Republic of Yemen

Ministry of Higher Education & Scientific Research

Emirates International University

Faculty of Medicine and Health Sciences

# Reference Values for Lipid Profile in Yemeni Adult Males

A graduation project submitted to Faculty to Medicine and Health Sciences
as requirement of the Bachelor Degree in Laboratory Medicine

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**2022$^{AD}$ / 1443$^{H}$**

# *Dedication*

We have no valuable and sufficient words to express our feeling and thanks, but we would to lovingly dedication this research to our respective parents and families, to the hundreds of people in community who are in pursuit of a healthy living, to our university, doctors, friends, and all supporters who were a backbone to us.

# *Acknowledgments*

The Prophet Muhammad Peace be upon him said: He who does not thank people does not thank ALLAH.

First of all, we thank ALLAH abundantly for granting us success and assistance in completing this study.

We wish to express our special thanks of gratitude to our **Prof. Waled Al-Dubai** for his guidance and constant supervision as well as valuable information he provided us with, which contributing to enriching the subject of our study in its various aspects.

We thankful and express our kind gratitude towards **Associate. prof. Dr /Abdulbasite Al-ghoury** the head of department, and **Assist. Prof. Dr/ Taha Alnosary**, and **Prof. Saleh Al-dhahry** Dean of Faculty of Medicine and Health Sciences.

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# List Of Abbreviations

| Item | Description |
|---|---|
| ABCA1 | ATP binding cassette transport A1 |
| ACAT | Acyl CoA:cholesterol acyltransferase |
| AGPAT | Acylglycerol-3-phosphate acyltransferases |
| AMP | Adenosine monophosphate |
| AMPK | Activated protein kinase |
| Apo B | Apo lipoprotein-B |
| ATP | Adenosine triphosphate |
| BMI | Body Mass Index |
| CDC | Center of Disease Control |
| CDP-DG | Cytidine diphosphate diacylglycerol |
| CETP | Cholesterol ester transfer protein |
| CHD | Coronary heart disease |
| CO2 | Carbone dioxide |
| CoA | Acetyl coenzyme A |
| DG | Diacylglycerol |
| DGAT | Diacylglycerol acyltransferase |
| DNA | Deoxyribonucleic acid |
| DPP | Dimethylallyl pyrophosphate |

| | |
|---|---|
| **ER** | Endoplasmic reticulum |
| **FH** | familial hypercholesterolemia |
| **FPP** | Farnesyl pyrophosphate |
| **G3P** | glycerol3-phosphate |
| **GPAT** | glycerol3-phosphate acyltransferase |
| **GPP** | Geranyl pyro – phosphate |
| **H2O** | Water |
| **HDL** | High density lipoprotein |
| **HDL-C** | High density lipoprotein-cholesterole |
| **HMG** | 3-hydroxy-3-methylglutaryl |
| **IDLs** | Intermediate density lipoprotein |
| **IPP** | Isopentenyl pyrophosphate |
| **LCAT** | lecithin:cholesterol acyltransferase |
| **LDL** | Low density lipoprotein |
| **LPA** | Lysophosphatidic acid |
| **NADPH** | Nicotinamide adenine dinucleotide phosphate |
| **PA** | phosphatidic acid |
| **PC** | phosphatidylcholine |
| **PE** | phosphatidylethanolamine |
| **PH** | Potential of hydrogen |
| **RIs** | Reference intervals |

| | |
|---|---|
| **SD** | Standard Deviation |
| **SLOS** | Smith-Lemli-Opitz syndrome |
| **SPSS** | Statical Package for the Social Sciences |
| **SR-A** | Scavenger receptor class A |
| **SR-B1** | scavenger receptor class B type 1 |
| **SRE** | Sterol regulatory element |
| **SREBP** | sterol regulatory element Binding protein |
| **TAGs** | Triglyceride |
| **TG** | Triglyceride |
| **USA** | United State Of America |
| **VLDL** | Very low Density Lipoprotein |

## Abstract

**Background:** The reference values obtained from western reagent kits cannot be effective for Yemeni population, and every laboratory should be established its own reference intervals for the optimal and true diagnosis in the clinical practice , so this study aimed to determine the reference values for blood lipids profiles in Yemeni adult males.

**Methods:** This study was cross-sectional study carried out on 120 Yemeni adult males aged 18 - 65 years in Sana'a city, Yemen, during 2022.

**Results:** All reference values of lipid profile of Yemeni adult males were different from the existing reference ranges. Triglycerides shows significant increase in serum level in ≥ 30 years group compare to < 30 years group (p-value =0.0003), but total cholesterol , HDL-Cholesterol and LDL-Cholesterol have non-significant change. There were significant positive correlation between BMI with total cholesterol and LDL-cholesterol (p-value = 0.0003, 0.049), and positive correlation between age with total cholesterol ,LDL-cholesterol and triglycerides (p-value= 0.012, 0.021, 00003). LDL-cholesterol equation that formulated by using linear regression can be used to predict LDL-cholesterol from total cholesterol (Adjusted R Square =0.906, and p-value = $6.5 \times 10^{-41}$).

**Conclusion:** The results of the study propose that the currently used reference intervals for lipid profile test are not quite representing the actual reference intervals of the healthy Yemeni adult males. Hence, it is more convenient and trustful to use the outcomes of this study which are established reference intervals rather than the currently used ones in the clinical practice.

# 1- Introduction

Reference values are used to describe the dispersion of variables in healthy individuals **(Yang *et al.*, 2014)**, or the range of normality or the range of value used from doctor to estimate patients state **(Smith *et al.*, 2009).**

They are usually reported as population-based reference intervals (RIs) comprising 95% of the healthy population. Lipid derivates in body the second source of energy for the body **(German.*et al.*, 2006)** but present of lipid in abnormal value in body regarded as risk factor for many cardiovascular disease **(Bastien *et al.*, 2014),** lipid level in body different from person to person depend on many factor include sex, age and weight **(Jousilahti *et al.*, 1999)** main causes of lipid variation due to hormone change **(Flock *et al.*, 2011)**, for evaluate lipid derivates level lead to measure cholesterol, triglyceride , LDL and HDL **(Richardson *et al.*, 2020)** regarded as lipid profiles. Reliable reference values are required for all tests in the clinical lab and must be provided by clinical labs and diagnostic test manufacturers **(Kushnir *et al.*, 2015).**

The reference intervals (often known as normal values or expected values) are poorly defined and certainly not determined by a uniform process **(Stedinger *et al.*, 2008).**

## 1.1- Cholesterol

### 1.1.1- Structure of cholesterol

Cholesterol is a very hydrophobic compound. It consists of four fused hydrocarbon rings (A-D) called the "steroid nucleus"), and it has an eight carbon,

branched hydrocarbon chain attached to carbon 17 **(Dring *et al.*, 2015).** Ring A has a hydroxyl group at carbon 3, and ring B has a double bond between carbon 5 and carbon 6 **(Pei *et al.*, 2013).**

## A. Sterols

Steroids with eight to ten carbon atoms in the side chain at carbon 17 and a hydroxyl group at carbon 3 are classified as sterols. Cholesterol is the major sterol in animal tissues. [Note: Plant sterols, such as β-sitosterol are poorly absorbed by humans **(Ogbe *et al.*, 2015).**

