Original Article

Clinical and echocardiographic features of children with rheumatic carditis: correlation with high sensitivity C-reactive protein.

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ABSTRACT

Background: Rheumatic fever (RF) and rheumatic heart disease (RHD) are leading causes of cardiovascular mortality and morbidity in developing countries.

Objectives: To describe the clinical and echocardiographic features of children with RF and RHD and compare these features with their serum C-reactive protein in 2 pediatric cardiology centers in Khartoum.

Methodology: It was a prospective cross sectional study. Patients were examined clinically and by echocardiography. Serum high sensitivity C-reactive protein (hsCRP) was measured from children with Acute RF as well as from healthy age and sex matched controls selected from children attending the clinics. Statistical Analysis Used: Mean and standard deviation, P value using Fisher's exact test.

Results: Sixty six patients (45% males) were enrolled. Mitral regurgitation (MR) was found in 65 patients (98%), it was severe in 42 patients (64%), combined with aortic regurgitation (AR) in 27 patients (41%) and with Mitral stenosis (MS) in 3 patients (4.5%). For patients with carditis, hsCRP ranged between 1.10 and 15 mg/l (mean 8.0817, SD 4.47). In the control group it was 0.6-1.3 mg/l (mean 0.93 SD 0.23) P<0.0001.Patients with Acute RF had hsCRP mean of 12.35 mg/l (SD 2.11) while those with chronic RHD had hsCRP mean of 7.34 mg/l (SD 4.16), P<0.0001.

Conclusion: RHD is manifested in our patients with severe valve damage dominated by MR and there is evidence of an ongoing inflammation during the chronic phase. RHD is manifested in a severe form in Sudan. High sensitivity CRP is elevated in acute phase as well as in the chronic phase.

Key Words: Rheumatic carditis, C-reactive protein.

Rheumatic fever (RF) and Rheumatic heart disease (RHD) are the leading causes of cardiovascular mortality and morbidity in developing countries. Prevalence rates in Sudan range from 2-14 per 100000 [1, 2]. Clinical and echocardiographic (echo) features are not fully delineated in this area. RF is a delayed autoimmune response to Group A streptococcal pharyngitis, and the clinical manifestation of the response and its severity in an individual is determined by host genetic susceptibility, the virulence of the infecting organism and the conducive environment. C-reactive protein (CRP) is a protein found in the blood and it is a "marker" of inflammation, its presence indicates a heightened state of inflammation in the body. There is growing evidence that serum CRP is elevated in these patients both in acute and chronic phases putting them at risk of increasing valve damage[3]. This study looked at the clinical and echo features in relation to the serum high sensitivity (hs) CRP.

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PATIENTS AND METHODS

The study was prospective cross sectional study carried at 2 pediatric cardiac clinics in Khartoum state; the main children's hospital, at the pediatric cardiology department and Sudan Heart Center from September 2011 to January 2012. After an informed consent, all patients with Acute RF (ARF) (with carditis), diagnosed

by the Jone's Criteria and confirmed by echo, were included. Physical examination (performed by the first author) and echo study (2-dimentional and Doppler performed by the second author) were done for each patient. Rheumatic MR was diagnosed by the characteristic echo features including thickening of the leaflet tips, superior malcoaptation of the anterior leaflet and restricted motion of the posterior leaflet. Rheumatic AR was diagnosed by the presence of irregular leaflet thickening and lack of coaptation4. High sensitivity C reactive protein (hs CRP) was done using ELISA method for each patient and from healthy age and sex matched controls selected from children attending the clinics. Mean and standard deviation, P value using Fisher's exact test were calculated.

RESULTS

Sixty six patients (45% males) were enrolled. The age ranged between 9-15 years (mean 11.3). Fifty eight patients (87.8%) had RHD and 8 (12.1%) had ARF with carditis. 57 cases (86.3%) were in New York Heart Association (NYHA) class I-II whereas 9 cases (13.6%) were in class III-IV. Fifty four patients were on penicillin prophylaxis, out of them, 31 patients had one or more doses missed (57.4%).

Echocardiographic Findings:

Table 1 summarizes the echo findings.

Mitral regurgitation (MR) was found in 65 patients (98.4%), it was isolated in 35 cases (53.8% of cases of MR), combined with aortic regurgitation (AR) in 27 cases (41.5%), and with mitral stenosis (MS) in 3 cases. AR was present in 28 patients (41.4%), it was isolated in only 1 patient. (1.5%).Tricuspid regurgitation (combined with other lesions) was found in 19 cases (28.7%).

MR was mild in 23 patients (35.3%), and severe in 42 (64.4%). AR was mild in 23 patients (85.1%) and severe in 5 (18.5%) of cases of AR. Pulmonary hypertension was present in 15 cases (22.7%) and a low ejection fraction was found in 7 cases (10.6%).

