ACTA MEDICA IRANICA
Vol. VIII 1965 P. 100-111

A PRELIMINARY STUDY OF SERUM ENZYMES LEVELS IN RHEUMATIC CARDITIS

M. Pazirandeh, M. D. ✡

The nature of Rheumatic Carditis has been debated for years and there are some who believe that the primary lesion lies in the myofibrils and thence the heart failure in acute rheumatic carditis can be easily explained(1). But some authors regard the Ashoff nodes to originate from interstitium or vessels and the subsequent failure to be due to secondary changes, probably a metabolic process of myofibrils(2). This process somehow affects the permeability of the myocardial cell and disequilibrates the Na, K ratio(3).

We have been interested in investigating these patients as to the possibility of their serum enzymes levels being raised(4). One can postualate that even if there is no real necrosis of myofibrils as it occurs in myocardial infarction, ther may be some leakage of cytoplasmic enzymes into the circulation due to altered cell membrane permeability in rheumatic carditis.

Material and Method :

The enzymes we have selected are aldolase, SGOT, MDH and LDH. During the study we abandoned M. D. H. because this proved to undergo too little changes as compared with those we noticed with other enzymes. We, on the other hand, substituted L. D. H. for M. D. H.

✡ Assistant Professor, Department of Internal Medicine, Ward 3, Pahlavi Hospital, Tehran University. Teheran.

For estimation of serum aldolase we used Boehringer's Reagent)5) and the readings were done first lot with Zeiss spectrophotometre (U. V. test) and the second lot (color test) with Beckman spectrophotometer. Both instruments gave equal results on a particular specimen.

Transaminases were estimated with Dade Reagents (color test) (6) and readings were done with B & L spectrophotometer and later Beckman spectrophotometer. We used Boehringers' Reagents for L. D. H. – the UV test – and the readings were carried out in Zeiss and later Beckman.

Selection of Patients

Thirty – four patients with rheumatic fever either associated with overt carditis or mild carditis were selected on the general medical wards and the two paediatric wards of Pahlavi Hospital. We tried to examine the patients and to take the specimen of blood as early as the first day of arrival - some before and some only shortly after treatment. We, however failed to get access to some of the patients on the first day.

We have made the diagnosis of rheumatic fever and rheumatic carditis on the conventional criteria which way be summarized here :

Rh. Fever
- migrating polyarthritis (JP/S mig.)
- high ESR
- age
- history of tonsilitis or/and high titre of ASOT.
- CRP+
- Skin lesions if present
- fever. Leucocytosis. anemia.

Rh. Carditis:
- new murmurs { Carey Coombs / Aortic Late diastolic murmur.
- changing murmurs
- changes of heart sounds
- pericardial rub or effusion
- gallop rythme ?
- third heard sound
- tachycardia disproportionate to fever
- subcutaneous Rh. nodes near the joints
- pleural effusion or Rh. pneumonia.

ECG changes:
- prolonged P–R interval, 0.12 - 0.20 s according to textbooks tables (4), (7), and (8).
- prolonged QTc interval, more than 0.42s or 0.44s (3), (7), and (8).☼
- B. B. B. or slurred R wave.
- Low voltage
- atrial fibrilation, flutter, and nodal rythme
- A - V block, 2:1, 3:1, wenkebach phenomenon
- ST segment depression or elevation
- T wave inversion or flat T wave.

A summary of clinical features, laboratory findings are shown in the following schedule together with the amount of serum enzymes.

Guide to the Schedule :

W – stands for ward
Pah – Pahlavi Hospital
Ped – Pediatric ward
Inf – Infectious ward
JP – Joint pain
S – swelling
Mig – migrating
Other manif. – consists of skin and extra cardiac lesions of Rh. fever.
☼ – used for+

Figures under the ASOT, ESR temp, and pulse are the initial findings and the figures under the first ones show(1) in case of temp and pulse the second readings after 24, 36 hours(2) in case of other findings second or third reading after a few days. In the column demonstrating heart sounds, changes of signs are shown under the initial sign. If signs are due to old rheumatic heart disease the nature of valvular lesions are written.

