Rheumatic Fever in Mahalla El-Koubra, Egypt: How accurate is the diagnosis?

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Abstract

Objectives: Rheumatic fever still causes 25- 40% of all cardiovascular disease in the world. This study was conducted to identify some epidemiological features of rheumatic fever, the accuracy of diagnosis and the possible familial tendency of the disease and studying the socio-demographic condition of sibling of rheumatic heart disease parents.

Methodology: a cross sectional study was conducted on 5095 persons receiving long acting penicillin for prophylaxis against rheumatic fever and 450 siblings of 229 family with history of rheumatic heart disease.

Results: Among studied persons only 36.8% were found to actually suffering from rheumatic fever, either rheumatic arthritis or rheumatic heart diseases. Females suffering rheumatic fever were 25.0%. Crowding index was significantly affecting the occurrence of the disease especially in rheumatic heart diseases. About a quarter of patients with rheumatic arthritis and 15.1% with rheumatic heart diseases reported regular intake of Long Acting Penicillin, these differences were not statistically significant. Rheumatic heart disease was diagnosed among 12% and rheumatic arthritis among 10% of siblings of patients with rheumatic heart disease. Multiple analysis model show that the most contributing determinants on the occurrence of rheumatic heart diseases are the following in decreasing orders; types of medical services, age of patients, mother occupations, education of patients, and gender.

Conclusion: Misdiagnosis of rheumatic fever is still high with poor compliance with long acting penicillin which may affect efforts for prevention of rheumatic fever complications. This reflects the implication for patients'health education and awareness. The presence of hereditary or familial tendency for rheumatic fever needs to be confirmed.

Keywords: Rheumatic Heart Diseases Rheumatic Arthritis Demographic Determinants Crowding index Mis- Diagnosis Complaints Medical Management Multiple Analysis Medical Services Types.

الحمى الروماتيزمية فى المحلة الكبرى، مصر: ما مدى دقة التشخيص؟

الأهداف: لا تزال الحمى الروماتيزمية لأمراض القلب والشرايين فى العالم تمثل ٢٥- ٤٠%. وقد أجريت هذه الدراسة لتحديد بعض الملامح الوبائية للحمى الروماتيزمية، فإن دقة التشخيص ودراسة الظروف الاجتماعية والديموجرافية بين الأخوة الآباء والاستعداد العائلى للأمراض شرطا لتحديد الأمراض الروماتيزمية وأمراض القلب.

المنهجية: أجريت دراسة مقطعية على ٥٠٩٥ شخص ممن تلقوا البنسلين طويل المفعول للوقاية من مرض الحمى الروماتيزمية ومن ٤٥٠ الأشقاء من ٢٢٩ أسرة.

النتائج: من بين الأشخاص التى أجريت عليهم الدراسة تم العثور على ٣٦,٨% فقط يعانى فعلا من الحمى الروماتيزمية، والتهاب المفاصل الروماتيزمية أو أمراض القلب الروماتيزمية ٢٥,٠% من الإناث يعانون الحمى الروماتيزمية. مؤشر الازدحام ذات دلالة احصائية على حدوث المرض خصوصا فى أمراض القلب الروماتيزمية. حوالى ربع المرضى الذين يعانون من التهاب المفاصل الروماتيزمية و١٥,١% الذين يعانون من أمراض القلب الروماتيزمية يتم علاجهم بانتظام بالبنسلين طويل المفعول، وكانت هذه الاختلافات ليست ذات دلالة إحصائية. تم تشخيص أمراض القلب الروماتيزمية بين ١٢% والتهاب المفاصل الروماتيزمية بين ١٠% من أخوة المرضى الذين يعانون من أمراض القلب الروماتيزمية. التحليل المتعدد أظهر أن أهم المحددات المؤثرة فى حدوث معظم أمراض القلب الروماتيزمية هى بالترتيب التنازلى كالآتى: نوع الخدمات الطبية، عمر المرضى، عمل الأم، وتعليم المرضى، والنوع.

الاستنتاج: إساءة تشخيص الحمى الروماتيزمية لا يزال مرتفعة مع ضعف الامتثال للعلاج بالبنسلين طويل المفعول والذى قد يؤثر على منع مضاعفات الحمى الروماتيزمية. هذا يعكس ضمنا مستوى والتثقيف الصحى للمرضى وتوعيتهم. وجود تأثير وراثى أو عائلى للحمى الروماتيزمية يحتاج إلى تأكيد فى بحوث مستقبلية.

