Clinical Profile of Hypertrophic Cardiomyopathy in a Tertiary Level Hospital

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Keywords:
Sudden cardiac death; Hypertrophic cardiomyopathy; Electrocardiogram; Echocardiogram.

Abstract:

Background*- Hypertrophic cardiomyopathy (HCM) is a genetically transmitted disease with diverse natural history for which the potential to produce adverse consequences has been emphasized. However, the possibility of this disease remaining clinically dormant for many years has not been as widely appreciated. Certainly, the clinical recognition of previously undiagnosed patients with HCM may be advantageous by permitting risk stratification for sudden cardiac death or for timely pharmacologic therapy when symptoms intervene. The purpose of this study was to assess the disease pattern and the extent to which hypertrophic cardiomyopathy (HCM) exists undetected in a suspected group of population never diagnosed to have any cardiovascular disease, referred from the primary care facilities to one of the largest tertiary level hospital of Bangladesh.*

Methods*-We prospectively conducted an echocardiographic survey in 3648 cases between 19-03-2009 to 03-08-2010 (18 months) in the cardiac centre of Combined Military Hospital, Dhaka, Bangladesh.*

Results*- A total of 3648 cases referred by primary care physicians underwent echocardiogram either to confirm a new diagnosis or to exclude obvious cardiovascular abnormalities. Hypertrophic cardiomyopathy was identified in 148 patients (4.06%) who was not known have any cardiac disease before. At diagnosis, age ranged from 20 to 83 years (mean 52.19) with male gender preponderance (85.81%). Ninety eight patients (67%) had no functional limitation and the remaining fifty patients reported with symptoms mostly giving multiple responses like chest pain (39.2%), palpitation (18.9%), dyspnoea (22.3%), unusual fatigability (16.9%) and syncope (6.8%). Twelve patients had strong suspicion of familial predisposition depending on the symptomatology of the familial tree but were confirmed only in 03 cases by echocardiography. Basal left ventricular outflow obstruction (gradients 20 to 76 mm Hg) was evident in 14 patients (9.45%). Relatively variable phenotypic expression of the disease was substantiated by diffuse thickening of left ventricular wall occurring more commonly than localized distributed hypertrophy (56.08% vs. 43.94%, respectively). Electrocardiogram was abnormal in almost 95% of cases and typical pattern of left ventricular hypertrophy was observed in 25.68% cases.*

Conclusion*-This prospectively assembled data show that HCM cases may remain asymptomatic, clinically dormant and undetectable for many years (often to advance ages) in our community. The actual prevalence of the disease in our community needs to be ascertained which might exceed the prevalence mentioned in the text books.*

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Introduction:

Hypertrophic cardiomyopathy (HCM) is believed to be the most common genetic cardiovascular disease of the heart muscle, with an overall prevalence of 1:500 to 1:1000, mostly inherited as an autosomal dominant manner characterized by a small left ventricular cavity and marked hypertrophy of the myocardium with myofibril disarray.[1-4] Indeed, HCM has been cited as the most frequent cause of sudden cardiac death in young people, including competitive athletes, stimulating an interest in the screening of large populations for this disease.[3,5-10] The extent to which HCM can remain clinically occult and undetected for many years remains unresolved.[7-10] The occurrence of unsuspected HCM in the general population has recently been reported to be 0.17% (about 1:500),[11] suggesting that this disease may be more common than previously thought. However, many of the clinical data available in HCM have been generated from a few tertiary referral centers in urban settings in the western countries, largely comprising highly selected, clinically manifested and preferentially referred patient populations.[1, 2, 12, 13] Therefore, in the present study, we performed echo-cardiography to all suspected cases referred by our primary physicians of different hospitals (26 centers) spread all over the country. This circumstance permitted us to prospectively

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assemble data relevant to the occurrence and clinical profile of HCM in a tertiary level hospital but predominantly reflecting apparently physically fit persons extracted from a large community-based population.

