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COMPARISON OF CLINICAL AND ECHOCARDIOGRAPHIC PROFILE OF RHEUMATIC FEVER IN CHILDREN: A CROSS SECTIONAL STUDY

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ABSTRACT
ARF / RHD in a developing country is very much preventable and has significant burden on public health resources.; It's cross sectional study of children of 5-15 yrs age, attending OPD or admitted to VIMS, Bellary satisfying the WHO RHD criterion. Mean age was 10.96 yrs with the M; F; 1.3:1. Clinical Profile has: carditis being commonest followed by fever, polyarthritis/ arthralgia and chorea. Overcrowding observed in 68 %, low socioeconomic status in 92%. Lab parameter mean Hb 10.85 gm%, elevated anti- ASO titer 68%, positive throat swab 64%, elevated CRP 68%, ESR 39.96, prolonged PR interval 12%, Mitral valve was the most commonly involved. Echo found significantly higher TR in patient than clinically. Additionally, echo detected subclinical patient and IE Children with ARF may present with joint symptoms or chorea, features that could be recognized by community health workers. Echo had advantage in detection of TR, subclinical cases and IE.

KEYWORDS: Rheumatic Fever, Rheumatic heart disease, Jones criteria, echocardiography.

INTRODUCTION
ARF/RHD is inflammatory disorder involving heart, brain, joint and skin. It occurs two to four weeks later as autoimmune sequela of pharyngeal infection with *Streptococcus pyogenes*, or Group A β haemolytic *Streptococcus*.[1] Among the other manifestations of ARF, carditis is the only one that causes death during acute stage of the disease and leads to long term sequelae in the form of CHF, strokes, infective endocarditis.

With global estimate of over 15 million cases, annual addition of 28200 new cases and 2,33,000 deaths, RHD imposes a substantial burden on health care systems.[2] Secondary prevention needs accurate detection of cases to improve use of prophylactic antibiotics and regular medical surveillance. Exact prevalence data are also highly desirable to facilitate health care planning. Though ARF and RHD have declined in many parts of the world, but still remains a major cause of morbidity and premature death in developing countries like India. Moreover, it leads as a major cause of cardiovascular morbidity and mortality.

According to recent surveys, the incidence of ARF varies from 0.2-0.75/1000 school age children 5-15 years of age.[3,4] It mainly effects children and young adults leads to significant social and economic losses.

Besides the ARF, it is to be emphasized that severe symptomatic RHD occurs in far younger age groups in developing countries like India compared to the West. Critical mitral stenosis with severe pulmonary hypertension and CHF may occur within 1-2 years of illness. Approximately, 50-60% of children with ARF later on develop valvular heart disease. Females are affected 3 times as often as males. Mitral valve is predominantly involved with aortic valve next in frequency and the tricuspid valve least frequently involved. Approximately 25,000 US dollar is needed for surgical intervention in RHD which can fund 1 year of an RHD screening program in a small developing nation.[5] So, early detection through screening programs can reduce the morbidity of chronic RHD and surgeries for heart valve repair or replacement.

Although Jones' criteria has been modified and revised , carditis in ARF remain under diagnosed leading to nearly 50% of established RHD not receiving prophylaxis, or over diagnosed, based on traditional characteristic auscultatory findings for diagnosis of carditis.[6–8] So, this study was undertaken to evaluate clinical features of this disease, various epidemiological factors affecting the course of this disease, and most importantly the role of echocardiography in a suspected or diagnosed case of RHD.

METHOD
Study design and setting
This study was cross sectional analytical study. After approval from Institutional Ethical Committee, this study

was carried out in the Department of Pediatrics, VIMS, Bellary over a period of one and half year from December 2009 to July 2011.

Participants

All children of 5-15 years of age group who fulfilled revised Jones criteria[8] were enrolled in the study. Exclusion criteria was**:** Children less than 5 year or more than 15 years of age**,** children already suffering from acquired heart disease from any cause proven to be other than RHD, children suffering from cardiomyopathies.

Procedure

All children who satisfied the modified Jones criteria and gave written informed consent from the parents were enrolled. A detailed clinical evaluation including history and examination was carried out for all subjects as per the proforma by doctor on duty. Socioeconomic status was classified on basis of modified BG Prasad.[9] After that following investigation was done in all case: Complete blood count, ECG, ESR, CRP, Throat culture, ASO titer and Echocardiography. Optional investigations were carried out for few patients including Rapid streptococcal antigen test and Chest X ray.