الكلمات المفتاحية: روماتزم القلب روماتزم المفاصل المحددات السكانية مؤشر الزحام التشخيص الخاطئ شكاوى المريض الرعاية الطبية التحليل المتعدد نوع الخدمة الطبية.

Introduction:

Rheumatic fever is no longer a significant health problem in most socio-economically advanced countries but it still causes (25- 40)% of all cardiovascular disease in the world. Rheumatic heart disease accounts for (25-50)% of all cardiac admissions internationally.[1] Regions of public health concern include the Middle East, the Indian subcontinent, and some areas of Africa and South America where as 20 million new cases occur each year.[2] Large proportion of children and adolescents who suffer from rheumatic fever are physically handicapped and psychologically deprived.[3]

The pathogenesis of rheumatic fever remains an enigma and specific treatment is not available, yet prevention of initial and recurrent attacks is possible by penicillin treatment.[1] In Egypt, rheumatic fever prevalence may reach 5.1 per 1000 in school children and it remains active during second and third decades of life.[4] El- Ghamrawy, (2003)[5] reported that the prevalence of rheumatic fever in Mahalla El- Koubra rural areas, Gharbia Governorate was 4% among children aging (5- 15) years. A genetic predisposition to develop rheumatic heart disease appears to be important in certain countries like India, Egypt and Turkey.[6]

WHO Expert Consultation Report, (2001)[7] revealed that the control of rheumatic fever and rheumatic heart disease in developing countries has been largely ineffective, because of poverty and its associated conditions such as substandard nutrition, overcrowding and inadequate housing. Limited infrastructure and resources for health care also contribute to the poor status of the control. Rheumatic fever recurrence and progression towards rheumatic heart disease can be stopped by antibiotic using long acting penicillin. The traditional regimen was four weekly prophylaxis schedules. WHO and the American Heart Association recommended a three weekly regimen for individuals living in high- risk areas.[8] Egyptian health authorities implanted Biweekly regimen.[9] Consequences of non- compliance with long acting penicillin prophylaxis are far reaching, both from an economic standpoint and in terms of morbidity and mortality.[10] Patient's failure to comply with their antibiotic regimen is a reason for the emergence of treatment- resistance strains of microbes.[11]

Objectives:

This study was conducted to study some epidemiological features of rheumatic disease in Egypt and to determine the accuracy of diagnosis by physicians, which is important for early detection and prevention through compliance with long acting penicillin use. In addition, the hypothesis of possible familial tendency was investigated.

Methodology:

The cross sectional research design was used to implement this study. This study was conducted at Mahalla El- Koubra Province, which is one of eight administrative areas of Gharbia Governorate, Egypt. Mahalla El- Koubra Province includes one city and 54 villages with a total population of 1,200,000.[12]

Study subjects included a group of 5095 patients (registered with the begening of the study) was referred to Rheumatic Fever Center at Mahalla El-Koubra who were diagnosed as having rheumatic fever. Another group of 450 siblings of 229 patients with cardiac surgery secondary to rheumatic affection during the period from 1st January, 2007 to 31st March 2010 were included.

Data Collection was done through direct face to face interview about the subjects included in this study. A pre- designed questionnaire was used for data collection. This questionnaire included; socio- demographic data, data related to history of manifestations of rheumatic fever, present clinical data and use of long acting penicillin. Diagnostic John's criteria used for diagnosis of rheumatic fever.

Investigations were conducted for Confirmation of diagnosis of rheumatic heart disease by subjecting all study target population to (ECG) and color Doppler echocardiography (G.E.Echo).

Statistical Analysis:

Data management and analysis: the collected data were organized and statistically analyzed using SPSS software statistical computer package version 12.[13] The number and percent distribution were calculated for each observed category and Chi square test, and regression multiple analysis used for statistical analysis The level of significance was adopted at (p<0.05).

Ethical Issues:

Confidentiality was guaranteed during the whole study period. The research team exerts no pressure of any kind on the target population to participate in the study. They were informed about the study, its objectives and expected benefits to them and the community as a whole to motivate them to participate in the study. A witnessed verbal consent was taken before starting data collections and investigations. Persons participating in the study were offered for free all needed medical services according to their health needs.

