Indian J Med Res 137, June 2013, pp 1121-1127

Epidemiological trends of RF/RHD in school children of Shimla in north India

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Received September 9, 2011

***Background & objectives*: There are no active surveillance studies reported from South East Asian Region to document the impact of change in socio-economic state on the prevalence of rheumatic fever/ rheumatic heart disease (RF/RHD) in children. Therefore, we conducted a study to determine the epidemiological trends of RF/RHD in school children of Shimla city and adjoining suburbs in north India and its association with change in socio-economic status.**

***Methods* : Active surveillance studies were conducted in 2007-2008 in urban and rural areas of Shimla, and 15145 school children, aged 5-15 yr were included and identical screening methodology as used in earlier similar survey conducted in 1992-1993 was used. The study samples were selected from schools of Shimla city and adjoining rural areas by multistage stratified cluster sampling method in both survey studies. After a relevant history and clinical examination by trained doctor, echocardiographic evaluation of suspected cases was done. An updated Jones (1992) criterion was used to diagnose cases of acute rheumatic fever (ARF) and identical 2D-morphological and Doppler criteria were used to diagnose RHD in both the survey studies. The socio-economic and healthcare transitions of study area were assessed during the study interval period.**

***Results*: Time trends of prevalence of RF/RHD revealed about five-fold decline from 2.98/1000 (95% C.I. 2.24-3.72/1000) in 1992-1993 to 0.59/1000 (95% C.I. 0.22-0.96/1000) in 2007-2008. (P<0.0001). While the prevalence of ARF and RHD with recurrence of activity was 0.176/1000 and 0.53/1000, respectively in 1992-1993, no case of RF was recorded in 2007-2008 study. Prevalence of RF/RHD was about two-fold higher in rural school children than urban school children in both the survey studies (4.42/1000 vs. 2.12/1000) and (0.88/1000 vs. 0.41/1000), respectively. The indices of socio-economic development revealed substantial improvement during this interim period.**

***Interpretation & conclusions*: The prevalence of RF/RHD has declined by five-fold over last 15 yr and appears to be largely contributed by improvement in socio-economic status and healthcare delivery systems. However, the role of change in the rheumatogenic characteristics of the streptococcal stains in the study area over a period of time in decline of RF/RHD cannot be ruled out. Policy interventions to improve living standards, existing healthcare facilities and awareness can go a long way in reducing the morbidity and mortality burden of RF/RHD in developing countries.**

Key words Environmental factors - GABHS - heart disease - India - prevalence - rheumatic fever - time trends

Rheumatic fever/rheumatic heart disease (RF/RHD) continues to be the commonest cause of valvular heart disease among children, adolescents and young adults in developing countries[1,2]. According to WHO, there are 15 million cases of RHD worldwide with 282,000 out of 0.5 million of acute rheumatic fever (ARF) cases developing RHD and 233,000 deaths due to RF/RHD annually[2]. The actual picture might be more serious because of undiagnosed RF/RHD cases and paucity of echocardiographic surveillance in detection of RF/RHD. Moreover, the quality of epidemiological data for reliable estimates of time trends in RF/RHD in developing countries is poor due to lack of prospective active surveillance studies adopting uniform screening methodology[2]. Also, there are no data available on the impact of change in socio-economic and healthcare factors on prevalence trends of RF/RHD in developing countries.

The prevalence of RF/RHD varies from country to country, within different geographical regions in the same country, rural to urban settings and within same region among populations having different level of human development indices[1,2]. The most striking examples of populations with a higher incidence of RF/RHD in the same geographical region have been the Aboriginals of Australia, Maoris of New Zealand. Though one can also suspect the role of ethnicity in predisposing to ARF and RHD, but studies in above mentioned populations have not shown any such association[3,4]. These epidemiological observations suggest that somehow environmental factors predispose to increased and rapid transmission of group A beta haemolytic streptococci (GABHS) pharyngitis, thus playing a major role in creating pockets with increased burden of RF/RHD in a region otherwise showing decreased prevalence. Also, GABHS as pathogens are versatile, in having the ability to change their virulence and antigenic characteristics dynamically through genetic recombination of different strains[2]. Moreover, it has also been shown that GABHS are capable of transmitting virulence marker alleles to commensal streptococci residing in throat[5]. Though the pathogenesis of streptococcal infection is complex, but repeated infections in childhood model the immune response before causing the first attack of rheumatic fever[6]. Thus, public health interventions directed towards preventing transmission of GABHS pharyngitis by early identification, prompt treatment and improved hygiene could be an important mean to decrease burden of RF/RHD. There are no time trend active surveillance studies from developing countries to assess the impact of change in socio-economic status on trends of prevalence of RF/RHD. The present study was, therefore, carried out to evaluate trends of RF/RHD and impact of change in the socio-economic status in school children aged 5-15 yr in Shimla, Himachal Pradesh, India, using identical screening methodologies as was followed in the first survey conducted in the same area by our group in 1992-1993.

