Review Article

Evaluation & Assessment of Chest Pain among Dyslipidemic Out-Door Patients without Prior Clinical Ischemic Heart Disease

Md. Nazmul Haque[1], Syeda Tasnuva Maria[2]

Abstract:

Dyslipidemia is a significant risk factor for atherosclerotic cardiovascular diseases, including ischemic heart disease. However, hypercholesterolemia patients without a history of clinical ischemic heart disease (IHD) may experience chest pain that presents diagnostic and management challenges. This review aims to summarize the existing literature and assess the prevalence of chest pain in this specific patient without having previous heart disease.

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Introduction:

Dyslipidemia is the imbalance of lipids such as [1,2]

- Total cholesterol,
- low-density lipoprotein cholesterol (LDL-C)
- Triglycerides
- High-density lipoprotein (HDL)

Here dyslipidemia mostly interchanging with hyperlipidemia. Atherosclerotic plaque formation is major in the development of cardiovascular disorder [3-5]. Lipids play an important role in the formation of plaque.

[A] Biochemistry of Lipids

Lipoproteins and apolipoproteins

Lipoproteins are complex plasma particles containing a core of cholesterol esters and triglycerides surrounded by free cholesterol, phospholipids, and apolipoproteins, and are classified based on size, density, and major lipid and apolipoprotein content[6]. Apolipoproteins, structural proteins that bind triglyceride and cholesterol and enable the formation of lipoproteins, enjoy important roles in lipoprotein structure and metabolism by acting as ligands for lipoprotein receptors and activators or inhibitors of enzymes involved in lipoprotein metabolism [6, 7]. The size, structure, and apolipoprotein content of the lipoproteins, namely chylomicrons (CM), very-low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and lipoprotein(a) [Lp(a)], crystallize into individualized atherosclerotic risk profiles for the specific lipoprotein [8, 9].

Chylomicrons and chylomicron remnants

CMs, the largest and least dense of the lipoproteins, are triglyceride rich, released from the intestine, and primarily responsible for delivery of dietary cholesterol and triglycerides to peripheral tissue and the liver [6, 10]. Removal of triglycerides from circulating CMs generates CM remnants that possess a considerably higher cholesterol concentration [6, 11].

Very-low-density lipoprotein (VLDL) and intermediate-density lipoprotein (IDL)

Triglyceride consumption by adipose tissue and the resulting cholesterol-rich CM remnants subsequently

1. Medicine Specialist & Cardiologist, BNS Haji Mohsin, Bangladesh Navy
2. UH & FPO, Upozila Health Complex, Manikganj.

Address of Correspondence: Md. Nazmul Haque, Medicine Specialist & Cardiologist, BNS Haji Mohsin, Bangladesh Navy. Phone : 01684042647 Email: dr.shiplu_01@yahoo.com

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reach the liver, which reorganizes triglycerides and cholesterol in the form of VLDL that are secreted into circulation and allow for lipoprotein lipase (LPL) mediated absorption of triglycerides by cardiomyocytes, skeletal muscle, and adipose tissue [4, 6]. CMs, CM remnants, and VLDL contain apolipoprotein C (Apo C), specifically Apo C-II, an essential cofactor for LPL, and transposition of triglycerides from circulating lipoproteins to tissue steadily increases the concentration of cholesterol and overall density of the lipoprotein while simultaneously decreasing the size [6, 13].

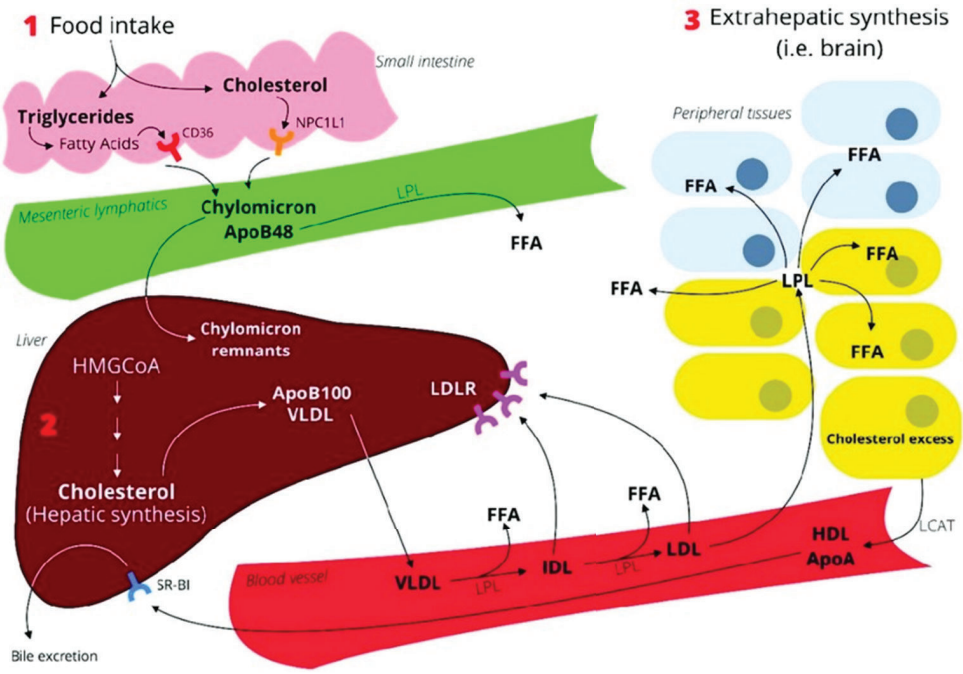
Low-density lipoprotein (LDL)

