

Original Research Article

Utility of world heart federation and modified World Health Organization echocardiographic diagnostic criteria of subclinical rheumatic heart disease in children of Manipur, India

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ABSTRACT

Background: A comparative prevalence studies using modified WHO and more stringent criteria of WHF2012 have not been conducted in this part of the country and so authors felt necessary to conduct such study in this North-eastern state of India.

Methods: In this cross-sectional study, 3600 children aged 5-15 years (11.07±2.86, 51.90% male) from randomly selected schools of Manipur were examined clinically and by 2D colour doppler echocardiography.

Results: Only one case of Clinical RHD with a combination of MR and AS was found, (prevalence of 0.28/1000) [CI: 0.04-1.97]. Echocardiography detected 3 cases of definite subclinical (prevalence rate of 0.83/1000 (CI: 0.27-2.58), 14 cases of borderline subclinical RHD (prevalence rate of 3.9)/1000 (CI: 2.30-6.56) befitting WHF 2012 criteria, and 61 cases of borderline subclinical RHD befitting modified WHO criteria (prevalence rate of 16.9/1000) [CI 1.3-2.1]. On follow up to 5 years, among the 3 cases with definite subclinical RHD, 2 had worsened and 1 remained non- progressive, while among the 14 subclinical borderline cases, 2 normalized, 6 remained non-progressive and 6 children were lost to follow up.

Conclusions: Prevalence of RHD using echocardiography is several folds higher compared to clinical examination alone. While the number is reduced by about half using WHF criteria. However, the importance of WHO criteria cannot simply be neglected, as all the subclinical cases by WHF criteria remains non-progressive, while one case of subclinical defined by WHO worsened on follow up.

Keywords: Echocardiography prevalence, Rheumatic heart disease, School children, Subclinical

INTRODUCTION

Worldwide rheumatic heart disease is still a major public health challenge especially in developing countries including India. Secondary prophylaxis by giving penicillin injection to prevent recurrent attacks of rheumatic fever (RF) thereby preventing further worsening of valve lesions has been accepted as the only

cost-effective strategy to decrease the disease burden.¹ Prevention will be more effective if the measure is instituted early in the course of the disease. Since, many RHD cases occur without definite noticeable history of RF, echocardiographic screening of high-risk population is suggested as a method for early detection of disease. Generally, echocardiography is more sensitive and specific to diagnose RHD compared to clinical

examination using stethoscope.²⁻⁸ However, definition of subclinical RHD is an evolving area. There are established American heart association (AHA) criteria for acute rheumatic fever (ARF) diagnosis but no such accepted criteria exist for RHD.

In 2001, a WHO expert committee established a consensus for the echocardiographic diagnosis of pathological regurgitation based on the detection of valve regurgitation by Doppler interrogation of the cardiac valves.⁹

In 2005, a joint WHO and NIH (National Institute of Health) established consensus case definition for RHD which were published 5 years later in 2010.¹⁰ Subclinical RHD may be defined as RHD detected on echocardiography without an associated clinically pathological cardiac murmur. According to some authors, the burden of subclinical RHD appears to be underestimated if one use WHO diagnostic criteria of RHD which accounts only for the Doppler abnormal characteristic but not morphological change.⁴

Subsequent to later studies using echocardiography for diagnosis of RHD, there has been concern for possible over diagnosis of the disease leading to overestimation of its burden. Accordingly, an international advisory group of experts in RHD screening and echocardiographic manifestations of RHD brought out a consensus WHF criteria for diagnosis of RHD.¹¹

The primary purpose of the study was to study the prevalence and long-term outcome of subclinical RHD in Manipur and to compare the prevalence using WHF and WHO criteria.

METHODS

The study was designed as a cross-sectional survey. The purpose of this study was to determine the prevalence of rheumatic heart disease in the age group 5-15 years with specific reference to the burden of subclinical cases and its possible long-term outcome in a follow up of 5 years. This was a part of the multisite extension study of rheumatic study (e rheumatic).¹² The study was conducted in Manipur, which has a unique geographical characteristic having a blend of valley and hilly areas covering a total area of 22,327 square kilometer. hosting a population of 25,70,390 inhabitants, giving a population density of 735 per sq.km in valley and 47 per sq.km in the hills as per 2011 census publication of Govt. of India.

