Cardiac Troponin T as Plasma Biomarker for Morbidity and Mortality in Preterm infants with Patent Ductus Arteriosus

Hanan Mostafa Abo Raya[(1)], Howyda Hosney El Gebaly[(1)], Mohamed Amin Mekawy[(2)], Maha Hassan Mohamed[(2)]
[(1)]Faculty of Postgraduate Childhood Studies- Ain Shams University, [(2)]Faculty of Medicine- Ain Shams University

Abstract

Background: PDA is the most common cardiovascular abnormality in preterm neonates. Left to right shunting across the PDA is associated with congestive heart failure and increased ventilatory dependence. Echocardiography remain the gold standard for diagnosing PDA. cTnT is a marker of cardiac injury.

Aim: To assess the rule of cTnT as a marker of cardiac injury in VLBW infants with clinically significant PDA and its relation to echocardiographic findings and clinical outcome.

Subjects and methods: Seventy- seven preterm infants born ≤ 1.5kg, were included, divided according to their diameter of PDA and whether having clinically significant PDA or not significant, into patients and control groups. For all neonates, echocardiography, CBC, CRP and cTnT measurement were done at 48 hours of life and as follow up 5- 7 days later.

Results: Fourty- one preterm infants with a mean gestational age of 31.7±1.57 weeks and birth weight of (1.38±0.2kg) were included as patients group, 36 preterm infants were included as control group with a mean gestational age of 32.2±0.9 weeks and birth weight of (1.63±0.2kg). On the second day, infants of the patient group had significantly higher mean cTnT levels (0.31±0.06 ng/dl) than those in control group (0.16±0.03 ng/dl). There were statistically significant decrease in LVESD in patients than in control group initially (9.00±1.94, 14.72±1.56, p= 0.023).

There was statistically significant increase in the number of the patients having right ventricular hypertrophy (p= 0.001), mild mitral regurgitation (p= 0.005), pulmonary stenosis (p= 0.03) and highly significant trivial tricuspid regurgitation (p= 0.000), and greater diameter of PDA (p= 0.000) in patient group than in control group in the first 48 hours.

Conclusion: cTnT in conjunction with echocardiography may provide the basis for early diagnosis and detection of complication of VLBW infants with hemodynamically significant PDA for trials of targeted medical treatment.

Keywords: cTnT, cardiac troponin, PDA, Patent ductus arteiosus, LVESD, left ventricular end systolic diameter, VLBW, very low birth weight

التربونين (ت) القلبى كعلامة بيولوجية للبلازما فى الحالات المرضية والوفيات فى الرضع المبتسرين ناقصى النمو ذوى أمراض ظاهرة فى القناة الشريانية السالكة

الخلفية: مرض القناة الشريانية السالكة (PDA) هو أكثر أمراض الأوعية القلبية شيوعا فى حديثى الولادة المبتسرين. يرتبط مفتاح التحويل من اليسار إلى اليمين في PDA بفشل القلب الاحتقانى والاعتماد المتزايد على الأكسجين. وتظل الموجات الصوتية على القلب هى المعيار الذهبى لتشخيص PDA، ويعد cTnT مؤشر لوجود إصابة بعضلة القلب.

الهدف: تهدف الدراسة إلى تحديد أهمية cTnT كمؤشر لوجود إصابة فى عضلة القلب فى حالات الأطفال المبتسرين الذين يعانون من PDA وعلاقته بنتائج الموجات الصوتية على القلب وشفاء المرضى.

الأساليب: تتكون العينة من ٧٧ طفل من المبتسرين المولودون بوزن ≤١,٥كجم، تم تقسيمهم وفق حالاتهم المرضية في PDA سواء كانت حادة بشكل دلالى أم غير دلالي، وقسمت العينة إلى مجموعتين: المرضى والضابطة. تم اجراء اختبارات الموجات الصوتية على القلب، CBC، CRP وcTnT لجميع الأطفال المبتسرين بعد ٤٨ ساعة من ولادتهم ومتابعة حالتهم بعد ٥- ٧ أيام.