LDL, derived from LPL/Apo C-II-mediated triglyceride removal from VLDL and IDL, is the lipoprotein responsible for cholesterol transport to peripheral tissue and the lipoprotein that has been extensively studied and directly implicated in the development of atherosclerosis [4, 5]. With an average size of 18–25 nm, LDL and the predominant apolipoprotein it contains, Apo B-100, undergo oxidation and other molecular modifications that are responsible for endothelial damage, macrophage chemoattraction, and pathologic arterial changes [1, 6, 14].

The metabolism of LDL, and thus the circulatory availability and arterial wall extravasation ability of LDL, is determined by the quantity of hepatic LDLR, as the concentration of LDL generated from the metabolism of VLDL and IDL is regulated by the amount of IDL that is absorbed into the liver via the LDLR prior to LPL-mediated triglyceride removal [6, 18]. Hepatic levels of LDLR are primarily modulated by hepatocyte cholesterol levels, with adequate cholesterol levels stimulating LDLR targeting for degradation by PCSK9, a protein synthesized by hepatocytes that binds the LDLR and promotes lysosomal LDLR degradation [5, 6, 17].

High-density lipoprotein (HDL)

HDL differs from VLDL, IDL, and LDL in size, lipid, and apolipoprotein content, role in cholesterol metabolic pathways, and antiatherogenic characteristics. HDL is responsible for peripheral cholesterol uptake and delivery to the liver- and cholesterol-derived hormone-producing organs, and it provides important antioxidant and anti-inflammatory functions that can inhibit atherosclerosis [4, 6, 18]. After cholesterol uptake from peripheral tissue and macrophages, HDL facilitates transfer to the liver via scavenger receptor class B type I (SR-B1), where the cholesterol can be converted into bile acids for excretion or be directly secreted into bile [18,19]. The apolipoprotein profile and receptors involved in cholesterol movement from HDL sheds light on some of the physiologic pathways involved in HDL attenuation of atherosclerosis and conversely the highly atherogenic contents and formulation of LDL.



A basic principle of prevention is that the intensity of risk-reduction therapy should be adjusted to a person's absolute risk. Hence, the first step in selection of LDL-lowering therapy is to assess a person's risk status. Risk assessment requires measurement of LDL cholesterol as part of lipoprotein analysis and identification of accompanying risk determinants.

[B] Lipid Profile Values:

In all adults aged 20 years or older, a fasting lipoprotein profile (total cholesterol, LDL cholesterol, high density lipoprotein (HDL) cholesterol, and triglyceride) should be obtained once every 5 years. If the testing opportunity is non fasting, only the values for total cholesterol and HDL cholesterol will be usable. In such a case, if total cholesterol is ≥ 200 mg/dL or HDL is <40 mg/dL, a follow-up lipoprotein profile is needed for appropriate management based on LDL [20,21]. The relationship between LDL cholesterol levels and CHD risk is continuous over a broad range of LDL levels from low to high. Therefore, ATP III adopts the classification of LDL cholesterol levels shown in Table 1, which also shows the classification of total and HDL cholesterol level

Table-I

LDL Cholesterol	
<100	Optimal
10D-129	Mear optimal/above optimal
130-159	Borderline high
160-169	High
≥190	Very high
Total Cholesterol	
<200	Desirable
200-239	Borderline high
≥240	High
HDL Cholesterol	
<40	Low
≥60	High

Risk determinants in addition to LDL-cholesterol include the presence or absence of CHD, other clinical forms of atherosclerotic disease, and the major risk factors other than LDL (see Table 2)[22]. (LDL is not counted among the risk factors in Table 2 because the purpose of counting those risk factors is to modify the treatment of LDL.) Based on these other risk determinants, ATP III identifies three categories of risk that modify the goals and modalities of LDL-lowering therapy[23]. Table III defines these categories and shows corresponding LDL-cholesterol-goals.

