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Original Research Article

The Role of Highly Sensitive Troponin I in Diagnosis and Prognosis of Dilated Cardiomyopathy in Pediatric Age Group

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Abstract

The aim of this study, is to evaluate the role of highly sensitive serum troponin I in diagnosis and prognosis of children with dilated cardiomyopathy. This study included 48 children with dilated cardiomyopathy with left ventricular dysfunction, that diagnosed clinically by history, clinical examination ,electrocardiography and echocardiography, including 2D-echocardiography, M-mode and Doppler study. Echocardiography regarded as the corner stone in the diagnosis of dilated cardiomyopathy. Those patient were subdivided to 15 children present with acute heart failure (Acute DCM) (8 female and 7 male), and 33 children who are known cases of dilated cardiomyopathy reported in the cardiology out clinic with chronic cardiac dysfunction (18 female and 15 male),both groups followed for one year with regular clinical, laboratory and echocardiographic evaluation during treatment coarse for cardiac dysfunction , another 48 control healthy child with same age groups involved in the study (25 female and 23male), the age of both patient and control groups ranging from 1month- 12 years. All patient had cardiac dysfunction at the time of attendance . We found that most patient with Dilated cardiomyopathy with acute left ventricular dysfunction had high serum level of highly sensitive troponin I at the time of presentation. Those patients with chronic Dilated , usually had serum troponin above the detectable limit and significantly more than control group. During follow up all patient show to decrease their serum troponin I level with improvement of their cardiac function till reaching normal or nearly normal level if Left ventricular function improved toward normal value, while those remain with left ventricular dysfunction for longer period despite treatment shown to have higher troponin level. This negative relationship between highly sensitive troponin I indicates that the highly sensitive troponin I is important for both diagnosis and prognosis of patient with dilated cardiomyopathy.

الخلاصة

ان هدف هذه الدراسة هو بيان نتيجة متابعة الأطفال المصابين باعتلال العضلة القلبية الموسع لسنة واحدة من العلاج والمتابعة ولبيان دور التروبونينiعالي الدقة في تشخيص هذه الحالات أو التكهن بمستقبلها وبسبب وجود الحالة المرضية واستمرار التوسع في عضلة القلب خلال هذه العملية المرضية لذا يوجد إصابات وتلف مستمر لخلايا العضلة القلبية وهذا يقود إلى ارتفاع معدل العلامات الحيوية البيولوجية القلبية التي تشمل التروبونينiعالي الدقة والذي عادة ما يوجد بصورة أعلى من مستوى التحديد لذا فان التروبونين يعتبر أداة جيدة للتشخيص. إن علامات شمول المرضى في هذه الدراسة هي الأطفال المصابين باعتلال العضلة القلبية الموسع بينما تم استبعاد أمراض وتشوهات القلب الولادية والخلقية واعتلال العضلة القلبية الوراثي العائلي من خلال النظر في التاريخ المرضي للعائلة.شملت هذه الدراسة ٤٨ طفل مصاب باعتلال عضلة القلب الموسع والذين يعانون من قصور وظائف البطين الأيسر ثم تشخيصهم سريريا بواسطة اخذ تاريخ المرض والفحص ألسريري وتخطيط القلب الكهربائي وفحص القلب بالايكو أحادي وثنائي الأبعاد والدوبلر.ويعتبر الايكو حجر الزاوية في تشخيص حالات اعتلال العضلة القلبية الموسع.وقد تم تقسيم هؤلاء المرضى إلى ١٥ طفل من الذين اظهروا قصور قلبي حاد عند حضورهم للمستشفى وكانو٨ إناث و٧ ذكور بالإضافة إلى ٣٣ طفل هم معروفين ومسجلين لدى سل الاستشارية القلبية ومعروفين بقصور وظيفي مزمن للبطين الأيسر وهم ١٨ إناث مقابل ١٥ ذكور. كلا المجموعتين تمت متابعتهم بعد بدء العلاج ولسنة كاملة بصورة منتظمة بالفحص السريري والمختبري وفحص الايكو