After entering the enterocytes, they are actively transported back into the intestinal lumen because some cholesterol is transported as well; plant sterols appear to reduce the absorption of dietary cholesterol. This has led to clinically useful dietary treatment of hypercholesterolemia **(Wang *et al.*, 2013).**

Daily ingestion of plant steroid esters (in the form of commercially available trans fatty acid–free margarine) is one of a number of dietary strategies leading to the reduction of plasma cholesterol levels **(Eckel *et al.*, 2007).**

## B. Cholesteryl esters

Most plasma cholesterol is in an esterified form (with a fatty acid attached at carbon 3), which makes the structure even more hydrophobic than free (esterified) cholesterol **(Ahmed *et al.*, 2021).**

Cholesteryl esters are not found in membranes, and are normally present only in low levels in most cells. Because of their hydrophobicity, cholesterol and its esters must be transported in association with protein as a component of a lipoprotein particle or be solubilized by phospholipids and bile salts in the bile **(Hu *et al.*, 2018).**

## 1.1.2- Synthesis of cholesterol

Cholesterol is synthesized by virtually all tissues in humans, although liver, intestine, adrenal cortex, and reproductive tissues, including ovaries, testes, and placenta, make the largest contributions to the body's cholesterol pool. As with fatty acids, all the carbon atoms in cholesterol are provided by acetate, and NADPH provides the reducing equivalents **(Kanmalar *et al.*, 2022)** the pathway is endergonic, being driven by hydrolysis of the high-energy thioester bond of acetyl coenzyme A (CoA) and the terminal phosphate bond of adenosine triphosphate (ATP). Synthesis requires enzymes in both the cytosol and the membrane of the smooth endoplasmic reticulum (ER). **(Krishna *et al.*, 2018)**.

The pathway is responsive to changes in cholesterol concentration, and regulatory mechanisms exist to balance the rate of cholesterol synthesis within the body against the rate of cholesterol excretion. An imbalance in this regulation can lead to an elevation in circulating levels of plasma cholesterol, with the potential for vascular disease **(Wang *et al.*, 2013).**

### A. Synthesis of 3-hydroxy-3-methylglutaryl (HMG) CoA

The first two reactions in the cholesterol synthetic pathway are similar to those in the pathway that produces ketone bodies. They result in the production of HMG CoA **(Wang *et al.*, 2014)**.

First, two acetyl CoA molecules condense to form acetoacetyl CoA. Next, a third molecule of acetyl CoA is added, producing HMG CoA, a six-carbon compound. [Note: Liver parenchymal cells contain two isoenzymes of HMG CoA synthase. The cytosolic enzyme participates in cholesterol synthesis, whereas the

mitochondrial enzyme functions in the pathway for ketone body synthesis **(Baynes *et al.*, 2018).**

## B. Synthesis of mevalonate

The next step, the reduction of HMG CoA to mevalonate, is catalyzed by HMG CoA reductase, and is the rate-limiting and key regulated step in cholesterol synthesis. It occurs in the cytosol, uses two molecules of NADPH as the reducing agent, and releases CoA, making the reaction irreversible. [Note: HMG CoA reductase is an intrinsic membrane protein of the ER, with the enzyme's catalytic domain projecting into the cytosol. Regulation of HMG CoA reductase activity is discussed below **(Hashemi *et al.*, 2017).**

## C. Synthesis of cholesterol

The reactions and enzymes involved in the synthesis of cholesterol from mevalonate.

1- Mevalonate is converted to 5-pyrophosphomevalonate in two steps, each of which transfers a phosphate group from ATP. 2- A five-carbon isoprene unit—isopentenyl pyrophosphate (IPP)— is formed by the decarboxylation of 5-pyrophosphomevalonate. The reaction requires ATP. [Note: IPP is the precursor of a family of molecules with diverse functions, the isoprenoids. Cholesterol is a sterol isoprenoid. Nonsterol isoprenoids include dolichol and ubiquinone (Coenzyme Q). 3- IPP is isomerized to 3,3-dimethylallyl pyrophosphate (DPP).4- IPP and DPP condense to form ten-carbon geranyl pyro - phosphate (GPP).5- A second molecule of IPP then condenses with GPP to form 15- carbon farnesyl pyrophosphate (FPP). [Note: Covalent attachmentof farnesyl to proteins, a process known as "prenylation," is one mechanism for anchoring proteins to plasma membranes.].6- Two molecules of

FPP combine, releasing pyrophosphate, and are reduced, forming the 30-carbon compound squalene. [Note: Squalene is formed from six isoprenoid units. Because three ATP are hydrolyzed per mevalonate residue converted to IPP, a total of 18 ATP are required to make the polyisoprenoid squalene.]7- Squalene is converted to the sterol lanosterol by a sequence of reactions catalyzed by ER-associated enzymes that use molecular oxygen and NADPH. The hydroxylation of squalene triggers the cyclization of the structure to lanosterol.

8- The conversion of lanosterol to cholesterol is a multistep process, resulting in the shortening of the carbon chain from 30 to 27 carbons, removal of the two methyl groups at carbon 4, migration of the double bond from carbon 8 to carbon 5, and reduction of the double bond between carbon 24 and carbon 25. [Note:This ER-associated pathway includes several different enzymatic reactions. Smith-Lemli-Opitz syndrome (SLOS), a relatively common autosomal recessive disorder of cholesterol biosynthesis, is caused by a partial deficiency in 7-dehydro cholesterol-7-reductase-an enzyme involved in the migration of the double bond. SLOS is one of several multisystem, embryonic malformation syndromes associated with impaired cholesterol synthesis (**Victor *et al.*, 2018**).

## D. Regulation of cholesterol synthesis

HMG CoA reductase, the rate-limiting enzyme, is the major control point for cholesterol biosynthesis, and is subject to different kinds of metabolic control:

### 1. Sterol-dependent regulation of gene expression:

Expression of the gene for HMG CoA reductase is controlled by the transcription factor, SREBP-2 (sterol regulatory element–binding protein-2) that binds DNA at the cis-acting sterol regulatory element (SRE) of the reductase gene. SREBP

is an integral protein of the ER membrane, and associates with a second ER membrane protein, SCAP (SREBP cleavage–activating protein). When sterol levels in the cell are low, the SREBP-SCAP complex is sent out of the ER to the Golgi. In the Golgi, SREBP is sequentially acted upon by two proteases, which generate a soluble fragment that enters the nucleus, binds the SRE, and functions as a transcription factor. This results in increased synthesis of HMG CoA reductase and, therefore, increased cholesterol synthesisIf sterols are abundant, however, they bind SCAP at its sterol-sensing domain and induce the binding of SCAP to yet other ER membrane proteins (insigs). This results in the retention of the SCAPS REBP complex in the ER, thus preventing the activation of SREBP, and leading to down-regulation of cholesterol synthesis.

## 2. Sterol-accelerated enzyme degradation:

The reductase itself is a sterol-sensing integral protein of the ER membrane. When sterol levels in the cell are high, the reductase binds to insig proteins. Binding leads to ubiquitination and proteasomal degradation of the reductase.

