk of mortality and cardiovascular diseases [19].

Statin treatment increases the survival in five main trials, absolute increase ranged from 3.33% to 0.43%, the change was 1.75%, which occurred in the largest trial. In primary prevention, statin treatment increased survival in six of the seven main trials, absolute change in survival ranged from −0.09% to 0.89%, median 0.49% [20].

In another study, over the 5.4 years' median follow-up period, simvastatin produced mean changes in HDL-C, LDL-C, and total cholesterol of +8%, -35%, and -25%, respectively, with few adverse effects [21]. In addition,

another study revealed statin therapy reduced mortality from coronary heart disease and overall mortality with a relative risk reduction of 24% [22].

The enthusiasm of statins prescription is based on primary and secondary prevention [22]. The Meta-analyzes showed a reduction in deaths from all causes by 9-14% in low-risk patients as primary prevention [23]. It is safe and can be broadly described because there is no increase in non-cardiovascular mortality [24].

CONCLUSION

Implementation of dyslipidemia education programs has an impact on adherence and proper dosing of anti-hyperlipidemic therapy. The education has helped to improve the practice of physicians, no matter which specialty, ongoing programs and national guidelines is a must in local societies. Results from the study have shown that substituting brands should be guided by a critical assessment using appropriate evaluation techniques.

ACKNOWLEDGMENTS : The authors are very thankful to all the associated medical staff, pharmacist and nurses in cardiology, endocrine and family medicine departments.

CONFLICT OF INTEREST : None

FINANCIAL SUPPORT : None

ETHICS STATEMENT : Saudi Heart Association supported and aprovaed the study.

REFERENCES

1. Wiviott SD, de Lemos JA, Cannon CP, Blazing M, Murphy SA, McCabe CH, et al. A tale of two trials. Circulation. 2006;113(11):1406-14.
2. Kennedy-Martin T, Curtis S, Faries D, Robinson S, Johnston J. A literature review on the representativeness of randomized controlled trial samples and implications for the external validity of trial results. Trials. 2015;16(1):495.
3. Howard BV, Ruotolo G, Robbins DC. Obesity and dyslipidemia. Endocrinol Metab Clin North Am. 2003;32(4):855-67.
4. Genest J, McPherson R, Frohlich J, Anderson T, Campbell N, Carpentier A, et al. 2009 Canadian Cardiovascular Society/Canadian guidelines for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease in the adult–2009 recommendations. Can J Cardiol. 2009;25(10):567-79.
5. Rodriguez F, Maron DJ, Knowles JW, Virani SS, Lin S, Heidenreich PA. Association between intensity of statin therapy and mortality in patients with atherosclerotic cardiovascular disease. JAMA Cardiol. 2017;2(1):47-54.
6. Navarese EP, Robinson JG, Kowalewski M, Kołodziejczak M, Andreotti F, Bliden K, et al. Association between baseline LDL-C level and total and cardiovascular mortality after LDL-C lowering: a systematic review and meta-analysis. Jama. 2018;319(15):1566-79.
7. Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk: the Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS). Eur Heart J. 2020;41(1):111-88.
8. Dimmeler S, Aicher A, Vasa M, Mildner-Rihm C, Adler K, Tiemann M, et al. HMG-CoA reductase inhibitors (statins) increase endothelial progenitor cells via the PI 3-kinase/Akt pathway. J Clin Investig. 2001;108(3):391-7.
9. Solomon A, Kåreholt I, Ngandu T, Wolozin B, MacDonald SW, Winblad B, et al. Serum total cholesterol, statins and cognition in non-demented elderly. Neurobiol Aging. 2009;30(6):1006-9.
10. Boren J, Chapman MJ, Krauss RM, Packard CJ, Bentzon JF, Binder CJ, et al. Low-density lipoproteins cause atherosclerotic cardiovascular disease: pathophysiological, genetic, and therapeutic insights: a consensus statement from the European Atherosclerosis Society Consensus Panel. Eur Heart J. 2020;41(24):2313-30.
11. Alasnag M, Awan Z, Al Ghamdi A, Al Modaimeigh H, Al Shemiri M. Improvement initiative in LDL-C management in Saudi Arabia: A call to action. IJC Heart Vasc. 2020;31:100667.

12. Sabatine MS, Giugliano RP, Keech AC, Honarpour N, Wiviott SD, Murphy SA, et al. Evolocumab and clinical outcomes in patients with cardiovascular disease. New Engl J Med. 2017;376(18):1713-22.
13. Arbaeen AM, Abdelaziz SA. Impact of Emblica Officinalis Pulp Aqueous Extract on Hyperglycemia and Hyperlipidemia in Diabetic Rats. Int J Pharm Phytopharmacol Res. 2020;10(3):130-8.
14. Krikke M, Hoogeveen RC, Hoepelman AI, Visseren FL, Arends JE. Cardiovascular risk prediction in HIV-infected patients: comparing the Framingham, atherosclerotic cardiovascular disease risk score (ASCVD), Systematic Coronary Risk Evaluation for the N etherlands (SCORE-NL) and Data Collection on Adverse Events of Anti-HIV Drugs (D: A: D) risk prediction models. HIV Med. 2016;17(4):289-97.
15. Paoletti R, Corsini A, Bellosta S. Pharmacological interactions of statins. Atheroscler Suppl. 2002;3(1):35-40.
16. Jones PH, Davidson MH, Stein EA, Bays HE, McKenney JM, Miller E, et al. Comparison of the efficacy and safety of rosuvastatin versus atorvastatin, simvastatin, and pravastatin across doses (STELLAR Trial). Am J Cardiol. 2003;92(2):152-60.
17. Keskitalo JE, Zolk O, Fromm MF, Kurkinen KJ, Neuvonen PJ, Niemi M. ABCG2 polymorphism markedly affects the pharmacokinetics of atorvastatin and rosuvastatin. Clin Pharmacol Ther. 2009;86(2):197-203.
18. Paoletti R, Fahmy M, Mahla G, Caplan R, Raza A. Rosuvastatin is more effective than pravastatin or simavastatin at improving the lipid profiles of hypercholesterolaemic patients. Atherosclerosis (Supplements)(Component). 2001;2(2):87.
19. Schubert J, Lindahl B, Melhus H, Renlund H, Leosdottir M, Yari A, et al. Low-density lipoprotein cholesterol reduction and statin intensity in myocardial infarction patients and major adverse outcomes: a Swedish nationwide cohort study. Eur Heart J. 2021;42(3):243-52.
20. Akunne OO, Godman B, Adedapo AD, Truter I, Fadare J. Statin prescribing among hypertensive patients in southwest Nigeria: findings and implications for the future. J Comp Eff Res. 2016;5(3):281-8. doi:10.2217/cer.15.65
21. Warren JB, Dimmitt SB, Stampfer HG. Cholesterol trials and mortality. Br J Clin Pharmacol. 2016;82(1):168-77.
22. Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet. 1994;344(8934):1383-9.
23. Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. New Engl J Med. 1998;339(19):1349-57.
24. Al Sifri SN, Almahmeed W, Azar S, Okkeh O, Bramlage P, Jünger C, et al. Results of the Dyslipidemia International Study (DYSIS)-Middle East: clinical perspective on the prevalence and characteristics of lipid abnormalities in the setting of chronic statin treatment. PLoS One. 2014;9(1):e84350.