Study Methods:

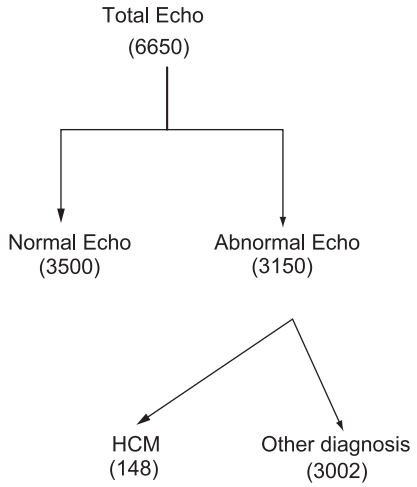
This study was conducted in Cardiac Center of Combined Military Hospital Dhaka Bangladesh. Mostly suspected defense personals (both serving and retired), civilians paid out of defense service, their family members and as well as their relatives representing a wide range of general population variety were included in this study and they were referred for echo-cardiography to have some sort of diagnosis or to rule out any cardiovascular diseases. Patients having atypical symptoms unexplained by corresponding ECG or abnormal ECG that did not correlate to the patient's presentations sent for diagnosis were accounted most in the selection of cases. Echocardiographic studies were performed by four experienced cardiologists.

Study was conducted from March 1999 to August 2009 (18 months). This diagnostic echocardiography program involved referred cases from 26 military hospitals all over the country.

Echocardiography was done with commercially available HP System 5 GE, Vivid-I, and Accusons Semens echocardiography machines using 2.5 MHz transducers for the purpose of diagnosis in a standard fashion. The following two-dimensional (2D) echo-cardiographic criteria are used to aid diagnosis: (i) unexplained maximal wall thickness >15 mm in any myocardial segment, or (ii) septal/posterior wall thickness ratio >1.3 in normotensive patients, or (iii) septal/posterior wall thickness ratio >1.5 in hypertensive patients in the absence of any other cardiac or systemic disease capable of producing the same magnitude of lefet ventricular hypertrophy observed[14,16]. Systolic anterior motion of anterior leaflet and abnormalities related to mitral valve supporting structures were also noted. Peak instantaneous left ventricular outflow tract gradient were estimated with continuous wave Doppler imaging under basal conditions.[17]

Results:

Echocardiographic diagnosis of HCM: Over the 18 months of study period, total 6650 echocardiograms were done in this centre, of which 3500 cases had normal echocardiography and among the remaining 3150 unknown cases, 148 cases were finalized to be diagnostic of HCM, who did not suffer from systemic hypertension or any other causes of ventricular wall hypertrophy (Flow chart-1).



Flow chart 1: *Echocardiographic Statistics of 18 months*

Indications for echocardiographic study: The 148 HCM patients identified for the first time in this study had their diagnostic echocardiograms performed for a variety of reasons. The primary clinical indications were: 1) predominantly, 12-lead ECG abnormalities suspicious of cardiovascular disease, 2) routine medical checkup for young defense service personnel or as a screening test prior to surgery or other medical treatment, 3) radiological evidence of pulmonary congestion or cardiomegaly 4) non-specific chest pain, palpitation, dyspnoea, fatigue or syncope, and 5) family history of sudden cardiac death (SCD). Most of the individuals had multiple indications because 95% cases showed abnormal ECG who also had many of the other indications mentioned above.

Clinical profile: At presentation patient's age ranged between 20 to 83 years (mean 52 ±13.85 years) having maximum age distribution between 30 to 70 years (88.5%), where 74 (50%) cases had age 50 years. Only 04 (2.70%) cases were found below the age of 30 years, whereas 13 (9%) cases were found above 70 years of age (Fig 1).

Male had clearly dominated the disease over female showing 85.61% and 14.18% respectively (Fig-2).