## 3. Sterol-independent phosphorylation/dephosphorylation:

HMG CoA reductase activity is controlled covalently through the actions of adenosine monophosphate (AMP)–activated protein kinase (AMPK) and a phosphoprotein phosphatase. The phosphorylated form of the enzyme is inactive, whereas the dephosphorylated form is active. [Note: AMPK is activated by AMP, so cholesterol synthesis, like fatty acid synthesis, is decreased when ATP availability is decreased (**Menzies *et al.*, 2018**).

### 4. Hormonal regulation:

The amount (and, therefore, the activity) of HMG CoA reductase is controlled hormonally. An increase in insulin and thyroxine favors up-regulation of the expression of the gene for HMG CoA reductase. Glucagon and the glucocorticoids have the opposite effect **(Ferrier *et al.*, 2017).**

### 5. Inhibition by drugs:

The statin drugs (atorvastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin, and simvastatin) are structural analogs of HMG CoA, and are (or are metabolized to) reversible, competitive inhibitors of HMG CoA reductase. They are used to decrease plasma cholesterol levels in patients with hypercholesterolemia **(Ferrier *et al.*, 2017).**

## 1.1.3- Degradation of cholesterol

The ring structure of cholesterol cannot be metabolized to CO2 and H2O in humans. Rather, the intact sterol nucleus is eliminated from the body by conversion to bile acids and bile salts, which are excreted in the feces, and by secretion of cholesterol into the bile, which transports it to the intestine for elimination. Some of the cholesterol in the intestine is modified by bacteria before excretion. The primary compounds made are the isomers coprostanol and cholestanol, which are reduced derivatives of cholesterol. Together with cholesterol, these compounds make up the bulk of neutral fecal sterols **(Feller *et al.*, 2021).**

## 1.2 Triglycerides:

Knowledge of the way in which triglyceride is transported in the blood and of the factors that influence the transport process is essential for a proper understanding

of the overall distribution of lipids in the plasma that is observed in health and disease **(Robert *et al.*, 2020).**

The following account deals with triglyceride transport in normal individuals and provides a basis for comparison with states of abnormal lipid metabolism.The concentration of lipoprotein triglyceride in the plasma at any given time must represent a balance between the rate of entry into the plasma and the rate of removal. A change in concentration may therefore be the result of a change in either or both of these factors. Moreover, a primary change in one may result in a secondary change in the other. Thus, perhaps the main question to be asked, in any situation where the plasma triglyceride concentration is abnormally high, is whether this is due to a rise in the rate of entry or to a fall in the rate of removal **( Nikolaev *et al.*, 2015).**

## Entry of Triglyceride

About 30 to 40% of our calorie intake is normally in the form of fatty acids contained in the dietary triglyceride. Digestion in the intestinal lumen breaks down this triglyceride into free fatty acids and monoglycerides, and these are absorbed by the intestinal cells and re-synthesized into triglyceride which is then released into the lymphatics in lipoproteins called chylomicrons **(Dima *et al.*, 2020).**

The liver is the second site of triglyceride release into the plasma. The source of the fatty acids present in the triglyceride entering the blood from this organ depends markedly on the nutritional state. Thus, in a fasting individual, fatty acids are mobilized from the adipose tissue stores and are transported in the plasma in unesterified form bound to the plasma albumin. Most are carried directly to tissues such as muscle and are oxidized **(Ferrier *et al.*, 2017).**

## Triglyceride synthesis

In most mammalian cell types, the glycerol3-phosphate (G3P) pathway is the principal route for the synthesis of TG, contributing over 90% of total TG synthesis **(Coleman *et al.*, 2000).**

The first and rate-limiting step of this pathway is the esterification of long-chain acyl-CoA to G3P, which is catalyzed by mitochondrial and microsomal G3P acyltransferase (GPAT) enzymes. Lysophosphatidic acid (LPA) molecules produced in this reaction are then acylated to form phosphatidic acid (PA) by the acylglycerol-3-phosphate acyltransferases (AGPAT) present in the ER membrane. PA can be converted into cytidine diphosphate diacylglycerol (CDP-DG), which is a substrate for the synthesis of certain glycerolphospholipids and cardiolipins **(Shindou *et al.*, 2009)** or can be dephosphorylated by phosphatidate phosphohydrolase (PAP, synonym Lipin) to form DG, which serve as precursor molecules for the synthesis of TG, as well as phosphatidylcholine (PC) and phosphatidylethanolamine (PE) (Coleman etal.,2000). DG acyltransferase (DGAT) catalyzes the acylation of DG, constituting the final step of TG synthesis (55). Newly synthesized TG molecules are then directed from ER lipid bilayer to form cytosolic lipid droplets **(Goh &, Silver., 2013).**

## 1.3- Low Density Lipoprotein

### 1.3.1- Metabolism of LDL

LDL particles contain much less triacylglycerol than their VLDL predecessors, and have a high concentration of cholesterol and cholesteryl esters.

## 1. Receptor-mediated endocytosis:

The primary function of LDL particles is to provide cholesterol to the peripheral tissues (or return it to the liver). They do so by binding to cell surface membrane LDL receptors that recognize apo B-100 (but not apo B-48). Because these LDL receptors can also bind apo-E, they are known as apo-B-100/apo E receptors. A summary of the uptake and degradation of LDL particles. A similar mechanism of receptor-mediated endocytosis is used for the cellular uptake and degradation of chylomicron remnants and IDLs by the liver. LDL receptors are negatively charged glycoproteins that are clustered in pits on cell membranes. The cytosolic side of the pit is coated with the protein clathrin, which stabilizes the shape of the pit. After binding, the LDL-receptor complex is internalized by endocytosis. [Note: A deficiency of functional LDL receptors causes a significant elevation in plasma LDL and, therefore, of plasma cholesterol. Patients with such deficiencies have Type II hyper - lipidemia (familial hypercholesterolemia, FH) and premature atherosclerosis. FH can also be caused by increased activity of a protease that degrades the receptor and by defects in apo B-100 that reduce its binding to the receptor.]. The vesicle containing LDL loses its clathrin coat and fuses with other similar vesicles, forming larger vesicles called endosomes.

The pH of the endosome falls (due to the proton-pumping activity of endosomal ATPase), which allows separation of the LDL from its receptor. The receptors then migrate to one side of the endosome, whereas the LDLs stay free within the lumen of the vesicle. [Note: This structure is called CURL—the Compartment for Uncoupling of Receptor and Ligand. The receptors can be recycled, whereas the lipoprotein remnants in the vesicle are transferred to lysosomes and

degraded by lyso-somal acid hydrolases, releasing free cholesterol, amino acids, fatty acids, and phospholipids. These compounds can be reutilized by the cell. [Note: Storage diseases caused by rare autosomal recessive deficiencies in the ability to hydrolyze lysosomal cholesteryl esters (Wolman disease), or to transport unesterified cholesterol out of the lysosome (Niemann-Pick disease, Type C) have been identified.] **(Van *et al.*, 2011).**

## 2. Effect of endocytosed cholesterol on cellular cholesterol homestasis:

The chylomicron remnant-, IDL-, and LDL-derived cholesterol affect cellular cholesterol content in several ways

First, HMG CoA reductase is inhibited by high cholesterol, as a result of which, de novo cholesterol synthesis decreases.