The diagnosis of acute rheumatic carditis in these cases is not relied on the presence of pre – existing signs but upon the other criteria such as characteristic ECG changes not related to valvular lesions. In the column relating to ECG changes the intervals which have been abnormal are underlined. In the column related to the enzymes some of the initial cases have only one enzym estimation. This is because we had only one or two reagents available at the time. MDH (malic dehydrogenase) did not show any change where other enzymes were raised. So we substituted LD_H (Lactic dehydrogenase) for it.

☼ Normal QTc range differs from one author to another. Goldman takes 0.42 in male and 0.43 in female as upper limits. So does Nadas (7), but according to Friedberg 0.44 is the upper limit of normal. We have regarded 0.44 or more as definite abnormal and 0.42 – 0.43 being as border – line. QT has been measured from the beginning of Q wave to the end of T wave in 2 or 3 leads.

NO.	NAME & WARD	DATE	AGE	EVIDENCE FOR RHEUMATIC FEVER								change of H. sounds
				JP/S	HIST. of TONSIL.	other manif.	ASOT	ESR	other findings	temp	pulse	
1 X	R.B.S. W1 Pah.	18/7/44	14 F.	L. Shoulder pain	R.F. at 6	Dyspnea Precord Pain Liver**	1250	41 36 Hb. 50%	CRP- Fib.5/3 B.Cul. neg. wbc11600	38.5 37.0	100 80	mitral valve dis. a. Fibrillation.
2 X	A.Y.A. W/3 Pah.	1/8/44	16 M	JP/S	Cholera Vacc.	Dyspnea	-	72	CRP * wbc4250 p 46 L40M8E6	37	100	mitral valve dis. Aortic incompetenc
3 X	Y.G.T. W/Ped Pah.	26/8/44 22/9/44	10 M	JP/S mig. nil	*	Liver ** no liver	625 333	120 2	CRP - Hb 11.4	37	130 100	Soft 1st. H. sound Loud P2 no P2
4 X	R.J.N. W/3 Pah.	14/9/44	18 F	JP no S	-	head ache	1250	80 15	blood cul. neg.	37 spikes of 38	110 100	mitral valve dis.
5	G.G.G. W/Ped. Pah.	14/7/44 26/7/44	12 M	JP/S mig. nil	* -	- -	625 -	78 -	Hb 10/6 CRP * -	39 37 -	124 92 -	Soft 1st. H. sound Loud 1st. H. sound
6	A.A.A. W/3 Pah.	26/7/44	16 M	JP/S mig.	Cold temp 38	-	333	92 26	-	37	90	Loud P2 Later normal
7	M.B. W/1 Pah.	26/7/44	21 M	JP no S later JP/S	General Malaise	A week later Pleural effusion and Peric. effusion	833 625	60 25 10	Hb 65% wbc16200 Poly 84 Mantoux Negative No AFB Rx. Peric.&(L) Pleural effusion	39 37 38-39	120	Soft heart Sounds. Loud P2 Diast. mm. at Apex (Carey coombs?)
8	M.A.M. W/Inf. Pah.	20/7/44	18 F	JP/S	*	Epistaxis	625	116 65	CRP ** Fib. 7 gm	37.5	105	Prolongation & Muffling 1st. H.sound
9	H.T.T. W/3 Pah.	22/8/44 1/9/44	17 M	JP/S	*	-	500	83	Fib. 4 gm	39 37	120 80	Split 1st. H. sound Loud P2
10	S.G.M. W/1 Pah.	11/7/44	19 F	no JP/S	R.F. 3yrs. ago	Dyspnea Palpitation	833 625 166	108 62 23	CRP - Fib. 5 gm	37	85	H. sounds are soft
11	M.E.K. W/3 Pah.	17/7/44	23 M	JPS mig	*	-	625	100	-	39 37	100 80	-