خلال فترة العلاج لهذا القصور القلبي الوظيفي. بالإضافة إلى ذلك شملت الدراسة ٤٨ طفل آخرين وهم من الأصحاء الذين اعتبروا كمجموعة قياسية معتمدة أو مجموعة السيطرة وكانوا ٢٥ من الإناث و٢٣ من الذكور وقد خضعوا لنفس الفحوصات التي خضع لها مجاميع المرضى المصابين.كانت أعمار المرضى ومجموعة السيطرة تتراوح بين (شهر واحد–إلى ١٢ سنة) وعند الفحص الأولي كان جميع المرضى يعانون من القصور القلبي الوظيفي للجانب الأيسر من القلب.لقد وجد في هذه الدراسة أن المرضى المصابين بالاعتلال القلبي الموسع المرافق لقصور قلبي وظيفي حاد لديهم مستوى عالي من التروبونين اعالي الدقة عند الفحص الأولي .أما المرضى الذين يعانون من الاعتلال القلبي المصاحب لعجز قلبي مزمن فنجد مستوى التروبونين الأعلى من المستوى الممكن اكتشافه بالمختبر وهو أعلى بصورة مميزة من مجموعة السيطرة القياسية المختارة. ومن خلال متابعة كلا المجموعتين من المرضى وجد بان مستوى التروبونين يظهر انخفاضا ملحوظا عند تحسن او زيادة وظيفة القلب الانقباضية لحين الوصول للحد الطبيعي أو القريب من الطبيعي, وبالمقابل فان المرضى الذين يبقى لديهم قصور قلبي رغم العلاج المستمر يبقى لديهم مستوى تروبونين عالي لديهم وهو أمر ملحوظ.

Introduction

Dilated cardiomyopathy (DCM) means congestive heart failure as a result of dilation and systolic dysfunction of cardiac ventricles (mainly the left ventricle). Children may have more deleterious consequences of low-level cardiomyocyte loss than adults due to both the length of subsequent survival and an insufficient potential for myocardial growth[1]. Troponine, a thin-filament contractile protein present in high concentrations in the myocardium but usually not in other tissues, is released rapidly after myocardial injury in direct proportion to the extent of injury. It persists in the serum for several days5. It is more cardio-specific, and persists longer and shows higher elevations relative to normal ranges[2]

To determine whether serum troponine would specifically detect myocardial damage in children, we examined biochemical markers of myocardial damage in three groups of children: acute DCM , Chronic DCM and normal control.

Materials andMethods

The participants belongs to both patients and control groups were selected and examined in the cardiology clinic of Karbala pediatric teaching hospital between April 2013 and October 2014, the type of test discussed for the parents , starting with history taking especially family history, and presence of familial cardiac disease ,some questionnaire about the age and degree of relatives of both parents, past medical history and antenatal history. Then measuring the weight and the height of the affected child, physical examination that involving measuring the temperature by mercury thermometer, heart rate with auscultation of the chest and palpation and auscultation of the precordium for presence of added sounds , also detection of partial oxygen pressure (SPO2),by using digital pulse oxymeter planted on terminal warm finger phalanx. Electrocardiography (ECG), were done for all patients, then ultrasonic examination of the heart by using, 2- D echocardiography, M-mode for assessment of cardiac function (Ejection Fraction and, Fractional Shortening), camber size, cardiac wall thickness in addition to Doppler study of cardiac valves for detection of valvular complications and presence of regurgitation, and to exclude other cardiac wall defects or congenital anomaly.Blood and serological tests included were, hemoglobin level (Hb) for each child and evaluation of serum high sensitivity troponin I .treatment of patient diagnosed with DCM involve mainly Digoxin,Furosamide and Enalopril.This regime of examination were repeated for all patient during the period of the study with regular spacing and periods after starting medical treatment for the first group (those with acute presentation), after 3 months,6 months and 1year, and for the second group (those who are known cases of dilated cardiomyopathy), after 6 month and 1 year.

Results

1-Dilated cardiomyopathy with acute LV dysfunction:

Troponin enzyme

At time of attendance , the Troponin enzymelevel was measured in patient and control groups. Troponin enzymesignificantly higher in patient group when compared with control group (p< 0.01) as shown in table (1).

Table1: The Troponin enzymelevel in patient with acute DCM and controlgroups

		Patients	Control	P Value
Troponin ng/dl	Attendance	1.37±1.06	0.05±0.036	**0.001****
	After 3 months	0.62±0.24		**0.001****
	After 6 months	0.45±0.24		**0.001****
	After 1 year	0.35±0.32		**0.001****