Second, synthesis of new LDL receptor protein is reduced by decreasing the expression of the LDL receptor gene, thus limiting further entry of LDL cholesterol into cells. [Note: Regulation of the LDL receptor gene involves a SRE and a SREBP (SREBP-2), as was seen in the regulation of the gene for HMG CoA reductase.

Third, if the cholesterol is not required immediately for some structural or synthetic purpose, it is esterified by acyl CoA:cholesterol acyltransferase (ACAT). ACAT transfers a fatty acid from a fatty acyl CoA derivative to cholesterol, producing a cholesteryl ester that can be stored in the cell. The activity of ACAT is enhanced in the presence of increased intracellular cholesterol **(Aguilar-Ballester *et al.*, 2020).**

## 1.4- High Density Lipoprotein

### 1.4.1- Metabolism of HDL

HDL comprises a heterogeneous family of lipoproteins with a complex metabolism that is not yet completely understood. HDL particles are formed in blood by the addition of lipid to apo A-1, an apolipo protein made by the liver and intestine and secreted into blood. Apo A-1 accounts for about 70% of the Apo-proteins in HDL. HDL performs a number of important functions, including the following **(Feldman *et al.*, 2021).**

### 1. HDL is a reservoir of Apo-lipoproteins:

HDL particles serve as a circulating reservoir of apo C-II (the apolipoprotein that is transferred to VLDL and chylomicrons, and is an activator of lipoprotein lipase), and apo E (the apolipoprotein required for the receptormediated endocytosis of IDLs and chylomicron remnants).

### 2. HDL uptake of unesterified cholesterol:

Nascent HDL are disk-shaped particles containing primarily phospholipid (largely phosphatidylcholine) and Apo-lipoproteins A, C, and E. They take up cholesterol from non-hepatic (peripheral) tissues and return it to the liver as cholesteryl esters. [Note: HDL particles are excellent acceptors of unesterified cholesterol as a result of their high concentration of phospholipids, which are important solubilizers of cholesterol.

### 3. Esterification of cholesterol:

When cholesterol is taken up by HDL, it is immediately esterified by the plasma enzyme lecithin: cholesterol acyltransferase (LCAT, also known as P[illegible] which

"P" stands for phosphatidylcholine). This enzyme is synthesized by the liver. LCAT binds to nascent HDL, and is activated by apo A-I. LCAT transfers the fatty acid from carbon 2 of phosphatidylcholine to cholesterol. This produces a hydrophobic cholesteryl ester, which is sequestered in the core of the HDL, and lyso phosphatidylcholine, which binds to albumin. [Note: Esterification maintains the cholesterol concentration gradient, allowing continued efflux of cholesterol to HDL.] As the discoidal nascent HDL accumulates cholesteryl esters, it first becomes aspherical, relatively cholesteryl ester–poor HDL3 and, eventually, a cholesteryl ester–rich HDL2 particle that carries these esters to the liver. Cholesterol ester transfer protein (CETP) moves some of the cholesteryl esters from HDL to VLDL in exchange for triacylglycerol, relieving product inhibition of LCAT. Because VLDL are catabolized to LDL, the cholesteryl esters are ultimately taken up by the liver.

### 4. Reverse cholesterol transport:

The selective transfer of cholesterol from peripheral cells to HDL, and from HDL to the liver for bile acid synthesis or disposal via the bile, and to steroidogenic cells for hormone synthesis, is a key component of cholesterol homeostasis. This is, in part, the basis for the inverse relationship seen between plasma HDL concentration and atherosclerosis, and for HDL's designation as the "good" cholesterol carrier. Reverse cholesterol transport involves efflux of cholesterol from peripheral cells to HDL, esterification of cholesterol by LCAT, binding of the cholesteryl ester–rich HDL (HDL2) to liver and steroidogenic cells, the selective transfer of the cholesteryl esters into these cells, and the release of lipid-depleted HDL (HDL3). The efflux of cholesterol from peripheral cells is mediated, at least in part, by the transport protein, ABCA1. [Note: Tangier disease is a very rare deficiency of ABCA1 and is characterized by the virtual absence of HDL particles due to degradation of lipid-poor

Apo A-1.] The uptake of cholesteryl esters by the liver is mediated by a cell-surface receptor, SR-B1 (scavenger receptor class B type 1) that binds HDL. It is not yet clear as to whether the HDL particle itself is taken up, the cholesteryl esters extracted, and the lipid-poor HDL released back into the blood, or if there is selective uptake of the cholesteryl ester alone. [Note: Hepatic lipase, with its ability to degrade both TAG and phospholipids, also participates in the conversion of HDL2 to HDL3.

## 1.5 Cholesterol and Cardiovascular diseases

Major risk factors for atherosclerosis include high plasma levels of low-density lipoprotein (LDL) cholesterol and lipoprotein(a), as well as low plasma concentrations of high-density lipoprotein (HDL) cholesterol **(Angelantonio *et al.*, 2009).** Because elevated LDL cholesterol levels are a major causal factor for coronary heart disease (CHD) and stroke and have been a primary target of therapy for more than thirty years, the potent HMG-CoA reductase inhibitors, statins have been developed to lower plasma LDL cholesterol levels and reduce the risk of adverse cardiovascular events **(Cholesterol Treatment Trialists Collaboration *et al.*, 2010).**

Moreover, reducing LDL cholesterol levels to below current guideline targets further inhibits atherogenesis and decreases adverse coronary events (Grundy et al., 2004). Many clinical studies have found that statins can reduce new adverse cardiovascular events and CHD mortality by ~ 35%, but even aggressive statin therapy can not completely eliminate cardiovascular risk. Approximately 65% of the patients treated with stat- ins still develop adverse cardiovascular events. Therefore, additional therapeutic interventions beyond statins are strongly needed to further reduce the risk of developing CHD and stroke **(Barter *et al.*, 2003).**

## Chapter one Introduction

Cholesterol is essential for all cells in the body and it is used extensively as a major structural component of cell membranes and as a substrate for the synthesis of other steroids such as bile acids, vitamin D, and sex hormones such as estradiol, progesterone, androsterone and testosterone, as well as adrenocortical hormones such as aldosterone and cortisone. The liver and small intestine are two crucial organs for cholesterol homeostasis. Indeed, high cholesterol biosynthesis in the liver leads to more very low-density lipoprotein (VLDL) secreted into plasma, thereby increasing plasma total and LDL cholesterol concentrations. Increased quantities of dietary cholesterol also cause plasma cholesterol concentrations to rise in most individuals. Accumulated evidence has clearly demonstrated that elevated total and LDL cholesterol levels in plasma are an important risk factor for the development of cardiovascular diseases in humans and laboratory animals **(Wang, 2013).**

Because CHD is still a leading cause of death and disability in the USA and Europe, the National Cholesterol Education Program Adult Treatment Panel III guidelines **(The National Cholesterol Education Program, 2001),** along with the 2012 update and the American Heart Association/ American College of Cardiology recommendations **(Greenland *et al.*, 2010),** have suggested a much lower target for plasma LDL cholesterol concentrations (i.e., < 100 mg/dL) for individuals at high risk for adverse cardiovascular events. In this way, the total number of patients requiring more aggressive cholesterol-lowering treatment increases substantially. Because the cholesterol carried in LDL particles is derived mainly from both de novo synthesis and absorption from the diet, a better understanding of the regulatory mechanisms of hepatic cholesterol biosynthesis and intestinal cholesterol absorption should lead to novel approaches to the treatment and the prevention of CHD and stroke. Therefore, despite major advances in the treatment of atherogenic lipoproteins, substantial

residual risk in patients with CHD and stroke is under intensive investigation. Many epidemiological investigations and clinical studies have clearly demonstrated that the cholesterol contained within HDL is inversely associated with risk of CHD and is a critical component of predicting its risk **(Wang *et al.*, 2017).**