..1

NO.	EVIDENCE FOR CARDITIS OR UNRELATED TO ACUEE CARDITIS									SGOT	LDH MDH	aldolase 3-8 u
	murmurs	P. rubs	gallop or 3rd H.sound	other findings	P-R rate	QTc	T	ST	R others			
1 X	-	-	-	Rx:heart ** mitral configuration	fib.	0.36	-	-	R.V. **	25 52	110 MDH	6 8
2 X	-	-	BP 90/30	Rx: heart **	-	-	neg. 1, avl	dep. 1,avl elev. 2,3,avf	LV *	14	50 mdh	8
3 X	Grade 3 apical syst. mm. " " "	to axilla	3rd H.S. no 3rd H.S.	Rx: nil	0.16 83	0.38	biph. 3	elev. 1,2,3 V3,4,5	notch P1-ed extra syst.	170 1200	340 LDH 760	17 48
4 X	liver ** later shrank	-	-	Rx: Heart**	0.20 110	0.38	flat 3	dep V6	notch -ed P	54 some days later	LDH 700	8
5	grade 4 apical syst. mm. grade 1 syst. mm.	to axilla	-	BP 90/60 Rx:heart normal	0.12 75	0.476	-	-	tall in prec. RV * -	120 next day: 70 30	- MDH 140	4 8
6	grade 1 apical syst. mm.		3rd H.sound later nil	-	0.20 72	0.42	-	-	-	44	150 MDH	9
7	grade 2 apical syst. mm.	prec. rub present rub	-	BP 80/60 BP 100/60	0.20 68 - -	0.45 0.46 0.435	- flat 1,2,3 avl neg. V4 -	- elev. 1,2 elev. 1,2,avl V5,6	P flat avl notch -ed 3	162 later 118 in 10 56	130 MDH - days: 57	18.6 - 9.7
8	-	-	-	-	low nodal rythm.	0.44	-	-	-	90	210 MDH	13
9	grade 2 apical syst. mm.	-	3rd H.sound no 3rd H.sound	- -	0.18 60 -	0.44 0.41	flat 3 upright 3	slight elev. 1	partial B.B.B C.C.W. rotation	52 35	- -	5.5 6
10	-	-	-	BP 90/60	0.14 85	0.443	flat avl	slight dep.3 & avl	slur: low volt avl	-	-	17
11	-	-	-	-	0.16 63	0.385	-	slight elev. avf, 2,3	-	50	-	13

NO	NAME & WARD	DATE	AGE	EVIDENCE FOR RHEUMATIC FEVER								change of H. sounds
				JP/S	hist. of tonsil	other minf.	ASOT	ESR	other findin	Temp	Pulse	
12	M.Z.K. W/1 Pah.	24/7/44	12 M	JP/S	-	4 previous attacks	-	134	-	40 37	100 80	Loud P2
13	Z.S. W/inf. Pah.	18/8/44	12 F	JP/S mig	?	dyspnea	1250 833	128	CRP- Hb 50%	39 37	120 90	mitral valv disease pul. Hyp.
14	N.A.Z. W/inf. Pah.	22/8/44	12 F	JP/S	*	-	833	120	fib. 4 gm	38.5 37	110 80	-
15	G.J.G. W/Ped. Pah.	8/9/44	13 M	JP/S mig	*	±	833	67	CRP**	38 37	115 100	-
16	M.S. W/3 Pah.	24/9/44	17 M	JP/S mig	*	-	2500	104 22 7	-	37	95 80	-
17	A.T. W/3 Pah.	30/9/44	19 M	JP/S mig	-	dyspnea on exertion	166	114	CRP-	38	100	mit. stenosis aortic incompeten.
18	F.H.A W/inf Pah.	2/11/44	22 M	JP/S	-	3rd attack	333	45	Hb. 60%	37.5	100 80	mitral stenosis
19	Z.B. W/inf Pah.	2/11/44	12 F	JP/S	-	chorea	333	70	CRP*	37?	80 ?	mild mitral stenosis
20	A.A.M. W/3 Pah.	7/7/44	14 M	JP/S	* chorea	dyspnea puffy-face odema*	100	70	Hb. 11.5gm	38.5	120 100 80	mitr. incom Aortic in-competence
21	H.A.B. W/2 Pah.	12/7/44	32 M	JP no S	-	previous attack ESR 123	625	94	Uric acid 3 mgm	37	100 80	-
22	Z.A.M. W/3 Pah.	12/7/44	18 F	JP/S mig	*	CRP *	500	80 23 6	Hb. 12.2 Wbc 14500 P.56 Myel. 8	37.5 37	120 80	mitral valve disease
23	P.R.E. W/1 Pah.	24/7/44	14 F	JP/S mig	*	-	1250 500	82 5	0	37	80	soft heart sounds
24	A.H.G. W/3 Pah.	27/7/44	16 M	JP/S mig	*	-	-	missed 3 days later 25	-	37	90	-