Material & Methods

Shimla, the capital city of State of Himachal Pradesh, India, is situated at 30°6´N latitude and 77°11´E longitude. A cross-sectional study was carried out by the Department of Cardiology, Indira Gandhi Medical College (IGMC), Shimla, in 2007-2008 in the Shimla city and in rural area of adjoining Kasumpatti - Sunni Block of Shimla district, India. Using similar methods of sampling, screening and similar criteria to diagnose RF/RHD as described earlier[7], prevalence of RF/RHD in same target population of school children aged 5-15 yr was determined. Similar sample size was taken in 2007-2008 study as was done in 1992-1993 survey (Table I). In 2007-2008 survey, there were 42,861 children in age range of 5-15 yr, studying in 305 schools located in urban and rural settings of study area. A total of 15,986 children of 71 out of 305 schools were randomly selected through stratified random sampling. Sample size in each stratum was proportional to number of students enrolled in each group; 841 children could not be examined due to being absent, even on repeated visits to the schools. It

Table I. Screening outcomes of study population in 1992-1993 and 2007-2008

Population (5-15 yr)	1992-1993	2007-2008
Total population	40950	42861
Total sample	16082	15986
Population screened	15080	15145
Suspected cases for echocardiography evaluation	150	239
Number reported for echocardiography evaluation	150	181
Definite RF/RHD	33 (2.18/1000)	7 (0.46/1000)
Probable RHD	12 (0.79/1000)	2 (0.13/1000)
CHD	34	28

CHD, congenital heart disease; RF, rheumatic fever; RHD, rheumatic heart disease

was ensured that the reason for absence was not due to sickness. Thus, overall participation rate was 94.8 per cent (15145). All eligible children from the selected school were examined by doctor who was trained in the Department of Cardiology to improve auscultatory and diagnostic skills to pick up cases of RF/RHD and heart disease. Each child was enquired about the history of receiving 3 weekly penicillin injections, breathlessness, joint pains, fever and abnormal involuntary movements of limbs at present or in the past. It was followed by a thorough cardiovascular examination done in school itself in standing, recumbent and left lateral decubitus position carefully auscultating all the areas for abnormal sounds and murmurs and relationship with posture and respiration. Children found to have any of the mentioned features in the history and/or physical examinations were referred to the department of Cardiology, IGMC, for echocardiographic evaluation. Echocardiography was done in left lateral decubitus position using 5 MHz phased array probe with HDI 3000 ATL echo machine, USA. Standard morphological & Doppler Criteria were used to diagnose definite and probable cases of RHD and updated Jones criteria (1992)[2] were used to diagnose RF. All suspected cases of RF or recurrence of RF activity were subjected to blood investigations (TLC, ESR, ASO titer and CRP), ECG and throat swab culture using the standard technique as described earlier. Throat swabs were cultured for isolating GABHS on blood agar plate. The data pertaining to changes in socio-economic standards, healthcare facilities and health indices in 1992-1993 and in 2007-2008 of Shimla district were obtained from the Department of Economics and Statistics of Himachal Pradesh Government[8,9].

Statistical analysis: SPSS version 16 (USA) was used for statistical analysis of data. Distributions of demographic characteristics of the study population in two survey studies were expressed as percentages for categorical variables and mean±SD for continuous variables. The prevalence of RF/RHD was reported as per 1000 study population with 95% confidence interval (CI). Difference in prevalence of RF/RHD in the two survey studies was analyzed using Z-test. Differences in the distribution of categorical variables presented as percentages in the two surveys were analyzed using Chi square and Fisher exact test. $P<0.05$ was taken as significant.

