Original Article

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Clinical profile and practice patterns of patients with severe hypercholesterolemia: A Hospital-based registry

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Abstract

Background: Severe hypercholesterolemia, defined as low-density lipoprotein cholesterol of ≥190mg/dL (≥4.9 mmol/L), has a high risk of atherosclerotic cardiovascular disease and premature and recurrent coronary events. Its prevalence may be as high as 5–7% in the general population. This registry aims to provide insights into clinical profiles and practice patterns among such patients treated at the tertiary cardiac hospital of Nepal.

Methods: This was a cross-sectional, observational, registry of the patients who were diagnosed with severe hypercholesterolemia from January 2022 to December 2022 in the National Heart Centre.

Results: In this registry, 119 cases were included. The mean age of patients was 53 years, with 56.3% being female. Of these patients, 74 (62.1%) were hypertensive, 16 (13.4%) had diabetes mellitus, and 16 (13.4%) used tobacco. A history of premature coronary artery disease was present in 15 (12.6%) patients, and premature peripheral vascular disease in 1 (0.8%) patient. A family history of premature coronary artery disease was reported in 4 (3.3%) patients, and a family history of total cholesterol levels >7.5 mmol/L was present in 20 (16.8%) patients. Tendon xanthoma was found in 4 (3.3%) cases, and arcus cornealis in 22 (18.4%) cases. The body mass index ranged from 15.2 to 43.2, with a mean of 26.3; over 60% of cases were overweight or obese. Rosuvastatin was used in 87 (73.1%) cases, atorvastatin in 32 (26.9%) cases, and ezetimibe 10 mg combined with atorvastatin in 18 (15.1%) cases. High doses of statins were administered in 93 (78.1%) cases.

Conclusion: Severe hypercholesterolemia hospital-based registry provides valuable information on severe hypercholesterolemia regarding the associated cardiovascular risk factors and its clinical presentation. Most of the patients were treated with high doses of statins as recommended by guidelines.

Keywords: Coronary artery disease; Familial hypercholesterolemia; High intensity statins; Severe Hypercholesterolemia;

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Introduction

Severe hypercholesterolemia is defined as Low-Density Lipoprotein Cholesterol (LDL-C) of ≥ 190mg/dL (≥ 4.9mmol/L).[1] Prevalence of severe hypercholesterolemia may be as high as 5–7% in the general population.[2,3] Patients with severe hypercholesterolemia have a high risk of Atherosclerotic Cardiovascular Disease (ASCVD) and premature and recurrent coronary events.[4] It is suggested that the risk of coronary artery disease (CAD) is accelerated by 10–20 years in men and 20–30 years in women with LDL-C levels ≥190 mg/dL.[2] The future risk of CAD remains 6-fold higher in those with LDL-C ≥190 mg/dL and no familial hypercholesterolemia-related mutations.[4]

Current guidelines recommend the initiation of high-intensity statin therapy in individuals with LDL-C ≥190 mg/dL without calculating 10-year ASCVD risk, due to their high lifetime risk for ASCVD events that are related to long-term exposure to markedly elevated LDL-C levels.[1,5,6] Initiation of high-intensity statin therapy is strongly recommended in this population to achieve a ≥50% reduction in LDL-C to adequately reduce their risk for future cardiovascular events.[1,7]

There is limited information available about this group of patients in Nepal. This registry aims to provide insights into clinical profiles and practice patterns among severe hypercholesterolemia patients treated at the tertiary cardiac hospital of Nepal.

Methods

This was a prospective, observational registry done at Shahid Gangalal National Heart Centre (SGNHC), Bansbari, Kathmandu,

Nepal. A web-based performa was designed to collect information about severe hypercholesterolemia patients. Cardiologists were given access to enter the patient's data. Data were entered by the treating cardiologists. All consecutive patients aged >18 years who were diagnosed with severe hypercholesterolemia in the National Heart Center from 2022 January to 2022 December were included. Age, gender, premature CAD in patients (men <55 y old, women <60 y old), premature cerebral or peripheral vascular disease (men <55 y old, women <60 y old), family history of Myocardial Infarction (MI) <50 y old in second-degree relative or <60 y old in first-degree relative, family history of Total Cholesterol (TC) >7.5 mmol/L in a first- or second-degree relative, hypertension, diabetes mellitus, tobacco use, Body Mass Index (BMI), tendon xanthoma and arcus cornealis in patients, total Cholesterol, triglyceride, High density lipoprotein, LDL, treatment received at the time of enrollment were entered in the web-based registry portal.

diabetes mellitus

Operational definitions are as follows:

Hypertension: Diagnosed case on lifestyle modification or medication

Diabetes Mellitus: Diagnosed case on lifestyle modification or Medication

Family history of premature Coronary artery disease: First-degree relatives who had CAD before 55 years in males and before 65 in Females.

