



## ROLE OF CHOLECYSTECTOMY ON POSTOPERATIVE LIPID PROFILE OF PATIENTS UNDERGOING SURGERY

Osama Jawed Khan<sup>1</sup>, Anam Taj<sup>2\*</sup>, Sana Ejaz<sup>3</sup>, Nimra Shaikh<sup>4</sup>, Rafia Haleem Shaikh<sup>5</sup>,  
Muhammad Hammad<sup>6</sup>

<sup>1</sup>Dow University of Health Sciences/ Dr Ruth K M Pfau Civil Hospital Karachi  
osama\_jawed@outlook.com

<sup>2\*</sup>Department of general surgery, DUHS / Dr.Ruth K.M. Pfau Civil Hospital Karachi  
dr.ana100@hotmail.com

<sup>3</sup>Department of general surgery, DUHS / Dr.Ruth K.M. Pfau Civil Hospital Karachi  
sanaejaz@hotmail.com

<sup>4</sup>Dow University of Health Sciences/ Dr Ruth K M Pfau Civil Hospital Karachi  
binte\_shaikh@hotmail.com

<sup>5</sup>Dow University of Health Sciences/ Dr Ruth K M Pfau Civil Hospital Karachi  
rafiashaikh37@gmail.com

<sup>6</sup>Dow University of Health Sciences/ Dr Ruth K M Pfau Civil Hospital Karachi  
hammad.ajmal@outlook.com

**\*Corresponding Author:** Anam Taj

\*Department of general surgery, DUHS / Dr.Ruth K.M. Pfau Civil Hospital Karachi  
dr.ana100@hotmail.com

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### Abstract

**Introduction:** Gallstone disease is an emerging health issue worldwide with its incidence on the rise. The development of gallstone disease is multifactorial, with risk factors including increased age, female sex, obesity, and the use of oral contraceptive pills.

**Objective:** To determine the mean change (pre and postoperative) in serum lipid profile in patients with cholelithiasis.

**Study design:** Quasi-Experimental Study.

**Setting:** This study was conducted at the Department of General Surgery, Dr. Ruth K.M Pfau Civil Hospital, Karachi, Pakistan from September 21, 2021 to March 20, 2022.

**Materials and methods:** All patients who fulfilled the inclusion criteria and visited Civil Hospital, Karachi were included in the study. Informed consent was taken after explaining the procedure, risks and benefits of the study. In our study, preoperative 3 ml blood samples after 12 hours fasting were taken from all the patients under aseptic conditions one day before surgery for assessing the preoperative lipid profile.

**Results:** The age of the patients ranged from 15 to 65 years with a median of 52.00. In the distribution of gender, 31 (35.2%) were male while 57 (64.8%) were female. Mean  $\pm$  standard of

change in pre and post-operative lipid profile after 1 week, total cholesterol was  $4.47 \pm 90.98$ , LDL  $5.54 \pm 28.82$ , HDL  $2.42 \pm 12.87$  while triglyceride was  $4.18 \pm 102.09$  and p-value found to be non-significant i.e. (P=0.646), (P=0.075), (P=0.081), (P=0.702) respectively. Mean  $\pm$  standard of change in pre and post-operative lipid profile after 1 month, total cholesterol was  $3.09 \pm 88.61$ , LDL  $18.78 \pm 42.13$ , HDL  $1.17 \pm 12.71$  while triglyceride was  $10.61 \pm 97.91$  and non-significant p-value was found in total cholesterol i.e. (P=0.744) HDL (P=0.390), triglyceride (P=0.312) where as p-value was found in LDL (P=0.0001).

**Conclusion:** It is to be concluded that a highly significant mean change was noted in LDL while insignificant changes were noted in TCL, HDL, and triglyceride in serum lipid profile in patients with cholelithiasis. Further large-scale work is recommended for the validation of current findings.

**Keywords:** Lipid Profile, Cholelithiasis, Mean change

### Introduction

Hyperlipidemia is a very big health issue worldwide. The prevalence of hyperlipidemia is increasing in developed as well as developing countries. Even in Pakistan, there is a rise in frequency due to a change in the lifestyle of the people. Every year a huge sum of money is spent on the use of anti-hyperlipidemic to control hyperlipidemia. Many studies have shown an association between abnormal lipid profile and gallstones and it has been one of the most prevalent gastrointestinal disease in recent year [1].

