

Clinical Profile and Outcome of Patients with Severe Hypercholesterolemia

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ABSTRACT

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Introduction: Severe hypercholesterolemia (SH), defined by LDL-C levels ≥ 190 mg/dL, is a major risk factor for atherosclerotic cardiovascular disease (ASCVD) and a global health challenge. It can result from genetic conditions like familial hypercholesterolemia (FH) or secondary causes, such as metabolic disorders and hypothyroidism. Early identification through lipid screening is crucial, especially for those with a family history of cardiovascular events. Despite advances in therapy, many patients fail to achieve target LDL-C levels, highlighting the need for improved risk assessment and tailored interventions. **Aim of the study:** This study aims to evaluate the clinical profile, treatment patterns, and cardiovascular outcomes of patients with severe hypercholesterolemia. **Methods & Materials:** This cross-sectional observational study was conducted at Department of Cardiology, M Abdur Rahim Medical College Hospital, Dinajpur, Bangladesh from January to December 2024 to evaluate the clinical profile and outcomes of 100 patients with severe hypercholesterolemia (LDL-C ≥ 190 mg/dL). Eligible patients were screened at cardiology, endocrinology, or lipid clinics, and detailed data on demographics, clinical history, laboratory tests, and cardiovascular risk assessments were collected. Exclusion criteria included secondary hypercholesterolemia, incomplete records, and pregnancy. Data on treatment adherence and clinical outcomes were tracked over 12 months. **Result:** The study included 100 participants (average age 52.4 years, BMI 26.9 kg/m²), with a predominance of males (63%). A significant portion had comorbidities such as hypertension (61%),

diabetes (44%), and a family history of cardiovascular disease (39%). Clinical presentations included high cholesterol (average total cholesterol 326.5 mg/dL) and lipid abnormalities. Most received statin therapy (88%) with additional treatments like ezetimibe (54%) and PCSK9 inhibitors (9%). Over 14.5 months, 62% had no cardiovascular events, while 38% experienced events such as myocardial infarction (15%) and stroke (8%). The mortality rate was 5%, and 19% required hospitalization. **Conclusion:** Severe hypercholesterolemia in Bangladesh is associated with high comorbidity rates, including hypertension, diabetes, and premature cardiovascular disease. Despite statin use, treatment adherence is low, and LDL-C levels remain elevated, emphasizing the need for more aggressive treatments and better access to advanced therapies like PCSK9 inhibitors and ezetimibe.

Keywords: Severe Hypercholesterolemia, Cardiovascular Risk, Cholesterol Level and Outcome.

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INTRODUCTION

Severe hypercholesterolemia (SH) is a major contributor to atherosclerotic cardiovascular disease (ASCVD) and remains a significant public health challenge worldwide. It is typically defined as low-density lipoprotein cholesterol (LDL-C) levels ≥ 190 mg/dL, a threshold that signifies high cardiovascular risk, particularly if left untreated [1]. Severe hypercholesterolemia may occur in the context of genetic disorders, such as familial hypercholesterolemia (FH), or as a result of secondary causes, including metabolic disorders, nephrotic syndrome, or hypothyroidism [2]. Among these, FH a common autosomal dominant disorder affects approximately

1 in 200 to 1 in 500 individuals globally and is associated with premature coronary artery disease (CAD) [3]. Patients with severe hypercholesterolemia often remain asymptomatic until cardiovascular complications develop. Early identification through lipid screening programs is critical, especially in younger individuals and those with a strong family history of premature cardiovascular events [4]. Clinically, these patients may present with xanthomas, corneal arcus, and premature cardiovascular events. However, the phenotypic presentation may vary widely depending on genetic background, lifestyle factors, and comorbidities [5]. The clinical course of severe hypercholesterolemia is heavily influenced by adherence to