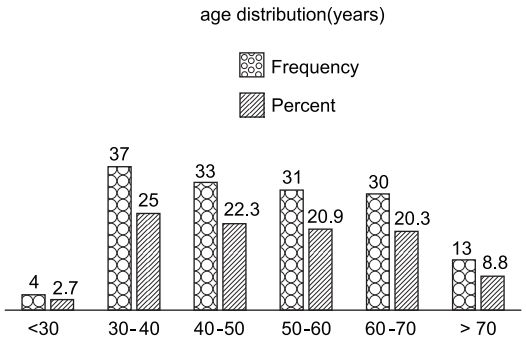


Fig-1: *Age distribution (n=148)*

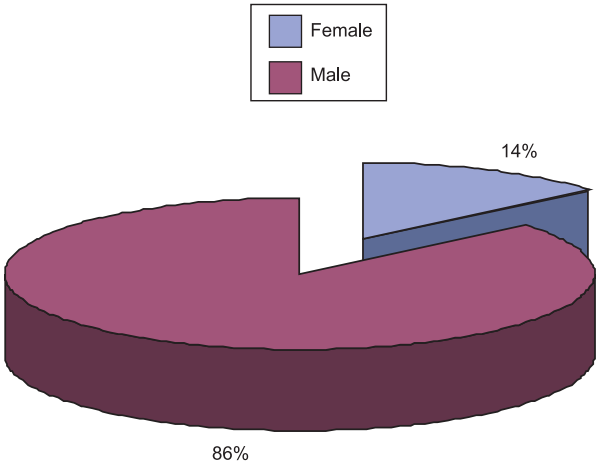


Fig-2: *Sex distribution (n=148)*

At the time of diagnosis, 98 patients (66.216%) were asymptomatic (Table-I), mostly reported for abnormal ECG finding (37.16%) followed by incidental diagnosis (25%) where echocardiography were done for routine medical check up. About 3% patients were detected following evaluation for abnormal precordial findings like systolic murmur and heaving apical impulse. Rest of the 50 (33.783%) cases were symptomatic, where most of them had more than one symptoms giving multiple response;39.2% had experienced atypical chest pain, 22.3% had exertional dyspnoea (functional class II to III), 18.9% had palpitation, 16.9% developed early fatigue and 6.8% had transient symptoms of syncope (Fig -3).

Table-I

Asymptomatic (n=98) individuals in the study population.

	Frequency	Percent
Incidental	37	25.51
Abnormal ECG	55	37.16
CXR Cardiomegaly	1	0.68
Abnormal precordial findings	5	3.38

*Multiple response

Patients aged more than 60 years presented more with symptoms compared to overall presentation, (45.28% vs 33.78%) (Table-II) but had less symptoms of chest pain compared to the younger group (20.8% vs 39.2%). On the other hand, the older patients (>60 years) presented more with syncope (11.3% vs 6.8%) compared to that of younger patients.

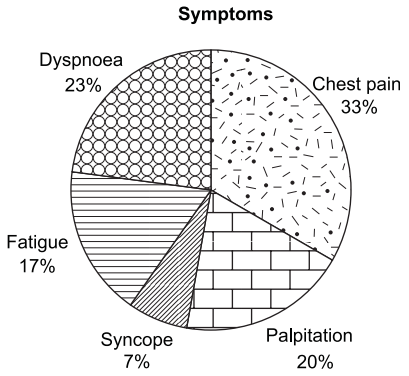


Fig.-3: *Distribution of symptoms (n=50)*

Table-II

Presentation above 60 years(n 53)

Age > 60 Yrs	Frequency	Percent
Asymptomatic	29	54.71
Symptomatic	24	45.28

Family history of HCM: Twelve patients (8.11%) had symptoms strongly suggestive of family history, 3 of them were documented by echo findings, 5 patients had family history of symptoms strongly suggestive of HCM and 4 had family history of sudden cardiac death (SCD) (Table -III)

Table-III

Family History (n = 12) of patients with HCM

Presentation in family	Frequency	Percent
Documented HCM in family	3	2.0
Syncope in family members	3	2.0
Palpitation in family members	2	1.4
History of SCD in Family	4	2.7

* Multiple responses

Electrocardiograms: Patients were mostly suspected by a variety of abnormal ECG (95% of cases) findings either isolated or multiple non-specific changes that could give no definitive diagnosis. However, multiple responses have been simplified by dominant changes to fit in the diagnosis of HCM. Very less number of individuals (5%) showed classically normal ECG (Table IV).