Results:

Among the studied 5095 persons attending Rheumatic Fever Center, those who give positive history only for rheumatic fever. Those 5095 were regestered at Mhala Rheumatic Heart Center database and then compelete clinincal examination, ECG and ECHO was done. The result of the examinatins show that 1876 patients with rhematic fever representing 36.8%. (14.7% with rheumatic heart disease and 22.1% with rheumatic arthritis) while the rest 2073 persons 40.7% were misdiagnosed by comparing clinical with Echo diagnoses and hence did not need long acting penicillin intake as previously recommended to them by their health care providers. On the other hand, 1146 persons 22.5% were examined for the first time without past history of rheumatic fever.

Sex difference in relation to diagnosis of rheumatic fever was found statistically significant (p= 0.001). Among studied cases confirmed to suffer from rheumatic arthritis, the majority were females (23.3% females versus 19.9% males). Among studied cases confirmed to suffer from rheumatic heart diseases, females represented 15.4% compared to 13.5% among males. Concerning age, only 23.8% of cases of rheumatic arthritis were above 16 years. Among cases of rheumatic heart disease, only 333 patients 18.4% were aged above 16 years. These differences in relation to age and diagnosis were statistically significant, (p= 0.001).

A trend of increased percentage of crowded index for rheumatic arthritis and rheumatic heart diseases was observed. For rheumatic heart diseases it was found to increase from 11.7% for crowding index of one to reach 17.8% for the index of >3. Among cases of rheumatic arthritis, the same trend was observed where it starts with 18.9% for crowding index of one to reach 2.8% for those having crowding index of more than three. These differences were statistically significant (p= 0.006). family income was low among a higher percentages of misdiagnosed cases as compared with cases of rheumatic arthritis or heart diseases which was found statistically significant (p= 0.024, i.e. it is less than 0.05) Table (1) and figure (1)

Concerning clinical symptoms of studied groups, the most frequent complaint for all groups was tonsillitis which was observed among nearly two thirds of each group. Previous tonsillectomy was highest among the group with rheumatic arthritis 45.4% and lowest among negative groups 925.1%. Intake of long acting penicillin was regular among 50.5% and 43.1% of cases with rheumatic arthritis and rheumatic heart diseases. The regimen of penicillin intake was mostly biweekly. Table (2)

A total of 450 siblings of parents with cardiac surgery secondary to rheumatic affection were studied. Among studied siblings, 99 patients (22%) were found to have rheumatic fever (45, 10% rheumatic arthritis diseases and 54 patients, 12% rheumatic heart disease). Siblings of parents with rheumatic disease were found positive for rheumatic arthritis among 3.1% of males and 6.9% of females while rheumatic heart disease was diagnosed among 5.3% of males and 6.7% of females. The observed high frequency of diagnosis of rheumatic affection among females compared to males was found statistically significant (p= 0.001). Rheumatic heart diseases tended to increase with increased age where it was 0.4% for those aged less than five years and increases to 4.9% for those aged 16 years and above. The percentage in relation to rheumatic arthritis was higher among age group (11- 15) 3.6%.

These differences were found statistically significant (p= 0.001) cases of rheumatic arthritis and heart diseases were found higher among urban residents (9.9% and 11.5%) respectively as compared to rural ones (3.1% and 4.0%), respectively. However, the difference in diagnosis in relation to residence was not statistically significant. Table (3)

Table (4) shows regression multiple analysis of the effects of independent determinants. The most contributing determinants on the occurrence of rheumatic heart diseases are the following in decreasing orders were medical services, age of patients, mother occupations, education of patients, and gender.

Table (1) Socio- demographic characteristics in relation to diagnosis among Studied Cases

| Socio- Demographic Characteristics		Mis- Diagnosed		Negative for RF/RHD*		Rheumatic Arthritis		Rheumatic Heart		Chi Square	P- value
		n	%	n	%	n	%	N	%		
Gender:	Males	686	38.0	515	28.6	358	19.9	243	13.5	59.80	0.001
	Females	1387	42.1	631	19.2	768	23.3	507	15.4		
Age In Years:	<5	83	26.8	165	53.2	43	13.9	19	6.1	477.5	0.001
	5- 10	455	32.9	486	35.0	271	19.6	173	12.5		
	11- 15	669	42.0	318	19.9	382	24.0	225	14.1		
	16+	866	48.0	177	9.8	430	23.8	333	18.4		
Crowding Index:	<1	314	45.4	166	24.0	130	18.9	81	11.7	23.0	0.006
	1- 3	1660	40.3	926	22.4	918	22.3	619	15.0		
	>3	99	35.2	54	19.2	78	27.8	50	17.8		
Family Income:	Low	348	36.4	222	23.2	232	24.3	153	16.1	9.4	0.024
	Middle	1725	41.7	924	22.3	894	21.6	597	14.4		