Outcome

Clinical profile

Rigorous cardiac auscultation was performed by two third year resident doctors and pathological murmur was detected based on traditional criteria.[10] Cardiac murmurs were considered pathological when associated with tachycardia or tachypnoea, abnormal pulses, precordial bulge, displaced apex beat, presence of thrill, abnormally loud or fixed second heart sound, diastolic murmur, loud or harsh murmur, or pan systolic murmur.

Pathological

Hemoglobin was estimated using Sahil's haemocytometer. Anemia was defined in children as per WHO criteria. Total WBC count and Differential count was done using Sysmex Auto analyser followed by cross examination by smear stained with Leishman stain. Total count of >11500 was considered as elevated. ESR done using Westegrens tube method. CRP was done using latex agglutination test. ASO titer were done using latex agglutination test and a titer of >333 Todd units or rising titre was considered positive. Throat swab was done taken for culture. ECG: 12 lead ECG was taken for all the cases and observed for heart rate, axis, rhythm, PR interval, QRS duration, QTc interval, morphology of P waves, QRS complex and T waves, presence of u waves, and chamber hypertrophy. Chest radiographs were taken for all the patients in posterior-anterior view and looked-for cardiomegaly, features suggestive of valvular lesions, hyperemic lung fields and other significant features.

Echocardiography

All the patients were subjected to 2 D Echo and color Doppler using standard Phillips HDI 4000 system by a trained cardiologist, Department of Medicine, VIMS. High frequency transducer (12-4 megahertz) was used and assessment was done, as per standard imaging technique recommended by the American Society of Echocardiography. First 2 D Echo was done in the parasternal long axis and short axis view, the apical four chamber and long axis view and the subcostal views then M mode echo followed by Color Doppler echocardiography. The observer was blinded to the clinical, pathological status while performing echo evaluation.

Subclinical carditis was defined by presence of silent rheumatic value features ((according to at least 1 of the 2 sets of echocardiographic criteria), acute and / or chronic, even in absence of a history of acute rheumatic fever. Two set of criteria[11] used is enumerated in Table 1.

Sample size

Sample size was based on number of the patients who attended the Department of pediatrics during study period and it was found to be 25.

Statistical analysis

Data from predesigned Performa was compiled in Microsoft excel for analysis. Demographic characteristics, clinical, pathological and echocardiography parameters were described as mean± standard deviation and proportion (percentage). Proportion of valvular lesion detected by clinical examination and echocardiography was compared using chi square test or Fisher's exact test as applicable. P value of less than 0.05 was considered significant. All analyses were done using commercially available software program Stata 11**,** Stata Corp LP, Texas, USA.

RESULTS

25 children were enrolled during study and. analyzed. Demographic characteristics of children are detailed in Table 2. Clinical profile of enrolled children with RHD/RF are described in fig 1. Mean age of presentation was 10.9 years with 56 percentage of cases being male. Clinical profile shows carditis seen in 92 % of patient with most of them having myocarditis (52%). Polyarthritis/ arthralgia seen in 48 % and chorea in 20 % of children. No patient presented with subcutaneous nodules and erythema marginatum. One patient died by refractory congestive heart failure with critical mitral stenosis and the mortality was 4%.

Mean ESR was 39 .96. While CRP, ASO was positive in 68 percentage of children, throat culture positive for group A streptococcal organism was seen in 64 children (Table 3).

Valvular involvement was observed in 76% case with mitral regurgitation commonest by both clinical examination and echocardiography (fig 2). Finding of MR, MS, AR and TS are similar both clinically and by echocardiography (Table 4). Moreover, echo detected

TR in significantly higher children than clinical examination. Echo detected sub clinical carditis and concomitant infective endocarditis (Table 4).

Table 1: Criteria Used to Define Subclinical RHD Using Echocardiography.

1.	**WHO criteria**
	Doppler criteria
	A regurgitant jet >1 cm in length
	A regurgitant jet in at least 2 planes
	A mosaic colour jet with a peak velocity _2.5 m/s
	The jet persists throughout systole or diastole
2.	**Combined criteria**
a.	Doppler criteria
	Any degree of valvular regurgitation seen in at least 2 planes
b.	Associated with at least 2 morphological signs
	Leaflet restriction
	Subvalvular thickening
	Valvular thickening

Table 2: Demography characteristics.