A variety of abnormal patterns and abnormalities were evident in the 12-lead ECG, either alone or in combination. Among which symmetrical T-wave inversion along with the features of LVH appeared to be the hallmark of ECG changes (66.89% and 25.68% respectively) in our study cases. Other changes were old Inferior MI (18.24%); old anterior MI (6.08%), left axis deviation (5.41%), conduction disturbances (1.35%) and Wolff-Parkinson's White sings (0.68%) (Table-IV). ECG finding of Symmetrical T wave inversion mainly found in the age group above 40 and this relationship was statistically significant (P <0.05) so becomes an important tool to detect HCM above 40.

Table-IV

Distribution of ECG abnormalities

Symmetrical T wave inversion	99	66.89
Left Ventricular Hypertrophy (LVH)	38	25.68
Inferior MI	27	18.24
Anterior MI	9	6.08
Left Axis Deviation	8	5.41
Conduction disturbance	2	1.35
WPW pattern ECG	1	0.68

* Multiple findings

Left ventricular hypertrophy: Relatively stronger phenotypic expression of the disease was substantiated by diffuse left ventricular wall thickening (when involving anterior wall, IVS, lateral wall and apical segments) occurring more commonly than localized (either IVS, apical or localized elsewhere) distributed hypertrophy (56.08% vs. 34.49%, respectively) (Fig 4).

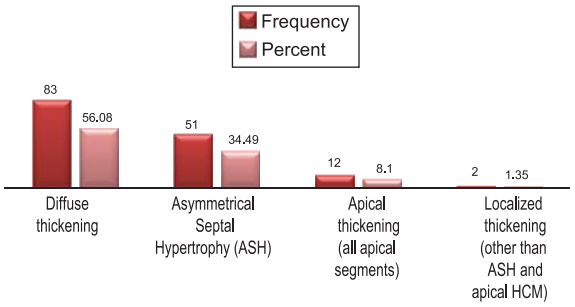


Fig.-4: *Distribution of left ventricular thickening among the study population.*

Maximum left ventricular wall thicknesses were 15 to 30 mm (mean18.3 mm) distributed among 138 patients, and 10 patients showed severe form of (30 mm) wall thickening.

Table-V

Other Echocardiographic findings among the study population.

	Frequency	Percentage
Systolic Anterior Motion of MV-apparatus (SAM)	44	29.73
Mitral Regurgitation (MR)	19	12.84
Aortic Regurgitation (AR)	9	6.08
Dynamic LVOT gradient	14	9.46
IVS thickening	134	90.54

* Multiple responses

Septal hypertrophy was involved in 134 cases (90.54%) either as an isolated thickening or as part of symmetrical thickening. So disproportionate thickening of IVS is also an important echocardiographic hallmark to raise strong suspicion that one might be dealing with a case of HCM.

Other echocardiographic findings- SAM of different amplitude was present in 44 patients (29.73%) but dynamic LVOT gradient was observed in only 14 cases (10%). Mitral regurgitation was identified by color flow imaging in 19 cases (12.83%) and AR was seen in 9 cases (6.08%) quantified as mild by color flow mapping (Table-10).

Outflow obstruction - 14 patients (9.46%) had LVOT obstruction under basal condition and peak instantaneous outflow gradients ranged between 20 to 82 mm Hg, 5 of them had marked outflow obstruction (50 mm Hg).