Results

A total of 15,145 students were screened in 2007-2008 with mean age of 11.07 ± 4.1 yr. There were 8890 boys (58.7%) and 6255 girls (41.3%). The distribution of gender, rural and urban background among study population in the two survey studies was similar. But the distribution of study population in the age group of 5-10 and 11-15 yr in the two surveys was different. Indicators of human development index revealed substantial improvement over a period of 15 years reflected by better health indicators in terms of increase in life expectancy, decrease in infant mortality rate, improved education and per capita income (Table II).

The decline in prevalence of overall RF/RHD recorded in 1992-1993 and 2007-2008 studies was statistically significant; ($P<0.0001$) 2.98/1000 (95% C.I. 2.24-3.72/1000 vs. 0.59/1000 (95% C.I. 0.22-0.96/1000), respectively (Table III). The difference in prevalence of definite cases of RF/RHD in two survey studies were also found to be significant ($P<0.0001$). No case of acute RF and/or recurrent RF was recorded in 2007-2008 compared to seven cases (0.23/1000) recorded in 1992-1993. Prevalence of RF/RHD was about two-fold higher in rural school children than urban school children in both studies 1992-1993 (4.42/1000 vs. 2.12/1000) and 2007-2008 (0.88/1000 vs. 0.41/1000), respectively. Prevalence of RF/RHD in children in age group of 11-15 yr was higher compared to 5-10 yr age group in both the survey studies of 1992-1993 and 2007-2008 (3.5/1000 vs. 2.29/1000 and 0.46/1000 vs. 0.13/1000), respectively. However, the difference in the distribution of proportion of cases in age group 5-10 and 11-15 yr recorded in the two surveys was not significant. In the present survey, 71.4 per cent of the definite cases of RF/RHD were aware of their disease and were on secondary prophylaxis, while 77.3 per cent of the cases were symptomatic but only 61.4 per cent were on secondary prophylaxis in 1992-1993 survey study.

Mitral valve followed by aortic and then tricuspid valve was the order of frequency in both the surveys. Proportion of patients with moderate to severe MR was higher in 1992-1993 (26.6%) compared to 11.1 per cent in 2007-2008 survey (Table IV). Similarly, proportion of patients of RHD with moderate to severe MS was significantly higher during 1992-1993 (4.4%) but no case of moderate to severe MS was detected in 2007-2008 survey. Since number of patients with mild and moderate to severe valvular dysfunction in 2007-2008 was less, distribution of cumulative severity of valvular dysfunction in both surveys was compared using Fisher exact test.

Table II. Comparison of demographic characteristics, socio-economic and healthcare parameters of the study area in 1992-1993 and 2007-2008

Population characteristics		2007-2008	1992-1993
Age (yr) (Mean±SD)		11.07±4.1	12.04±3.12
Age groups; N (%) (yr)	5-10	8890 (58.7)	6544 (43.4)
	11-15	6255 (41.2)	8536 (56.6)
Gender; N (%)	Boys	8890 (58.7)	8113 (53.8)
	Girls	6255 (41.2)	6967 (46.2)
School background; N (%)	Urban	9526 (62.9)	9425 (62.5)
	Rural	5619 (37.1)	5655 (37.6)
Economic parameters[10]	Per capita income at current price	₹12047	₹ 41059
	GDP of HP State at current price	₹47826.8 million (Economic survey 2010-2011)	Rs. 282980.4 million (Economic survey 2010-2011)
Education status[7,9]	Literacy rate (%)	64.6	79.1
Crowding indices[7,9] (Shimla district)	Population density (per km^2)	121	141
	Per household dwelling	5	5
Healthcare facilities[7,9]	Number of healthcare institutions providing services to every 100,000 individuals	30	20
Expenditures on health services[7,9]	Annual expenditures on health services (million)	₹68.5038	₹198.1261
Health Indicators[7,9]	Infant mortality rate	69/1000 live births	49/1000 live births
	Overall death rate	8.9/1000	6.9/1000
	Life expectancy at birth	62.4 yr	66.1 yr

Superscript numerals indicate reference numbers

Table III. Comparison of prevalence of RF/RHD (diagnostic categories) in urban and rural school children in 2007-2008 and 1992-1993