Cholecystectomy has been proven beneficial in patients with symptomatic gallstones [2] and it could play a role in patients facing devastating consequences of dyslipidemia refractory to medical treatment or in long term compliance issues due to difficulty in following patients living in remote areas. Early cholecystectomy is a daycare procedure and doesn't have an adverse effect on body physiology in the long run and could be considered as primary treatment in providing dyslipidemia patients benefit [3].

Bile consisting of bile acids is stored in gall bladder which is released into the duodenum, via the common bile duct through the major duodenal papilla during digestion after cholecystokinin (CCK) secretion, when fatty foods enter the digestive tract. Digestion occurs mostly in the upper intestine (the duodenum), where the bile is released. About 95% of the bile acid, from the bile that is delivered to the duodenum, will be recycled by enterohepatic circulation. The presence of biliary acids in the intestines helps in the digestion of fats and other substances. If the gallbladder is removed, the bile in the liver will directly enter the upper part of the intestine. As a result, bile acid circulates faster, thus exposing the enterohepatic system to a greater bile acid reflux [3]. Lipid and bile acid metabolism are functionally interrelated but how gallbladder removal affects lipids is not well understood. Therefore, the goal of this study is to determine the changes in serum lipid levels (serum TG, total cholesterol, HDL, and LDL) in patients after cholecystectomy [1]. In a study conducted by Kuldeep Singh concluded that serum total lipids, serum cholesterol, serum LDL cholesterol and serum triglycerides levels decrease and serum HDL cholesterol increase after cholecystectomy [4]. Similar results in LDL and TG has also been noted in study conducted by Jindal N et al. [5]. In another work done in The Medical and Health Welfare trust (MHWT), Uttara Model Town, Dhaka, Bangladesh, cholecystectomy has a significant effect on lipid profile pre and postoperatively however the results are complex and further studies are warranted [6]. Study conducted by Osman et al compare the pre and post lipid profile in patient undergoing laparoscopic cholecystectomy. The baseline LDL, HDL, total cholesterol and triglycerides were  $120 \pm 38.2$ ,  $45.8 \pm 11.9$ ,  $180 \pm 51.6$  and  $128.1 \pm 66.5$ . Lipid profile after 2 months post cholecystectomy were LDL  $101.2 \pm 39.4$ , HDL  $46.2 \pm 15.1$ , total cholesterol  $178.5 \pm 52.8$  and triglycerides  $123.6 \pm 41.7$  [7].

Though lipid and bile acids metabolisms are functionally correlated [8], how cholecystectomy affects lipid profile is not well-comprehended. High lipid profile readings, consisting of elevations in

chylomicron, low-density lipoprotein (LDL), very-low-density lipoprotein (VLDL), and intermediate-density lipoprotein (IDL) levels, are becoming increasingly prevalent, especially with the spreading factors among the Asian population, such as urban residence, increasing age, especially 40 years; physical inactivity, overweight and obesity, diabetes mellitus, frequent fast food consumption, and so on. This, in turn, raises concerns about the effective management of such conditions [9,10].

## **OBJECTIVE**

To determine mean change (pre and postoperative) in serum lipid profile in patients with cholelithiasis.

## **MATERIAL and METHODS**

This Quasi Experimental Study was conducted at Department of General Surgery, Dr. Ruth K.M Pfau Civil Hospital, Karachi from *September 21, 2021* to *March 20, 2022*.

## **SAMPLE SIZE**

Sample size was calculated by using G power sample size calculator. By using the mean of HDL at baseline  $45.8 \pm 11.9$  and 1 week after cholecystectomy  $42.7 \pm 11.2$ <sup>7</sup>, assuming correlation value 0.5, power 80% and confidence interval 95%. The required sample size for this study was 88.

## **SAMPLING TECHNIQUE**

Non-Probability, Consecutive Sampling.

## **INCLUSION CRITERIA**

- Patient between age groups 15-65 years of age.
- Patient had symptomatic gallstones (patients had on and off pain (VAS>3) in the right upper quadrant region with or without vomiting and ultrasonographic evidence of gallstone).
- Patients had gall stone symptoms for 4 weeks or more (irrespective of number and size of stone).
- ASA class <3.
- Patient underwent cholecystectomy (open or laparoscopic).

## **EXCLUSION CRITERIA**

- Patients who were malnourished.
- Patients with the presence of gallbladder malignancy.
- Patients who were pregnant.
- Patient already diagnosed dyslipidemia and took lipid lowering medication.
- Emergency cholecystectomy.

