

Lipid Profile: Parametric test sounds simple but significant in diagnostic approach

Arun Kumar

Professor and Head, Department of Biochemistry, Krishna Mohan Medical College and Hospital, Sonkh Road, Mathura, Uttar Pradesh-281123

Correspondence:

Dr. Arun Kumar,
Professor and Head, Department
of Biochemistry, Krishna
Mohan Medical College
and Hospital, Sonkh Road,
Mathura, Uttar Pradesh-281123.
Mobile: 07584089886.
E-mail: arun732003@gmail.com

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ABSTRACT

Lipid profile test is usually requested by physician to determine the subject's risk of coronary heart diseases. The items in the panel of profile have shown to be fantastic indicators as prognostic and diagnostic tools in analyzing the risk of subject who is likely to have a heart attack or stroke in future. This test is very significant in diagnosis of wide variety of diseases and could be used as a marker. The other important area of concern is the risk caused solely by low density lipoprotein (LDL) which is recognized as an important risk factor for coronary artery disease (CAD) and is the main target for lipid lowering therapy. Apart from the lipid profile as a prognostic tool in cardiovascular diseases, the concomitant measurement of plasma hsCRP levels is highly recommended as it acts as an inflammatory marker. Apart from cardiovascular diseases, there are many more diseases where lipid profile may serve as a prognostic factor. One such is in cancer patients. In some malignant diseases, the serum cholesterol is altered significantly. The lipid profile prognostic significance can also be observed in patients with falciparum malaria. The diagnostic importance of lipid profile changes can also be exploited in cases with acute pancreatitis. Even in cases of liver disorder the lipid parameters are affected.

Key words: Lipid Profile, Diagnostic Significance, NCEP-ATP, Inflammation, Acute Pancreatitis, Cancer, Malaria

What does lipid profile means?

It is a group of tests that physician requests to diagnostic laboratory of biochemistry to determine the subjects risk of coronary heart diseases. The items in the panel of profile have shown to be fantastic indicators as prognostic and diagnostic tools in analyzing the risk of subject who is likely to have a heart attack or stroke in future, which could be due to blockage of blood flow or hardening of the arteries which in technical terms means atherosclerosis.

What are the parameters usually included when someone calls for lipid profile

Mostly it includes determination of Total cholesterol (TC), High density lipoprotein cholesterol (HDL-C), Low density lipoprotein cholesterol (LDL-C) and Triacylglycerol (TAG). Sometimes just by measuring these parameters the risk assessments cannot be fully justified so the physician calls for an extended profile. It means inclusion of some more parameters which is currently emerging biomarkers which concomitantly helps the physician in having a clear picture of the patients, how much likely they are going to

be in the risk of cardiovascular disease. The parameters included in extended assay are Apolipoprotein A-I, Apolipoprotein B, High sensitivity C-reactive proteins, Lipoprotein (a), small-low density lipoprotein (sLDL), Apolipoprotein A-II, Apolipoprotein C-II, Apolipoprotein C-III and Apolipoprotein E.

Now the major concern is the ratio of total cholesterol/HDL-C ratio, Triacylglycerol/HDL-C ratio what we consider it as lipid of atherogenic potential. This risk is mainly based on the these ratios along with the variable parameters like age, sex in addition to conventional risk factors like smoking, diet, exercise, sedentary life style, obesity, hypertension, diabetes.¹ The best part is to keep our HDL-c always on the higher side (> 65 mg/dl) so that one can enjoy the benefit of one risk factor being subtracted.

Usually the blood sample for lipid profile assay is collected after twelve hours fasting, except water is permitted but if avoided results could be better. It is not necessary to get your lipid profile checked when you are in hospital with some ailment but it is recommended for all healthy individuals to get there blood tested for lipid profile once every one year even they do not have any risk for heart diseases.