2.2 EVDENCE FOR CARDITIS OR UNRELATED TO ACUTE CARDITIS

murmurs	P.rubs	Gallop or 3rd HH.sound	other findings	P-R rate	QTC	T	ST	R others	SGOT	MDH LDH	aldolase
grade 2 syst. mm.	apical (old?)	-	-	0.14 110	0.46	neg 3	-	partial B.B.B.	56	94 MDH	10
!-	-	-	Rx: mit. configuration	0.18 100	-	-	-	P.puln. RV **	28	30 MDH	6.5
-!	-	-	-	0.16 80	0.44	neg 3	-	-	24	-	5
grade 2 systolic	apical mm.	-	Rx: heart *	0.16 100	0.435	-	-	-	28	150 LDH	9.7
!-	-	-	-	0.14 72	0.46	-	-	-	84	470 LDH	10.5
no liver	enlargement		BP 110/45	0.24 100 0.20 75	0.52 -	neg 3 -	elev. 1,2,avf elev. 2,3	slurr R	22 20	-	13.7
-	-	-	Rx: normal	0.16 100	0.49	-	-	slurr	70	260 LDH	4
-	-	-	-	0.16 120	0.45	-	-	-	20	-	4.6
Petence	-	-	BP 110/55	0.16 110	0.36	slight	elev. 3	slurr CC.C.W. rot. LV *	-	-	5.5
-	-	-	-	N O T	T A K E N			N O T	45	-	-
-	-	-	Rx: heart *	0.18 72	0.40	neg. avl	elev. 2,3 avf	LV**	44 Later 30	-	-
Grade 2 systolic	apical mm.	-	-	0.16 82	0.42	biphasic avl	-	slurr avf,3	10	50 MDH	9
grade 2 syst. mm.	apical -	-	BP 95/65	0.16 90	0.415	-	-	-	22	-	10

NO	NAME & WARD	DATE	AGE	EVIDENCE FOR RHEUMATIC FEVER								TAGE (3)
				JP/S	hist. of tonsil	other manif.	ASOT	ESR	other findings	temp.	pulse	change of H. sounds
25	A.H.S. W/2 Pah.	10/8/44	17 M	JP/S	*	-	-	missed in 21 days 20	-	37	90	-
26	A.S.S. W/inf. Pah.	10/8/44	24 M	JP/S mis	*	-	-	75	fib. 4.6gm wbc 12800 poly80	38.9 37	100 80	-
27	R.A.N. W/1 Pah.	18/8/44	28 F	JP/S	cold	-	-	65	-	38 37	110 70	-
28	H.R.N. W/3 Pah.	22/8/44	25 M	JP no S	*	-	625	94	fib. 4.6 gm	37	90 80	-
29	M.A.V. W/3 Pah.	29/8/44	14 M	JP/S mig	-	-	-	90	-	37	90	aortic incompetence
30	E.A.E. W/inf. Pah.	22/9/44	14 M	JP/S mig	*	-	-	37	CRP *	37.8	80 90	loud P2
31	Z.M.E. W/ped. Pah.	9/9/44	12 F	JP/S mig	*	-	1250 625	57 6	Hb. 13.4gm	37	114 90	-
32	P.M.S. W/inf. Pah.	8/9/44	21 M	JP/S	*	-	500	35	CRP - fib. 4 gm	39.5 37	100 80	-
33	F.M.A. W/inf. Pah.	11/10/44	18 M	JP no S	*	-	-	100	-	39 37	110 80	-
34	M.B.S. W/inf. Pah.	2/11/44	17 M	JP/S	-	3rd attack	625	115	-	40 37	130 70	loud p2 loud 1st heart sound

