



## Case Report

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# HETEROZYGOUS FAMILIAL HYPOBETALIPOPROTEINEMIA DETECTED DURING PERIODIC EXAMINATION IN A FAMILY MEDICINE OUTPATIENT CLINIC: A CASE REPORT

 **Melih Kiran<sup>1</sup>**

<sup>1</sup>Çankaya District Health Directorate, Ankara, Türkiye

### Correspondence:

Melih Kiran (e-mail: drkiranmelih@gmail.com)

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## Abstract

Familial hypobetalipoproteinemia (FHBL) is a rare, genetically inherited cause of hypocholesterolemia. Although it usually presents asymptotically, it can occasionally lead to clinical outcomes such as hepatic steatosis. In this case, a 37-year-old male patient presented to a family medicine outpatient clinic for a routine health check. His physical examination and vital signs were within normal limits. Laboratory investigations revealed markedly low LDL and total cholesterol levels and elevated triglycerides. Additionally, mild elevations in liver enzymes and grade 1-2 hepatic steatosis on abdominal ultrasonography were detected. A presumptive diagnosis of heterozygous familial hypobetalipoproteinemia was considered, and the patient was referred to the endocrinology clinic for further evaluation. This case demonstrates how periodic health screening in asymptomatic individuals can contribute to the early detection of rare metabolic disorders. Family physicians are competent in evaluating patients holistically and initiating appropriate referrals based on clinical and laboratory findings.

**Keywords:** Familial hypobetalipoproteinemia, hypocholesterolemia, hepatic steatosis, periodic health examination, family medicine, lipid disorders.

## Introduction

Family medicine serves as the cornerstone of primary healthcare and plays a central role in the provision of preventive services. As emphasised by the Ministry of Health and the Turkish Association of Family Physicians, periodic health examinations enable the early detection of diseases before the appearance of symptoms. Within this scope, periodic health examinations are effective in screening for systemic conditions such as cardiometabolic diseases, dyslipidemia, hypertension, and obesity.<sup>1</sup> According to the literature, family physicians are expected to effectively assess patient needs, formulate initial diagnostic impressions, and coordinate care through appropriate referrals within the healthcare system.<sup>2</sup>

Heterozygous familial hypobetalipoproteinemia (FHBL) is a rare lipoprotein metabolism disorder caused by heterozygous mutations in the MTTP and apoB genes.<sup>5</sup> In most cases, patients are asymptomatic, and the condition is detected either incidentally through lipid profiling or during family screening of patients with homozygous abetalipoproteinemia.<sup>5</sup> Except for certain specific mutations, most individuals with FHBL have a reduced risk of atherosclerosis.<sup>3</sup> These patients generally do not require initial assessment or continuous follow-up. However, in many cases, LDL cholesterol levels may be one-third to one-fourth of normal, and mild deficiencies of fat-soluble vitamins may develop over time. Hepatic steatosis and, less frequently, severe liver complications may develop.<sup>4,7</sup>

Therefore, patients with extremely low levels of apoB-containing lipoproteins should be monitored regularly.<sup>9</sup> Initial evaluation and follow-up should include assessment of fat-soluble vitamin levels, hepatobiliary ultrasonography, and liver function tests. In cases with vitamin deficiencies, treatment is typically initiated at near-daily doses, without the need for high doses, and adjustments are made based on biochemical responses. In addition, the presence of metabolic comorbidities such as obesity and type 2 diabetes in patients with heterozygous FHBL may contribute to the development of hepatic fibrosis.<sup>3,6</sup>

## Case Report

A 37-year-old male patient presented to the family medicine outpatient clinic for a periodic health examination, without any active complaints. He reported no history of smoking or alcohol use. His family history was unremarkable. His height was 186 cm, weight 113 kg, and body mass index (BMI) was calculated as 32.7 kg/m<sup>2</sup> (obesity class I). His blood pressure was 127/68 mmHg, and his heart rate was 76 bpm. Physical examination findings were within normal limits.

The patient provided a fasting blood sample after approximately 8 hours of fasting. Laboratory results revealed markedly low LDL and total cholesterol levels, and elevated triglycerides. To exclude possible laboratory error and perform further testing, the patient was invited again to give another blood sample after an 8-hour fast. Additionally, abdominal ultrasonography revealed grade 1–2 hepatic steatosis. The biochemical parameters from the two separate fasting blood samples are summarised in Tables 1 and 2.

