

Hypolipidemia: How Common Is It!!

Lydia W Jeris¹, Mohamed Thayub², Sarasa Bharati³, Kotturathu Mammen Cherian⁴

Received on: 31 October 2022; Accepted on: 16 November 2022; Published on: 03 January 2023

ABSTRACT

Aim: To throw light on the causes and complication of hypocholesterolemia.

Background: Hypocholesterolemia is defined as total cholesterol and low-density lipoprotein (LDL) level below the fifth percentile of the general population. It is usually an incidental finding on routine lipid screening and thus much clinical importance is not given to the same. Though the first case of hypocholesterolemia was published in 1911, decades have passed since then with only a handful of cases of hypocholesterolemia being reported implying either a general lack of knowledge regarding the causes and consequences of low cholesterol or a lack of awareness in the diagnosis of hypocholesterolemia. Hypocholesterolemia can be caused due to many reasons and can lead to many complications as well.

Case description: We report three cases of hypocholesterolemia, which had very low levels of total cholesterol and LDL at our tertiary cardiac specialty hospital over a period of one year. Hypocholesterolemia in our cases could be attributed to a combination of statins, liver dysfunction, critical illness, and chronic inflammation. More extensive work needs to be done on this subject as the incidence of hypocholesterolemia is on the rise.

Conclusion: Hypocholesterolemia is equally dangerous as compared to hypercholesterolemia and more research work needs to be undertaken in this field.

Clinical significance: Understanding the causes and complications of hypocholesterolemia as well as knowing the underlying molecular basis is of crucial importance as it would provide new insights into the management of hypercholesterolemia and cardiovascular diseases in particular.

Keywords: Case report, Critical illness, Hypocholesterolemia, Statins.

Indian Journal of Medical Biochemistry (2022): 10.5005/jp-journals-10054-0202

BACKGROUND

Hypolipidemia is defined as total cholesterol and serum LDL below the fifth percentile of the general population adjusted for age, gender, and race. It is usually an incidental finding on routine lipid screening and thus thought may not be clinically important. Though hypercholesterolemia is considered a risk factor for many diseases, hypocholesterolemia is definitely associated with many diseases such as cancer, depression, hemorrhagic stroke, aortic dissection, nosocomial infection, and even depression.¹ Recently, it is becoming evident that hypolipidemia follows when managed with statins. Though the first case of hypocholesterolemia was published in 1911,² decades have passed since then with only a dozen more cases of hypocholesterolemia reported implying either a general lack of knowledge regarding the causes and consequences of low cholesterol or lack of awareness in the diagnosis of hypocholesterolemia. Further, the critical level to define hypocholesterolemia is also not yet clear. Hypocholesterolemia is also a significant prognostic indicator denoting increased morbidity and mortality.

CASE DESCRIPTION

We would like to report three cases of hypolipidemia seen at the tertiary cardiac specialty hospital over a period of one year.

The first case was that of a 68-year-old man who had sought treatment for coronary artery disease. He was well-built (73 kg) and had a history of diabetes and hypertension for several years. He had undergone a coronary artery bypass graft for triple vessel disease. Initial investigation at that time disclosed all routine parameters to be normal including lipid profile (total cholesterol: 125 mg/dL) except serology, which showed reactivity to

^{1,3}Department of Pathology, Frontier Lifeline Hospital, Chennai, Tamil Nadu, India

²Department of Clinical Pharmacy, Frontier Lifeline Hospital, Chennai, Tamil Nadu, India

⁴Department of Cardiothoracic Surgery, Frontier Lifeline Hospital, Chennai, Tamil Nadu, India

Corresponding Author: Lydia W Jeris, Department of Pathology, Frontier Lifeline Hospital, Chennai, Tamil Nadu, India, Phone: +91 9790315145, e-mail: lydiajeris@gmail.com

How to cite this article: Jeris LW, Thayub M, Bharati S, *et al.* Hypolipidemia: How Common Is It!! *Indian J Med Biochem* 2022; 26(1):34–36.