**p value < 0.01 is highly significant

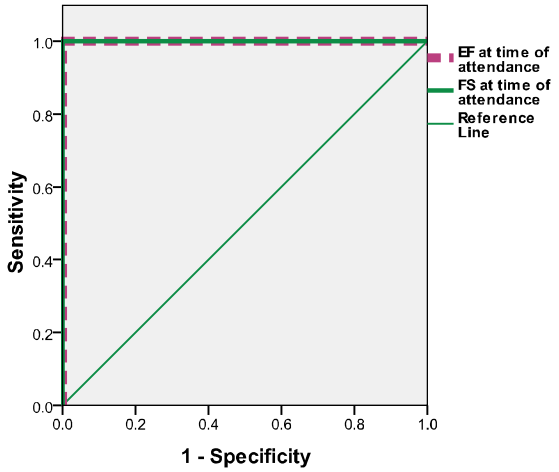
After 3 month , the Troponin enzymewas significantly decreased when compared with its level at time of attendance, (p<0.001). as shown in table (2), it was insignificantly decrease after 6 months of follow up, while its level was significantly decrease after 1 year of treatment (p<0.05), but still higher level than control group.

Table 2: The Troponin enzymein patient with acute DCM after 3,6 and one year of treatment

	Troponin ng/dl	MEAN±*SD*	P Value	P Value	P Value
Acute CMP	Attendance	1.37±1.06	**0.006****		
	After 3 months	0.62±0.24		0.089	
	After 6 months	0.45±0.24			**0.040***
	After one year	0.35±0.32			

**p value < 0.01 is highly significant
*p value < 0.05 is significant

The area under the curve (AUC) of troponin enzyme at time of attendance was 0.94, indicating a sensitivity of 93 % and specificity of100 % respectively, at cut off value of0.16,table(3)andfigure(1and2).



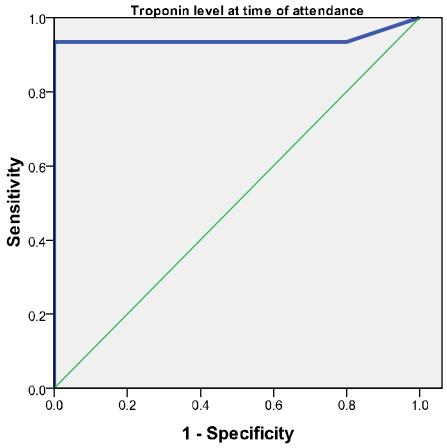


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Figure 1 and 2: Receiver operating characteristic (ROC) curve of EF, FSpatient with DCM as compared to control group**.**

Table 3: Receiver operating characteristic (ROC) curve of EF, FS and troponin enzyme in patient with DCM as compared to control group

	Area	Cut off point	sensitivity	Specificity	P value	95% CI	
						Lower Bound	Upper Bound
Troponin ng/dl	0.94	0.16	93	100	0.001**	.000	1.000
EF%	1.000	57	100	100	0.001**	1.000	1.000
FS%	1.000	26	100	100	0.001**	1.000	1.000

**p value < 0.01 is highly significant

1 Ejection fraction (EF)

The EF was measured in patient and control groups at time of attendance. It was significantly lower in patient group when compared with control group at the time of attendance,after 3, 6 months and after 1 year ($p < 0.001$) as shown in table (4).

Table 4: The ejection fraction in patient with acute DCM and control groups

		Patients	**Control**	**P Value**
EF%	**Attendance**	41.66±5.66	69.33±3.15	**0.001****
	After 3 months	55.06±4.68		**0.001****
	After 6 months	58.00±6.74		**0.001****
	After 1 year	60.00±6.85		**0.001****

**p value < 0.01 is highly significant

After 3 month , the EF was significantly increased when compared with its level at time of attendance ($p<0.001$), as shown in table (5). Also its level significantly increase after 6 month ($p<0.05$) and insignificantly increase after one year of treatment ($p >0.05$) as shown in table (5).

Table 5: The ejection fraction in patient with acute DCM after 3 ,6 and one year of treatment

	EF%	MEAN±*SD*	P Value	P Value	P Value
Acute CMP	**Attendance**	41.66±5.66	**0.001****		
	After 3 months	55.06±4.68		**0.01***	
	After 6 months	58.00±6.74			0.076
	After one year	60.00±6.85			

**p value < 0.01 is highly significant
*p value < 0.05 is significant

Correlation between Troponin Level and Ejection Fraction (EF)

There were a significant negative correlation between troponin level and EF after 6 months and after one year ($p<0.01$) ,that is mean that, the higher the level of troponin , the lower the level of the ejection fraction , and decreasing troponin level gradually reflect the improving of the level of the EF . as shown in table (6).

