Value of Cardiac Myosin Binding Protein C In The Assessment Of Pediatric Heart Failure

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Abstract

Background:

Heart failure is one of the cardiovascular diseases that have high mortality and morbidity, especially in children. Early diagnosis of HF is crucial for early management and for improving risk stratification for death from HF.Cardiac Myosin Binding Protein C is a cardiomyocyte-specific sarcomeric protein, which regulates both sarcomeric structure and function. It is easily soluble and releasable from the sarcomere. Moreover, the large size of it and its release into the circulation inresponse tocardiac injurymakes it one of the promising cardiac biomarkers for detection of cardiac injury. As 87% of new onset case of heart failure reach the diagnosis when the patient reaches the state of sever decompensation.

Theaim of this study was to investigate the clinical value of Cardiac Myosin Binding Protein C level as a diagnostic and prognostic biomarker in Pediatric Heart Failure.

Methods:

This was a comparative cross sectional study which was done on 2 groups;

Group I (study group) cases with acute heart failure, were collected from Pediatric ICU at Banha university Hospital, at time of admission and group II (Control group) which comprised healthychild, age and sex matched with patients in group I.

Results:

Our study showed the Echocardiographic diagnosis, VSD (33.3%) & Dilated cardiomyopathy (23.3%) were the most predominant echocardiography among our cases. Mean value of LVEDD was statistically significant higher among cases group than control group. Mean value of LVESD was statistically significanthigher among cases group than control group. Mean value of FS% was statistically significant lower among cases group than control group. Mean value of EF% was statistically significant lower among cases group than control group. The current study showed that mean value of hemoglobin (Hb) was statistically significant lower among cases group than control group. This study showed that, mean value of WBCs was lower among cases than controls. There was no statistically significant difference between cases group and control group regarding CRP. The present study revealed that mean value of Cardiac Myosin binding protein was statistically significanthigher among cases group with the mean (78.28± 34.38 ng/dl) than control group. Regarding Modified ROSS among cases group, percentage of patients with class II was (13.3%), III and IV were (43.3%) each. This study showed that, the percentage of died was (13.3%) and discharged was (86.7%)among cases group. In our study, there was negative statistically significant correlation between Cardiac Myosin binding protein and EF% and FS%.This study showed that, Cardiac Myosin Binding Protein C level was directly proportional to the severity of heart failure (Modified ROSS) and the severity of pulmonary hypertension as well.The recent study showed that mean value of Cardiac Myosin binding protein C was statisticallysignificant higher among died than discharged. Regarding Diagnostic accuracy of Cardiac Myosin binding protein, Sensitivity was 95%, Specificity was 89%, PPV was 93.1%, NPV was 88.3% and accuracy was 90%.

Conclusion:

The results obtained in our study revealed that Myosin Binding Protein C is useful as a diagnostic and prognostic biomarker in Pediatric Heart Failure.

Key words: Cardiac Myosin Binding Protein C -Pediatric Heart Failure

Introduction:

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Heart failure (HF) was defined as failure of the heart to supply the blood essential for the metabolic demands of body [(1).]
Heart failure is one of the cardiovascular diseases that have high mortality and morbidity, especially in children. Early diagnosis of HF is crucial for early management and for improving risk stratification for death from HF [(2).]
Cardiac biomarkers are useful diagnostic and prognostic tools, especially in patients who have atypical signs and symptoms. High adverse outcome in HF led to the search for ideal cardiac biomarker that could diagnose early HF, predict outcome, reflect response to treatment and help in staging of heart failure with its associated risk [(3).]
cMyBP-C is a cardiomyocyte-specific sarcomeric protein, which regulates both sarcomeric structure and function. It is easily soluble and releasable from the sarcomere. Moreover, the large size of it and its release into the circulation inresponse tocardiac injurymakes it one of the promising cardiac biomarkers for detection of cardiac injury [(4).]
It is confirmed that cardiac stress is associated with decreased level of cMyBP-C phosphorylation, activate cleavage of intact cMyBP-C and release of 140-KDacardiac protein. 140-KDa is a truncated fragment, which is increased in diseased heart and compete for the normal cMyBP-C binding site to actin and myosin. Thus, interfering with cardiac contractility that causes heart failure. This finding suggests that plasma level of cMyBP-C could be used for early diagnosis of heart failure and predicting its severity [(5).]
There is lack of the literature regarding the role of cMyBP-C as a biomarker in HF [(6).]
Theaim of this study was to investigate the clinical value of Cardiac Myosin Binding Protein C level as a diagnostic and prognostic biomarker in Pediatric Heart Failure.