All the existing 9 districts of the state were covered and about 50 schools, both government and private were randomly selected. The principals of these schools were initially approached formally and obtained consent forms duly signed by the parents or class masters.

This study was cleared by the ethical committee of the institute (JNIMS Imphal). The enrollment and initial

study were conducted from mid-2012 to 2014, while the follow-up study was done 4-5 years later.

The onsite physician took a brief history and examined the child. Anthropometric parameters were recorded. Clinical examination was performed to find out features of respiratory distress, cyanosis, cardiomegaly, congestive heart failure, abnormal heart sounds, murmurs etc. Color doppler echocardiography was performed, using a portable echo machine (Sonosite M Turbo, USA) for all children in the study by the cardiologist in the team who has been blinded initially from the finding of clinical examination.

Operational Definition of Echocardiographic criteria

WHO definition of subclinical RHD requires pathological regurgitation lesion fulfilling all 4 criteria of: regurgitation identified in at least two planes, a regurgitant jet greater than 1cm seen in at least 2 planes, a mosaic color jet with peak velocity greater than 2.5 m/s and pan systolic/pan diastolic regurgitation of the mitral and aortic valves, respectively.

The modified World health organization (WHO) criteria requires above criteria combined with at least 2 morphologic signs including leaflet restriction, sub valvular thickening, and valve leaflet thickening.¹³ Other criteria for diagnosing “definite” RHD by echocardiography included mitral stenosis, mitral valve involvement with aortic regurgitation (AR) in the absence of alternative cause for AR, and isolated mitral regurgitation with documented history of RF.

WHF (2012) criteria requires additional criteria in Doppler characteristics of longer jet length of >2 cm for MR and higher jet velocities of > 3 m/s for both MR and AR for being defined as pathological.

Definite subclinical RHD by this criterion is defined by pathological MR or AR and at least two morphological features of RHD of the MV or AV, or MS mean gradient >4 mmHg, or combination of borderline disease of both the AV and MV.

Borderline subclinical definition of the case requires any one of these features viz. minimum of two morphological features of RHD of the MV without pathological MR or MS, or pathological MR, or pathological AR.

Children detected with any abnormality were advised for subsequent treatment and further follow up study at JNIMS. Of the 3 subclinical definite RHD fulfilling WHF criteria, 2 received oral while 1 received injectable prophylactic penicillin.

Statistical analysis

The data are presented as mean (SD) or number (%). Prevalence was reported per thousand populations with

95% CIs. The association of categorical data with RHD was analysed using chi-square test and continuous variables were analysed using t-test for independent samples/Wilcoxon rank sum test (for non-normal data). A multivariate logistic regression analysis was performed to identify the predictors of RHD in this population. The model included age, gender, type of school (government or private) overcrowding (defined as >4 persons living in a room) and type of house (Kutch/brick). A p-value of <0.05 was considered significant. The data were analysed using Stata 13.0 (STATA Corp, USA).

RESULTS

A total of 3600 children were screened for echocardiographic evidence of RHD over a period of two years. Out of this, 214 subjects were found to have some deficiencies in the demographic data and hence excluded, and the calculation and presentation of the demographic profile was done from 3386 subjects.

The mean age was 11.07 ± 2.86 years (range 5-15 years) and 51.9% were male. Children aged 5-10 years were comparatively less comprising of 41% of the total study population while the highest representation was from the age range of 12-15 years of age.

Table 1: Baseline characteristics of the study subjects.

Characteristics	Mean /Median \pm SD	Range /proportion
Age (years)	11.6 ± 2.86	5 to 15
Class	5 ± 2.78	1 to 10
Boys	1758	51.90
Number of family members	6.05 ± 2.12	2-24
Number of rooms	3.59 ± 1.76	1-15
Weight (kg)	34.38 ± 12.07	10-83
Height (cm)	136.44 ± 16.52	86.9-179.5
Waist circumference (cm)*	60.2 ± 8.12	27-97
2423 subjects		
BMI	17.80 ± 3.76	10.95-29.98
Overcrowding (>4persons/room)	235	6.94
Systolic BP	110.14 ± 12.34	61-167
Diastolic BP	70.58 ± 9.61	29-108

*Information was available in 2423 subjects.