النتائج: تم تصنيف ٤١ طفل من المبتسرين ذوى متوسط العمر الجنينى ١,٥٧ ±٣١,٧ أسبوع وزن عند الميلاد ٠,٢ ±١,٣٨كجم بأنهم مجموعة المرضى و٣٦ طفلا من المبتسرين بأنهم المجموعة الضابطة بمتوسط عمر جنينى ٠,٩ ±٣٢,٢ أسبوع ووزن عند الميلاد ٠,٢ ±١,٦٣كجم. فى اليوم الثاني، وأظهر الرضع فى مجموعة المرضى مستويات cTnT مرتفعة دلاليا ٠,٠٦ ±٠,٣١ ng/dl أعلى من المجموعة الضابطة ٠,٠٣ ±٠,١٦ ng/dl. أظهرت النتائج وجود انخفاض ذو دلالة إحصائية في LVESD فى مجموعة المرضى عن المجموعة الضابطة P= 0.023. كما أظهرت النتائج أيضا وجود انخفاض ذو دلالة إحصائية فى عدد المرضى المصابين بتضخم البطين الأيمن P= 0.001، ارتجاع الصمام المترالي P= 0.005، وضيق الصمام الرئوي p= 0.03، كما أظهروا وجود مستويات مرتفعة دلاليا فى ارتجاع الصمام الثلاثى التنوءات، وقطر أكبر من PDA p= 0.000 فى مجموعة المرضى أكثر من المجموعة الضابطة خلال ٤٨ ساعة الأولى.

الاستنتاج: cTnT مع الموجات فوق الصوتية على القلب قد يساهمان فى وضع الأساس للتشخيص المبكر والكشف عن المضاعفات في VLBW ذوي PDA عند إجراء لتجارب بهدف وضع العلاج الطبى المستهدف.

Introduction:

Patent ductus arteriosus (PDA) is the most common cardiovascular abnormality in preterm neonates, occurring in about 33% of infants less than 30 weeks gestation and in up to 60% of infants less than 28 weeks gestation. Left to right shunting across the PDA is associated with congestive heart failure, increased ventilatory dependence, pulmonary or intraventricular hemorrhages (Van and Chemtobs, 2015). Echocardiography remain the gold standard for diagnosing PDA (Costa et.al., 2007). Myocardial ischemia and its effect on cardiac function can be assessed by electrocardiogram (ECG), echocardiography, assay of biochemical markers and autopsy (San Jay A, 2004).

Biochemical markers of myocardial ischemia include creatine kinase and cTnT. The advantage of cTnT over the other markers, it's cardiac specificity, unaffected by trauma, mode of delivery, birth weight and sex (Uzodimma et.al., 2012). cTnT exists as both cytoplasmic and structural protein, the cytoplasmic pool is the source of cTnT released into the circulation within 4 to 6 hours and peaks at 24 to 36 hours after injury. The structural protein is responsible for the second blunted peak that occurs 2 to 4 days after injury (Kemp et.al., 2004). cTnT is the marker of cardiac injury and mortality in preterm infants (Costa et.al., 2007). Elevated cTnT levels have been found in preterm infants with RDS and PDA (San Jay, 2004).

Objective:

This study was done to assess the role of cTnT as marker of cardiac injury in VLBW infants with clinically significant PDA twice in first two and five days of life and its relation to echocardiographic findings and clinical outcome.

Subjects and Methods:

This case control study was conducted in Al Demerdash Neonatal Intensive Care Unit between April 2013- April 2014. It included neonates weighting less than 1.5 kg born during this period. They were classified by clinical examinations and echocardiography into two groups:

- Patients group: 41 VLBW with clinically significant PDA manifested with presence of heart murmur, tachycardia, hyperactive, precordium and increase in amplitude pulse. Ductal diameter> 1.6 mm was considered significant
- Control group: 36 VLBW without clinically significant PDA. We excluded preterms neonates with congenital malformations isolated or multiple, genetic syndromes or severe asphyxia and persistent pulmonary hypertension.