Patients and Methods:

Subjects:

This was a comparative cross sectional study which includes 60 children. They were divided into two groups;
Group I (study group): 30 cases with acute heart failure, were collected from Pediatric ICU of Banha university Hospital, at time of admission.
and group II (Control group): 30 cases which comprised healthy child , age and sex matched with patients in group I .
Sample size was calculated using an appropriate statistical software.

Inclusion criteria:

- ✓ Age from one month-10 years.
- ✓ Both sexes were included.
- ✓ Infants and children with heart failure.
- ✓ Patient with heart failure due to either acquired or congenital heart disease.

Exclusion criteria:

- ☒ Infants (neonates) < one month and patients> 10 years old.
- ☒ Patients suffering from any other diseases as autoimmune, malignancy and inflammatory conditions.

Methods:

1-History taking:

- Personal history; age, sex, complaint.
- history of present illness and manifestations of left and right cardiac decompensation e.g. Cough,orthopnea,cyanosis,exercise tolerance, syncopal episodes, feeding difficulties and sweating with feeding.
- Past history of diseases, operations, or medication.
- Family history of congenital heart diseases or cardiomyopathy.

2-Clinical examination:

➢ **General examination including:**

- Anthropometric measurements**:** height, weight.
- Vital signs measurements: heart rate, respiratory rate, blood pressure and temperature.

➢ **Systemic examination including:**

- Complete local cardiac examination: inspection, palpation, percussion and auscultation.
- Complete Chest examination.
- Complete abdominal examination.

3-Assessment of severity of heart failure using modified ROSS score CHF was classified to Class I, II, III and IV. [(7)]

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Class I	No limitations or symptoms.
Class II	**Infants**: Mild tachypnea or diaphoresis with feeding. **Older children**: Mild to moderate dyspnea on exertion.
Class III	**Infants**: Growth failure and marked tachypnea or diaphoresis with feeding. **Older children**: Marked dyspnea on exertion.
Class IV	Symptoms at rest such as tachypnea, retractions,Grunting, or diaphoresis.

(7).

4- Investigations:

- **Plain X-ray chest:**
  Cardiothoracic ratio was measured in the patient group for assessment of cardiomegaly.

- **Echocardiography (two dimensional, M-mode &Doppler) :**
  Was done in the patient and control groups with measurement of ejection fraction (EF), fraction shortening (FS), left ventricular end diastolic dimension (LVEDD) and left ventricular end systolic dimension (LVESD) using Philipsaffiniti 50 C Ultrasound**.**

The Ejection fraction (EF)of the left heart, known as the left ventricular ejection fraction (LVEF), is calculated by

$$\mathbf{EF(\%)} = \frac{\text{LVEDV} - \text{LVESV}}{\text{LVEDV}} \times 100$$

Fraction shortening (FS) is the fraction of any diastolic dimension that is lost in systol

$$\mathbf{FS\ (\%)} = \frac{\mathbf{LVEDD} - \mathbf{LVESD}}{\mathbf{LVEDD}} \times 100$$

➢ **Laboratory investigations:**

- **Complete blood count:**
  CBC was done for all samples for red blood cell (RBC) count, hemoglobinlevel, hematocrit value & WBC count and platelet count.

- **C-reactive protein (CRP):**done by slide assay for patient and control groups.

- **Plasma level of Cardiac Myosin binding protein C (c My BP- C):**
  at time of admissionby ELISA technique.