The HDL particles were first found in the 1960s after isolation by ultracentrifugation. After a method to precipitate apoB-containing lipoproteins was established, it could determine the cholesterol content of HDL in individual healthy subjects and patients with CHD. As a result, large scale epidemiological studies on the relationship between the plasma concentrations of HDL cholesterol and the prevalence of CHD were extensively performed. The Framingham Heart Study showed the first compelling evidence of the strong inverse association between HDL cholesterol concentrations and CHD. Based on these epidemiological findings, a widely acknowledged concept was proposed that HDL might have properties that protect against CHD, leading to the idea that HDL is the "good" cholesterol, as opposed to LDL "bad" cholesterol. As a result, a new concept was addressed that therapeutic intervention to raise plasma HDL cholesterol concentrations would reduce risk of CHD, which was supported by a series of animal studies in the 1980s and 1990s. Subsequently, many advances were made in understanding the molecular and genetic regulation of plasma HDL metabolism. Animal studies have found that the infusion of HDL into rabbits reduces a risk of developing diet-induced atherosclerosis.13 In addition, atherosclerosis is protected in mice overexpressing apolipoprotein A-I (apoA-I), the major HDL protein, even a high-cholesterol and high-fat diet is fed. A further study that is performed in mice with pre-existing atherosclerosis finds that overexpression of apoA-I leads to regression of pre-existing atherosclerotic disease. Taken together, these animal studies and preclinical results

match the epidemiological investigations and clinical studies, as well as strongly support the hypothesis that HDL is a key target for a novel therapeutic approach to reducing risks of developing atherosclerosis. However, human genetic analysis and some failed clinical trials have created skepticism about the importance of HDL on the prevention and the treatment of CHD. Despite the properties of HDL consistent with atheroprotection **(Wang *et al.*, 2017).**

## 1.6 Literature review

The reference values of lipid profile in Burkina Faso (Koumaré et al., 2015) in adult males the reference range for serum total cholesterol was 2.93–5.81 mmol/l, for HDL was 0.65–1.77 mmol/l, and for LDL was 1.18–3.99 mmol/l, in Iraq (Baqi etal ., 2021), in adult males the reference range for serum total cholesterol was 107-236 mg/dl, for serum triglyceride was 48-246 mg/dl, for HDL was 25-60 mg/dl, and for LDL was 63 -164 mg/dl, in Iran (Fallahzadeh et al .,2021) the reference range for serum total cholesterol was 109-275 mg/dl, for HDL was 29-62 mg/dl, and for LDL was 45 -177 mg/dl, in India (Yuthika et al., 2014) the reference range for serum total cholesterol was 85-212 mg/dl, for serum triglyceride was 61-156 mg/dl, for HDL was 20-62 mg/dl, and for LDL was 50 -147 mg/dl, in Venezuela (Bermudez et al., 2012) the reference range for serum total cholesterol was 107-269 mg/dl, for serum triglyceride was 33-207 mg/dl, for HDL was 30-76 mg/dl, and for LDL was 45 -195 mg/dl.

## 1.7 Justification

Reference value is influenced by several factors like gender, age, race, ethnicity, environment, sample type, analytical procedures, instruments and geographical location of the healthy individuals, so there is absolute need for reference values in clinical chemistry lab for all biochemical parameters, so the aim of this study is to establish reference interval for lipid profile among Yemeni adult males.

## 2-Objectives of the study

### 2.1- General objective.

To estimate reference interval for lipid profile among Yemeni adult males.

### 2.2- Specific objectives

1. To compare lipid profiles between different age groups.

2. To determine the correlation between Cholesterol, Triglyceride, LDL and HDL with Body Mass Index and age among adult males.

3.To formulate Equation to predict values of LDL-cholesterol from total cholesterol

# 3. Materials and Methods:

## 3.1 Materials:

**Table (1) Equipment and instruments**

| | Name of test | Equipment | Company | Supplier |
|---|---|---|---|---|
| 1 | Lipid profile | Bts-350 Semi Automatic Analyzer | Biosystem | EU |
| 2 | Weight | Seca | seca | Germany |
| 3 | Height | Seca | seca | Germany |
| 4 | For collecting blood samples | Vacuum tubes-gel, , syringe, centrifuge, | Kangjian | China |

## 3.2 Reagents:

### 3.2.1 HDL cholesterol kit consist of:

| | |
|---|---|
| Phosphotungstate | 14 mmol/L |
| Magnesium chloride | 1 mmol/L |
| Preservative | 1 × 4 ml |
| HD L cholesterol standared | 50 mg/dL |
| HDL cholesterol concentration | 23 mg/dl |

### 3.2.2. Triglyceride kit (GPL, Germany) consist of:

| | |
|---|---|
| Reagent 1: Pipes buffer (PH 7.5) | 50 mmol/l |
| 4-chlorophenol | 5.0 mmol/l |
| Magnesium ions | 4.7 mmol/l |
| ATP | 1.0 mmol/l |
| Lipase = | 1.0 U/ml |
| Peroxidase = | 0.5 U/ml |
| Glycerol kinase = | 0.4 U/ml |

| | |
|---|---|
| Sodium azide | 0.05 % |
| Reagent 2: 4-aminoantipyrine | 0.4 mmol/l |
| Glycerol-3-phosphate oxidase = | 1.5 U/ml |
| Sodium azide | 0.095 % |

### 3.2.3. LDL-Cholesterol kit consist of::

1 x 10 ml Precipitant solution.

Dropper for 100 tests.

Ready-to-use.

The concentrations in the reagent solution are:

| | |
|---|---|
| Polyvinyl sulphate | 0.7 g/L |
| EDTA Na | 2 5.0 mM |
| Polyethyleneglycol monomethyl ether | 170 g/L |
| Stabilizers | |

### 3.2.4 Cholesterol kit ( Human ,Germany ) consist of :

| | |
|---|---|
| Reagent 1 : Phosphate buffer ( PH 6.5 ) | 100 mmol/l |
| 4-Aminophenazone | 0.25 mmol/l |
| Phenol | 5.0 mmol/l |
| Peroxidase | > 5.0 KU /l |
| Cholesterol esterase | > 150 U/l |
| Cholesterol oxidase | > 100 U/l |
| Sodium azide | 0.05 % |
| Reagent 2 : Cholesterol standard | 5.17 mmol/l |

## 3. 3 Method:

### 3.3.1 Study design:

Descriptive cross-sectional study

### 3.3.2 Study setting:

Sana'a city, Yemen during 2022

### 3.3.3 Sample size:

The sample size calculated for a cross sectional study by the Epi Info statistical program version 20 (CDC, Atlanta, USA). The minimum sample size required for estimation of the reference values (2.5 and 97.5 percentiles) is 120 to obtain reliable estimates (Bishop *et al*, 2018; Burtis *et al*, 2015).