Majority of the subjects (78.9%) were living in Kuccha house (made of bamboo/wood and mud), in rural areas (67%), and about a third (42.5%) were studying in government school. The base line characteristics are given in Table 1.

Clinical examination did not reveal any significant cardinal symptoms of heart disease except one. In the population studied, 102 (3%) subjects had complaint of joint pain, and characteristics of the pain were not typical

of RF. It may be noted that 2 out of 3 definite subclinical and 4 out of 14 borderline subclinical cases had history of joint pain.

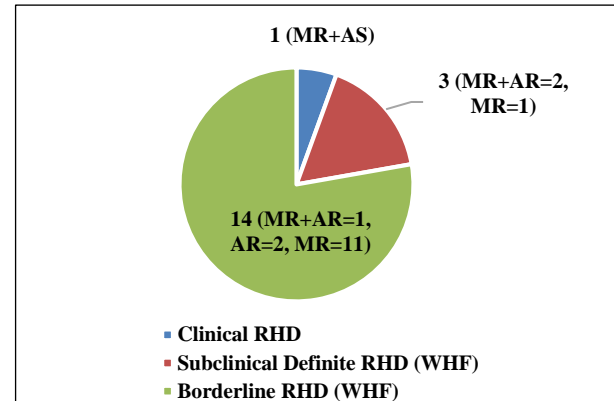


Figure 1: Distribution of valve lesions in all spectrum of RHD.

Significant murmur was detectable in only 1 subject who complained of mild exertional dyspnea and palpitation, who have moderate degree aortic stenosis (AS) combined with mild mitral regurgitation (MR) on echocardiography giving a diagnosis of clinical RHD with a prevalence rate of 0.28/1000 (CI: 0.04-1.97).

In the subclinical category in whom no significant murmur was detectable, echocardiography revealed mitral regurgitation (MR) as the most common lesion, while isolated aortic regurgitation (AR) was found in 6 individuals and a combination of MR and AR were detected in 7 subjects.

The distribution of the valve lesions across all spectrums of the clinical and subclinical cases, depending on the criteria of detection used is depicted in Figure 1.

Risk factors

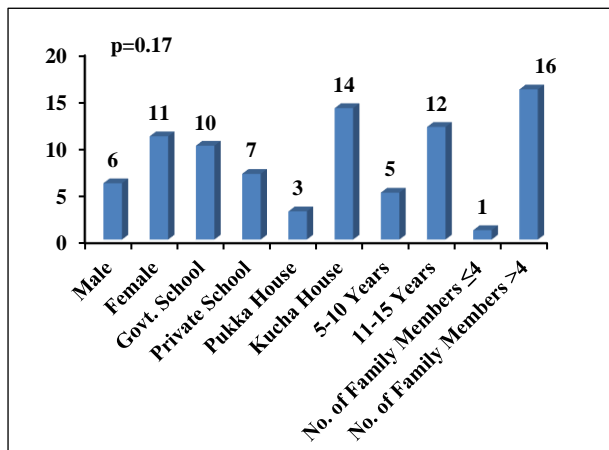
Compared to non-RHD group, children with suspected RHD appear to belong to older age group and higher class.

Majority of the children in the RHD group are found living in kuccha house and attending government school which may reflect lower socio-economy (Table 2). However, these variables were not statistically significant.

Among the 17 subjects detected to have echocardiographic evidence of clinical and subclinical RHD, subgroup analysis revealed relative apparent association of the disease with variables like older age, female gender, crowded and kuccha dwellers. However, these variables when subjected to multivariate regression analysis did not show statistically significant association (Figure 2).

Table 2: Comparison of the baseline characteristics of RHD and non RHD children.