**Table 1.** First Laboratory Results (18.02.2025)

Laboratory Parameter	Value	Unit	Reference Range
Glucose	82	mg/dL	70 - 99
Urea	39	mg/dL	19 - 49
Creatinine	1.09	mg/dL	0.7 - 1.3
AST	32	U/L	< 35
ALT	64	U/L	< 50
LDH	164	U/L	120 - 246
Total Cholesterol	81	mg/dL	< 200
Triglycerides	245	mg/dL	< 150
HDL	23	mg/dL	> 40
LDL	9	mg/dL	< 100
VLDL	49	mg/dL	10 - 40
TSH	1.2	μIU/mL	0.55 - 4.78
Ferritin	47	ng/mL	22 - 322
Vitamin B12	214	pg/mL	211 - 911
Vitamin D	12	ng/mL	30 - 100

\*Abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase; HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very low-density lipoprotein; TSH, thyroid-stimulating hormone.\*

**Table 2.** Second Laboratory Results (25.02.2025)

Laboratory Parameter	Value	Unit	Reference Range
Glucose	87.0	mg/dL	70 - 99
Urea	34.0	mg/dL	19 - 49
Creatinine	1.13	mg/dL	0.7 - 1.3
AST	42.0	U/L	< 35
ALT	79.0	U/L	< 50
LDH	205.0	U/L	120 - 246
Total Cholesterol	88.0	mg/dL	< 200
Triglycerides	222.0	mg/dL	< 150
HDL	24.0	mg/dL	> 40
LDL	20.0	mg/dL	< 100
VLDL	44.0	mg/dL	10 - 40
HbA1c	5.5	%	< 5.7
Apolipoprotein B	51.0	mg/dL	66 - 144
INR	1.0	-	0.8 - 1.2
GGT	62.0	U/L	< 73
ALP	101.0	U/L	53 - 128
Albumin	48.0	g/L	32 - 48
Total Protein	89.0	g/L	57 - 82

\*Abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase; HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very low-density lipoprotein; TSH, thyroid-stimulating hormone; INR, international normalized ratio; GGT, gamma-glutamyl transferase; ALP, alkaline phosphatase.\*

## Discussion

Hypocholesterolemia is a laboratory finding that is often overlooked, yet it may indicate underlying significant conditions.<sup>8</sup> Once secondary causes are excluded, primary hypolipidemic disorders should be considered, especially in cases with markedly low LDL and total cholesterol levels. In this case, periodic screening in an asymptomatic individual revealed significantly low lipid levels, leading to a presumptive diagnosis of heterozygous familial hypobetalipoproteinemia.

FHBL is an autosomal dominant lipid disorder caused most often by heterozygous mutations in the apoB gene. In affected individuals, LDL cholesterol levels may be reduced to one-third or one-fourth of normal values. Most patients are asymptomatic and diagnosed incidentally through lipid screening.<sup>3</sup> Although atherosclerosis risk is generally reduced in FHBL, the condition may be mistakenly regarded as benign. However, hepatic steatosis and, albeit rarely, progressive liver disease have been reported in some cases.<sup>3,4</sup>

In our case, abdominal ultrasonography revealed grade 1–2 hepatic steatosis, along with mild elevations in liver enzymes. These findings are consistent with the literature. According to the 2023 guidelines of the Turkish Society of Endocrinology and Metabolism, patients with FHBL should undergo assessment of fat-soluble vitamin levels, hepatobiliary ultrasonography, and liver function tests.<sup>3</sup> The presence of metabolic comorbidities such as obesity and type 2 diabetes mellitus may further contribute to the development of hepatic fibrosis in these individuals.<sup>6</sup> Given the patient's obesity and hepatic steatosis, the clinical picture was initially consistent with the recently updated definition of Metabolically Dysregulated-Associated Steatotic Liver Disease (MASLD). However, the incidental finding of profound hypocholesterolemia distinguished this case from typical MASLD, redirecting the diagnosis towards a primary lipid disorder such as FHBL. Evaluating such patients with awareness of MASLD criteria is crucial to identify metabolic risks; however, rare genetic etiologies must not be overlooked.

This case demonstrates that periodic examinations may reveal rare metabolic disorders even in asymptomatic individuals. Family physicians are equipped to assess the clinical context of laboratory findings and to make appropriate referrals based on preliminary diagnoses. In family medicine practice, instead of evaluating the patient solely based on complaints, conducting comprehensive periodic examinations and basic biochemical tests is important both for individual health and in terms of societal healthcare costs.

Family medicine is a continuous and holistic discipline that supports individuals not only in times of illness but also during periods of health. Family physicians provide guidance not only in disease prevention but also in helping patients understand their conditions, access reliable health information, and maintain healthy behaviours. In this context, they play a key role in the management of rare diseases by empowering patients to actively participate in their own care. As emphasised by the World Organisation of Family Doctors (WONCA), the role of the family physician extends beyond clinical intervention to include patient-centred education, behavioural support, and ongoing guidance within the healthcare system.<sup>10</sup>

Periodic health examinations in family medicine outpatient clinics provide an important opportunity for the early detection of serious metabolic disturbances, even in individuals without symptoms. This case exemplifies the recognition of a rare lipid disorder at the primary care level and its appropriate referral to a specialised department. Family physicians serve not only as the initial point of contact in the healthcare system but also hold a critical role in establishing preliminary diagnoses, performing holistic assessments, and ensuring timely specialist referrals.

**Ethical Considerations:** Written informed consent was obtained from the patient, and all personal information has been kept confidential.

**Conflict of Interest:** The authors declare no conflict of interest.

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