ORIGINAL ARTICLE

NATURAL HISTORY OF RHEUMATIC HEART DISEASE, A 12 YEARS OBSERVATIONAL STUDY "PENICILLIN BITES THE MUSCLE BUT HEALS THE HEART"

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Background: Rheumatic Heart Disease (RHD) is a major cause of cardiovascular morbidity and mortality in young individuals, in developing countries. Long term studies regarding natural history of RHD in Pakistan have not been reported in literature. We present our follow up observations on RHD patients at the end of 12 years since our first survey conducted in rural communities in 1994. **Methods:** Our study patients were known cases of RHD, diagnosed in cross sectional survey of rural areas of Rahimyar Khan in 1994. Second survey conducted in 2006, in which these RHD patients were evaluated in detail with history/Physical examination, 12 lead ECG, X-ray chest PA view and Echo/Doppler studies at Sheikh Zayed Medical College Rahimyar Khan. **Results**: Out of 57 patients enrolled in 1994, 21 patients (37%) were available for further evaluation. Overall mortality was 23%. Male to female ratio was 1:1.62. Age ranges between 20–80 years with mean of 43 years. Only 6 patients (29%) were taking rheumatic prophylaxis (RP) and six patients had recurrent RF. Five patients (24%) developed new aortic regurgitation (AR) and 38% increased in grade of severity of lesions on Echo (none of them was on RP). Regression of mild lesions noted in six patients (all of them were on RP). Two patients underwent surgery. 10% developed new atrial fibrillation. **Conclusion**: Unabated RF/RHD led to a very high mortality. Favourable out come observed with prophylaxis even for short period on mild or moderate RHD. Patients not on RP had severe diseases. This small study is a big blow to our claims of combating RF/RHD in the 21st century.

Keywords: Heart, rheumatic, natural history, penicillin

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INTRODUCTION

Rheumatic Heart Disease (RHD) is still a major public health problem in developing nations. RHD causes at least 200000–250000 premature deaths every year,[1] and is one of the leading cause of cardiovascular deaths in children and young adults in developing countries.[2] It is estimated that there are over 15 million cases of RHD worldwide, with 282,000 new cases and 233,000 deaths annually.[3] Recent echocardiographic based studies from these regions had shown marked increased in recognized prevalence of RHD.[4–7]

Similar new studies published from Pakistan have established no decline in prevalence of Rheumatic Fever (RF)/ RHD in past thirty years.[8–11] The natural history of RF/RHD have been reported from others parts of the world however no study to date have been published from Pakistan depicting the natural course of this crippling disease in our country.[12,13] In rural areas of Pakistan where poverty prevails and lack of medical facilities lead to unabated natural course of RHD. Long-term follow-up studies of RHD from the under privileged areas like ours, remote district of Punjab need to be addressed. RHD patients in our initial survey of a rural community in 1994 were reviewed in a follow up study at the completion of 12 years.

The objective was to study the natural history of RHD and the impact of RF prophylaxis (RP) on natural course of disease.

MATERIAL AND METHODS

In this cross sectional follow up study a field team visited each household having known RHD patients in all 11 villages detected during 1996 survey in Rahimyar Khan Tehsil (sub district) and noted the current status of these patients in September 2006. Patients were requested to attend our institution for further workup. In those who died cause of death and adherence to rheumatic prophylaxis was determined by interrogating the family of deceased. Patients reluctant to follow up and investigations were convinced and incentives were offered including free transport facility to hospital.

Detail history particularly regarding rheumatic prophylaxis (RP), hospitalization, surgical procedures or any other cardiac events were inquired. Physical examination was carried out to document recent clinical findings. Investigations like 12 leads ECG, X-Ray chest PA view were done and Echo/Doppler studies were performed using Nemio 35 Toshiba, Japan echocardiographic system. Latest findings were compared with the previous ones and differences were highlighted.

The data was analyzed using SPSS-10 Chicago Illinois with student *t*-test and *p*-value of 0.05 was considered significant.

RESULTS

Out of 57 patients enrolled in year 1994, 16 (28%) cases were lost to twelve years follow up (5 migrated, and 11 could not be traced). Out of 41 traceable patients, 20 patients could not be evaluated (13 patients expired and 7 patients refused examination). Thus 21/41 (51%) patients were available for further evaluation.

Male to female ratio was 1:1.62. Age ranges between 20–80 years with mean of 43years. Eleven patient expired due to cardiac causes during 12 years period causing overall mortality of 27% (Excluded two patient died due to non-cardiac causes). None of them was on rheumatic prophylaxis. The details of valvular lesion and cause of death is shown in table-1. The highest mortality was noted in mitral stenosis (MS)/mitral regurgitation (MR) followed by isolated MS and one patient had mixed aortic valve disease.

Despite strong recommendation of RP to all patients picked up at initial survey, only 6 out of 21 available patients were taking RP (28%). None of the expired patients were on RP, (except few injections were taken after initial diagnosis). If we exclude 23 patients (lost + refused) only 18% were on RP. Six patients developed recurrent RF (28%), among them only one was on RP thus the rate of recurrent RF on RP is 0.01 per patient per year. Arthritis/ arthralgia were dominant manifestation in recurrent rheumatic fever.

Six patients (28%) developed new valvular lesions, i.e., five aortic regurgitation (AR) and one MS). 38% patients with known valvular disease, showed increase in severity of lesions on echo. Interestingly none of them was on RP. Regression of mild lesions was observed in six patients. All of them were on RP. Two patients underwent surgery and both are alive. 10% developed new atrial fibrillation.