RF/RHD= Rheumatic fever or Rheumatic Heart Disease
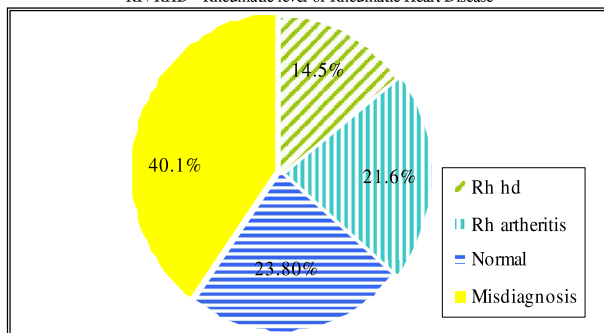
Fig. (1) Distibution of main diagnosis of the studied group, 5095 patients, p=0.00

Table (2) Clinical data in relation to diagnosis among Studied Cases

Clinical Symptoms		Mis- Diagnosed (N= 2073)		Negative for RF/RHD* (n= 1146)		Rheumatic arthritis (n= 1126)		Rheumatic heart (n= 750)	
		n	%	n	%	n	%	n	%
Complaints	Tonsillitis	1351	62.5	707	61.7	746	66.3	459	61.2
	Sore Throat	119	5.7	63	5.5	95	8.4	45	6.0
	Arthritis	7	0.3	3	0.3	20	1.8	0	0.0
	Dyspnea On Effort	7	0.3	4	0.3	1	0.1	0	0.0
	None	589	28.4	369	32.2	264	23.4	264	32.8
Previousosillectomy		861	41.5	288	25.1	511	45.4	285	38.0
Intake Of LAP:	Regular	1247	60.2	0	0.0	569	50.5	323	43.1
	Irregular	826	39.8	0	0.0	394	35.0	235	31.3
Regimen Of LAP Intake:	Biweekly	1513	73.0	0	0.0	713	63.3	402	53.6
	Every 3 Weeks	81	3.9	0	0.0	26	2.3	15	2.0
	Every 4 Weeks	394	19.0	0	0.0	198	17.6	116	15.5

RF/RHD= Rheumatic fever or Rheumatic Heart Disease

Table (3): Socio- demographic characteristics of siblings of parents with cardiac surgery secondary to RHD in relation to diagnosis among Studied Cases

Socio- Demographic Characteristics		Mis- Diagnosed		Negative for RF/RHD*		Rheumatic Arthritis		Rheumatic Heart		Chi Square	P- Value
		n	%	n	%	n	%	n	%		
Gender	Males	15	3.3	166	36.9	14	3.1	24	5.3	30.2	0.001
	Females	16	3.6	154	34.2	31	6.9	30	6.7		
Age In Years:	<5	0	0.0	53	11.8	9	2.0	2	0.4	37.6	0.001
	5- 10	9	2.0	126	28.0	7	1.6	14	3.1		
	11- 15	13	2.9	90	20.0	16	3.6	16	3.6		
	16+	9	2.0	51	11.3	13	2.9	22	4.9		
Residence	Urban	22	7.1	223	71.5	31	9.9	36	11.5	0.24	0.970
	Rural	9	2.0	97	21.6	14	3.1	18	4.0		

RF/RHD= Rheumatic fever or Rheumatic Heart Disease

Table (4): Multiple regression analysis of the effects of independent determinants on rheumatic heart diseases [by ECHO]

The Effects Of Independent Determinants	Standardized Beta	T- Test	P- Value
Coefficients	0.031	2.3	0.021
Gender	0.113	6.9	0.001
Age	0.074	4.9	0.001
Education Of Patients	- 0.003	- 0.19	0.850
Father Occupations	- 0.078	- 5.6	0.001
Mother Occupations	- 0.001	0.06	0.949
Smoking	0.176	13.2	0.001
Medical Services Types	0.022	1.6	0.113
Income	0.031	1.5	0.139
Family Size	- 0.035	- 1.4	0.164
Room Number	0.004	0.16	0.877
Crowded Index	0.011	0.67	0.503
Ventilation	0.031	2.3	0.021