Diagnostic category	2007-2008 N (Prevalence per 1000)			1992-1993 N (Prevalence per 1000)			
	Urban	Rural	Overall prevalence N (Prevalence per 1000) [95% C.I.]	Urban	Rural	Overall prevalence N (Prevalence per 1000) [95% C.I.]	2-tailed significance of difference in prevalence of RF/ RHD between 1992-1993 & 2007-2008 survey
Definite RHD[1]	3 (0.31)	4 (0.71)	7 (0.46) [0.43 to 0.49]	13 (1.37)	20 (3.53)	33 (2.18) [1.48 to 2.88]	*P*<0.0001
Acute RF[2]	0	0	0	2 (0.212)	1 (0.176)	3 (0.198)	
Recurrent RF[3]	0	0	0	1(0.106)	3 (0.530)	4 (0.265)	
Probable RHD[4]	1 (0.10)	1 (0.18)	2 (0.13)	7 (0.742)	5 (0.884)	12 (0.795)	
Definite +Probable RHD[5]	4 (0.41)	5 (0.88)	9 (0.59) [0.22 to 0.96]	20 (2.12)	25 (4.42)	45 (2.98) [2.24 to 3.72]	*P*<0.0001

1, 4, 5; based on WHO criteria for diagnosis in RHD1; 2, 3; based on updated Jones criteria (1992)[1]

Tabl IV. Comparison of frequency & distribution of severity of valvular dysfunction in 1992-1993 and 2006-2007 surveys

Valvular lesion	Mild valvular dysfunction		Odds ratio (95%C.I.)	Moderate to severe valvular dysfunction		Odds ratio (95%C.I.)
	2007-2008 No. (%)	1992-1993 No. (%)		2007-2008 No. (%)	1992-1993 No. (%)	
MR	3 (33.3)	16 (35.5)	2.56 (0.41-20.2)	1 (11.1)	12 (26.6)	0.33 (0.04-2.0)
AR	1(11.1)	3 (6.6)		1 (11.1)	4 (8.8)	
TR	2 (22.2)	4 (8.8)		0	3 (6.6)	
MS	1 (11.1)	3 (6.6)		0	2 (4.4)	
TS	0	0		0	0	
Total	7 (77.7)	26 (57.7)		2(22.2)	21(46.6)	

MR, mitral regurgitation; AR, aortic regurgitation; TR, tricuspid regurgitation; MS, mitral stenosis; TS, tricuspid stenosis

Discussion

Impact of change in human development index on time trends of RF/RHD was evaluated in school children by two-point estimation of prevalence of RF/RHD after a gap of 15 years in same study area using similar screening methods. Comparison of prevalence of RF/RHD estimated in these two survey studies revealed significant five-fold decline. Although a decline has been observed in the prevalence of RF/RHD in both rural and urban school children in 2007-2008 study, but rural-urban gradient has continued to prevail in both studies. No case of acute RF and/or recurrent RF was detected in 2007-2008 survey compared to seven cases in 1992-1993 survey. Comparison of frequency distribution of cases of RF/RHD in age groups of 5-10 and 11-16 yr in these two surveys suggested trends in demographic shift in the distribution of cases with late age of onset; a pattern also observed in countries with declining prevalence of RF/RHD[2]. Thus, these observations suggest declining trends in the incidence of acute and recurrent RF, severity of RF/RHD and trends of its late age of onset possibly because of improvement in living standards and healthcare services ensuring effective and early treatment of GABHS pharyngitis; similar findings have been observed in other developed countries in 1950-1970s[2].

Studies after year 2000 showed a declining trend of rheumatic fever in different parts of India (Table V). The reported variability in prevalence could be due to different diagnostic methods used, different study populations with variable state of socio-economic and health transitions, apart from the changes in virulence of GABHS. Hence, periodic surveys need to be done in same study area to document actual time trends in epidemiology of RF/RHD.

Since the school dropout rates in the study area was less than 2 per cent, it is unlikely that observed low prevalence of RF/RHD in present survey study could be attributed to it[28]. The difference in the proportion of children in the two age groups could be one of the reasons for the observed lower prevalence of RF/RHD in the latest survey, as there was a trend of higher proportion of cases in the age group of 11-15 yr in both surveys. Overall numbers of RF/RHD cases detected in 2007-2008 were nine compared to 45 in 1992-1993 survey. It is unlikely that this significant difference in the number of cases observed is primarily related to different demographic profile of these two surveys. In many populations, higher prevalence of RF/RHD has been reported in females[2] though the reasons for this are still unclear.