### 3.3.4 Inclusion criteria

Adults male with normal BMI.

### 3.3.5 Exclusion criteria

Smokers, adult's male with disease or abnormal BMI

### 3.3.6 Data collection

A questionnaire for each adult's males will be filled with the participant's information (This includes the age, weight, heights). **Body mass index (BMI)** was computed as weight in kilograms (kg) divided by height in meters squared (m2)

### 3.3.7 Specimen collection

A four ml of venous whole blood will be collected from donor to plan tube for serum for lipid profiles, after overnight fasting.

### 3.3.8 Total cholesterol assay:

#### 3.3.8.1 Principle :

Cholesterol is determined after enzymatic hydrolysis and oxidation. The indicator quinoneamine is formed from hydrogen peroxide and 4-aminoantipyrine in the presence of phenol and peroxidase . The color intensity formed is measured at 500 nm.

Cholesterol ester + $H_2O$ $\xrightarrow{CHE}$ cholesterol + fatty acids

Cholesterol + $O_2$ $\xrightarrow{CHO}$ cholestene-3-one + $H_2O_2$

$2H_2O_2$ + phenol + 4-aminoantipyrine $\xrightarrow{POD}$ quinonemine +$H_2O$

CHE: Cholesterol esterase.

CHO: Cholesterol oxidase

#### 3.3.8.2 Procedure :

To three tubes labeled sample, standard and blank, 1 ml of working reagent were pipeted, followed by 10 µl of serum sample, standard solution and distilled water were added respectively, then mixed and incubated at 37 C° for 5 minutes. The absorbance of sample and standard was measured within 60 minutes, spectrophotometrically at 500 nm against the reagent blank.

#### 3.3.8.3 Calculation:

The concentration of total cholesterol was calculated according to the following equation:

Concentration of cholesterol in the sample (mmol/l ) = Absorbance of sample X concentration of standard /Absorbance of standard.

### 3.3.9 Triglycerides assay:

#### 3.3.9.1 Principle :

Triglycerides are determined after enzymatic hydrolysis with lipase the indicator is quinoneimine formed from hydrogen peroxide , 4-aminoantipyrine and 4-chlorophenol under the catalytic influence of peroxidase .The color intensity formed is measured at 500 nm .

Triglycerides $\xrightarrow{\text{lipase}}$ glycerol + fatty acids

Glycerol + ATP $\xrightarrow{\text{GK}}$ glycerol-3-phosphate + ADP

glycerol-3-phosphate + $O_2$ $\xrightarrow{\text{G.P.O}}$ dihydroxyacetone phosphate + $H_2O_2$

$2H_2O_2$ + 4-aminophenazone + 4-chlorophenol $\xrightarrow{\text{P.O.D}}$ quinoneimine + $4H_2O$ .

GK: Glycerol kinase.

GPO: Glycerol-3-phosphate oxidase.

POD: Peroxidase.

#### 3.3.9.2 Procedure :

To three tubes labeled sample, standard and blank, 1 ml of working reagent were pipetted, followed by 10 µl of serum sample, standard solution and water respectively, then mixed and incubated at 37 C° for 5 minutes.The absorbance were then measured spectrophotometrically witin 60 minutes of the test and standard against reagent blank at 500 nm .

#### 3.3.9.3 Calculation :

The concentration of triglycerides was calculated according to the following equation :

Triglycerides concentration (mmol/l) =Absorbance of sample X concentration of standard /Absorbance of standard.

### 3.3.10 HDL-cholesterol assay

#### 3.3.10.1 Principle

The chylomicrons, Very low density lipoproteins (VLDL) and low density lipoproteins (LDL) of serum are precipitated by phosphotungstic acid and magnesium ions. After centrifugation, High density lipoproteins (HDL) are in the supernatant. HDL content in supernatant is measured by an enzymatic Method.

#### 3.3.10.2 Procedure

**1.preiceptation**

We added 30 µL of serum to 300 µL of HDL reagent, then we mixed well, allowed the mixture to stand for 10 min, a room temperature, then we mixed again and centrifuged for 10 min, at 4000 rpm.After centrifugation we separated the clear supernatant from the precipitate to determine the HDL-cholesterol concentration using the cholesterol reagent method.

**2-HDL measurement**

| | Blank | Sample | Standard |
|---|---|---|---|
| Cholesterol Reagent | 1000 µL | 1000 µL | 1000 µL |
| Standard (HDL) | ------ | ----- | 50 µL |
| HDL supernatant | ------ | 50 µL | |

We mixed and incubated for 5 min.at 37Co. Then we measured the absorbance

**3.Calculation**

$$\text{HDL Cholesterol Conc.(mg/dl)} = \frac{\text{Absorbance of sample}}{\text{Absorbance of standard}} \times N \times 11$$

Where , 11= dilution factor of the sample

N= Standard concentration (50 mg/dl)

**3.3.11 LDL-cholesterol assay**

**3.3.11.1 Principle**

LDL-Cholesterol can be determined as the difference between Total Cholesterol and the Cholesterol content of the supernatant after precipitation of the LDL fraction by Polyvinyl sulphate (PVS) in the presence of Polyethylene-glycol monomethyl ether.

**3.3.11.2 Procedure**

**1. Precipitation reaction**

| | |
|---|---|
| Precipitant solution | 0.1 ml (3 drops) |
| Sample | 0.2 ml |

Mixed well and let stand for 15 min. aprox. at room temperature (20-25°C).

Centrifuge at 2,000 x g/15 min.

The Cholesterol concentration in the supernatant was determine.

**Calculations**

**LDL-cholesterol (mg\dl) =** total Cholesterol (mg\dl) -1.5 X supernatant Cholestero (mg\dl)

### 3.3.9 Statistical analysis

All data were collected then analyzed using statistical software (SPSS Version 20; SPSS Inc, Chicago, USA). The quantitative data will be expressed as mean ±Standard deviation (SD) when the data was normal distributed or expressed as median and interquartile range when the data was not normal distributed. The reference values include 95% of the test results and bounded by the 2.5 and 97.5 percentiles. In normally distributed data, the 2.5th and 97.5th percentiles were determined parametrically, but in non-normally distributed data, the 2.5th and 97.5th percentiles were determined non-parametrically. Kolmogorov-Smirnov Test was performed to distinguish between parametric and non-parametric data. Liner regression used to estimate LDL-cholesterol equation from total cholesterol. The significant differences were indicated if P-value was ≤ 0.05.

## 4-Results

This study included 120 adult males with a mean age of 29.9 ± 10.7 years and a mean body mass index (BMI) of 21.8 ± 2.3 kg/m2. The mean ± SD and 95% reference values (2.5th – 97.5th percentiles) for biochemical tests for parametric and non-parametric data are shown in Table 2. All reference values of lipid profile of Yemeni adult males were different from the existing reference ranges.