Discussion:

Rheumatic fever remains highly prevalent in developing countries, where overcrowding and poor access to health care persist. The true incidence of acute rheumatic fever and prevalence of rheumatic heart disease in these areas are not known because relevant epidemiological data are not available.[7]

In the present study, out of 5095 studied persons, 36.8% were properly diagnosed cases of rheumatic fever, while 40.7% were found to be misdiagnosed and receive long acting penicillin (LAP) without need. This may be explained by the fact that although the criteria for diagnosis of rheumatic fever are well known, the clinical symptoms needed to make a diagnosis do not always arise concurrently and the initial illness may be mild and short lived. Also the diagnosis will be missed if appropriate investigations are not

carried out during the acute illness. On the other hand too much reliance on a solely elevated.

Anti streptolysin O titer (ASOT) as an investigation for evidence of streptococcal throat infections preceding rheumatic fever can result in unnecessary treatment. Not all individuals experiencing an untreated group A beta- hemolytic streptococci (GABS) will develop acute rheumatic fever. Moreover, not all strains of GABS will trigger an acute attack even in a highly susceptible host.[13,14] DeRosa et al., 2006,[14,15] reported that despite the widespread application of Jone's criteria for diagnosis of rheumatic fever, many cases either under diagnosed or over diagnosed. A study in Menoufia (1994) revealed that a significant number of children 39.6% were not diagnosed prior to the study and this was due to mild symptoms, inadequate medical supervision and unavailability of echocardiography.[16, 15]

Among those correctly diagnosed to have rheumatic fever, 40% were confirmed to have rheumatic heart disease, while 60% were suffering from rheumatic arthritis. World Heart Federation, Rheumatic Heart Disease Program (2006)[17,16] reported that arthritis is the most common symptom in up to 75% of first episodes of Rheumatic Fever. A Community based rheumatic fever/ rheumatic heart disease cohort in India (2002)[18,17] revealed that arthritis was reported among 58.9% of studied group, while carditis was found among 22.3%. In Egypt, Abdel Megeid (1999)[19,18] found that arthritis was common symptom of rheumatic activities 72% compared to only 2% carditis. Khriestetal, (2003)[20,19] in his study in Jordan found that arthritis was the most common major manifestation 88% and carditis was second commonest 48%. Also Ozeretal 2005,[21,20] in Turkey reported that arthritis was present in 33% , while carditis represented 25%.

The present study showed statistically significant difference in distribution of rheumatic fever in relation to sex where that the majority of studied confirmed cases were females 68%. This in agreement with that reported by Abdel Megeid, (1999)[19] where 60% of rheumatic cases were females. This may be attributed to the fact that females in low socioeconomic classes spend more time indoors under bad housing conditions with greater liability to repeated streptococcal infections. Due to sex preference in our community, mothers usually care for boys more than girls especially among low social classes. 18Studies in Saudi Arabia and Sudan have reported higher rates of rheumatic heart diseases among females.[21] Opposite to that Hassab (1997) in Oman failed to report statistical significant difference between males and females regarding the rate of rheumatic heart disease.[22]

Concerning age, the majority of cases were below 16 years. Thakuret al., (1996) reported that no significant difference between the age groups (5- 10) and (11- 16) years.[23] Refat et al., (1994) in Menoufia, Egypt found that older children (10- 12) had higher prevalence rate of rheumatic heart disease than younger ones.[15] Kumar et al, (2000) in India reported that most of studied cases were aged (6- 20) years.[17]

With increased family size as represented by crowding index of the studied persons, there is increase in the rate of rheumatic fever. This is in agreement with Abdel Megeid (1999) in Egypt and Kumar (2002) in India.[17,18] Number of rooms and crowding index were significantly affecting the prevalence rate of rheumatic fever in this study as these factors favor transmission of GABS infections and indicate low socioeconomic standard with poor living conditions and health care services. 9Many studies proved the same result.[8, 15, 23,24] On the other hand, AbolFotouh in Saudi Arabia proved no significant

difference was detected between children living in homes of higher crowding index than those living in homes of lower crowding index.[25]

As regards family income, the majority of studied persons reported having middle socio- economic level without significant difference between rheumatic and normal cases. WHO (2004) reported that poverty is a determinant of higher incidence of rheumatic fever.[8] It is also proved by Refat 1994 in Menoufia, Egypt[15] While Abol Fotouh 1996 in Saudi Arabia proved no significant relation. [25]