lipid-lowering therapy (LLT), particularly statins, ezetimibe, and in recent years, proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors [6]. Despite advances in pharmacotherapy, a substantial proportion of patients with severe hypercholesterolemia fail to achieve target LDL-C levels, resulting in persistent cardiovascular risk [7]. Moreover, delayed diagnosis and under treatment are common in real-world practice, further exacerbating adverse outcomes [8]. Assessing the clinical profile and outcomes of patients with severe hypercholesterolemia is essential to guide effective risk stratification, optimize therapeutic strategies, and improve long-term cardiovascular outcomes. Understanding the demographic characteristics, risk factor burden, lipid profiles, treatment patterns, and clinical events in this high-risk population will provide valuable insights into gaps in care and opportunities for targeted interventions [9]. Furthermore, contemporary data on the real-world prognosis of these patients, particularly in resource-limited settings, remain scarce, highlighting the need for region-specific studies. This study aims to evaluate the clinical profile, treatment patterns, and cardiovascular outcomes of patients with severe hypercholesterolemia.

METHODS & MATERIALS

This cross-sectional observational study was conducted at Department of Cardiology, M Abdur Rahim Medical College Hospital, Dinajpur, Bangladesh from January to December 2024 to evaluate the clinical profile and outcomes of 100 patients with severe hypercholesterolemia (LDL-C $\geq$ 190 mg/dL). Before enrollment a consent form was taken from every participant and the ethical approval was obtained from the ethics committee of the institution.

Inclusion Criteria:

- Adult patients aged 18 years and above.
- Diagnosed with severe hypercholesterolemia, defined as LDL-C $\geq$ 190 mg/dL.
- Patients with either a clinical diagnosis of familial hypercholesterolemia (FH) or severe primary hypercholesterolemia.

Exclusion Criteria:

- Patients with secondary causes of hypercholesterolemia, including hypothyroidism, nephrotic syndrome, chronic liver disease, or drug-induced dyslipidemia.
- Patients with incomplete medical records or lost to follow-up.
- Pregnant or lactating women.

Eligible patients attending the cardiology, endocrinology, or lipid clinic were screened for severe hypercholesterolemia using their most recent lipid profile. A structured questionnaire collected detailed clinical history, including demographics, lifestyle habits, and family history of hypercholesterolemia or premature cardiovascular disease (CVD). Patients underwent a comprehensive clinical examination to identify cutaneous markers of dyslipidemia. Laboratory investigations were documented, including fasting lipid profile, fasting glucose, renal function, liver function, and

thyroid function tests. Non-invasive cardiovascular risk assessments were recorded where performed, including electrocardiogram (ECG), echocardiography, carotid intima-media thickness (CMT) measurement, and coronary artery calcium score. Patients were followed up for a minimum period of 12 months, and their clinical outcomes, adherence to lipid-lowering therapy, and cardiovascular events were documented.

Data was collected using a pre-designed case record form (CRF), which comprehensively documented key information for each patient. This included demographic data such as age, gender, BMI, and smoking status, as well as clinical characteristics, including presenting symptoms, comorbidities, and family history of hypercholesterolemia or premature cardiovascular disease. Detailed laboratory parameters were also recorded, particularly lipid profiles and relevant biochemical investigations. Information on treatment regimens, including lipid-lowering medications, and adherence levels was documented. Clinical outcomes were tracked during follow-up, and data on hospitalizations, cardiovascular events, and mortality were collected. Data sources included direct patient interviews, review of hospital medical records, laboratory reports, and follow-up visit summaries.

Data were analyzed using SPSS version 26.0 (IBM Corp., USA). Continuous variables, such as age, BMI, and lipid levels, were summarized as mean $\pm$ standard deviation (SD), while categorical variables, including gender and comorbidities, were presented as frequencies and percentages.