All our patients were subjected to detailed obstetric, perinatal, and postnatal history, maternal history of complication especially hypertension, mode of delivery, Apgar score at one and five minutes, intake of medications as intropic agents, diuretics, brufen or indomethacin. Thorough clinical examination including chest, cardiac, abdominal and neurological examinations. Assessment of vital signs and signs of cardiac decompensation like congestive heart failure, tachycardia, tachypnea, cardiomegaly, hepatomegaly, up to gallop rhythm. Measuring of the weight, recording the type of feeding whether enteral or parenteral, feeding intolerance. Manifestations of RDS, using surfactant or oxygen up to mechanical ventilation.

Hemodynamically significant PDA was considered if there is bounding pulses, wide pulse pressure and hyperdynamic precordium with systolic murmur at the upper left sternal border.

Investigations were done including CBC, CRP, cTnT by ELISA two times initially on the second day of life and follow up on the fifth to seventh day. cTnT measurement were taken following echocardiographic twice as second day and at the end of the first week. A sample of 1 ml of blood was collected in lithium heparine bottle and centrifuged and the plasma frozen at- 20°c for MAGLUM I electro chemiluminescent enzyme linked immunosorbent assay, which has a lower limit of detection of 0.01 pg/l.

Echocardiographic studies were done initially and follow up by the end of the first week were performed using standard neonatal windows including apical, parasternal, subcostal and high parasternal windows. Two dimensional, M mode imaging were recorded. The following echocardiographic findings were determined in each study:

1. Ductal diameter: absolute diameter in millimeter from high parasternal view (ductal diameter> 1.6mm was considered significant).
2. Left ventricular end systolic diameter (mm).
3. Left ventricular end diastolic diameters (mm).
4. Fraction Shortening (%).
5. Ejection Fraction (%).
6. Inter ventricular septal diameter (mm).
7. Right ventricular diameter (mm).
8. Trivial Mitral Valve Regurgitation.
9. Aortic Valve Regurgitation.
10. Tricuspid Valve Regurgitation.
11. Pulmonary Stenosis.

Ethical aspect of the study:

Written informed consent was obtained from the parents after explanation of the aim of the study, its benefits and expected risks for their infants if they participate in the study. All the patients data were confidential, neither the data nor the collected samples were used in other researches. Approval was taken to conduct this research from the Ethical Committee of the Faculty of Postgraduate Childhood Studies Ain Shams University, the Ethical Committee of the Faculty of Medicine Ain Shams University and the Ethical Committee of the National Research Center (NRC).

Statistical Analysis:

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 20. The qualitative data were presented as number and percentages while quantitative data were presented as mean, standard deviations and ranges when parametric distribution while non- parametric distribution were presented as median with interquartile range (IQR) using Mann Whitney test (z) test.

The comparison between groups regarding qualitative data was done by using Chi- square test and/ or Fisher exact test when the expected count in any cell found less than 5.

Comparison between two independent groups regarding quantitative data with parametric distribution was done by using Independent t- test and paired t- test comment.

Spearman correlation coefficients were used to assess the correlation between two quantitative parameters in the same group.

The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p- value was considered significant as the following: P> 0.05: Non significant, P <0.05: Significant, P <0.01: Highly significant.

Results:

Our preterm infants were divided into two groups: patients group (41) infants with clinically significant PDA, control group (36) infants without clinically significant PDA, Clinical and demographic data as shown in table (1):

Table (1) Comparison between patients group and control group as regard some clinical and demographic data

		Patients Group No. = 41	Control Group No. = 36	X^2/T	P- Value
Gender	Male	21 (51.2%)	12 (33.3%)	2.504	0.114
	Female	20 (48.8%)	24 (66.7%)		
Gestational Age (Weeks)	Mean±SD	31.71 ± 1.57	32.22 ±0.93	- 1.721#	0.089
	Range	28- 34	31- 34		
Parity	Primigravida	11 (26.8%)	16 (44.4%)	13.359	0.010*
	One	25 (61.0%)	10 (27.8%)		
	Two	3 (7.3%)	8 (22.2%)		
	Three	2 (4.9%)	0 (0.0%)		
	Four	0 (0.0%)	2 (5.6%)		
Single/Multiple pregnancy	One	25 (61.0%)	30 (83.3%)	6.628	0.036*
	Two	11 (26.8%)	6 (16.7%)		
	Three	5 (12.2%)	0 (0.0%)		
Delivery Mode	NVD	28 (68.3%)	6 (16.7%)	20.719	0.000**
	CS	13 (31.7%)	30 (83.3%)		
Maternal complications	Negative	32 (78.0%)	30 (83.3%)	0.341	0.559
	Positive	9 (22.0%)	6 (16.7%)		
Weight (Kg)	Mean±SD	1.38 ±0.20	1.63 ±0.25	- 4.830#	0.000**
	Range	0.9- 1.9	1.3- 2.25		