Full Name: Human Myosin Binding Protein C, Cardiac (MYBPC3) ELISA Kit.

Intended Use
This kit is used to assay The Myosin Binding Protein C, Cardiac(MYBPC3) in the sample of human's serum, blood, plasma and other related tissue Liquid.

Methodology of measurement of serum cardiac myosin binding protein-c:

Specimen collection and preparation:
About 2 ml of peripheral venous blood were withdrawn on plain tubes.
Samples were lefted to be clotted within 30 min, centrifuged and the separated serum samples were aliquoted and stored at -30°c for cardiac myosin binding protein-c assessment and assay.

Test procedure:
Preparing reagents, samples and standards **then** adding prepared samples, standards and antibodies labeled with enzyme reacting 60 minutes at 37°C **then** plate washed five times, adding chromogen solution A,B reacting 10 minutes at 37°C **then** adding stop solution **then** measuring the OD value within 10 minutes**then** calculation by taking the standard density as the horizontal, the OD value for vertical , drawing the standard curve on graph paper, finding out the corresponding density according to the sample OD value by the sample curve.

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Ethical considerations:
Informed consents were obtained from all cases and control's guardians included in this study which were approved by the local ethical committee of Banha University.

Statistical Analysis
Data analysis was performed using the software SPSS (Statistical Package for the Social Sciences) version 24. Quantitative variables were described using their means and standard deviations.
The clinical and laboratory data were statistically analyzed to obtain:

(1)Descriptive statistics:
a· $\bar{x}$ =mean
b· SD =standard deviation
c·Range

(2)Analytical studies:

a·Comparison between means using:-
Unpaired student t-test for comparison between 2 groups with independent parametric data.

b·Correlation statistics using:-
Pearson correlation coefficient between paramedic data.
P value, probability of chance, indicates significance when $P \leq 0.05$ and highly significant when$P \leq 0.001$.

Results:

This table shows that there were no statistically significant difference between cases group and control group regarding demographic data. Male and female were equal in our study **Table (1)**.

This table shows that Tachypnea (100%), Diaphoresis with feeding(76.6%) and Exertional dyspnea (50%),were the most predominant complaints among cases group **Table (2)**.
Tachycardia was present among our cases (100%). Cardiomegaly was (**63.3**%) among our cases **Table (3)**.
Mean value of **LVEDD** was statisticallysignificant higher among cases group than control group.
Mean value of **LVESD** was statistically significant higher among cases group than control group.
Mean value of **FS%** was statisticallysignificant lower among cases group than control group.
Mean value of **EF%** was statistically significant lower among cases group than control group.
Table (4).
Mean value of **Hb** was statistically significantlower among cases group than control group.
Mean value of **Platelet** was statistically significant lower among cases group than control group.
Mean value of **WBC** was statistically significant lower among cases group than control group.

There was no statistically significant difference between cases group and control group regarding CRP**Table (5).**
Mean value of Cardiac Myosin binding proteinc was statistically significant higher among cases group than control group **Table (6)**.
Regarding Modified ROSS among cases group,percentage of patients with class II was (13.3%), III and IV were (43.3%) each **Table (7)**.
Regarding outcome, the percentage of died among cases was (13.3%) and discharged was (86.7%). Cause of death: 1 case post TGA atrial switch operation myocardial dysfunction &3 cases after open heart reconstructive repair of complete Atrio-Ventricular Canal defect due to cardiogenic shock **Table (8)**.
There was statistically significant positive correlation between Cardiac Myosin binding protein and (Age, Weight), there was statistically significant positive correlation between Cardiac Myosin binding protein and (Heart rate, Respiratory rate). And there was negative statistically significant correlation between Cardiac Myosin binding protein and EF% and FS%, while there was no statistically significant differences between Cardiac Myosin binding protein and other numerical data**Table (9)**.
There was statistically significant positive correlation between Cardiac Myosin Binding Protein Cand severity of heart failure (Modified ROSS Classification)**Table (10)**.