## **DATA COLLECTION**

Study was conducted after taking approval from CPSP and ethical review committee of the institute. All patient fulfilling the inclusion criteria were enrolled in the study from OPD of Dr. Ruth Pfau civil hospital. Demographic details and clinical history were taken at the time of admission. Preoperative 3 ml blood samples after 12 hours fasting were taken from all the patients under aseptic conditions one day before surgery for assessing the preoperative lipid profile. Laparoscopic or open cholecystectomy was carried out in all the patients under the hands of skilled and experienced surgeons (consultants had at least 5 years of post-fellowship experience). Postoperative 3 ml samples were obtained at one week and one month postoperatively and sent to the laboratory for assessment of postoperative lipid profile. Various serum lipid parameters that were analyzed were included total cholesterol (TC), Low -density lipoprotein (LDL), High - density lipoprotein cholesterol (HDL-C), and Triglycerides (TGs). All the findings of qualitative and quantitative variables such as age, gender, height, weight, BMI, place of residence, diabetes, hypertension, smoking, duration of symptoms, size of stone and ASA class were noted in a predesigned performa.

**DATA ANALYSIS**

All the results were recorded in the Microsoft Excel sheet and were analyzed by SPSS version 24. For quantitative variable like age, duration of stone, size of stone, height, weight, BMI, preoperative and postoperative total cholesterol (Tc), Low-density lipoprotein (LDL), High-density lipoprotein (HDL), triglyceride (Tg), mean±SD/median(IQR) were computed. Normality of data was assessed by using Shapiro Wilk test. However, frequency and percentage were computed for qualitative variables like gender, place of residence, ASA status, smoking, hypertension and diabetes. Difference between preoperative and post-operative lipid profile was assessed by applying paired ‘t’ test / Wilcoxon Sign Rank test. Effect modifiers like age, gender, place of residence, BMI, duration of symptoms, ASA class, diabetes, hypertension and smoking were addressed through stratifications. Poststratification paired t test was applied. P ≤0.05 was taken as significant.

**RESULTS**

In this study 88 patients were included to assess the mean change (pre and postoperative) in serum lipid profile in patients with cholelithiasis and the results were analyzed. The distribution of continuous variables was tested by applying Shapiro-Wilk test for age (P=0.0001), weight (P=0.003), height (P=0.001), body mass index (P=0.0001), duration of symptoms (P=0.0001), size of stone (P=0.0001), pre-total cholesterol (P=0.0001), post-total cholesterol after 1 week (P=0.001), post-total cholesterol after 1 month (P=0.0001), pre-LDL (P=0.002), post-LDL after 1 week (P=0.003), post-LDL after 1 month (P=0.009), pre-HDL (P=0.0001), post-HDL after 1 week (P=0.0001), post-HDL after 1 month (P=0.0001), pre-triglyceride (P=0.0001), post-triglyceride after 1 week (P=0.0001) and post-triglyceride after 1 month (P=0.0001).

**Table 01:** Descriptive data of patients

VARIABLE	MEAN±SD	P-VALUE
Age	48.45±13.49	0.0001
Weight	79.94±10.49	0.003
Height	168.18±8.17	0.001
Body Mass Index	27.14±4.67	0.0001
Duration of Symptoms	10.36±4.48	0.0001
Size of Stone	8.13±1.91	0.0001
Pre-Total Cholesterol	182.28±73.87	0.0001
Post-Total Cholesterol after 1 week	177.81±46.21	0.001
Post-Total Cholesterol after 1 month	179.19±54.40	0.0001
Pre-LDL	123.42±29.87	0.002
Post-LDL after 1 week	117.88±28.60	0.003
Post-LDL after 1 month	104.64±34.07	0.009
Pre-HDL	44.36±12.12	0.0001
Post-HDL after 1 week	41.94±11.42	0.0001
Post-HDL after 1 month	43.19±12.47	0.0001
Pre-Triglyceride	132.78±88.16	0.0001
Post-Triglyceride after 1 week	128.60±58.39	0.0001
Post-Triglyceride after 1 month	122.17±43.26	0.0001