**Table (2) Lipid profile reference values for Yemeni adult males**

| Analyte | Unit | Mean ± SD | Percentile | | Reference values |
|---|---|---|---|---|---|
| | | | 2.5th | 97.5th | |
| Total cholesterol | (mmol/l) | 4.5±0.7 | 3.2 | 5.7 | 3.1-5.9 |
| | (mg/dl) | 174 ±27 | 124 | 221 | 120-228 |
| Triglycerides | (mmol/l) | 1.0±0.5 | 0.2 | 2.1 | 0.2-2.1 |
| | (mg/dl) | 90±45 | 18 | 189 | 18-189 |
| HDL-Cholesterol | (mmol/l) | 1.06±0.22 | 0.55 | 1.5 | 0.55-1.5 |
| | (mg/dl) | 41.1±8.5 | 21.3 | 58 | 21.3-58 |
| LDL-Cholesterol | (mmol/l) | 3.1±0.66 | 1.8 | 4.2 | 1.78-4.4 |
| | (mg/dl) | 120±25.6 | 69.8 | 162.9 | 69 -170.7 |

Table (3) shows significant increase in serum level of triglycerides in ≥ 30 years group compare to < 30 years group (p-value =0.0003), but total cholesterol , HDL-Cholesterol and LDL-Cholesterol have non-significant change.

**Table (3) Comparison between lipid profile according to Age groups**

| Variables | < 30 years group (69 participants) | ≥ 30 years group (51 participants) | P-value |
|---|---|---|---|
| **Total cholesterol (mmol/L)** | 4.4±0.7 | 4.6±0.6 | 0.244 |
| **Triglycerides (mmol/L)** | 0.7 (0.9) | 1.3 (0.8) | **0.0003** |
| **HDL-Cholesterol (mmol/L)** | 1.1 (0.3) | 1.1 (0.22) | 0.831 |
| **LDL-Cholesterol (mmol/L)** | 3.0±0.6 | 3.2±0.7 | 0.135 |

Data were expressed as Mean ±SD for total cholesterol , and LDL-Cholesterol, but for HDL-Cholesterol and triglycerides presented as Median (Interquartile Range).

Table (4) shows significant positive correlation between BMI with total cholesterol and LDL-cholesterol (p-value = 0.0003, 0.049), also shows positive correlation between age with total cholesterol ,LDL-cholesterol and triglycerides (p-value= 0.012, 0.021, 00003).

**Table (3) Correlation between age , body mass index (BMI) and lipid profile**

| | | Total cholesterol (mmol/l) | Triglycerides (mmol/l) | LDL-cholesterol (mmol/l) | HDL-cholesterol (mmol/l) |
|---|---|---|---|---|---|
| BMI ($Kg/m^2$) | r | 0.437 | 0.16 | 0.33 | 0.09 |
| | p-value | **0.0003** | 0.17 | **0.012** | 0.4 |
| Age (Years) | r | 0.2 | 0.39 | 0.24 | 0.01 |
| | p-value | **0.049** | **0.00003** | **0.021** | 0.9 |

r =Correlation Coefficient

Table (5) shows Variables used to estimate linear Regression Equation to predict values of LDL-cholesterol, [LDL-cholesterol is dependent variable (Y)] and can be predicted from total cholesterol [independent variable (X)],so the equation derived from linear regression: [Y = -0.826+0.834 X].

**LDL-cholesterol (Y) = Constant + B x cholesterol (X)**

LDL-cholesterol = -0.826 + 0.834 x cholesterol

Example: If serum cholesterol level was 5.2 mmol/l , what is the LDL- Cholesterol Level?

LDL-cholesterol = -0.826 + 0.834 x 5.2 = 3.5 mmol/l

**Table (5)** Variables used to estimate Linear Regression Equation to predict values of LDL-cholesterol from total cholesterol

| | B | Adjusted R Square | F | P-value |
|---|---|---|---|---|
| Cholesterol | 0.834 | 0.906* | 739.5 | $6.5 \times 10^{-41}$ |
| Constant | -.0826 | | | $2.2 \times 10^{-7}$ |

* The value of adjusted R Square (90.6 %) indicates that: Total cholesterol level interpreted 90.6 % of LDL- Cholesterol level during fasting and the rest of percentage (9.4 %) may be explained by Other lipoproteins.

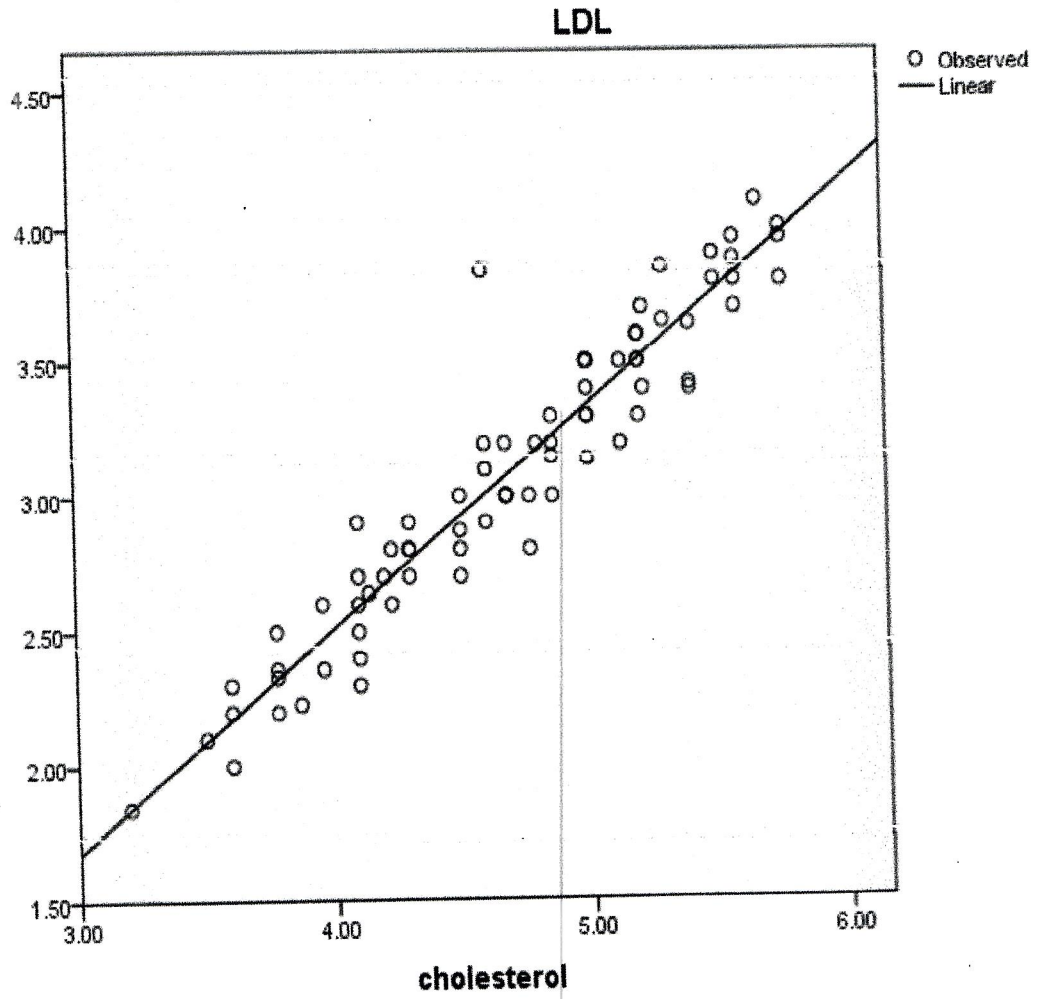


Figure (1): Linear model of regression for relationship between LDL- Cholesterol and Total-cholesterol

## 5-Discussion

Biochemical tests are essential in the diagnosis and monitoring of diseases and requiring optimal reference range for accurate interpretation of laboratory tests. The total cholesterol, LDL, HDL, and triglycerides are requested routinely by physicians for patients to assess risk factors and as follow-up investigations for cardiovascular diseases. According to the recommendations of the International Federation of Clinical Chemistry (IFCC) and national cholesterol education programme (NCEP), every laboratory should establish their own set of reference limits (Solberg., 1987).