Tonsillitis was common among both persons suffering from rheumatic fever and those not. Rheumatic fever can follow upper respiratory tract infections, but not all individuals experiencing untreated GABS infections will develop rheumatic fever. It is estimated that only 3% of the human population has a genetic predisposition.[26] Bassili et al. (2000) found that a history of tonsillitis was found among only one third of the studied children.[9] While other studies reported that tonsillitis was significantly associated with occurrence of rheumatic fever/ rheumatic heart disease.[18,27] Tonsillectomy was significantly higher among persons who diagnosed as a rheumatic fever patients incorrectly and confirmed cases of rheumatic fever than normal peers as most of families take the decision of tonsillectomy after recurrent attacks of tonsillitis and rheumatic fever may be already established. Abdel Megeid (1999) found that 66% of studied persons gave no history of treatment of tonsillitis and there was significant association between treatment of tonsillitis and recurrence of Rheumatic fever.[19]

A relatively high percentage in the present study was found to use LAP regularly. Nearly two thirds used LAP biweekly. This may be due to low level of awareness of the disease in the community and inadequate expertise of health care providers.[16] Low level of compliance was reported also in other studies as in Menoufia, Egypt 1994 where compliance rate was 41.8% and in Helwan, Egypt, it was 34%. The main cause of incompliance was child refusal due to pain associated with injection.[15,18] On the other hand higher rates of compliance were recorded by Bassili et al 2000 in Alexandria 64.6% and Kumar et al, (2002) where compliance rate was 92%.[9,17]

Studies on the serum penicillin levels in Egyptian children have shown a drop in the serum penicillin concentration to below therapeutic level during the third week following the injection of LAP. Consequently, a two weekly regimen is now implemented for Egyptian children rather than the previous 4- weekly regimen.[28,29]

In the present study 22% of siblings of parents with cardiac surgery secondary to rheumatic heart disease were found to have Rheumatic fever (12% confirmed RH heart disease and 10% RH arthritis). This may denote that Rheumatic fever is a disease of familial tendency either because of genetic predisposition or environmental conditions shared by both parents and siblings and favoring the occurrence of rheumatic fever. The disease is autoimmune in nature and most likely results in part from the production of auto reactive antibodies.[30] A genetic predisposition to develop RH disease appears to be important in certain countries like India, Egypt and Turkey.[31] Antigenic simulation between streptococcal antigens, mainly M- protein epitopes and human tissues, such as heart valves, brain proteins, synovial tissue and cartilage as the triggering factor leading to autoimmunity in individuals with genetic predisposition.[32] Environmental factors are said to play a major role in modulating the genetic predisposition to the problem of RH disease.[33]

A previous study in Al- Mahalla Al- Koubra/Gharbia Governorate, Egypt

(2003) reported that the prevalence of Rheumatic fever was 4% in children aged (5- 15) years,[5] and 3.4/ 1000 in Menoufia (1994).[15]Another study in Alexandria showed a prevalence of rheumatic fever of 6.2/ 1000 in (1998)[27] these studies showed a prevalence of rheumatic fever in the Egyptian community which is much lower than that observed in the present study among siblings of patients with past history of surgery due to complications of rheumatic heart disease. This may indicate that siblings of patients with past history of rheumatic affection are at higher risk of acquiring rheumatic fever more than their peers in the community borne to parents not suffering from the disease.

Conclusion:

Misdiagnosis of rheumatic fever is still high augmented by poor compliance with long acting penicillin still one of the major challenges facing prevention and control of rheumatic fever. . Siblings of patients with rheumatic heart diseases seem to have higher prevalence of rheumatic fever compared to prevalence rates obtained from community based studies. This may indicate the presence of hereditary or familial tendency for rheumatic fever affection that needs to be confirmed.

Recommendations:

1. Establish a national RF program within the MOHP.
2. Establish Rh Fever surveillance system to assess the magnitude of the problem and monitor the implementation of the health programs all over the country.
3. Review and update the Rh F national guidelines and disseminate it widely for working in The PHCS.
4. Health Education Programs and community advocacy to orient people about the high importance of compliance on LAP for prevention of RHD.
5. Include screening of RF in school health program.
6. Support the implementation of Genetic research to investigate the genetic hypothesis predisposition role in RF and RHD development.

Acknowledgment:

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