The age of the patients ranged from 15 to 65 years with a median of 52.00 and with an interquartile range 18 and C.I (45.60---51.31). The weight of the patients ranged from 55 to 101 kg with a median of 80.00 with interquartile range 17 and C.I (77.72----82.17). The height of the patients ranged from 155 to 182 cm with a median of 167.50 with interquartile range 15 and C.I (166.45----169.91). The body mass index of the patients ranged from 19.72 to 38.86 kg/m<sup>2</sup> with a median of 26.28 with interquartile range 3.32 and C.I (26.15----28.13). The duration of symptoms of the patients ranged from 4 to 20 weeks with a median of 10.00 with interquartile range 7 and C.I (9.41-11.31). The

size of stone of the patients ranged from 5 to 10 mm with a median of 9.00 with interquartile range 4 and C.I (7.72----8.53). The post-triglyceride after 1 month of the patients ranged from 70 to 240 mg/dl with a median of 120.00 with interquartile range 59 and C.I(113.00----131.34). Mean  $\pm$  standard of change in pre and post operative lipid profile after 1 week, total cholesterol was  $4.47\pm 90.98$ , LDL  $5.54\pm 28.82$ , HDL  $2.42\pm 12.87$  while triglyceride was  $4.18\pm 102.09$  and p value found to be non-significant i.e. (P=0.646), (P=0.075), (P=0.081), (P=0.702) respectively.

**Table 02:** Comparison of pre-operative lipid profile and post-operative lipid profile after 1 week

LIPID PROFILE	MEAN $\pm$ SD PRE-OPERATIVE	MEAN $\pm$ SD POST-OPERATIVE	CHANGE	P-VALUE
Total Cholesterol	182.28 $\pm$ 73.87	177.81 $\pm$ 46.210	4.47 $\pm$ 90.98	0.646
LDL	123.42 $\pm$ 29.87	117.88 $\pm$ 28.60	5.54 $\pm$ 28.82	0.075
HDL	44.36 $\pm$ 12.12	41.94 $\pm$ 11.42	2.42 $\pm$ 12.87	0.081
Triglyceride	132.78 $\pm$ 88.16	128.60 $\pm$ 58.39	4.18 $\pm$ 102.09	0.702

Applied Paired Sample t-test

Mean  $\pm$  standard of change in pre and post operative lipid profile after 1 month, total cholesterol was  $3.09\pm 88.61$ , LDL  $18.78\pm 42.13$ , HDL  $1.17\pm 12.71$  while triglyceride was  $10.61\pm 97.91$  and non-significant p-value was found in total cholesterol i.e. (P=0.744), HDL (P=0.390), triglyceride (P=0.312) whereas significant p-value was found in LDL (P=0.0001).

**Table 03:** Comparison of pre-operative lipid profile and post-operative lipid profile after 1 month

LIPID PROFILE	MEAN $\pm$ SD PRE- OPERATIVE	MEAN $\pm$ SD POST- OPERATIVE	CHANGE	P-VALUE
Total Cholesterol	182.28 $\pm$ 73.87	179.19 $\pm$ 54.40	3.09 $\pm$ 88.61	0.744
LDL	123.42 $\pm$ 29.87	104.64 $\pm$ 34.07	18.78 $\pm$ 42.13	0.0001
HDL	44.36 $\pm$ 12.12	43.19 $\pm$ 12.47	1.17 $\pm$ 12.71	0.390
Triglyceride	132.78 $\pm$ 88.16	122.17 $\pm$ 43.26	10.61 $\pm$ 97.91	0.312

Applied Paired Sample t-test

Stratification of age, gender, place of residence, body mass index, duration of symptoms, ASA status, diabetes mellitus, hypertension and smoking status were done with respect to pre & post postoperative serum lipid profile in order to find statistical differences of significance.

**Table 04:** Stratification of diabetes mellitus with pre-operative lipid profile and post-operative lipid profile after 1 month

DIABETES MELLITUS	LIPID PROFILE	MEAN $\pm$ SD PRE-OPERATIVE	MEAN $\pm$ SD POST-OPERATIVE	CHANGE	P-VALUE
DIABETIC (n=25)	Total Cholesterol	185.56 $\pm$ 67.21	172.68 $\pm$ 57.64	12.88 $\pm$ 93.48	0.497
	LDL	172.68 $\pm$ 57.64	114.08 $\pm$ 31.03	15.20 $\pm$ 35.51	0.043
	HDL	46.40 $\pm$ 14.00	40.96 $\pm$ 10.33	5.44 $\pm$ 13.44	0.054
	Triglyceride	127.72 $\pm$ 76.43	119.20 $\pm$ 35.58	8.52 $\pm$ 84.98	0.621
NON-DIABETIC (n=63)	Total Cholesterol	180.98 $\pm$ 76.83	181.78 $\pm$ 53.32	-0.79 $\pm$ 87.08	0.943
	LDL	127.13 $\pm$ 28.82	106.92 $\pm$ 34.73	20.20 $\pm$ 44.66	0.001
	HDL	43.56 $\pm$ 11.31	44.08 $\pm$ 13.19	-0.52 $\pm$ 12.11	0.733
	Triglyceride	134.79 $\pm$ 92.90	123.35 $\pm$ 46.16	11.44 $\pm$ 103.22	0.382