Characteristics	RH RHD (17 subjects)		Non RHD (3369 subjects)		P-value
	Mean/Proportion/Median	SD	Mean/Proportion/Median	SD	
Age (years)	11.71	2.25	11.06	2.86	1.00
Class	5	-	5	-	1.00
Number of family members	6	-	6	-	1.00
Number of rooms	3	-	3	-	1.00
Weight (kg)	36.24	13.11	34.37	12.07	0.86
Height (cm)	142.77	16.63	136.30	16.63	0.94
Waist circumference (cm)	59.64	7.57	60.15	8.38	0.94
BMI	17.06	2.85	17.76	2.81	1.0
Systolic BP	112.94	12.63	110.13	12.34	1.0
Diastolic BP	71.17	11.11	70.58	9.61	1.0
Government vs private schools	10/7=1.42	-	1432/1617=0.88	-	0.64
Kucha/pukka house	14/3=4.33	-	2658/711=3.73	-	0.83
Male/female	6/11=0.54	-	1752/1617=1.08	-	0.08

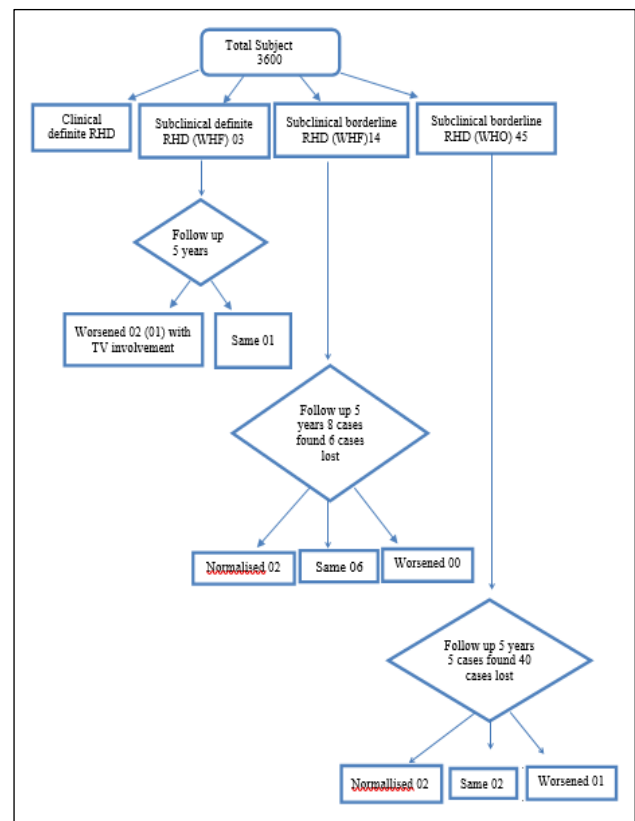
**Figure 2: Association of RHD among various subgroups of the 17 subjects.**

Follow up

Studies for the subclinical cases conducted 4-5 years later could find only a few of the subjects, 3 out of 3 (100%) in definite WHF group, 8 out of 14 (57%) in Borderline WHF group, 5 out of 45 (11%) in borderline subclinical WHO criteria befitting group.

The most probable reason of inability to follow up the majority of the borderline cases lies in the fact that these individuals were relatively older studying in higher classes leading to school transfer following upgradation to higher grades in other schools.

Two out of 3 definite subclinical cases showed worsening of the disease process in terms of increased thickness of valve and increased jet length of the regurgitant jet, while one was found to have developed mild but significant tricuspid involvement.

**Figure 3: Flow chart of selective follow up echocardiography study done after 5 years.**

Among the Borderline subclinical (WHF) cases, 2 got normalized while 6 were found non-progressive. Of all the very few cases of Borderline subclinical (WHO) cases, 1 found worsened in terms of increased MR jet length (25%) with persistence of valve thickening, while 2 got normalized and another 2 remained non-progressive (Figure 3).

The changes authors noticed in terms of resolution of the valvular pathology were mainly in the reduction or disappearance of the regurgitant lesion by Doppler which were more common and earlier than the morphological changes.

Hence, authors could not neglect the single borderline (WHO) case which showed progression of the MR jet length (25%) even if the morphological features were seen static.