Discussion:

Patient selection and HCM disease spectrum: Our perception on clinical spectrum of HCM has been greatly influenced by the experience of large tertiary referral institutions which have dominated the available published data.[1, 2, 12, 13] These conventional HCM referral patterns specially directed high risk patients for management and follow up in such institutions and as a result certain subgroups of silent cases have not been adequately represented either in their published reports or within the presently existing concepts of the disease spectrum. For example, asymptomatic or mildly symptomatic patients have largely been absent from many published reports on HCM.[7, 8] These observations logically raise questions regarding the extent to which some HCM patients may remain undetected within the community. Though in a prior study,[11] previously unsuspected HCM was identified by echocardiography in 0.17% of 4,111 subjects (or about 1:500) from the general population, but genotype selected HCM pedigrees has demonstrated that many asymptomatic cases or with mild phenotypic expressions of HCM detectable only by echocardiography [3, 19] who otherwise might not have been easily identified clinically. So our commitment in this study was to observe to which extent of ages an individual with HCM can remain asymptomatic or non-specifically barely symptomatic, find out more HCM patients in the primary level by providing echocardiographic facility to the suspected cases and provide risk stratification strategy and further cardiac plan to reduce or delay disease complication.

We designed this prospective study to facilitate a) early detection of HCM cases, b) emphasize on their clinical presentation and c) to promote the mechanism of suspicion in the primary level which should be extended to the general population reporting to primary health care physician located at different parts of the country. Fraction of HCM cases (4.05%) were high in our study compared to the other studies (0.17%) carried out among general population [11], and other reporting conducted among the unsuspected general populations (0.19%),[20] because our cases either had overt disease expression in the form of atypical symptoms or abnormal ECG findings out of 3648 cases who had no previous cardiac diagnosis. 6% of HCM cases, who neither had ECG changes nor do any symptoms along with predominant portion of asymptomatic cases, indicate that a large number of patient remains undetected in the community could be identified by the primary health care physicians simply by providing echocardiographic facilities to these selected individuals. But the lack of echocardiographic facilities in the rural level makes it impossible to find out the exact disease prevalence in our country. If it would have been possible, more silent cases could have been identified well ahead and related symptoms and complication could have been delayed or prevented by effective cardiac management planning. Another explanation of high incidence in our study in possibly due to extensive screening in all level of military medical facility which is sometimes not possible in general population.

The present HCM patients diagnosed for the first time showed more or less similar phonotypical expression clinically consistent with HCM in populations removed from the selection bias characteristic of tertiary referral centers but we got more number of male patients (86%) but less number of totally asymptomatic patients (54.7%) over age 60 years.[14, 15, 21, 22] Age of our patients ranged from 20 to 83 (mean 52.18) years, where 2.7% had age below 30 and 9% had age above 70 years. These observations, all underline the importance of recognizing HCM as a disease compatible with advanced age and normal longevity, and often associated with little or no disability. Such a perspective is largely unappreciated in the available HCM published data. [1, 2, 23-26]

In contrast to referral center populations, more of our patients (56%) showed symmetrical or diffuse hypertrophy of left ventricular wall and asymmetrical septal hypertrophy (35%), we got more cases of apical hypertrophy (8.10%) and very less number of localized thickenings when compared to referral center population.[14] Phenotypic expression on the 12-lead ECG [21] was

also considered to be similar where 25.68% showed features of left ventricular hypertrophy and the classical finding of ST segment changes and symmetrical T-wave inversion was preset in 67% of cases, which was mainly found in the age group above 40 and this relationship was statistically significant, thereby should receive maximum attention for early detection of HCM above 40 and it's onward prevention. Pathological Q-wave was present in 24.32% in inferior and anterior leads. Most all of our cases (95%) created suspicion following meticulous scrutiny of ECG which showed some changes supported with or without atypical cardiovascular symptoms or done due to some other requirements became very important diagnostic tool for detecting HCM in the general population though lot of abnormal ECG did not show HCM.

Conclusions:

This prospectively assembled data show that majority of HCM cases may remain asymptomatic, clinically dormant and undetectable for many years (often to advance ages) in our community. The role of primary care is important in early detection of HCM cases when an abnormal ECG supported by atypical cardiovascular symptoms are well addressed and intended to rule out structural heart disease by an echocardiography, thereby stratifying potential risk to prevent sudden cardiac death and avoid incapacitating cardiac complication. The actual prevalence of the disease in our community needs to be ascertained which might exceed the prevalence mentioned in the text books.

Conflict of Interest - None.

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