Source of support: Nil

Conflict of interest: None

Anti-Hepatitis B core antibody (anti-HBc antibody). He was started on a statin (atorvastatin) 20 mg soon after surgery. The patient came for a follow-up after one year with acute febrile illness possibly sepsis, and all routine parameters were again tested at which time he was found to have very low total cholesterol: 40 mg/dL. Other lipid parameters were also low (serum triglyceride: 34 mg/dL, high density lipoprotein (HDL): 16 mg/dL, LDL: 20 mg/dL). In addition, the aspartate aminotransferase (AST) level was high (1490 IU/L) indicative of high activity such as an abnormal liver function. As the lipid levels were low, the dose of statin was tapered down to 10 mg.

The second case was that of a 65-year-old man, who was euglycemic and normotensive with a body mass index (BMI) of 22. He had the acute coronary syndrome, severe left ventricular

dysfunction, atrial fibrillation and cardiogenic shock, and hence rescue percutaneous coronary intervention (PCI) was done. The lipid profile during this period was within the reference interval. On analyzing the medication history, he was found to be on atorvastatin 40 mg once daily and had shown regular compliance. He was admitted 5 years later for acute heart failure syndrome, chronic atrial fibrillation, acute chronic kidney disease, and acute liver failure. Total cholesterol during this admission was 43 mg/dL (triglyceride: 71 mg/dL, HDL: 6 mg/dL, LDL: 11 mg/dL). Bilirubin was elevated (total: 11 mg/dL, direct: 7 mg/dL, alkaline phosphatase: 323 IU/L, urea: 114 mg/dL, serum creatinine: 2.9 mg/dL, hemoglobin: 9 gm/dL). As the lipid parameters were markedly reduced, atorvastatin was discontinued.

The third case was that of a 54-year-old man with a BMI of 18, who had sick-sinus syndrome and right ventricular outflow tract (RVOT) ectopics for which he had permanent pacemaker implantation done and during that time lipid profile was normal. He came with complaints of giddiness and mild dyspnea on exertion 2 years after the procedure. Routine lab investigation showed a very low serum LDL level (LDL: 1.2 mg/dL, serum total cholesterol: 53 mg/dL, serum triglycerides: 34 mg/dL, and HDL: 40 mg/dL). He was not on any lipid-lowering agent.

DISCUSSION

Hypocholesterolemia is defined as total cholesterol and serum LDL below the fifth percentile of the general population adjusted for age, gender, and race. Though the first case of hypocholesterolemia was reported by Chauffard in 1911, more than a century has passed and only a few studies pertaining to this are available. There is a general lacuna in the knowledge regarding the cause and consequences of hypocholesterolemia. A consensus on the definitive cut-off value to define hypocholesterolemia based on various lipid parameters is also currently not available. It is usually an incidental finding and patients are generally asymptomatic. There also exists a racial difference in the incidence of hypocholesterolemia.

Hypocholesterolemia occurs either because of reduced production or increased clearance of cholesterol. The cause could be primary or secondary. Inherited causes include abetalipoproteinemia, chylomicron retention disease, and hypobetalipoproteinemia. Primary hypocholesterolemia is rare compared to secondary hypocholesterolemia.

There are many causes of secondary hypocholesterolemia. In anemia, hypocholesterolemia could be a cause as well as a consequence as there is increased cholesterol requirement due to the proliferation of erythrocytes as well as deficiency of cholesterol leading to rigidity of RBCs, lysis, and anemia.³ Thyrotoxicosis is another cause where there is increased catabolism of LDL by LDL receptors leading to decreased LDL levels.⁴ In critical illness, there are multiple reasons for hypocholesterolemia such as downregulation of hepatic synthesis, loss of apoprotein, and accelerated cholesterol catabolism. Hypocholesterolemia also serves as a marker for sepsis and is a sign of increased mortality.⁵ There is also an inverse relationship between the severity of critical illness and the levels of total cholesterol, HDL, and LDL.

Hypocholesterolemia can occur in chronic illness as there is constant exposure to Interleukin (IL-6, IL-10), and tumor necrosis factor (TNF). Malignant cells have an increased LDL receptor activity, leading to hypocholesterolemia.⁶ Nutrition also plays a role

in the occurrence of hypocholesterolemia. Either malnutrition or malabsorption can lead to hypocholesterolemia.⁷ Chronic hepatic insufficiency can also be a cause as the liver is the main site for lipid metabolism.⁸

Certain clinical conditions are commonly associated with hypocholesterolemia such as septicemia, malignancies, inflammatory bowel disease, critically ill patients, polytrauma, postoperative patients, protracted hypovolemic shock, etc. Hypocholesterolemia can also lead to many complications such as diarrhea, steatorrhea, failure to thrive, malabsorption of fat-soluble vitamins, neurological involvement with demyelination, elevated transaminase, hepatomegaly due to hepatic steatosis, acanthocytosis, anemia, and susceptibility to infection.^{9,10} The use of statins and newer potent medications like proprotein convertase subtilisin/kexin type 9 (PCSK9) antagonists could also contribute to lower LDL levels.

