

# Familial Hypercholesterolemia (FH) Awareness Amongst Physicians in Mumbai, India

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## Abstract

**Background:** Familial Hypercholesterolemia (FH) is a common genetic disorder affecting low density lipoprotein cholesterol (LDL-C) metabolism. Prolong exposure to elevated LDL-C results in the development of atherosclerotic lesions and a substantially increased risk of Coronary Artery Disease (CAD). In contrast, early detection and effective treatment of FH can result in a significant improvement in clinical outcomes. Despite these data, FH remains largely underdiagnosed and untreated.

**Objective:** To assess the awareness, knowledge, and clinical practices of FH by General Physicians (GPs) in Mumbai.

**Methods:** Physicians were requested to complete a survey comprising Multiple Choice questions (MCQs) on FH. The questionnaire inquired about; familiarity and awareness of the disorder, clinical description, prevalence, inheritance and their opinions on FH clinical services.

**Results:** Of the 79 GPs surveyed, 31% of them correctly described FH and only 28% knew about its prevalence. 51% perceived themselves to have an above moderate familiarity with this disorder. 46% of them were aware of the risk of cardiovascular disease (CVD) associated with FH. 80% of GPs were unsure or unaware of whether they had FH patients under their care. 50% and 33% of physicians identified statins as monotherapy and statin & ezetimibe as a combination therapy for FH respectively.

**Conclusion & Interpretation:** Immediate attention should be focused on increasing awareness and knowledge about FH in India. Establishment of lipid clinic network will aid in improving care and clinical practices.

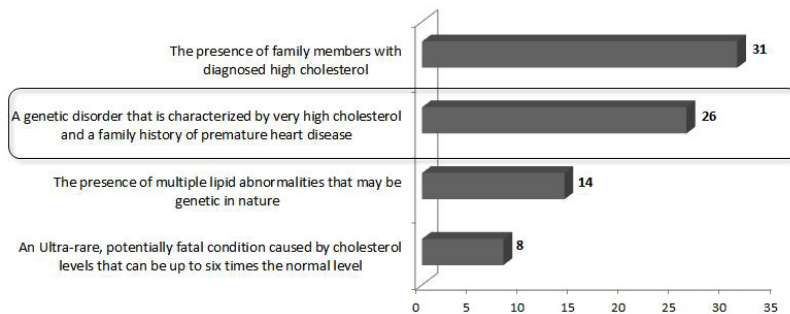
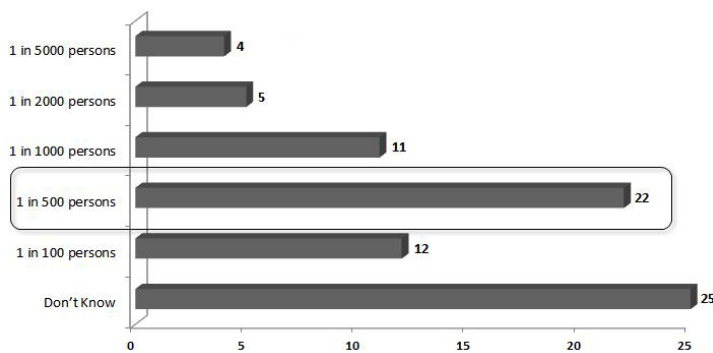
## Introduction

Familial Hypercholesterolemia (FH) is an inherited disorder characterized by elevated serum LDL cholesterol levels, which result in excess deposition of cholesterol in tissues, and it is amongst the most common autosomal dominant diseases encountered in clinical medicine.<sup>1,2</sup> FH is caused by mutations in the genes coding for the Low Density Lipoprotein Receptor (LDLR), apolipoprotein B (ApoB) or Proprotein Convertase Subtilase/Kexin type 9 (PCSK9).<sup>3</sup> Heterozygous FH (HeFH) is not an uncommon disorder, with an estimated prevalence of 1 in 500 in the western world. Homozygous FH (HoFH), although uncommon (prevalence is less than one per million in the general population), is a critical

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**Table 1: Summary of GPs responses to questions about FH awareness, knowledge and practice**

Awareness	
Familiarity of FH rated as above average	51%
Awareness about FH guidelines	31%
Awareness about lipid specialists	15%
Knowledge	
Correctly described FH	33%
Correctly identified lipid profile	33%
Correctly identified prevalence of FH in the community	28%
Correctly identified the transmission rate of FH to first degree relatives	46%
Correctly identified the CVD risk in untreated FH patients	33%
Correctly identified that genetic testing was not required to accurately diagnose FH	33%
Selected statins to best treat hypercholesterolemia	50%
Selected a combination of statin and ezetimibe to treat severe hypercholesterolemia	33%
Practice	
Screened patients with premature CVD for FH, including screening family members	31%
Unaware or unsure whether they had patients under their care	86%
Performed routine family screening of patients with FH	52%
The most prevalent age for screening young people in family with FH was 13-18 years, which was selected by	49%
Referred patients to lipid specialists	13%
Opinions on detection	
Selected GP's as the most effective health care provider for the early detection of FH	50%
Selected interpretive commenting on lipid profiles to highlight patients at risk of FH	86%

**Fig. 1: Clinical Definition of FH****Fig. 2: Prevalence of FH**

condition which commences in the first few years of life.