Applied Paired Sample t-test

## DISCUSSION

Gallstones disease is a chronic recurrent hepatobiliary disease. It is one of the emerging health problems worldwide and is becoming more common with an incidence of 1.4 per 100 persons [13,14]. Biliary stones are categorized into three main types: cholesterol, pigment, or mixed. Biliary stones formation is a complex process. It is governed by major factors: supersaturation of bile secreted, concentration of bile in the gallbladder, crystal nucleation, and abnormal gall bladder emptying [15].

Gallstone disease is an interaction between genetic and environmental factors. The prevalence increases with age; as an aging population, this justifies the rise in its rate. Females carry a higher incidence by two to three folds because of sex steroids and pregnancy changes. Oral contraceptives increase cholesterol secretion and decrease bile acids, resulting in the supersaturation of bile and increasing lithogenicity [16]. Presentation differs among patients, from asymptomatic and discovered incidentally. The most prevalent symptom is severe abdominal pain, requiring investigations and treatment. By the time they become symptomatic, many patients need surgical intervention. Based on the evidence, more than 50% of patients with gall stones have some sort of lipid disorder [17]. Though lipid and bile acids metabolisms are functionally correlated, how cholecystectomy affects lipid profile is not well-comprehended. High lipid profile readings, consisting of elevations in chylomicron, low-density lipoprotein (LDL), very-low-density lipoprotein (VLDL), and IDL levels, are becoming increasingly prevalent, especially with the spreading factors such as urban residence, increasing age, especially 40 years; physical inactivity, overweight and obesity, diabetes mellitus, frequent fast food consumption, and so on [18]. Most of the gallstones patients presents with severe abdominal pain requiring investigations and treatment. Many of them need surgical intervention by the time they are symptomatic [19,20]. If the gallbladder is removed, the bile in the liver will directly enter the upper part of the intestine. As a result, BA circulate faster, thus exposing the enterohepatic system to a greater BA flux. Lipid and BA metabolisms are functionally interrelated [21]. Gallstone disease is one of the frequent gastrointestinal diseases that can be characterized by asymptomatic gall stones to acute cholecystitis [22,23]. About 10–15% of the adult population is known to present gall stones with obesity, advanced age, metabolic syndrome, liver disease and female gender as the common risk factors.

## CONCLUSION

It is to be concluded that a highly significant mean change was noted in LDL while insignificant changes were noted in TCL, HDL, and triglyceride in serum lipid profile in patients with cholelithiasis. Further large-scale work is recommended for the validation of current findings.

## REFERENCES

1. Gill GS, Gupta K. Pre- and post-operative comparative analysis of serum lipid profile in patients with cholelithiasis. *Int J Appl Basic Med Res.* 2017;7(3):186-8.
2. Singh DDP, Sharma DMPC, Mahar DN, Bhat DH, Shahnawaz D. Assessment of serum lipid profile in patients undergoing laparoscopic cholecystectomy. *Int J Surg Sci.* 2019;3 (3):212-4.
3. Ahi KS, Singh RP, Kaur H, Moudgil A. Serum lipid profile in pre and post cholecystectomy patients. *Int J Anatomy Radiol Surg.* 2017;6(2):1-6.
4. Haq AMM, Giasuddin ASM. Effect of cholecystectomy on lipid profile in Bangladeshi patients with cholelithiasis. *J Metab Syndrome.* 2016;05(01).
5. Osman A, Ibrahim AH, Alzamil AM, Alkhalifa AM, Badghaish DA, Al-Dera FH, et al. Is Cholecystectomy in patients with symptomatic uncomplicated cholelithiasis beneficial in improving the lipid profile? *Cureus.* 2020;12(1):e6729.
6. Haq AM, Giasuddin A, Jhuma K, Choudhury M. Effect of cholecystectomy on lipid profile in Bangladeshi patients with cholelithiasis. *J Metabolic Syndr.* 2015;4:192.
7. Faxon DP, Fuster V, Libby P, Beckman JA, Hiatt WR, Thompson RW, et al. Atherosclerotic Vascular Disease Conference: Writing Group III: pathophysiology. *Circulation.* 2004;109 (21):2617-25.
8. Vodnala D, Rubenfire M, Brook RD. Secondary causes of dyslipidemia. *Am J Cardiol.* 2012;110(6):823-5.
9. Catapano AL, Graham I, De Backer G, Wiklund O, Chapman MJ, Drexel H, et al. 2016 ESC/EAS Guidelines for the Management of Dyslipidaemias. *Eur Heart J.* 2016;37(39): 2999-3058.
10. Nissen SE, Stroes E, Dent-Acosta RE, Rosenson RS, Lehman SJ, Sattar N, et al. Efficacy and tolerability of evolocumab vs ezetimibe in patients with muscle-related statin intolerance: the GAUSS-3 randomized clinical trial. *JAMA.* 2016;315(15):1580-90.