Smoker: Patients were considered as smokers if they report any smoking consumption within the last 1 year of study enrollment.

Tobacco consumer: Patients were considered as Tobacco if they report any tobacco consumption within the last 1 year of study enrollment.

A BMI less than 18.5 was considered underweight, a BMI of 18.5 to <24.9, was considered as healthy weight, a BMI of 25.0 to <30 was considered overweight, BMI of≥30.0 was considered obese.[8]

Data were analyzed using the statistical software, SPSS version 20. Ethical approval for this study was taken from the Institutional Review Committee of SGNHC. Informed written consent after proper counseling regarding the nature and purpose of the study was taken from each respondent.

Results

During the study period, 119 patients were enrolled in the study. Age ranged from 25 years to 77 years with a mean age of 53 years. Among them 67(56.3%) were female and 52 (43.7%) were males. Among the 119 patients enrolled in this study 74 (62.1%) were hypertensive,16 (13.4%) were Diabetes mellitus patients, and 16(13.4%) patients consumed tobacco. History of premature CAD was diagnosed in 15 (12.6%) patients, a history of premature Peripheral Artery Disease (PAD) in 1(0.8%) patient, a family history of premature CAD was present in 4 (3.3%), and family history of TC>7.5mmol/L was present in 20 (16.8%) patients, Tendon Xanthoma in 4 (3.3%) cases, arcus cornealis in 22 (18.4%) cases as shown in Table 1.

Table 1. Baseline characteristic n=119

Variable	n	%
Male	53	43.7
Female	67	56.3
Hypertension	74	62.1
DM	16	13.4
Smoking/Tobacco consumer	16	13.4
Premature CAD	15	12.6
Premature PVD	1	0.8
Family History of Premature CAD	4	3.3
Family history of TC>7.5mmol/L	20	16.8
Tendon Xanthoma	4	3.3
Arcus Cornealis	22	18.4

BMI ranged from 15.2 to 43.2 with a mean of 26.3. More than 60% of cases were overweight, and obese as shown in Table 2.

Table 2: Classification as per BMI

BMI	n	%
<18.5 (Underweight)	4	3.3
18.5-<25 (Normal)	38	31.9
24.9-<30 (Overweight)	56	47
30-39.9 (Obese)	21	17.4

Table 3 Lipid profile levels

	Range	Mean
TC	6.3-17.0	7.9mmol/L
TG	0.7-5.4	1.9mmol/L
HDL	0.8-2.1	1.1mmol/L
LDL	4.9-12.7	5.8 mmol/L

Rosuvastatin was used in 87 (73.1%) cases, Dose ranged from 10 to 40mg with a mean of 23.9mg, Atorvastatin in 32 (26.9%) cases, with Dose ranging from 10 mg to 80 mg with a mean of 47.1 mg. Ezetimibe combined with atorvastatin was used in 18(15.1%) cases, in all cases 10 mg of Ezetmibe was used. High-intensity atorvastatin of 40 mg or more was used in 20 (16.8%) cases, Low intensity was used in 12 (10.0%) cases. High-intensity rosuvastatin 20 mg or more was used in 73(61.3%) cases, and Low-intensity rosuvastatin was used in 14 (11.7%) cases. Over 93 (78.1%) cases were treated with high doses of statin as shown in Table 4

Table 4 Statin and their dose (n=119)

Statin Dose	Number	%

Atorvastatin	32	26.9
10	1	0.8
20	2	1.6
30	9	7.5
40	8	6.7
70	9	7.5
80	3	
Mean Atorvastation dose	47.1 mg	
Exetimibie+Atovastatin	18 case	15.1
Atorvastation 30+10	9	7.5
Ator 70+10	8	6.7
Ator 20+10	1	0.8
Rosuvastatin	87	73.1
10	14	11.7
20	49	41.1
40	24	201
Mean Rosuvastation Dose	23.9mg	

Discussion

Individuals with severe hypercholesterolemia are at significantly increased lifetime risk of CAD. One study involving over 68,000 subjects followed for up to 30 years found that those with LDL-C ≥190 mg/dL had a 2–5 fold increased risk of CAD compared to those with LDL-C <130 mg/dL.[2] Further, CAD occurred 10–20 years earlier in men and 20–30 years earlier in women with LDL-C≥190 mg/dL than in people with LDL-C<130.[9]

In our study patient's ages ranged from 25 years to 77 years with a mean age of 53 years. Among them 67(56.3%) were female and 52 (43.7%) were male. In a study done by Candace L. Jackson, there were 27,963 patients with a recorded LDL-C value. Of these patients, 388 had severe hypercholesterolemia (1.4%). The median age was 57 years, and 66% were women.[9] The exact number of very high LDL patients in Nepal is not known. In a cross-sectional study done on 454 participants by Limbu et al, a cluster sampling method was used through different health camps conducted in Kathmandu valley and found severe hypercholesterolemia in 5.8% of cases.[10] In a study done by Karki et al., fasting lipid profile of 2218 blood samples taken from patients attending a private clinic in Kathmandu found that 26 (1.1%) cases have severe hypercholetraolmia.[11]