There are at least 20 million people with FH worldwide, majority remain undetected and current treatment is often suboptimal.<sup>4</sup> These affected individuals have a 10- to 20- fold increased risk of developing premature Coronary Artery Disease (CAD).<sup>5</sup>

Burden of CAD is also due to rise in coronary risk factors like diabetes, hypertension and dyslipidemia.<sup>6</sup> Indians are known to have an increased prevalence of CAD compared to other ethnic groups and have been escalated by 11% in the last decade.<sup>7</sup> Also, it is estimated that 52% of CAD related deaths occur below the age of 50 years and around 25% of acute myocardial

infarction (AMI) below the age of 40 years in India.<sup>8</sup>

Due to lack of awareness amongst physicians and general public, the diagnosis for FH is often started only after the irreversible consequences of atherosclerosis.<sup>9</sup> FH remains underdiagnosed till date in various parts of the world, including India. Many individuals and families with FH may simply be overlooked amongst patients with heart disease caused by more common risk factors such as atherogenic dyslipidemia, metabolic disorders, smoking, central obesity or physical inactivity. As a result most of them are undertreated for genetically elevated cholesterol levels.<sup>10</sup>

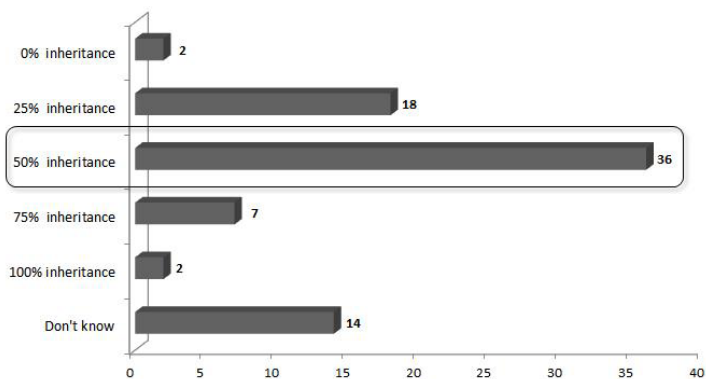
Due to lack of trained lipid specialist and services, patients with dyslipidemia are examined by GPs. The major barrier to FH management would be lack of understanding with respect to diagnosis and management of FH [10]. Our survey explores the knowledge of the GPs regarding identification of FH and its risk factors, and evaluation & management of FH.

## Materials and Methods:

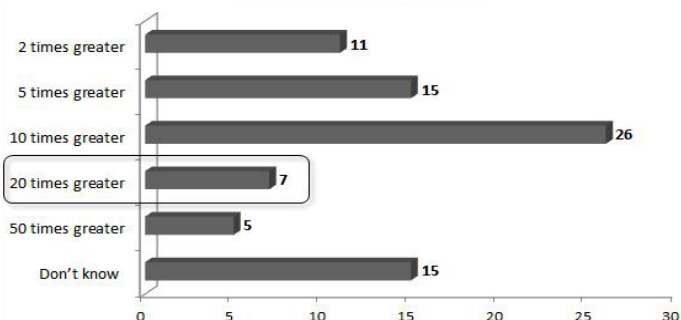
A small cross-sectional survey was conducted in P.D Hinduja Hospital and Medical research Center, Mumbai. 79 GPs associated with modern medicine participated in the survey. Questions were formulated based on expert recommendations and guidelines.<sup>4</sup> Hard copies with Multiple Choice questions (MCQs) were distributed to GPs, who completed it voluntarily. Questionnaire inquired about the following aspects of FH: familiarity & awareness with the condition, clinical description, prevalence, inheritance and their opinions on FH clinical services. Data was entered and analysed in MS Excel. Descriptive statistics are presented as percentages for the discrete variables.

## Results

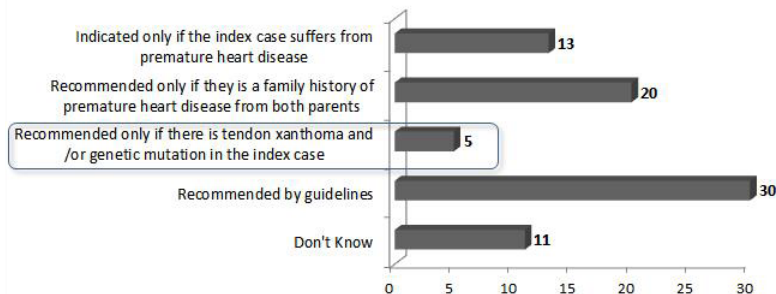
Total of 79 physicians were included in the survey. The results of the questionnaire concerning awareness, knowledge, practice and opinions on detection are summarized in Table 1. 31 % of physicians selected the correct clinical description of FH (Figure 1). 28% of them identified the prevalence of FH as 1:500, and 32% of physicians selected "Don't Know" to