Table 6: Correlation between troponin level and EF

EF%	Control	PATIENTS			
		at time of attendance	after 3 months	after 6 months	after 1 years
r	0.031	0.128	-0.377	**-0.930**	**-0.926**
P	0.913	0.648	0.166	**0.001****	**0.001****

**p value < 0.01 is highly significant

2-Dilated Cardiomyopathy with Chronic LV Dysfunction

1-Troponin Enzyme

At time of attendance, the Troponin enzymelevel was measured in patient and control groups. Troponin enzymesignificantly higher in patient group when compared with control group at the time of attendance, after 6 months and one year ($p < 0.01$) as shown in table (7).

Table 7: The Troponin enzymelevel in patient with chronic DCM and control groups

		Patients	Control	P Value
Troponin ng/dl	**Attendance**	0.28±0.20	0.06±0.056	**0.001****
	After 6 months	0.29±0.19		**0.001****
	After one year	0.31±0.26		**0.001****

**p value < 0.01 is highly significant, *p value < 0.05 is significant

After 6 month, the Troponin enzymewas insignificantly increased when compared with its level at time of attendance, ($p>0.05$). as shown in table (8). Also its level was insignificantly increase after 1 year of treatment ($p<0.05$), but its level still higher than control group .

Table 8 : The Troponin enzymein patient with chronic DCM at the time of attendance, after 6months and one year of treatment.

	Troponin ng/d	MEAN±SD	P Value	P Value
Chronic DCM	**Attendance**	0.28±0.20	**0.818**	
	After 3 months	0.29±0.19		**0.430**
	After one year	0.31±0.26		

**p value < 0.01 is highly significant, *p value < 0.05 is significant

The area under the curve (AUC) of troponin enzyme at time of attendance was 0.815, indicating a sensitivity and specificity of 73 % and 97 % respectively, at cut off value of 0.17ng/dl, table (9) figure (3 and 4).

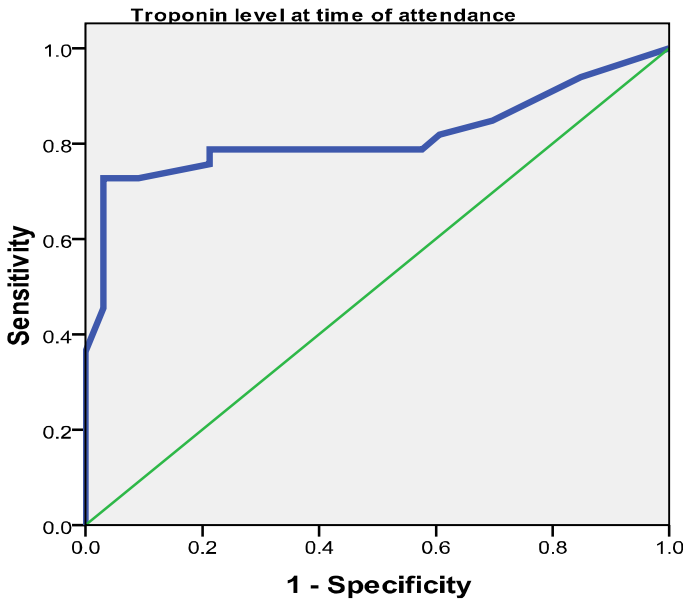

Figure3: Receiver operating characteristic (ROC) curve of EF, FS and in patient with DCM as compared to control group

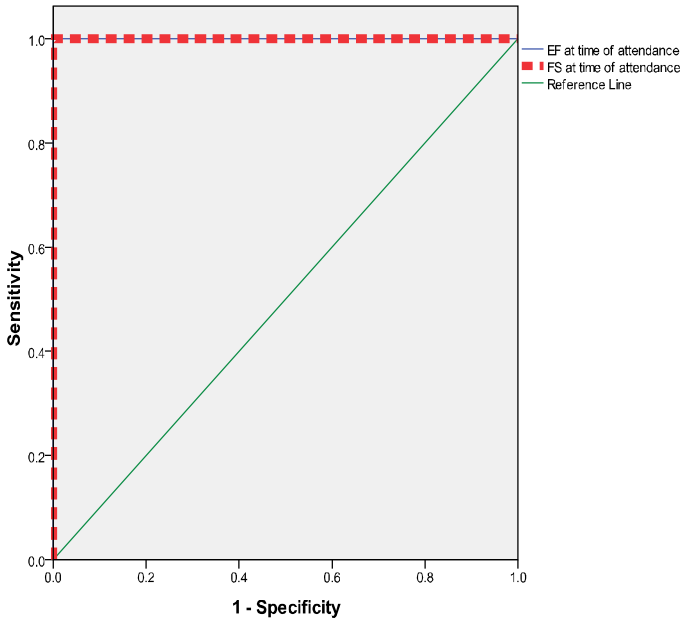

Figure 4: Receiver operating characteristic (ROC) curve of EF, FS and troponin in patient with DCM as compared to control group