Table-II

- Cigarette smoking
- Hypertension (BP >140/90 mmHg or on anti-hypertensive medication)
- low MDI cholesterol (40 mg/dl)
- Family history of premature CUD (CUD in male **first** degree relative -55 years: CUD in female first degree relative —65 years)
- Age (men >45 years: women >55 years)*

In ATP III, diabetes is regarded as a CHD risk equivalent

HDL cholesterol >60 mg/dl counts as a negative risk factor: its presence removes one factor from the total count

Table-III

Risk Category	LDL Goal (mg/dL)
CHD and CHD risk equivalents	—100
Multiple (2+) risk factors*	<130
Zero to one risk factor	<160

*Risk factors (hot modify the LDL god are fated m Table 3

The category of highest risk consists of CHD and CHD risk equivalents. The latter carry a risk for major coronary events equal to that of established CHD, i.e., >20% per 10 years (i.e., more than 20 of 100 such individuals will develop CHD or have a recurrent CHD event within 10 years). CHD risk equivalents comprise:

[C] Chest Pain:

Chest pain is a very common complaint. Many patients are well aware that it is a warning of potential life-threatening disorders and seek evaluation for minimal symptoms. Other patients, including many with serious disease, minimize or ignore its warnings [24]. Pain perception (both character and severity) varies greatly between individuals as well as between men and women. However, described, chest pain should never be dismissed without an explanation of its cause.

Pathophysiology of Chest Pain

The heart, lungs, esophagus, and great vessels provide afferent visceral input through the same thoracic autonomic ganglia. A painful stimulus in these organs is typically perceived as originating in the chest, but because afferent nerve fibers overlap in the dorsal ganglia, thoracic pain may be felt (as referred pain) anywhere between the umbilicus and the ear, including the upper

extremities.

Painful stimuli from thoracic organs can cause discomfort described as pressure, tearing, gas with the urge to eructate, indigestion, burning or aching. Uncommonly, other descriptions of chest pain are given such as stabbing or sharp needle-like pain. When the sensation is visceral in origin, many patients deny they are having pain and insist it is merely “discomfort.”

Etiology of Chest Pain

Mostly chest pain divides by cardiac & non-cardiac origin [24]

Cardiac chest pain is mainly caused by coronary heart disease that has Pressure, fullness, burning or tightness in the chest. Crushing or searing pain that spreads to the back, neck, jaw, shoulders, and one or both arms. Pain that lasts more than a few minutes, gets worse with activity, goes away and comes back, or varies in intensity [25].

Non-cardiac causes such as - musculoskeletal, gastrointestinal, pulmonary, and psychogenic factor [26].

Causes of Chest Pain in Patients Who Seek Care in a Primary Care Office[3-67]

Table-IV

Etiology of chest pain	% of patients with diagnosis
Musculoskeletal conditions (including costochondritis)	29%-36%
Nonspecific chest pain	11%-16%
Gastrointestinal disease	10%-19%
Stable CAD	8%-10%
Psychosocial or psychiatric disease	8%-17%
Pulmonary disease (pneumonia, pneumothorax, lung cancer)	5%-20%
Other cardiovascular disease (pulmonary embolus, heart failure)	3.5%-5%
Unstable CAD	1.5%

Abbreviation: CAD, coronary artery disease.

Objectives:

To summarize the existing literature and assess the prevalence of chest pain in this specific dyslipidemia/ hyperlipidemia patient population.

To improve understanding the etiology of chest pain

Try to find out the prevalence of chest pain among dyslipidemia patient who doesn’t have previous clinical ischemic heart symptoms/disease.

Try to give encouragement for further research.

Methods:

Observational -Descriptive Study

Here comprehensive search of medical databases, including Google Scholar, PubMed, Embase, and relevant academic sources/journals/publications, was conducted to identify relevant studies published from 2000 to 2023.

Results:

The review revealed a considerable assessment of chest pain among dyslipidemia outpatients without a prior clinical diagnosis of IHD.

Comprehensive analysis data showing mostly dyslipidemic outdoor patient without prior IHD presented with atypical chest pain needed diagnostic test, risk stratifications tools, individualized assessment are essential components of patient care in this population [27].

Furthermore, the potential role of statin/Fenofibrate therapy in modifying chest pain symptoms warrants further investigation.

Few cases are associated statin induced myalgia chest / myocarditis / hypertriglyceridemia induced pancreatitis were reported as non-cardiac chest pain [28-32].

Discussion:

Reviewing the data tells the fact that hyperlipidemia, marked by high levels of cholesterol and triglycerides, has been identified as a significant risk factor for atherosclerosis, a condition where plaque accumulates in the arteries.

Analyzing previous data there is arising an observation- Could this contribute to chest pain in those without a prior heart disease [28]?

It seems plausible. Even in the absence of established heart disease, the gradual buildup of plaque in the coronary arteries could compromise blood flow to the heart muscle, triggering ischemia chest pain.

So, if any hyperlipidemic patient presenting with chest pain though having no previous heart disease should give great emphasis for evaluation of recent development cardio-vascular disease.

Conclusion:

This review highlights the significant prevalence of chest pain among dyslipidemia outpatients without previous clinical IHD.

Healthcare providers/Physicians must be vigilant in evaluating these patients, considering a broad range of

differential diagnoses and tailoring their approach to individual patient needs.

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