11. Vallejo-Vaz AJ, Robertson M, Catapano AL, Watts GF, Kastelein JJ, Packard CJ, et al. Low-density lipoprotein cholesterol lowering for the primary prevention of cardiovascular disease among men with primary elevations of low-density lipoprotein cholesterol levels of 190 mg/dl or above: analyses from the WOSCOPS (West of Scotland Coronary Prevention Study) 5-year randomized trial and 20-year observational follow-up. *Circulation*. 2017;136(20):1878-91.
12. Ford I, Murray H, McCowan C, Packard CJ. Long-term safety and efficacy of lowering low-density lipoprotein cholesterol with statin therapy: 20-year follow-up of West of Scotland Coronary Prevention Study. *Circulation*. 2016;133(11):1073-80.
13. Chen X, Yan XR, Zhang LP. Ursodeoxycholic acid after common bile duct stones removal for prevention of recurrence: a systematic review and meta-analysis of randomized controlled trials. *Medicine (Baltimore)*. 2018;97(45):e13086.
14. Ibrahim M, Sarvepalli S, Morris-Stiff G, Rizk M, Bhatt A, Walsh RM, et al. Gallstones: watch and wait, or intervene? *Cleve Clin J Med*. 2018;85(4):323-31.
15. Kruger AJ, Modi RM, Hinton A, Conwell DL, Krishna SG. Physicians infrequently miss choledocholithiasis prior to cholecystectomy in the United States. *Dig Liver Dis*. 2018;50(2):207-8.
16. Parkin E, Stott M, Brockbank J, Galloway S, Welch I, Macdonald A. Patient-reported outcomes for acute gallstone pathology. *World J Surg*. 2017;41(5):1234-8.
17. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem*. 1972;18(6):499-502.
18. Catapano AL, Graham I, De Backer G, Wiklund O, Chapman MJ, Drexel H, et al. 2016 ESC/EAS Guidelines for the Management of Dyslipidaemias. *Rev Esp Cardiol (Engl Ed)*. 2017;70(2):115.
19. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019;139(25):e1082-143.
20. Meeusen JW, Snozek CL, Baumann NA, Jaffe AS, Saenger AK. Reliability of calculated low-density lipoprotein cholesterol. *Am J Cardiol*. 2015;116(4):538-40.
21. Martin SS, Blaha MJ, Elshazly MB, Toth PP, Kwiterovich PO, Blumenthal RS, et al. Comparison of a novel method vs the Friedewald equation for estimating low-density lipoprotein cholesterol levels from the standard lipid profile. *JAMA*. 2013;310(19):2061-8.
22. Herink M, Ito MK. Medication Induced Changes in Lipid and Lipoproteins. In: Feingold KR, Anawalt B, Boyce A, Chrousos G, de Herder WW, Dhatariya K, Dungan K, Hershman JM, Hofland J, Kalra S, Kaltsas G, Koch C, Kopp P, Korbonits M, Kovacs CS, Kuohung W, Laferrère B, Levy M, McGee EA, McLachlan R, Morley JE, New M, Purnell J, Sahay R, Singer F, Sperling MA, Stratakis CA, Trencle DL, Wilson DP, editors. *Endotext*. MDText.com, Inc.; South Dartmouth (MA): May 10, 2018.
23. Gooding HC, Rodday AM, Wong JB, Gillman MW, Lloyd-Jones DM, Leslie LK, et al. Application of pediatric and adult guidelines for treatment of lipid levels among US adolescents transitioning to young adulthood. *JAMA Pediatr*. 2015;169(6):569-74.