There was statistically significant difference between Cardiac Myosin binding protein C (c My BP- C) in relation to pulmonary hypertension and controls. Also there wasstatisticallysignificantpositive correlation between Cardiac Myosin binding protein C and severity of pulmonary hypertension (PHTN).**Table (11)**.
Mean value of Cardiac Myosin binding protein C was statisticallysignificanthigher among died than discharged**Table(12)**.
Regarding Diagnostic accuracy of Cardiac Myosin binding protein, Sensitivity was 95%, Specificity was 89%, PPV was 93.1%, NPV was 88.3% and accuracy was 90% **Table (13)**.

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Table (1): Comparison between study group and Control group regarding demographic data.

			Cases group	Control group	X^2	P. value
sex	female	No.	15	12	.606	.436
		%	50.0%	40.0%		
	male	No.	15	18		
		%	50.0%	60.0%		
Age (years)	Mean ± SD		1.85 ± 1.42	1.1 ± 1.62	t.test.274	.806

Table (2): complaints among cases group.

		No.(30)	%
complaint	Tachypnea	30	100
	Exertional dyspnea	15	50
	Diaphoresis with feeding	23	76.6
	Grunting	13	43.3
	Cyanosis	5	16.6
	Growth failure	12	40

Table (3):clinical Manifestations of heart failure among cases group.

	N(30)	%
Cardiomegaly	19	63.3
Tachypnea	30	100
Tachycardia	30	100
Retraction	13	43.3
Cold extremities	30	100
Delay CRT	17	56.7
Basal crepitations	17	56.6
Murmur	22	73.3
Hepatomegaly	16	53.3
Edema	21	70.0
Ascites	No	0.0

Table (4): Comparison between Cases group and Control group regarding echocardiographic measurements.

		Cases group	Control group	t.test	P. value
LVEDD	Mean ± SD	29.46± 11.05	21.70± 1.98	3.789	.000
LVESD	Mean ± SD	22.26± 8.62	13.81± 1.23	5.311	.000
EF%	Mean ± SD	44.13± 9.09	65.13± 3.87	-11.629	.000
FS%	Mean ± SD	24.53± 3.57	36.28± 2.11	-15.503	.000

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LVPWd	**Mean ± SD**	4.46± 1.79	4.8±0.88	-.912	.366
IVSd	**Mean ± SD**	5.03± 2.10	5.75±0.86	-1.721	.091

Table (5): Comparison between Cases group and Control group regarding Laboratory tests.

			Cases group	Control group	t.test	P. value
CBC	**Hb (gm/dl)**	**Mean ± SD**	10.53± .535	11.41± 1.99	2.330	.023
	WBC ($\times 10^3/\mu L$)	**Mean ± SD**	5.16± .951	.1074± .161	-16.312	.000
	Platelet ($\times 10^3/\mu L$)	**Mean ± SD**	236.20± 35.48	260.46± 34.88	-2.671	.010
CRP	**(mg/L)**	**Mean ± SD**	2.79± 2.36	2.66± 1.57	.260	.796

Table (6): Comparison between Cases group and Control group regarding Cardiac Myosin binding protein C (c My BP-C).

		Cases group	Control group	t.test	P. value
Cardiac Myosin binding protein C (c My BP- C) (ng/ml)	**Mean ± SD**	78.28± 34.38	23.36± 10.65	8.356	.000

Table (7): Modified ROSS (degree of heart failure) among cases group.

		No.(30)	%
Modified ROSS	**I**	0	0
	II	4	13.3
	III	13	43.3
	IV	13	43.3

Table (8): OUTCOME among cases group.

		No.(30)	%
OUTCOME	**died**	4	13.3
	discharged	26	86.7

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Table (9): Correlation between Cardiac Myosin binding protein C (c My BP- C) and other data.