Table 9: Receiver operating characteristic (ROC) curve of EF , FS and troponin enzyme in patient with DCM as compared to control group

	Area	Cut off point	sensitivity	Specificity	P value	95% C.I. Interval	
						Lower Bound	Upper Bound
Troponin ng/dl	.815	0.17	73	97	0.001**	.702	.929
EF%	1.000	57	100	100	0.001**	1.000	1.000
FS%	1.000	27	100	100	0.001**	1.000	1.000

**p value < 0.01 is highly significant , *p value < 0.05 is significant

Echocardiographic Findings

Ejection Fraction (EF)

The EF was measured in patient and control groups at time of attendance. It was significantly lower in patient group when compared with control group ($p < 0.001$) as shown in table (10).

Table 10: The ejection fraction in patient with acute DCM and control groups

		Patients	Control	P Value
EF%	**Attendance**	38.27±9.28	66.57±3.02	**0.001****
	After 6 months	47.30±9.36		**0.001****
	After one year	54.94±11.23		**0.001****

**p value< 0.01 is highly significant, *p value < 0.05 is significant

After 6 month, the EF was significantly increased when compared with its level at time of attendance ($p<0.001$), as shown in table (10). Also its level significantly increase after 1 year of treatment ($p<0.01$).

Table 11: The ejection fraction in patient with acute DCM after 3 ,6 and one year of treatment

	EF%	MEAN±SD	P Value	P Value
Chronic DCM	Attendance	38.27±9.28	0.001**	
	After 6 months	47.30±9.36		0.001**
	After one year	54.94±11.23		

**p value < 0.01 is highly significant, *p value < 0.05 is significant

Correlation Between Troponin Level and EF in Chronic DCM

There were a significant negative correlation between troponin level and EF after 6 months and after one year ($p<0.01$) as shown in table (12).

Table 12: Correlation between troponin level and EF

EF%	Control	PATIENTS		
		at time of attendance	after 6 months	after 1 years
r	0.281	-0.027	-0.590	-0.893
P	0.113	0.881	0.001**	0.001**

**p value < 0.01 is highly significant, *p value < 0.05 is significant

Discussion

1-Dilated Cardiomyopathy with Acute LV Dysfunction:

In this study we found that the children who had a high level of serum troponin, were had low cardiac output state and cardiac function and there is a negative relationship between the level of serum troponin and cardiac function, this is also consistence with other studies [3,4]and because of this negative relationship of cardiac troponinI and LV function, so troponin also regarded as an important prognostic marker, as decreasing level of CTroponinI when it measured serially, indicates good prognostic indicator of improving cardiac function and this is consistence with the study of [5.6,7] .After 3 month , the Troponin enzymewas significantly decreased when compared with its level at time of attendance, it was insignificantly decrease after 6 months of follow up, while its level was significantly decrease after 1 year of treatment as shown in table (1), which may indicates improvement in the cardiac function during the course of the treatment, which also consistent with other studies [4]

2- Dilated Cardiomyopathy with Chronic LV Dysfunction:

serial measurement of troponin I in chronic DCM shows that many patient

had troponin value above the limit of detection, this high level of troponin is probably due to continuous myocyte injury and remodeling. Similar to acute DCM, the rising level of troponin is a marker of worse prognosis, so troponin is considered also a good and sensitive important indicator not only for diagnosis but also prognosis,like other important biomarkers such asnatriuretic peptide, and also a good marker predicting the need for frequent hospitalization, or predicting the risk of death [9,8,10] In this study, At time of attendance, the Troponin enzymelevel in children with chronic dilated cardiomyopathy was measured in patient and control groups. Troponin enzymesignificantly higher in patient group when compared with control group as shown in table (7). After 6 month, the Troponin enzymewas insignificantly increased when compared with its level at time of attendance. Also its level was insignificantly increase after 1 year of treatment as shown in table**.**

Conclusion

Serum troponin I is significantly high in some patient of DCM with acute cardiac dilatation (acute DCM) and heart failure , may be due to viral myocarditis induce cardiomyopathy., while the level in those with chronic LV dysfunction is still higher than normal children and above the detected limit but not reach to the level of significance. The level of troponin decline to normal range with improving the cardiac function, so ,the highly sensitive serum troponin I is not only important in diagnosis but also in the prognosis of the progression of DCM.

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