3 EVIDENCE FOR CARDITIS OR UNRELATED TO ACUTE CARDITIS											
murmurs	P. rubs	Gallop or 3rd H.sound	other findings	P-R Rate	QTC	T	ST	R others	SGOT	LDH MDH	aldolase
grade 2 syst. mm.	apical -	-	-	0.20 74	0.415	-	elev. 2,3, avf	-	29	-	7
-	-	-	-	not taken		-	-	-	39	-	5.5
-	-	-	-	0.20 70	0.435	-	-	C.C.W. rotation	24	30 MDH	9
-	-	-	-	0.16 75	0.43	flat3	-	-	28	-	3
-	-	-	BP 105/35	0.16 90	0.405	flat avl	elev. 1,2,3	-	40	250 LDH	5
-	-	-	-	0.12 75	0.42	flat3	-	-	22	130 LDH	4.8
grade 1 apical syst. mm.	-	-	-	not taken	. . . .	. . . .	. . . .	. . . .	28	170 LDH	6.5
grade 2 pul. syst. mm.	-	-	-	not taken		-	-	-	32	150 LDH	4.8
-	-	-	-	Not taken		-	-	-	26	-	6
grade 2 apical syst. mm.		3rd heart sound	-	0.18 60	0.42	-	-	-	34	-	7

The normal range for SGOT is 0 - 40 U
Aldolase 3 - 8 U. Bruns
MDH 50 - 200 U
LDH 200 - 500 U. Wroblcusky.

Result

Amongst 34 cases four patients, i. e., 1. 2, 3, 4 had rather advanced old rheumatic heart disease, their serum enzymes arenot taken into consideration if they are raised though they were not necessarily in congestive heart failure. These are marked by X.

Cases of definite acute rheumatic carditis are numbers 5,6,7.8 and 9 who showed obvious clinical evidence of acute carditis. The remainder of cases fall into two groups, one group uncomplicated rheumatic fever without carditis (unfortunately on some of them ECG's were missed to be done. Clinical findings were. however, confidently typical of rheumatic fever without carditis) cases 20 through 34. The second group are those who showed some trivial clinical evidence of acute carditis or did not show any at all on the clinical grounds but did show some kind of abnormality in ECG. These are the cases 10 through 19.

We have put the second group in the category of mild carditis. The patients with overt carditis had raised serum enzymes levels notably SGOT and/or aldolase. MDH was rarely raised and LDH very uncommonly elevated.

In the cases with minimal or slight carditis serum enzymes, SGOT or aldolase or both were slightly raised, except cases, 13, 14. and 19 who showed no rise and case 15 had suspected carditis.

A QTc interval of 0.44 or more was more commonly associated with rheumatic carditis and with raised serum enzyme levels than a prologed P-R interval.

A QTc interval of 0.43 could be associated with a normal serum enzyme or only slightly raised SGOT or aldolase.

Of the cases with raised enzymes 12 had abnormal ECG's amongst which 6 had a QTc longer than 0.44. There were three cases with a QTc in border-line range and slightly raised enzyme, that is, number 15, 23, 27. A prolonged PR interval was less constantly associated with raised serum enzymes. There were only cases 4, 6, in whom the PR and SGOT were abnormal while QTc was normal. In other four cases 13, 17, 19 and 25 in whom PR intervals were prologed the enzymes were normal or if the latter was raised QTc was prolonged too.

There was incidentally noted that T wave in leads 3 was flat or inverted (neg.) in the majority of cases of carditis. A loud P2 was heard early in most cases of rheumatic fever probably unrelated to acute carditis.

CONCLUSION :

In view of the fact that in rheumatic carditis permeability of the cell membrane is altered, though there may be no real necrosis of myofibrills, an attempt has been mad to estimate the serum enzymes levels in acute carditis. In cases with overt carditis as diagnosed by new harsh murmurs, gallop, 3rd heart sound or pericardial rubs etc... there are raised SGOT and less frequently aldolase.

In cases where carditis is suspected as evidenced by a 3rd heart sound or soft heart sounds or only ECG changes SGOT and less commonly aldolase are aised though rather slightly. A prolonged QTc 0,44 or longer was more commonly associated with rheumatic carditis than a prolonged PR and a QTc between 0.42 and 0.44 provided that there are no other causes for such an abnormality. We take it for granted that our patients who did not show any other abnormal signs were not suffering from any other disease such as hypokalemia or hypocalcemia etc. A loud P2 on auscultation of early rheumatic fever unrelated to carditis was noted in most cases. A flat T or inverted T wave in lead 3 was commonly noted in cases of carditis or suspected cases. MDH and less commonly LDH were proved to be insensitive in rheumatic carditis.