Correlation	Pearson's correlation	
	r	P
Age (year) *(c My BP- C)	.628	.000
Weight (kg) * (c My BP- C)	.396	.030
Heart rate * (c My BP- C)	.372	.043
Temperature * (c My BP- C)	.276	.141
Respiratory rate * (c My BP- C)	.509	.004
Systolic blood pressure * (c My BP- C)	.186	.324
Diastolic blood pressure * (c My BP- C)	.132	.486
LVEDD * (c My BP- C)	.152	.424
LVESD * (c My BP- C)	.145	.443
FS% * (c My BP- C)	-.041	.030
LVPWd * (c My BP- C)	-.003	.989
IVSd * (c My BP- C)	.069	.718
EF% * (c My BP- C)	-.345	.042
Hb * (c My BP- C)	-.153	.420
WBC * (c My BP- C)	.261	.164
Platelet * (c My BP- C)	.170	.370
CRP * (c My BP- C)	-.094	.620

Table (10): Relation between Cardiac Myosin binding protein C (c My BP- C) and degree of heart failure.

		ROSS			t.test	F. value	LSD
		II	III	IV			
Cardiac Myosin binding protein C (c My BP- C) (ng / ml)	Mean ± SD	46.77± 1.96	60.97± 13.26	105.29±35.14	13.828	0.000	P1=0.054 P2=0.005 P3=0.000

Table (11): Relation between Cardiac Myosin binding protein C (c My BP- C) in relation to pulmonary hypertension (PHTN) and control cases.

	Positive pulmonary hypertension			Negative PHTNNo.= 10	Control No.=30	F.test	P. value	LSD
	Mild No.= 3	Moderate No.=12	Severe No.=5					

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(c My BP- C) (ng / ml)	**Mean ± SD**	41.2.77 ± 1.52	65.32 ± 9.1	106.32 ±29.14	30.12± 8.32	23.36 ± 10.65	76.736	0.000	P1=0.000 P2=0.000 P3=0.000 P4=0.000 P5=0.000 P6=0.000 P7=0.000 P8=0.000 P9=0.000 P10=0.076

P1 --- mild and moderate,p2 ----- mild and severe, p3-----mild and Negative pulmonary hypertension,p4 ----- mild and control.
P5--- moderate and severe, p6---moderate and Negative pulmonary hypertension, P7---moderate and control.
P8----- severe and Negative pulmonary hypertension, p9------ severe and control.
P10----- Negative pulmonary hypertension and control.
There was statistically significant difference between Cardiac Myosin binding protein C(c My BP- C) in relation to pulmonary hypertension and controls.

Table (12): Relation between Cardiac Myosin binding protein C (c My BP- C) and OUTCOME.

		OUTCOME		**t.test**	**P. value**
		died	**discharged**		
Cardiac Myosin binding protein C (c My BP- C) (ng/ml)	**Mean ± SD**	143.75± 41.16	68.21± 19.41	38.196	0.000

Table (13): Diagnostic accuracy of Cardiac Myosin binding protein C (c My BP- C) in diagnosis of cases.

	Cut off value	**AUC**	**Sensitivity**	**Specificity**	**PPV**	**NPV**	**Accuracy**
Cardiac Myosin binding protein C (c My BP- C) ng/ml	87	.991	95%	89%	93.1%	88.3%	90%

Discussion
This study showed that, there was no statistically significant difference between cases and control regarding age**.** The mean age among cases was (1.85 ± 1.42) years.

In a study conducted by **El- Amrousy et al., [(6),]** the mean age of the patient group was 16.92 months, while the mean age of the control group was 18.36 months with non-significant difference between both groups.

Our results showed that Tachypnea (100%), Diaphoresis with feeding(76.6%) and Exertional dyspnea (50%),were the most predominant complaints among cases group. While Grunting was (43.3%), Cyanosis was (16.6%) and Growth failure was (40%).

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Maqbool et al., [8] found clinically CCF (Cardiac Congestive Failure) is a syndrome of breathlessness and fatigue which commonly is associated with cardiac disease.
A study done by **Den Boer et al.,** [9] found tachycardia in 5% of the patients and tachypnea in 24%. Also a study done by **Zoair et al.,** [10] showed tachycardia in 100% of the patients, tachypnea in 93.33%,hepatomegaly in 100% and murmur in 80%.