Characters	**n=25**
Age (Years)*	10.96 ± 2.39
Male#	14 (56%)
Socioeconomic status # Class III Class IV Class V	 02 (08%) 17 (68%) 06 (24%)
Resident# Rural Urban	 18(72%) 07(28%)
Overcrowding#	17(68%)

Data expressed as mean± SD* and proportion# (percentage)

Table 3: Diagnostic profile.

Parameters	**N=25**
Hb%*	10.85±1.7
Tc*	9618±3837
Neutrophils*	60.52±11.51
Lymphocytes*	33.84±11.68
Monocytes*	3.16±2.29
Eosinophils*	3.00±3.23
ESR*	39.96±26.29
CRP#	17 (68%)
ASLO#	17 (68%)
Throat culture#	16 (64%)
ECG (PR prolong) #	03 (12%)
X- ray features# Cardiomegaly Pericardial effusion PAH MS	 14(56) 05(20) 02(08) 05(20)

Table 4: Chi square test/ Fisher's exact test comparing echo with clinical examination.

Valvular lesions	n=25 Clinical	n=25 Echo	P value*
MS	06 (24%)	10 (40%)	0.22
MR	18 (72%)	21 (84%)	0.30
AR	01 (04%)	01 (04%)	-
TS	00 (00%)	03 (12%)	0.11
TR	00 (00%)	13 (52%)	0.001
AS	00	00	

Data expressed as proportion (percentage)

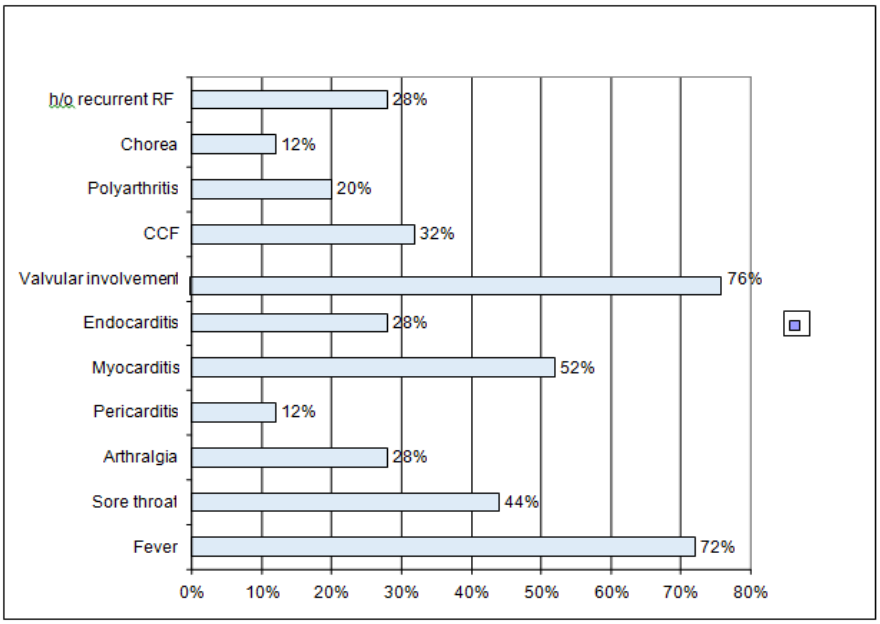

Fig. 1: Clinical profile.

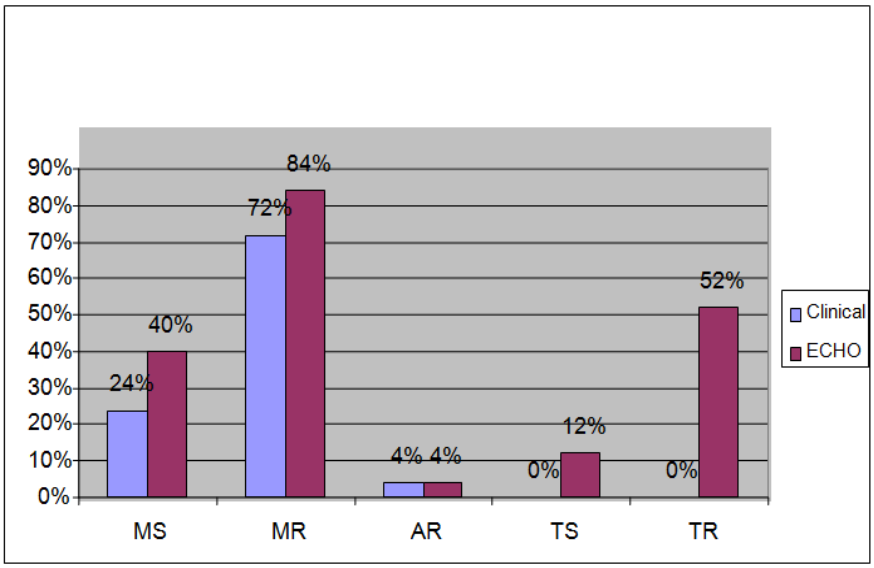

Fig. 2: Comparison of echo and clinical evaluation of valvular lesion.