High sensitivity CRP:

The normal range of hsCRP according to our lab is as follows:

Females (5-18yrs): less than 1.9mg/l

Males (5-13yrs): less than 1.45 mg/l.

Males (14-18yrs): less than 2.13mg/l.

For patients with carditis, hsCRP ranged between 1.10 and 15 mg/l (mean 8.0817, SD 4.47). In the control group it was 0.6-1.3 mg/l (mean 0.93 SD 0.23) P<0.0001 (Table 2). Patients with ARF had hsCRP mean of 12.35 mg/l (SD 2.11) while those with chronic RHD had hsCRP mean of 7.34 mg/l (SD 4.16), P<0.0001 (Table 3).

Patients with a single valve lesion (33 cases) had hsCRP mean of 5.35 mg/l (SD 2.96) and those with multiple lesions (33 cases) had a mean of 9.2568 mg/l (SD 4.28) P=0.06

Patients with mild valvular lesions had a mean hsCRP of 7.5274 mg/l (SD 4.55) and those with severe MR mean of 8.4998 mg/l (SD 4.43), P=0.4 (Table 4).

Table 1: Echocardiographic Findings

Lesion	Frequency	Percent
Isolated MR	35	53
Mild	23	65.7
Severe	12	35.2
MR+AR (all severe MR)	27	40.9
MS/MR	3	4.5
Isolated AR	1	1.5
Total	66	100.0

DISCUSSION

The clinical and echo features in this cohort of patients showed predominant chronic RHD with severe valve damage. The patients presented with established valve lesions indicating late diagnosis

Table 2: Comparison between Cases and Control Group hsCRP

Category		N	Minimum	Maximum	Mean	Std. Deviation
Cases	hsCRP	66				
	Valid N	66	1.10	15.00	8.0817	4.47459*
Controls	hsCRP	10				
	Valid N	10	0.60	1.30	0.9300	0.23594

* P<0.0001

with possible recurrent episodes. Those who had been diagnosed and put on secondary prophylaxis are mostly non compliant. In addition, multi valve affection was common raising concerns about the efficacy of secondary prophylaxis in such patients. It is obvious that secondary prophylaxis alone is not enough to control the devastating sequelae of ARF; moreover, RHD control programs in Africa proved that combining secondary prophylaxis with primary prophylaxis, health awareness, surveillance and advocacy is the way to achieve a better control[5].

The echo patterns of valve affection in this study showed predominance of MR followed by combined MR and AR, findings that are comparable to those reported in Sudan as well as other countries with similar prevalence of ARF and RHD. However the lesions in our patients tended to be more severe with higher frequency of pulmonary hypertension and low ejection fraction, probably related to late diagnosis and more relapses[6,7,8]. The pathogenesis of rheumatic carditis and mechanisms of progressive valve destruction are not yet fully understood.

Table 3: Comparison between hsCRP in acute RHD and chronic RHD

	Type of Carditis	N	Mean	Std. Deviation	Std. Error Mean
Hs CRP	Acute	8	12.3500	2.11862	0.74905*
	Chronic	58	7.3497	4.16711	0.54717

*P<0.0001

Host genetic susceptibility, the virulence of the infecting organism, and the environment which is conducive all contributed to the severity of cardiac affection. The role of continuing inflammation indicated by the high level of hsCRP, well as the role of hsCRP as a causative factor of valve damage had been recently raised[9]. This study proved that patients in the chronic phase continued to have high level of hsCRP compared to controls. Those with multiple valve affection tended to have higher hsCRP levels, though not reaching statistical significance. The severity of the lesion did not correlate statistically with the level of hsCRP, probably because many patients had multiple valve affection.

Table 4: Comparison between hs CRP in patients with one valve versus multiple valves lesions

	Valves affected	N	Mean	Std. Deviation	Std. Error Mean
Hs CRP	One valve	33	5.3536	2.96140	0.63137
	Multiple valves	33	9.2568*	4.28460	0.64593

*P<0.06

We have also observed an ongoing inflammation in a study that looked at the level of cytokines in patients with RHD which revealed a high level of tumor necrosis factor alpha[10].

Therefore, hsCRP may be considered as a test for monitoring patients with ARF and RHD, however, the implications of increased hsCRP on treatment needs to be further studied. Potential therapeutic options include prolonged use of anti inflammatory or immune modulating drugs to test their effectiveness in controlling the ongoing inflammation.

In conclusion, RHD is manifested in our patients with severe valve damage dominated by MR and there is evidence of an ongoing inflammation during the chronic phase.

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