Our study showed that the Mean value of **LVEDD** was statistically significanthigher among cases group than control group.
Mean value of **LVESD** was statistically significant higher among cases group than control group.
Mean value of **FS%** was statistically significantlower among cases group than control group.
Mean value of **EF%** was statistically significantlower among cases group than control group.

A study done by **El Amrousy and El-Mahdy,** [11] showed that ejection fraction and fraction shorteningwere significant loweramong cases group than control group, while left ventricular end diastolic dimension and left ventricular end systolic dimensionwere significant higher among cases group than control group. In a study done by **Hajdusek et al,** [12]showed mean ejection fraction in the patient group was significant lowerthan control group, also showed mean left ventricular end diastolic dimension in the patients wassignificant higherthan control group.
Our study showed that mean value of **Hb**was statistically lower among cases group than control group.
This is in agreement with the study of**ElAmrousy and El-Mahdy,** [11]found that, Hemoglobin (HB) levelwas significantly lower in children with HF than healthy control group ($P < 0.001$). **Khatab et al.** [13] reported that there was a significant decrease in hemoglobin of the patients in relation to the control. **Anand,** [14] the causes of anemia in heart failure are not entirely clear. Specific causes of anemia such as hematinic abnormalities are seen only in a minority of subjects. Renal dysfunction and neurohormonal and proinflammatory cytokine activation appear to contribute to anemia of chronic disease in the majority of the patients, resulting in inappropriate erythropoietin production and defective iron utilization Our study showed that, mean value of WBCs was lower among cases than controls.
This disagrees with **El Amrousy and El-Mahdy,** [11]who found that, Total leukocytic count was significantly higher in patient group than control group ($P < 0.001$).The cause of that WBCs was lower among cases than controls in our study is dilutional by neurohormonal compensatory mechanism to circulatory failure.

The present study revealed that mean value of Cardiac Myosin binding protein was statistically higher among cases group than control group.In our study for children with acute heart failure at time of admission ranged from 42 – 201 ng/ml with mean 78.28± 34.38 ng/ml and level in the control group ranged from 10.4 – 43.9 ng/ml with mean 23.36± 10.65 ng/ml.

In agreement with **El Amrousy*et al.*** [6] as they mentioned that there was a significant increase in plasma levels of cMyBP-C in children with HF at time of admission as compared to control group.The plasma level of cMyBP-C before treatment ranged from 49 – 223 ng/ml with mean 122.44 ng/ml and the level in control group ranged between8-54 ng/dl with mean of 24.4 ± 9.83 ng/ml.
This agreed with **Jeong et al.** [15]who reported increased plasma levels of cMyBP-C in patients with heart failure with or without preserved ejection fraction as compared to healthy control group.
This coincidence with **El-Moghazy et al.** [1] who aimed to explore the role of cMyBP-C as a biomarker in heart failure in children. They reported that there was a significant increase in the plasma level of cMyBP-C in children with heart failure at time of admission and before receivingany anti failure treatment ranged from 10 – 90 ng/ml with mean (76±30.50ng/ml) and level in the control group ranged from 10 – 40 ng/ml with mean 46.30±26.47 ng/ml.

In our study, there was negative statistically significant correlation between Cardiac Myosin binding protein and EF% and FS%.
A study done by **El Amrousy et al., [6],** which showed significant negative correlation between plasma level of cardiac myosin binding protein-C in patients at time of admission and their ejection fraction, also showed significant negative correlation between its plasma level in patients at admission and their fraction shortening. In a study conducted by**Aimo et al., [16],** 71% of the patient group had left ventricular ejection fraction $<$ 40% and 61% had $\leq$ 35%, over a 26-month median follow up patients with left ventricular $\leq$ 35% and $<$ 40% both hada significantly worse prognosis for cardiovascular death.
In a study done by**Khatab et al.** [13] There was a significant negative correlation between ejection fraction of the patients group at admission (before treatment) and plasma level of cardiac myosin binding protein-C as the patients with the ejection fraction $<$ 50 was with higher plasma levels of cardiac myosin binding protein-C and the ejection fraction was $>$ 50 in the patients with lower plasma level of cardiac myosin binding protein-C, also found negative correlation between fraction shortening in the patients at admission and their plasma level of cardiac myosin binding protein-C.
Regarding Modified ROSS among cases group, II was (13.3%), III and IV were (43.3%) each.