Summary

Thirty four patients with rheumatic fever are studied on ward 3 of Pahlavi Hospital with a view to finding out their serum enzyme levels.

Five cases had obvious rheumatic carditis who showed raised SGOT and serum aldolase.

The cases with minimal evidence of carditis, clinically or electrocardiographically, had only slightl serum enzyme elevation.

Résumé

Trent quatre malades atteints de rhumatisme articulaire aigu furent étudiés dans le 3éme service medical de l'Hopital Pahlavi en vue de determiner leurs taux serique en enzymes.

Le taux serique de SGOT et aldolase fut elevé dans cinq malades atteints de cardite rhumatismal evident.

Le taux des enzyme fut peu élevé chez les malades qui avaient des signes cliniques et electrocardiagraphiques descretes de la cardite.

Le taux de MDH et LDH reste inchange.

I am very grateful to Professor K. Armin and Dr Nafissl of Department of pathdogy and Medical Research Loboratory for permitting me to use their laboratory and to Professor F. Moatazedi, chairman, Department of Medicine for his encouragement and helps.

✿✿ Many thanks to my colleages at The Medical wards for allowing me to examine their patients.

References

1- Murphy G. E. (1960), Medicine 39, 289
2- Wedum B. G. (1963), Ann. of Rh. Disease 29, 127
3- Kaplan M. H. (1957), Circulation, 16, 621
4- Friedberg C. K. (1957) Diseases of the heart, W. B. Saunders Co: Filadelphia and London.
5- Brune F. (1954), Aldolase U. V. test, Biochemica, Boehringer, Germany
6- Reitman-Frankel (1963), Modified method of SGOT Dade Reagents Inc. Miami, Florida.
7- Nadas A. S. (1963), Pediatric Cardiology, W. B. Saunders Co.; Philadelphia and London.
8- Goldman M. J. (1962), Principal of Clinical Electrocardiography, Lange Medical Publications, Los Altos, California.
9- Bergmeyer H. U. (1963), Method of Enzymatic analysis, Academic Press, London.
10- Wilkinson J. H. (1962) An Introduction to diagnostic enzymology, Arnold, London.

ACTA MEDICA IRANICA
Vol. VIII, 1965, P. 112-117

A PROPOS D'UN CAS D'ANGIOMATOSE ENCEPHALO-TRIGEMINEE SANS CALCIFICATION CEREBRALE VISIBLE ✿

Par E. Tchehrazi ✿✿ et Dj. Brimani ✿✿✿

Notre malade est une petite fille agée de 10 ans hospitalisée le 22 Avril 1964 dans la clinique neurologique de la Faculté de Médecine à l'hôpital Pahlavi pour épilepsie Bravais-jacksonienne gauche avec angiomatose diffuse prédominant dans le domaine du trijumeau droit. L'histoire de la malade nous révèle qu'elle a toujours présenté des crises convulsives de l'hémicorps gauche, à raison d'une à plusieurs par jour avec perte de connaissance en cas d'atteinte de l'hémiface gauche.

Dès l'abord, l'aspect lagophtalmique et angiomateux de la malade est frappant, l'angiome occupant toute l'hémiface droite, le nez et une partie de l'hémiface gauche avec atteinte des lèvres, surtout la lèvre inférieure très épaisse et pendante.

Par ailleurs, on trouve surtout des taches angiomateuses au niveau du bras droit, de la région fessière droite, de la jambe droite et la face externe des grandes lèvres, de même on rencontre ces mêmes taches au niveau des muqueuses en particulier la face interne de la joue droite et de la conjonctive de l'oeil droit.

A l'examen neurologique, on note une hémiparésie gauche avec hémiatrophie légère prédominant nettement sur la main gauche.

Les réflexes ostéo-tendineux rotuliens, achilléens, bicipitaux, tricipitaux, stylo-radiaux et cubito-pronateurs sont très légèrement exagérés à gauche. Il y a signe de BABINSKI à gauche alors que le réflexe cutané plantaire

✿ Rapport présenté à la Société Française de Neurologie, le 3 Mars 1965 Paris.

✿✿ Professeur de Neurologie à la Faculté de Medecine de Téhéran. Directeur de l'Institut de Neuro – Psychiatrie.

✿✿✿ Chef de Clinique Neurologique à la Faculté de Medecine de Téhéran.