If you are known to have any remarkable risk factor and also if you are already on lipid lowering drugs (statins), than it is always advised to get it checked at frequent intervals say at six months interval and if your pocket does not permit than at least get your total cholesterol test done and if found drastically on the higher reference range than go for a total lipid profile assay along with the extended lipid profile and additive parameters as mentioned above to really know at how risk you are and also it would get you to check the effectiveness of your statins therapy.

Though for children and adolescents lipid testing is usually not called for routinely but it is always advised to check their profile too in case they have familial history of cardiovascular risks or death due to myocardial infarction, as the tendency for them to develop in future is always on the higher side. By seeing the children who are obese and have high blood pressure, parents of those are advised to check the lipid profile for their children. These children must get their lipid profile done when they are between two to ten years old as it is recommended by the American Academy of Pediatrics.

Soon when you get your laboratory reports of lipid profile, your physician determines the risk at what you are in after taking in consideration with your additive risks and then it would be considered whether you must start with lipid lowering drugs or just advised to be of low fat diet and exercise.

Our idea should be always to be on the safer side and our lipid profile should adhere to the guidelines laid down by National Cholesterol Education Program (NCEP).

As per NCEP², the following are the values of lipid profile-

LDL-Cholesterol: <100 mg/dl (2.59 mmol/l)

Borderline high: 130-159 mg/dl (3.37-4.12 mmol/l)

High: 160-189 mg/dl (4.15-4.90 mmol/l)

Very high: > 190 mg/dl (4.90 mmol/l)

If you would find your LDL-C is \leq 130 mg/dl than you are in safe zone but if increases, than you are approaching to risk. Keep a check on your diet pattern and if never go for brisk walking, you must start at least 30 min/day to burn your fat and calories.

As far as Total cholesterol is concerned

Desirable range of Total -Cholesterol: <200 mg/dl (5.18 mmol/l)

Borderline high: 200-239 mg/dl (5.18-6.18 mmol/l)

High: \geq 240 mg/dl (6.22 mmol/l)

It is always advisable to keep your HDL-Cholesterol always towards higher side because it is a negative risk factor and it is considered as good cholesterol and it is also called as a scavenger lipoprotein as it decreases the load of lipids from other circulating lipoproteins (lipids + proteins). Moreover HDL-C is associated with arylesterase activity (the enzyme which decreases the generation of free radicals and does not allow other lipoproteins to get oxidized, means much more atherogenic.

As per NCEP guidelines the risk increases when your HDL-C is well below >40 mg/dl (1.0 mmol/l) for men and for women > 50 mg/dl (1.3 mmol/l). The average risk is when it is between 40-50 mg/dl (1.0-1.3 mmol/l) for men and 50-59 mg/dl (1.3-1.5 mmol/l) for women. And as your HDL-C tends to be on higher side you are much safe and your levels should be >60 mg/dl for both genders (1.55 mmol/l).

As far as Triglycerides (TG) are concerned the desirable range should be <150 mg/dl(1.70 mmol/l), borderline high is from 150-159 mg/dl(1.7-2.2 mmol/l), high is from 200-499 mg/dl (2.3-5.6 mmol/l) and very high when found >500mg/dl(5.6 mmol/l).

The latest recommendation of American College of Cardiology and American heart Association in combination with national Heart, Lung and Blood Institute have released four new guidelines- The cholesterol management guidelines, a risk assessment guideline, obesity, and lifestyle recommendations.

Now when the physician gets aware of your lipid profile status, the first step in the treatment is advice the patient to change his life style specifically targeting their dietary pattern, consisting of low cholesterol and also motivate them to go for mild to moderate exercise. If it is observed that these two parameters are not adequate enough to lower the cholesterol than the next step is to begin with drug therapy. These days several class of drugs being marketed mainly to lower the cholesterol, mainly statins. First to begin with a low dosage and drastically adjust the dose depending on the lipid profile values and the dose is adjusted.