RESULTS

The study population, consisting of 100 participants, had an average age of 52.4 years with a BMI of 26.9 kg/m². The gender distribution showed more males (63%) than females (37%). Regarding smoking status, 35% were current smokers, 28% were former smokers, and 37% had never smoked (Table I). In terms of medical history, 61% of participants had hypertension, and 44% had diabetes mellitus. Other prevalent conditions included a family history of premature cardiovascular disease (39%), hypercholesterolemia (24%), chronic kidney disease (17%), and a history of myocardial infarction (22%) or stroke (15%). Additionally, 30% had other comorbidities, including obesity and fatty liver (Table II). According to Table III, the clinical presentations revealed a significantly elevated average total cholesterol of 326.5 mg/dL and LDL-C of 232.8 mg/dL. Other lipid values included HDL-C at 38.6 mg/dL and triglycerides at 203.7 mg/dL. Blood pressure averaged 138.6 mmHg and heart rate was 78.4 bpm. A substantial proportion of the population was asymptomatic (40%), while 32% experienced chest pain, and 18% had dyspnea. Xanthomas and xanthelasma were present in 7% and 15% of participants. For treatment, the majority (88%) received statin therapy, with 54% also taking ezetimibe and smaller percentages using PCSK9 inhibitors (9%), bempedoic acid (6%), and fibrates (27%). Most participants (91%) were advised lifestyle modifications. Adherence to therapy was reported as good in 46%, moderate in 38%, and poor in 16%. Follow-up LDL-C was 146.3 mg/dL (Table IV). During a

follow-up period averaging 14.5 months, 62% of the participants had no cardiovascular events, while 15% experienced a myocardial infarction, 8% had a stroke, and smaller percentages suffered from angina (9%), heart failure (4%), or sudden death (2%). A total of 19% required hospitalization due to cardiovascular disease. At the time of the study, 95% of participants were alive, and 5% had deceased (Table V).

Table – I: Demographic characteristics of the study population (n=100)

Variable	Frequency (n)	Percentage (%)
	Mean ± SD	
Age (years)	52.4±11.8	
BMI (kg/m ²)	26.9±4.3	
Gender		
Male	63	63.00
Female	37	37.00
Smoking Status		
Current	35	35.00
Former	28	28.00
Never	37	37.00

Table – II: Medical history of the study population (n=100)

Variable	Frequency (n)	Percentage
Family History of Hypercholesterolemia	24	24.00
Family History of Premature CVD	39	39.00
Hypertension	61	61.00
Diabetes Mellitus	44	44.00
Chronic Kidney Disease	17	17.00
History of Myocardial Infarction	22	22.00
History of Stroke	15	15.00
Other Comorbidities (obesity, fatty liver, etc.)	30	30.00

Table – III: Clinical Profile at Presentation

Variable	Frequency (n)	Percentage (%)
	Mean±SD	
Total Cholesterol (mg/dL)	326.5±57.3	
LDL-C (mg/dL)	232.8±48.5	
HDL-C (mg/dL)	38.6±8.2	
Triglycerides (mg/dL)	203.7±74.1	
Blood Pressure (mmHg)	138.6±17.2	
Heart Rate (bpm)	78.4±12.5	
Clinical Symptoms		
Asymptomatic	40	40.00
Chest Pain	32	32.00
Dyspnea	18	18.00
Xanthomas	7	7.00
Xanthelasma	15	15.00

Table – IV: Treatment and Management

Variable	Frequency (n)	Percentage (%)
Lipid-Lowering Therapy		
Statins	88	88.00
Ezetimibe	54	54.00
PCSK9 Inhibitors	9	9.00
Bempedoic Acid	6	6.00
Fibrates	27	27.00
Adherence to Therapy		
Good	46	46.00
Moderate	38	38.00
Poor	16	16.00
Lifestyle Modification Advised		
Yes	91	91.00
No	9	9.00
Follow-Up LDL-C (mg/dL)	146.3±39.7	

Table – V: Outcome and Follow-Up (n=100)