Table-1: Detail of expired patients by age, sex and type of lesion

Age* (Years)	Sex	Type & grade of Lesions**	Cause of Death
31	M	Mod. AS/AR.	Cardiac
19	F	Mild MS	Cardiac
54	M	Mild MR.	Cardiac
32	F	Tight MS.	Cardiac
50	F	Mod. AR.	Cardiac
22	M	Mod. MS. Mild to mod. AR.	Non Cardiac
42	F	Tight MS (Pliable). Mild- mod.MR.	Cardiac
20	F	Mod. AR/MR.	Cardiac
43	F	Mild AS/MR.	Cardiac
12	F	Severe MR.	Cardiac
65	F	Mod. MS.	Cardiac
27	M	Severe MS. (Ca++). Restenosis.	Cardiac
55	F	Mod. AR. Mild MR. Mild MS.	Non Cardiac

*Age at the time of death **Initial diagnosis in year 1994

Table-2: Impact of rheumatic prophylaxis on natural history of rheumatic heart disease

Variable of Nature History	No (%) of patients	Taking RP	Not taking RP
Progression of lesion	6/21 (28%)	0	6
New lesion	6/21 (28%)	0	6
Recurrent RF	6/21 (28%)	1	5
Regression of Lesion	8/21 (38%)	8	0
New atrial fibrillation	2/21 (10%)	0	2
Valvular Surgery	2/21 (10%)	0	2
Death	11/41(27%)	0	11
Survival rate	28/41(73%)	10/10(100%)	21/32(65%)

p-value=0.00

DISCUSSION

The high mortality in our series (27%) over 12 years of follow up period is probably the highest reported in literature. Ravisha MS *et al*[15] in their follow up of 550 children described mortality of 4.18%. In our study among those expired nine were females and four males. Majority of male patients were of bread earning age and females of child bearing age except 3 who were less than twenty years. The high mortality in these age groups had great impact on family in terms of economical loss and other liabilities. Only 2 patients under went surgery rest of the patients with moderate/severe lesions were unable to afford this costly mode of treatment and ultimately met their fate. The major risk factors adversely effecting survival was non compliance to chemoprophylaxis, underlying moderate/severe RHD, inadequate medical follow up, poor socioeconomic and hygienic conditions and endemic of streptococcal sore throat. Among 21 patients available for follow up 33% developed sore throat indicating high prevalence of Group-A streptococci.

Appearance of new lesions and increased in severity of existing lesions revealed underlying carditis due to recurrent RF. Similar observations was reported by Majeed *et al*[13] from Kuwait in their six years follow up. In another natural history study of RF, the severity of valvular lesions was shown to increase proportionately with the increase in number of recurrent attacks of carditis.[14] It seems that sub clinical recurrent RF is more common than full blown picture of RF. This is speculated due to the absence of typical picture or manifestation of RF. Only 28% gave history of arthralgia/arthritis and 33% complained of frequent sore throats. Increase incidence of carditis followed by arthritis has been reported in a large series of Indian children followed for 31 years.[15] Chorea, erythemia marginatum and subcutaneous nodules were not reported. Therefore absence of these manifestations in recurrence should be particularly noted and due importance to arthralgia should be given in diagnosing recurrent RF.

Regression of lesions was noted in patients who were on regular RP. This phenomenon has been described by Kawakita S[16] from Japan, in their follow

up studies over ten years 287 patients with carditis showed that cardiac murmur disappeared in 44.9% of their patients within 4 years through use of antibiotic prophylaxis. Similar findings have been reported by Lue HC *et al*.[17] Such apparent recovery is related to adherence to chemoprophylaxis. Another study from Saudi Arabia has highlighted that 70% patients of MR lost their murmur following regular RP for a period of 5 years in contrast to disappearance of murmur in 30% of MR patients on irregular RP.[12] Our findings are echo based showing statistically significant regression of lesions in patients on regular RP versus deterioration in severity of valvular lesions in patients without RP. Therefore it is important to implement secondary prophylaxis effectively at early stages to revert the natural course of RHD.

The most distressing fact in this study of natural history of RHD is extremely poor compliance to RP in spite of strong recommendations at initial survey leading to fatal outcome in the form of high mortality and morbidity. This may be due to ignorance, poor socioeconomic conditions and lack of medical follow up. Many workers from other part of the world had reported low compliance rate[15] in their follow up studies however our rate is perhaps the lowest one. The recurrence rate of RF who received continuous prophylaxis was higher than reported in another 5-year's follow up study from India (0.01 *vs.* 0.006 per patient per year).[18] This indicates more virulent and endemic nature of streptococcal infection in this area. Further studies are recommended to evaluate the serotyping of streptococci prevalent in this setting.

CONCLUSION

Poverty and ignorance about the disease are important factors responsible for a very a high prevalence of RF/RHD, in rural communities of Pakistan. Unabated natural course of the disease led to a very high mortality and morbidity. Inappropriate medical facilities, underestimating the significance and non-compliance with rheumatic prophylaxis played havoc with the situation. It has been shown that mild to moderate RHD is strikingly responding to RP, even if given for shorter period of time. Although we are limited by the loss of almost fifty percent of our cases during the time span of 12 years but we manage to accomplish our solo endeavour in country, the task of unveiling the natural course of the disease. Our goals should be to educate people, emphasize health care providers and motivate government officials about the importance of rheumatic prophylaxis in halting the deadly natural course of Rheumatic Heart Disease particularly in rural population of a developing country, like Pakistan.

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