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In a study done by**El Amrousy and El-Mahdy, [11]**23.3% of the patients were class II, 46.7% were class III and 30% were class IV.
Granström *et al.* [17], reported that 23.3% of the patients were class II, 46.7% were class III, and 30% were class IV.

This study showed that, the percentage of died was (13.3%) and discharged was (86.7%)
This agreed with **El Amrousy and El-Mahdy, [11]**who found that, the percentage of Non-survived cases was (20 %).

The recent study showed that mean value of Cardiac Myosin binding protein C was statistically higher among died than discharged.
In a study conducted by **El Amrousy et al., [6],**showed that before treatment there was significant high level of cardiac myosin binding protein-C in died compared to recovered.
This is in agreement with the study of **Anand*et al.*[18]**who demonstrated an increased mortality risk with rising cMyBP-C concentration in patients suffering from aortic stenosis.In a study done by**Khatab et al. [13]**showed that mean plasma level of cardiac myosin binding protein-C in the patients who died before treatment was significant higher than its level in the patients who recovered.
The recent study showed thatthere was a significant positive correlation between plasma level of cardiac myosin binding protein-C in the patients group at time of admission and increased severity of heart failure(Ross classification) of it, as its level inthe patients with class II was less than in class III and class IV.Also class III was less than class IV.

In agreement with **El-Moghazy et al. [1]**plasma level of cardiac myosin binding protein-C in class II Ross classification was lower than class III and also class III was lower than classIV. A significant positive correlation between plasma level of cardiac myosin binding protein-C in the patients group at admission and Ross classification of it.
In a study conducted by **Chen et al., [19],** showed that the severity of heart failure symptoms based on Ross classification correlates best with elevations in pulmonary capillary wedge pressure, as the worse Ross classification was most strongly associated with pulmonary capillary wedge pressure › 22 mmHg which correlates with our study.

There was statistically significant difference between Cardiac Myosin binding protein C (c My BP- C) in relation to pulmonary hypertension and controls. Also there wasstatisticallysignificant positive correlation between Cardiac Myosin binding protein C and severity of pulmonary hypertension (PHTN). Also there wasstatisticallysignificant positive correlation between severity of heart failure and severity of pulmonary hypertension (PHTN) as well.
This coincidence with **El-Moghazy et al. [1]** who foundhigh statistical significant difference among three levels of ROSS classification of the studied patients regarding levels of cMyBP-C, which was higher among patients of grade IV followed by grade III and the least among patients of grade II.
Regarding Diagnostic accuracy of Cardiac Myosin binding protein,Cut off value was 87ng/ml Sensitivity was 95%, Specificity was 89%,AUCwas 0.991,PPV was 93.1%, NPV was 88.3% and accuracy was 90%.
A study done by **El-Amrousy et al., [6]** showed at cutoff point higher than 45 ng/ml, sensitivity was 100%, specificity was 96% and AUC was 0.999.
El-Moghazy et al.[1] reported that, ROC curve analysis was performed to evaluate plasma levels of cMyBP-C as a prognostic predictor in patients with acute heart failure. The cutoff point value for cMyBP-C was 63.3, with sensitivity of 81.8%, specificity of 75% with 0.068 area under ROC curve and accuracy of 91.3%. This made cMyBP-c helpful in prediction of adverse outcome and identification of high-risk patients.

Conclusion:
The results obtained in our study revealed that Myosin Binding Protein C is useful as a diagnostic and prognostic biomarker in Pediatric Heart Failure.
Level of cardiac Myosin Binding Protein C can predict severity, complicationsand period of hospital admission among cases.

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