For knowledge for the commoners, the lipid profile consists of TC, LDL-C, VLDL-C, HDL-C, TG. All these lipoproteins are classified based on the content and composition of cholesterol, protein and triglycerides. LDL contains highest cholesterol concentration, VLDL contains highest TG and HDL contains the highest amount of protein. Usually as mentioned earlier HDL is always been beneficial for its scavenging properties. The VLDL is derived by Friedwald's equation of TG/5 as it contains maximum TG.

Since TG is considered to be dangerous due to its atherogenic nature, their ability to initiate or fasten the process of atherogenesis, which causes the deposition of atheromas, lipid and calcium in the arterial lumen, so the risk of heart disease and stroke is directly related to VLDL concentrations. In technical term all cholesterol coming from Non-HDL-c fragment are considered to be atherogenic, they can cause narrowing of blood vessels and blockages.

Sometimes we must be aware when exactly the sample for lipid profile needs to be collected, because it might cause pre-analytical errors in results if the standard operating procedure is not followed. Ideally, if this test is done with 12-hours fasting (no food and drink, except water) the results could be more accurate. For those who are smokers, try avoiding smoking at least 24 hours before as it might affect the results.

With the advent of latest researches, now the concept of lipid profile analysis has changed and we keep adding the latest concepts based on the findings of researches. Now the latest NCEP ATP-IV (Adult Treatment Panel) guidelines focus on ASCVD risk reduction, New perspective on LDL-C and Non-HDL-C treatment goals, Global risk assessment for Primary prevention, Role of Biomarkers and Non-Invasive tests.

It would take some time for a commoner to digest this very fact and get it recognized in public. So it is wiser to continue with the already familiar and proven measurements of LDL-C/HDL-C ratio as it provides key information regarding coronary heart disease risk and is a better predictor than LDL-C alone. The salient points one must remember is to target the levels for both LDL-C and HDL-C to understand the risk of heart disease as its substantiated with several epidemiological and clinical studies for being the excellent monitor for checking the effectiveness of lipid lowering therapies. Also if one

could get the ratio of these two parameters, we could literally judge the two way traffic of cholesterol entering and leaving arterial intima.

Now the point is why we switch on to the ratio of LDL-C/HDL-C, it is because this ratio is not affected by dietary cholesterol as it increases both LDL and HDL cholesterol, with a minimal change in the LDL-C/HDL-C ratio. If to be more precise it is predicted to increase 0.01 unit per 100 milligrams/day increase in dietary cholesterol, an amount unlikely to impact cardiovascular disease risk. In a large cohort study, the use of LDL-C/HDL-C ratio did not offer any advantage over the traditional lipid ratio of TC/HDL-C in terms of measuring prediction of future coronary events.³

The other important area of concern is the risk caused solely by low density lipoprotein (LDL) which is recognized as an important risk factor for coronary artery disease (CAD) and is the main target for lipid lowering therapy. The LDL particles are heterogeneous in nature respect to its size, density, chemical composition and electrical charge and certain particle of LDL being more atherogenic compared to others. Reports from several case control and prospective studies from different parts of the world have established an association between small dense LDL particles and increased risk of CHD.⁴ The association of small dense LDL is well correlated with other well-recognized risk factors such as increased plasma triglycerides and apolipoprotein B as well as decreased HDL cholesterol levels.⁵

It is said that the atherogenicity of small dense LDL is based on a number of factors. The small dense LDL particles are highly susceptibility to oxidation and there by the affinity for their receptors decreases with more affinity to bind to the arterial wall and its permeability towards the arterial cells more readily increases. Furthermore the small dense LDL particle also has a negative effect on endothelial function.⁵

Apart from the lipid profile as a prognostic tool in cardiovascular diseases, the concomitant measurement of plasma hsCRP levels is highly recommended as it acts as an inflammatory marker.⁶ It is said that irrespective of different treatment strategies the basal plasma hsCRP levels are always on the higher side. So it becomes immense important to analyze both plasma hsCRP level and TC/HDL-C ratio independently to predict future cardiovascular events⁷ and confirming hsCRP for its role as a biomarkers in clinical risk stratification especially in patients undergoing medical treatment.