DISCUSSION

In the past few decades, prevalence of RHD had been reported from various parts of the world in a range varying from 1.8 to 11/1000 depending on different methods of examination and criteria of diagnosis used. Previous studies in India conducted in the past decade involving clinical detection of RHD validated by echocardiography showed a prevalence of 0.6-0.8/1000 in school children.^{14,15}

Echocardiography has been accepted as the best initial tool to diagnose RHD. Earlier studies using only the color Doppler echocardiography criteria of WHO which did not count the morphological changes of the valve structure revealed several fold increased prevalence of the disease compared to clinical examination alone. Detection of the morphological changes of valve by rheumatic process is another extremely important aspect to be noted as there are practically no diseases which can induce similar changes in children apart from the rheumatic process. Later studies which incorporated a minimum of two morphological criteria in addition to the color Doppler defect improved the specificity and alleviated its overestimation to some extent which however has been criticized by some for possible underestimation of the disease burden. Marijon E et al, in their study have shown that inclusion of morphological criteria in addition to the standard WHO can improve the case detection rate by 3-fold.⁴ In one such study conducted in rural north India, Anita et al found a prevalence of clinical and subclinical RHD as 0.8/1000 and 20.4/1000 respectively.¹⁶

Contrary to all these studies, present study found the lowest prevalence of clinical (0.28/1000), and subclinical definite (0.83/1000) and subclinical borderline 3.9/1000 RHD cases using WHF criteria. If authors apply the less stringent modified WHO criteria, the total estimate of the subclinical case would be 61 giving a prevalence of 16.9/1000, which was still less compared to 20/1000 as found by Anita et al, in their study using modified WHO criteria.

Some setbacks have been observed in the inability of follow up study to reexamine all the suspected individuals particularly in the borderline cases where only 8 out of 14 (57%), 5 out of 45 (11%) in the category

of WHF and WHO befitting subclinical RHD cases respectively.

Importance of the stringent criteria of WHF in avoidance of overestimation of subclinical RHD and its influence on subsequent long-term outcome in 5 years has been exemplified by the fact that 2 out of 3 definite subclinical case has worsened while none of the borderline cases did.

The author feels that authors cannot simply discard the WHO criteria (including modified one) if authors aim to estimate the true burden of RHD in a community and take up measures to lessen it. The importance of WHO criteria can be visualized from the observational discrepancy in the outcome, as noted in the group of subclinical RHD cases according to WHO criteria, where 1 out of the 5 subjects examined subsequently found worsened or progressed significantly.

Even if the number of cases followed up in this group was very few, the finding may not be out rightly ignored. This impression is based on the author's experience and observation in the routine hospital practice over the preceding more than 10 years when quite a good number of ARF cases, some of them even in heart failure, on follow up over 6-12 months were found to have minimal residual findings leading to missing out of these cases owing to criteria short of WHF. What is more interesting is that few of these patients later presented to us, about 1-2 years, with features of ARF again. These individuals, who could have been prevented by proper prophylaxis measures from further progression or recurrence, would be missed out by any study using stringent criteria of WHF for case detection.

RHD is still found to be a common heart disease in the routine hospital practice. Based on these observations and findings it may be assumed that WHF criteria may be too stringent to be used in the detection of subclinical cases here in this part of the country where RHD is still very common.

There appears to be a missing link between this very low prevalence of clinical or subclinical RHD in the school children in present study and higher prevalence of RHD cases encountered in the routine clinical practices. In the study by Anita et al, most of the subclinical cases on follow up for 2 years were found non-progressive or regressed hence giving an impression that penicillin prophylaxis to prevent from further progression in such individuals will not be justified or cost effective. There has been no agreement as to how these subclinical cases would be treated or given prophylaxis. Though most of the ARF recovers and leave no residual changes, further changes in valve morphology in subsequent attacks of ARF may be influenced by some other unknown factors besides geographical factors, general health, nutrition and possibly immune status of the individuals. This variable response and subsequent impact on estimation of disease burden would only be well addressed to if authors

conduct larger study incorporating the modified WHO criteria as well.

The merit of the present study was that each and every child was examined echo cardio graphically by a single cardiologist who has adequate experience.

The major limitations of this study were the small sample size and poor coverage of the subjects in follow up particularly in the category of borderline subclinical RHD cases defined by modified WHO criteria.

CONCLUSION

Present study shows that compared to other studies, cases of RHD as defined by WHF (both clinical and subclinical) are rare in the school going children of this part of the country. Most of these subclinical cases on medium term follow up over 5 years do not show progression of the disease. However, true burden of the disease however in this part of the country may better be estimated by conducting larger study involving longer effective follow up in both cases of subclinical RHD defined by WHF and modified WHO criteria as well.

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