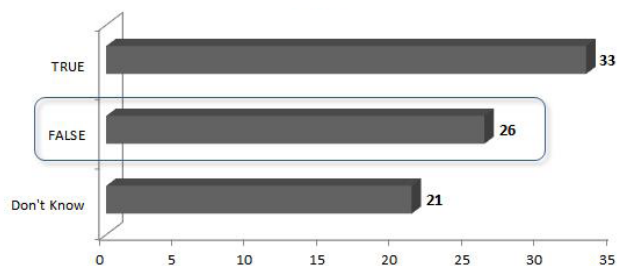
**Fig. 3: Inheritance of FH in 1st Degree Relatives**



**Fig. 4: Coronary Heart Disease risk in FH compared with general population**



**Fig. 5: After diagnosing an Index case, family cascade testing is?**



**Fig. 6: An accurate diagnosis of Familial Hypercholesterolemia can only be made via genetic test**

the prevalence question (Figure 2). 46% of the respondents correctly identified the heritability of FH as an autosomal dominant disorder (Figure 3). Only 9% of physicians think that CVD risk in untreated FH patients as 20 times greater in general population with 66%

selecting its lower risk associated with CAD (Figure 4). 80% of the physicians think family cascade testing is when the index case suffers from premature heart disease or has a family history of it, on the contrary this test is done only if there is tendon xanthoma and /

or genetic mutation in the index case (Figure 5). 42% of them identified that diagnosis of FH is not necessarily done via genetic testing (Figure 6).

Figure 1, 2, 3, 4, 5, 6: Summary of Physicians' responses to familial hypercholesterolemia (FH) questionnaire (n=79). correct answers are highlighted and numbers adjacent to bars indicate the responders.

## Discussion

Cross sectional survey was conducted to determine the awareness, knowledge, and clinical practices of FH by modern medicine physicians in Mumbai. Risk factors and description of premature CAD, cascade screening of relatives, the role of health care providers, specialist clinical services and drug treatment for FH were assessed. The overall knowledge regarding FH among GPs is less. Our results are concordant with the previous studies conducted by Ragarajan et al. and Pang et al., showing a significant gap in knowledge and awareness in Chennai, India (8) and Asia (11) respectively.

Despite recognition of patients with FH are at risk for premature CAD, they are still under-diagnosed. Hypercholesterolemia (monogenic and multifactorial) may affect 1 in 20 subjects in the general population<sup>11</sup> and recent studies suggests heterozygous FH may be more common than 1:500.<sup>12</sup>

Asia has the largest numbers of FH patients compared to Africans, Americans or Europeans, however there is a major shortfall in the detection and treatment.<sup>10</sup> Given the autosomal dominant inheritance pattern of FH, first degree relatives have a 50% chance of having FH, making cascade screening an effective method of detecting FH in families.<sup>13</sup> Also, screening programmes should be conducted which include molecular methods as well as measurement of cholesterol concentrations to identify as many persons at high CVD risk as possible.<sup>14</sup>

Patients with dyslipidemia within the community going to GP is a viable target of detection. Thus, further work and research is required to develop and raise physicians' knowledge with clinical tools for FH detection. The gap in healthcare provision, knowledge and effective strategies requires a collective effort for harnessing the combined

potential of individual cohorts across the globe. For instance, the potential for global collaborations to inform public health policy reliably about major non-communicable diseases has been successfully demonstrated by international consortia such as the Non-Communicable Diseases consortium or the Emerging Risk Factors collaboration. In this context, more initiatives like the European Atherosclerosis Society FH Studies Collaboration (EAS FHSC) should be developed which aims to form a database or registry for HoFH patients.<sup>15</sup> Also, to form a country specific criteria and guidelines, prevalence of dyslipidemic patients with classical clinical symptoms of FH such as high cholesterol, xanthomata and xanthelasmas or corneal arcus is necessary.<sup>16, 17</sup>

Lastly, in recent years, novel therapies for rare dyslipidemias such as FH have been identified. These agents (i.e. MTP-, apoB- and PCSK9 inhibitors, HDL- mimetic infusions and potentially gene therapy) are in different stages of development. Several of these agents are already available for clinical use. Novel agents are expected to be very expensive and their side effects are not fully known due to fact that only few patients have been enrolled in the trials that provided the basis for drug indication. This emphasizes the pivotal need to gather more insight into the clinical aspects of FH.

### Conclusion

This survey suggests that there is a substantial deficit in awareness and knowledge regarding FH among

the GPs in Mumbai. This issue can be addressed by conducting educational sessions on FH for doctors in India. In addition, knowledge regarding FH can be improved by the use of posters and leaflets displayed in hospitals. Also, implementation of country specific guidelines and awareness programs is essential to improve the care of FH.

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