These two parameters are the strongest predictors of future cardiovascular events even in healthy subjects irrespective of gender. The cut-off point for hsCRP is >0.1 mg/dl and for ratio it is >4.8. If they shoot to higher levels, it is indicative of future cardiovascular events, especially in those receiving medical treatment.

Research findings state an association of HDL-C and TG with the mortality in patients with heart failure.⁸ It is demonstrated that higher serum HDL and lower serum TG were associated with lower mortality in patients with symptomatic heart failure of different etiologies.⁹ The protective role of HDL-C may be explained on the basis of endotoxin- lipoprotein hypothesis, which means that serum lipoproteins modulate inflammatory immune function and HDL-C has antioxidant, anti-inflammatory and anti-thrombic properties. It has been hypothesized that serum lipids measured in the early period of stroke are predictive of stroke severity and outcome. The levels of TG and HDL-C were significantly lower in patients.

An expert panel formed by the National Lipid Association (NLA) currently recommends a enormous expansion in the use of new biomarkers for the diagnosis and management of cardiovascular disease.

The consensus panel recommends that the use of LDL particle number for initial clinical risk assessment of CVD is reasonable for many patients at intermediate risk, including patients with a family history of coronary heart disease (CHD) and recurrent cardiac events. In addition, LDL particle number should be considered in the risk assessment of selected patients with known CHD or CHD risk equivalent.

The panel also recommends that LDL particle number for on-treatment management of CVD risk is reasonable for many patients at intermediate risk, including patients with coronary heart disease, a CHD risk equivalent and in patients with recurrent cardiac events. LDL particle number should be considered in the management of selected patients with a family history of CHD.

Apart from cardiovascular diseases, there are many more diseases where lipid profile may serve as a prognostic factor. One such is in cancer patients. In these patients, there is drastic lowering of plasma TC, HDL-C which is considered as non-specific prognostic parameters in patients.¹⁰ The prognosis of women with early-stage breast cancer is affected by certain metabolic factors, namely insulin and body mass index. Higher levels of TC were observed amongst low grade tumors.

In some malignant diseases, the serum cholesterol is altered significantly. It has been proposed that alteration in serum cholesterol in the proliferating tissues and in blood could reflect its role in carcinogenesis.¹¹ The link of lipids with cancer might be affirmed as lipids have an integral role in the maintenance of cellular integrity. Also, it is observed that antineoplastic therapies have an influence on lipid profile.

The lipid profile prognostic significance can also be observed in patients with falciparum malaria.¹² In these patients the most remarkable feature is severe elevations of serum TG and VLDL which on treatment declines.

The diagnostic importance of lipid profile changes can also be exploited in cases with acute pancreatitis. Acute pancreatitis (AP) is a common systemic inflammatory disorder of the pancreas. Levels of serum total cholesterol, HDL cholesterol and LDL cholesterol are significantly lower in patients with severe acute pancreatitis in first two days of episode.¹³ Also the level of HDL-C falls significantly in alcoholic and hypertriglyceridemic AP cases denote the severity of the disease.

Even in cases of liver disorder the lipid parameters are affected. Since lipids are essential components of biological membranes, free molecules and metabolic regulators that control cellular function and homeostasis. Liver plays an immense role in lipid metabolism. Dyslipidemia seen in chronic liver disease differs from the other causes of secondary dyslipidemia.¹⁴

Thus, it could be realized that just by simple measurement of lipid profile, we can arrive with so many diagnostic features of it and its clinical usefulness too. In a nutshell only little have been discovered about the lipids and many more are awaited from the future researches with respect to its diagnostic and prognostic implications in management of diseases.

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Orcid ID: Dr. Arun Kumar - <http://orcid.org/0000-0003-2057-9163>

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