In our first case, the cause is clear, i.e., treatment with statins. In addition, liver dysfunction as indicated by a very high AST could possibly be the immediate causative factor. Hypocholesterolemia in the second case could be attributed to chronic inflammation, critical illness, liver dysfunction, and statins. The third case had the lowest level of LDL with 1.2 mg/dL, and the cause for hypocholesterolemia remains unexplained. All three patients had previous lipid profiles, which were within normal thus excluding primary disorders of hypocholesterolemia. The diet habits of all three cases were found to be nonvegetarian in nature. As the lipid parameters were found to be low, the dosage of statin was decreased in the first case and was stopped in the second case. This management led to a slight increase in the level of lipid parameters after 3 months but has not yet come to the normal reference range as other factors mentioned above could also be contributing to hypocholesterolemia in our cases.

CONCLUSION

Hypocholesterolemia is a rare entity in literature. However, anecdotal information relates to the presence of a sizeable number of such cases seen mainly by treating physicians. Pathologists relying on literature have to record the same which might induce anecdotes to become articles. It is time to realize that hypocholesterolemia is equally dangerous as compared to hypercholesterolemia and more research work needs to be undertaken in this field.

CLINICAL SIGNIFICANCE

Identifying hypocholesterolemia is important as it could lead to many complications such as cell membrane damage, intracerebral hemorrhage, adrenal failure, sepsis, and increased disease mortality. This is being presented to invite further work to bring about the various causes and consequences of hypocholesterolemia. Hypocholesterolemia is an index of pathophysiological frailty and may be indicative of impending danger offering an unfavorable prognostic sign.

REFERENCES

1. Elmehdawi RR. Hypolipidemia: A word of caution. *Libyan J Med* 2008;3:84–90. DOI: 10.4176/071221.
2. Wilson R, Barletta FJ, Tyburski GJ. Hypocholesterolemia in sepsis and critically ill or injured patients. *Crit Care* 2003;7:413–414. DOI: 10.1186/cc2390.

3. Pok SJ, Deutsch E, Nemesánszky E, et al. Cholesterol deficiency. A pathogenetic factor in chronic anemias? Preliminary report of a study in three states. *MMW Munch Med Wochenschr* 1978;120(23):807–812. German. PMID: 307148.
4. Liberopoulos EN, Elisaf MS. Dyslipidemia in patients with thyroid disorders. *Hormones* 2002;1(4):218–223. DOI: 10.14310/horm.2002.1170.
5. Giovannini I, Boldrini G, Chiarla C, et al. Pathophysiologic correlates of hypocholesterolemia in critically ill surgical patients. *Intensive Care Med* 1999;25:748–751. DOI: 10.1007/s001340050940.
6. Peterson C, Vitols S, Rudling M, et al. Hypocholesterolemia in cancer patients may be caused by elevated LDL receptor activities in malignant cells. *Med Oncol Tumor Pharmacother* 1985;2:143–147. <https://doi.org/10.1007/BF02934541>.
7. Brar P, Kwon GY, Holleran S, et al. Change in lipid profile in celiac disease: beneficial effect of gluten-free diet. *Am J Med* 2006; 119:786–790. <https://doi.org/10.1016/j.amjmed.2005.12.025>.
8. D'Arienzo A, Manguso F, Scaglione G. Prognostic value of progressive decrease in serum cholesterol in predicting survival in Child-Pugh C viral cirrhosis. *Scand J Gastroenterol* 1998;33(11):1213–1218. DOI: 10.1080/00365529850172593.
9. Lévesque H, Gancel A, Pertuet S, et al. Hypocholesterolemia: prevalence, diagnostic and prognostic value. Study in a department of internal medicine. *Presse Med* 1991;20:1935–1938. PMID: 1837087.
10. Crook MA, Velauthar U, Moran L, et al. Hypocholesterolemia in a hospital population. *Ann Clin Biochem* 1999;36:613–616. DOI: 10.1177/000456329903600508.