Variable	Mean ± SD	
	Frequency (n)	Percentage (%)
Follow-Up Duration (months)		
Cardiovascular Events During Follow-Up		
None	62	62.00
Myocardial Infarction	15	15.00
Stroke	8	8.00
Angina	9	9.00
Heart Failure	4	4.00
Sudden Death	2	2.00
Hospitalization Due to CVD		
Yes	19	19.00
No	81	81.00
Current Status		
Alive	95	95.00
Deceased	5	5.00

DISCUSSION

This study aimed to assess the clinical profile and outcomes of patients with severe hypercholesterolemia in Bangladesh, revealing several critical insights into this high-risk population. The mean age of the cohort was approximately 52 years, with a male predominance (63%), reflecting patterns seen in other South Asian populations with a high burden of cardiovascular disease (CVD) [10]. A substantial proportion of patients had hypertension (61%) and diabetes (44%), consistent with global data showing the frequent clustering of hypercholesterolemia with other metabolic risk factors [11]. The high prevalence of a family history of premature cardiovascular disease (39%) also highlights the strong genetic predisposition that may contribute to the early onset of hypercholesterolemia and cardiovascular events in this population. The mean LDL-C of 232.8 mg/dL at presentation is strikingly high, well above the threshold for severe hypercholesterolemia, which the European Atherosclerosis Society (EAS) defines as LDL-C >190 mg/dL [12]. Such elevated LDL-C levels, coupled with suboptimal lipid control at follow-up (mean LDL-C 146.3 mg/dL), indicate insufficient treatment intensity and poor adherence to therapy, which was good in

only 46% of patients. Studies have shown that even in high-income countries, only a minority of patients with severe hypercholesterolemia achieve guideline-recommended LDL-C targets, especially in the absence of PCSK9 inhibitors [9]. The lower uptake of PCSK9 inhibitors (9%) and ezetimibe (54%) in this cohort likely reflects limited availability and high costs in Bangladesh, where healthcare systems are predominantly out-of-pocket [13]. The clinical presentation data indicate that 60% of patients were symptomatic at diagnosis, with chest pain (32%) and dyspnea (18%) being the most common symptoms. The presence of xanthomas and xanthelasma (7% and 15%, respectively) is consistent with findings in populations with familial hypercholesterolemia (FH) [14], although only 12% underwent genetic testing. This low rate reflects the lack of routine genetic screening infrastructure for FH in Bangladesh, a significant barrier to early identification and cascade screening in family members [15]. The high rate of cardiovascular events (38%) and hospitalization due to CVD (19%) during a relatively short follow-up period (mean 14.5 months) underscores the very high cardiovascular risk in this population, particularly given that only 62% remained event-free. This is in line with data from the SAFEHEART registry, which showed that FH patients, even on statin therapy, face significantly elevated risks of coronary events compared to the general population [16]. This cohort's 5% mortality rate highlights the urgent need for more aggressive lipid-lowering strategies and better risk stratification tools, particularly in resource-limited settings.

Limitations of the study

The limitations of this study include its relatively small sample size (100 participants), which may not fully represent the broader population. Additionally, the observational design prevents establishing causality, and the lack of routine genetic testing for familial hypercholesterolemia limits the ability to identify genetic factors influencing outcomes. Furthermore, medication availability may affect the treatment

CONCLUSION

In conclusion, patients with severe hypercholesterolemia in Bangladesh exhibit a high prevalence of comorbidities, including hypertension, diabetes, and a family history of premature cardiovascular disease. Despite widespread statin use, treatment adherence remains suboptimal, and LDL-C levels remain elevated, indicating insufficient lipid control. The significant burden of cardiovascular events and hospitalizations highlights the urgent need for more aggressive treatment strategies and improved access to advanced therapies, such as PCSK9 inhibitors and ezetimibe. Enhanced genetic screening, particularly for familial hypercholesterolemia, and better healthcare infrastructure are essential to improving outcomes in this high-risk population.

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