In this study, the 95% reference range for serum total cholesterol was 120-228 mg/dl, for serum triglyceride was 18-189 mg/dl, for HDL was 21.3-58 mg/dl, and for LDL was 69 -170.7 mg/dl, so the upper limit of reference values of serum total cholesterol, triglyceride and LDL were higher than manufacturer's reference values of reagent kits but the lower limit of reference value of serum HDL was lower than manufacturer's reference values, this may be attribute to differences in lifestyle (sedentary or active), different dietary habits, and low physical activity, socio-economic status, race, geographical differences and genetics. The reference values of this study was in agreement with other studies in Iraq (Baqi etal ., 2021) the reference range for serum total cholesterol was 107-236 mg/dl, for serum triglyceride was 48-246 mg/dl, for HDL was 25-60 mg/dl, and for LDL was 63 -164 mg/dl, , in Iran (Fallahzadeh et al .,2021) the reference range for serum total cholesterol was 109-275 mg/dl, for HDL was 29-62 mg/dl, and for LDL was 45 - 177 mg/dl, in India (Yuthika et al., 2014) the reference range for serum total cholesterol was 85-212 mg/dl, for serum triglyceride was 61-156 mg/dl, for HDL was 20-62 mg/dl, and for LDL was 50 -147 mg/dl, in

Venezuela (Bermudez et al., 2012) the reference range for serum total cholesterol was 107-269 mg/dl, for serum triglyceride was 33-207 mg/dl, for HDL was 30-76 mg/dl, and for LDL was 45 -195 mg/dl.

There was significant increase in serum level of triglycerides in ≥ 30 years group compare to < 30 years group (p-value =0.0003), also there were positive correlation between age with total cholesterol ,LDL-cholesterol and triglycerides (p-value= 0.012, 0.021, 00003), these may be attributed to delay clearance of plasma lipoproteins that transport lipids due to decrease the activity of lipoprotein lipase , because the activity of lipoprotein lipase decreased with age (Spitler & Davies ., 2020), also there was significant positive correlation between BMI with total cholesterol and LDL-cholesterol (p-value = 0.0003, 0.049), and this maybe attribute to the fact, HDL-cholesterol decrease with increasing degrees of BMI among children, and adults (Yammoto **etal., 1988).**

Total cholesterol was a significant predictor of LDL- cholesterol (p-value= $6.5 \times 10^{-41}$), by using Linear regression to develop a good equation that predicts LDL-cholesterol from known total cholesterol values, because total cholesterol accounted for 90.6 % ($r^2$) variation in low-density lipoprotein values, so predicting LDL- cholesterol value from total cholesterol value offers an advantage in lab , because LDL-cholesterol cannot be assayed directly.

**LDL-cholesterol = -0.826 + 0.834 x cholesterol**

## 6-Conclusion

This study concluded to the following:

In this study, the results of the study propose that the currently used reference intervals for lipid profile test are not quite representing the actual reference intervals of the healthy Yemeni adult males. Hence, it is more convenient and trustful to use the outcomes of this study which are established reference intervals rather than the currently used ones in the clinical practice.

## 7-Recommendation

**We recommended the following:**

1-Further work up involving large number of Yemeni adult males.

2-Future studies to determine the reference range for other biochemical blood parameters.

3-Further work up involving large number of Yemeni adult females.

4-Using equation of this study for determination LDL-cholesterol

## 8-Refernces

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## الملخص العربي

**الخلفية:** القيم المرجعية التي تم الحصول عليها من الكواشف الغربية لا يمكن أن تكون فعالة بالنسبة للسكان اليمنيين ، ويجب إنشاء قيم مرجعية خاصة لكل مختبر للتشخيص الأمثل والصحيح في الممارسة السريرية ، لذلك هدفت هذه الدراسة إلى تحديد القيم المرجعية لدهون الدم في الذكور اليمنيين البالغين.

**المنهجية:** أجريت هذه الدراسة المقطعية على ١٢٠ شاب يمني بالغ تتراوح أعمارهم بين ١٨ و ٦٥ سنة في مدينة صنعاء ، اليمن ، خلال عام ٢٠٢٢.

**النتائج:** كانت جميع القيم المرجعية للدهون للذكور اليمنيين البالغين مختلفة عن القيم المرجعية الحالية. تظهر الدهون الثلاثية زيادة ذو دلاله في مستوى المصل في مجموعة ≤ ٣٠ عامًا مقارنة بمجموعة أقل من ٣٠ عامًا (القيمة الاحتمالية = ٠.٠٠٠٣) ، لكن الكوليسترول الكلي وكوليسترول البروتين الدهني عالي الكثافة وكوليسترول البروتين الدهني منخفض الكثافة ليس لها تغير كبير. كانت هناك علاقة ارتباط طرديه بين مؤشر كتلة الجسم والكولسترول الكلي والكوليسترول الضار (القيمة الاحتمالية = ٠.٠٠٠٣، ٠.٠٤٩) ، وهناك علاقة طرديه بين العمر مع الكوليسترول الكلي وكوليسترول البروتين الدهني منخفض الكثافة والدهون الثلاثية (القيمة الاحتمالية = ٠.٠١٢ ، ٠.٠٢١ ، ٠.٠٠٠٣). يمكن استخدام معادلة كوليسترول البروتين الدهني منخفض الكثافة التي تمت صياغتها باستخدام الانحدار الخطي للتنبؤ بكوليسترول البروتين الدهني منخفض الكثافة من الكوليسترول الكلي (مربع R المعدل = ٠.٩٠٦ ، والقيمة الاحتمالية = ٦.٥ × ١٠-٤١).

**الاستنتاج:** تبين نتائج الدراسة أن القيم المرجعية المستخدمة حاليًا لفحوصات الدهون لا تمثل القيم المرجعية الفعلية للذكور اليمنيين الأصحاء. ومن ثم ، فمن الملائم والأكثر ثقة استخدام القيم المرجعية لهذه الدراسة بدلاً من تلك المستخدمة حاليًا في الممارسة السريرية.

الجمهورية اليمنية
وزارة التعليم العالي والبحث العلمي
الجامعة الإماراتية الدولية
كلية الطب والعلوم الصحية

# القيم المرجعية للدهون في الذكور اليمنيين البالغين

مشروع تخرج مقدم لكلية الطب والعلوم الصحية كمتطلب للحصول على درجة البكالوريوس في الطب المخبري مقدم من:

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أستاذ الكيمياء الحيوية في كلية الطب والعلوم الصحية

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