Since we did not study the profile of GABHS strains prevalent in the study area, the role of change in the virulent character of GABHS strains cannot be ruled out. In another school survey study in Shimla district conducted during 2007-2009 revealed that 1.5 per cent of the school children were GABHS carriers and 4.5% had GABHS pharyngitis on the basis of throat cultures. Emm-typing of these GABHS isolates revealed rheumatogenic strains prevalent in north India. Another study by Dhanda *et al* in 2000-2003 revealed that the GABHS isolates from throats of children in north India carried highly virulent antigens[29]. Cross-section design of the study was another limitation of the present survey.

Though studies in Mozambique and Cambodia[30] have shown a 10-fold higher prevalence of RF/RHD using echocardiography based methods compared to clinical screening method, whether echocardiography

based screening is the way to assess true prevalence of RF/RHD is still not known.

In conclusion, the prevalence of RF/RHD has declined in children aged 5-15 yr in Shimla and adjoining rural areas over the last 15 yr; however prevalence continues to be higher in rural population in general. The decline in prevalence of RF/RHD appears primarily due to improvement in healthcare delivery system and socio-economic status, thus providing an important insight in planning preventive strategies for control and prevention. Prospective longitudinal follow up observational studies are needed to have an insight about its true clinical state.

Table V. Studies conducted on RF/RHD from 1957-2006 in India

Place of Study	Rural/ Urban/ Combined	Year	Age group (yr)	Method (Clinical/ Echo)	Sample size	RHD Prevalence/ 1000	RF Incidence/ 1000
Different Indian States[11]	Combined	1978	School children	Clinical		6-11	
Different Indian States[14]	Combined	1978	Employees Insurance data	Clinical		1.3	10.9
Vellore, Tamil Nadu[12]	Rural	1975-1978	4-16	Clinical	3890	4.4	1.7,1.6,0
Balabhgarh, Haryana[13]	Rural	1982-1990	5-15	Clinical	22729	1.0	
Varanasi, Uttar Pradesh[14]	Combined	1982-1990	5-15	Clinical	12190	5.4	
Vellore, Tamil Nadu[14]	Predominantly Rural	1982-1990	5-15	Clinical	13509	2.2	
Delhi[15]	Urban	1984-1994	5-10	Clinical	40000	3.9	0.384
Anand, Gujarat[16]	Rural	1986	8-18	Clinical	11346	2.03	0.384
Ludhiana, Punjab[17]	Combined	1987	6-16	Clinical	6005	1.3	0.700
Ambala, Haryana[18]	Rural	1988-1991	General population	Echo	114610	0.09	
Ambala, Haryana[18]	Rural	1988-1991	5-15	Echo	31200	2.1	0.54
Shimla, Himachal Pradesh[9]	Combined	1992-1993	5-16	Clinical	15080	2.98 Rural-4.8, Urban-1.98	
Churu, Rajasthan[19]	Rural	1992	5-15	Clinical	10168	0.334	
Jammu Tawi[20]	Combined	1992	6-16	Echo	10263	1.36	
Agra, Uttar Pradesh[21]	Urban	1993	5-15	Echo	8449	1.42 Slums -4.1 Urban-0.6	
Srinagar, J&K[22]	Rural	1999-2000	5-15	Echo where needed	4125	5.09	
Kanpur, Uttar Pradesh[23]	Combined	2000	7-15	Clinical	3963	4.54 Urban-2.54, Rural-7.42	0.75 Urban-0.42, Rural-1.20
Vellore, Tamil Nadu[24]	Rural	2001-2002	6-18	Echo	22989	0.68	
Bikaner, Rajasthan[25]	Urban	2003-2004	5-14	Echo	3292	0.67	
Gorakhpur, Uttar Pradesh[26]	Urban	2003-2006	4-18	Echo	118212	0.5	
Cochin, Kerala[27]	Combined	2003-2006	5-16	Echo	25033	0.1	
Present study	Combined	2007-2008	5-16	Echo in suspected cases	15145	0.59/1000	No Cases recorded

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