Abbreviation RHF**:** Rheumatic Fever; RHD: Rheumatic heart disease; echo: echocardiography; IE: infective endocarditis; MR: mitral regurgitation; MS: mitral stenosis; TR: tricuspid regurgitations: tricuspid stenosis; AR: aortic regurgitation; AS: Aortic stenosis.

DISCUSSION

Acute rheumatic fever and its long-term sequel RHD is still a major burning problem in children, adolescents and young adults in developing countries like India. Unfortunately, carditis is the only presentation of ARF that causes death during acute stage or leads to permanent damage with long term morbidity and mortality due to RHD and CHF.

Mean age of study subjects in the present study was similar to study done on Nepali children in the age group of 5-15 years by Rayamahi et al[12] and in a retrospective analysis by Ravish et al.[13] So, the age distribution probably has not changed over a span of past years as well as remains similar for the underdeveloped countries, though the presentation is early in comparison to developed countries where majority of patients tend to present in late adolescence and adult life.

The study observed RHF is more common in male than female. It's similar to the previous study in south Asia.[12] In the world, wide epidemiology of RHD for the WHO SEAR region, males were 57.4 % which is comparable to the present study.[14]

Demographic determinants as expected showed overcrowding as major risk factor and subjects mostly residing in rural area than urban area and belonged to low socioeconomic status. This suggest disease is common in rural area in developing countries.

Fever is the commonest manifestation and joint symptoms are also seen in good percentage of patients. Study by Tunks RD et al at Vanderbilt Children's hospital noted that 80% patients satisfied Jones criteria and 91% of cases had joint symptoms.[15] Also, majority of the patients have presented with carditis or clinically apparent valvular involvement which not only shows the late presentation but also the missed earlier episodes of ARF as majority of patients do not give past history suggestive of ARF.

Study also showed MR as the commonest valvular lesion and mitral valve being the commonest valve involved. This contrasts with the adult population where MS tends to be commonest lesion. Aortic valve is also involved in a significant number of patients.

Majority of the patients were anemic which was also a comorbidity in cases of CCF and valvular involvement. Chest X-ray a simple tool may help in detecting valvular lesion like MS, and pulmonary artery hypertension along with clinical examination.

Echocardiography showed most commonly mitral valvular involvement and is comparable to other study (16). Compared to clinical examination, echo showed a significant TR in children whereas Reddy et al found TR, AR and MR was significantly detected by echo than clinically. MS did not have statistically significant values in either of the study, though a greater number of patients were picked up by echo in both the studies which is nevertheless important. This can probably be explained on basis of a small sample size in the present study. Also, the patients who were studied in the present study were the ones who presented to institute after they became symptomatic and had established valvular heart lesions at presentation which were easy to identify clinically.

Subclinical carditis, missed clinically but picked up by echo, was observed in a total of 32% cases in this study. In total echo added extra information to clinical diagnosis in 56% of the cases.

In a screening study conducted on randomly selected school children of age group of 6-17 years in Cambodia, 8 out of 3677 children clinically fitted in the diagnosis RHD whereas echo picked up 79 cases of RHD in the same group.[17] In Mozambique, 5 out of 2170 children clinically having RHD whereas echo picked up 66 cases.[17]

CONCLUSION

Children have lesser age of presentation in India compared to peers in developed countries. Most children had well-established heart disease owning to delated age of presentation. MR is the commonest valvular lesion in childhood unlike adulthood. Children also had either joint symptoms or chorea. They may help in early detection rates of ARF in resource limited countries.

Echocardiography is important in not only to pick up subclinical cases but also detect associated Infective endocarditis. We suggest large scale study in high risk group, those belonging to low socioeconomic status and overcrowding to probe plausible role of echo as screening tool in RHD.

Competing interest. None.

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