In our study family history of TC>7.5mmol/L was present in 16.8% of cases. An important consideration in cases of severe hypercholesterolemia is the potential diagnosis of familial hypercholesterolemia (FH).[11] FH is an autosomal dominant disorder that causes premature CVD due to lifelong elevated LDL-C.[13,14] The heterozygous form of FH is estimated to occur in 1 in 250 to 1 in 500 people, while the incidence of the homozygous form is 1 in 250,000 to 1 in 1 million.[9,15,16] Studies using genetic testing for diagnosis report a 2% prevalence of FH in those with LDL-C 190 mg/dL.[4] An analysis from the NHANES study using clinical criteria reported a 7% prevalence.[17] It is estimated that at least 20 million people with FH worldwide, but 80% are unaware of their diagnosis.[9] The prevalence of FH increases progressively at higher LDL-C thresholds. Both the Simon Broome and AHA diagnostic criteria delineate an LDL-C level above 190 mg/dL as raising the potential for FH, which should then be supported and confirmed by additional clinical criteria.[9] National Lipid Association Guidelines state that an LDL-C 190 mg/dL should raise suspicion for FH and that detailed family history should be collected in all such individuals.[18]

To improve the diagnosis and treatment of FH among severe hypercholesterolemia patients we need to increase awareness. We need to understand current practice regarding the evaluation and management of these patients and apply it in our clinical practice. The 2013 ACC/AHA Cholesterol Guidelines recommended high-intensity statin therapy in all those ages 20 years and older with LDL-C ≥190 mg/dL, without calculation of the estimated 10-year risk of atherosclerotic cardiovascular disease due to their high lifetime risk for ASCVD events that are related to long-term exposure to markedly elevated LDL-C levels.[18] This recommendation was based on extensive data that have demonstrated a benefit in LDL-C reduction, as patients with LDL-C ≥190 mg/dL were excluded from most clinical trials due to their probable need for cholesterol-lowering therapies.[1] In our study all the patients were not treated with high-dose statins. Every effort should be made to treat these patients with high doses of statin. LDL-C reduction ≥50% was recommended as the initial goal, and a potential need for non-statin therapies to achieve optimal LDL-C levels was recognized.[1]

Current guidelines recommend consideration of adding ezetimibe or proprotein convertase subtilisin/kexin 9 (PCSK9) inhibitors in high-risk patients, such as those with LDL-C ≥190 mg/dL, who have<50% reduction in LDL-C on maximally tolerated statin therapy.[1] But they were not adequately managed with statins, or other lipid-lowering medications,[9] only a small proportion of those diagnosed receive optimal therapy.[9,19] A study done by Candace L. Jackson showed that 36% of patients with an LDL-C 190 mg/dL had no record of having ever been prescribed a statin.[9] A general practice electronic health record in Australia found that 44% of patients with an LDL-C ≥190 mg/dL had never taken a statin[20] as well and an analysis of statin prescription rates from a national clinical registry showed that 34% of patients with an LDL-C ≥190 mg/dL did not have a statin prescription.[9] Almost 90% of patients had not been prescribed another lipid-lowering medication, such as PCSK9 inhibitors, ezetimibe, niacin, fibrates, or bile acid binding resin, and only 5% were currently on one of these medications.[21] But in our study all the patients were treated with statins, many with high-dose statins. Few of them were treated with ezetimibe. PCSK 9 was not used as it is not available in Nepal. Until PCSK9 inhibitors become available, it is crucial to educate physicians on the importance of using high doses of statins combined with ezetimibe for these patients.

A registry like this can significantly enhance awareness of severe hypercholesterolemia and its management options among both the general public and physicians. These data were collected from the web portal by the treating physicians. The patients included in this study exhibit diverse clinical backgrounds: some underwent general check-ups, others were admitted, and some sought evaluation for additional risk factors such as hypertension and diabetes. There may be variation in the LDL levels as LDL levels were not tested in the same laboratory, different methods of LDL calculation may have been used, and fasting or non-fasting samples were collected. As this was just an observational study, we did not have the effect of different doses of statins, and changes in the LDL level cannot be mentioned.

In conclusion

The hospital-based registry on severe hypercholesterolemia offers significant insights into the related cardiovascular risk factors, its clinical presentation, and its management. Most of the patients were treated with high doses of statins as recommended by guidelines. Every effort should be made to diagnose and treat these patients.

Conflicts of interest

There are no conflicts of interest.

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