#Independent t- test χ^2: chi- square test, P> 0.05: Non significant,
*P <0.05: Significant **P <0.001: Highly significant, Data were expressed as a number (%) or mean±SD

1. There is highly significant difference between two groups as regards parity, para one mother, were more frequent in patients group than in control group (p<0.01).
2. Multiple pregnancy was statistically more frequent in patients group (p< 0.036). Normal vaginal delivery was significantly more common in patients group (p< 0.036) than in control group (p= 0.0001). The weight of the newborn was significantly less in patients group than in control group (p= 0.0001).

Table (2) Comparison between patients group and control group as regard Apgar score

		Patients Group No. = 41	Control Group No. = 36	(Z)	P- Value
Apgar At 1 Min	Median	3	4	- 2.366	0.018*
	IQR	3- 4	3- 4		
Apgar At 5 Mins	Median	7	7	- 2.547	0.011*
	IQR	7- 7.5	7- 8		

Z= Mann Whitney Test, P> 0.05: Non significant,
*P <0.05: Significant **P <0.001: Highly significant

1. Data were expressed as a median and IQR (inter quantile range)
2. There is significant decrease in Apgar score at 1 and 5 minutes between patients and control group.

The following table (3) shows some clinical and laboratory data of included neonates.

Table (3) Comparison between patients and control groups as regard some clinical and laboratory data

		Patients Group		Control Group		Independent T-Test	
		No.	%	No.	%	T/X^2*	P-Value
Respiratory							
O_2 Therapy	Positive	25	61	16	44.4	2.104	0.147
	Negative	16	39	20	55.69		
Ventilator Use	Positive	28	68.3	12	33.3	9.358	0.002
	Negative	13	31.7	24	66.7		
Days On Mechanical Ventilation	Mean±SD	2.95±2.81		2.028±2.833		1.433	0.156
	Range	0- 7		0- 7			
Surfactant	Positive	27	68.3	12	33.3	9.385	0.002
	Negative	13	31.7	24	66.7		
Cardiac							
Pulse	Bradycardia	23	56.1	24	66.7	0.900	0.343
	Tachycardia	18	43.9	12	33.3		
Blood Pressure	Normal	27	65.9	24	66.7	0.006	0.940
	Hypotensive	14	34.1	12	33.3		
Heart Failure	Positive	11	26.8	8	22.2	0.219	0.640
	Negative	30	73.2	28	77.8		
Use Of Inotropics	Positive	11	26.8	0	0	11.208	0.001
	Negative	30	73.2	36	100		
Use Of Diuretics	Positive	6	14.6	2	5.6	1.697	0.193
	Negative	35	85.4	34	94.4		
Use Of Brufen Or Endomethacin	Positive	11	26.8	0	0	11.26	0.001
	Negative	30	73.2	36	100		
Outcome	Live	40	97.6	36	100	0.980	0.346
	Died	1	2.4	0	0		
Feeding							
Intravenous Fluids	Positive	39	95.1	30	83.3	2.861	0.091
	Negative	2	4.9	6	16.7		
Enteral Feeding	Positive	15	36.6	30	83.3	17.248	0.000
	Negative	26	63.4	6	16.7		
Parental Feeding	Positive	12	29.3	10	27.8	0.021	0.885
	Negative	29	70.7	26	72.2		
Laboratory							
Hb (Gm/Dl)	Mean±SD	14.70 ± 2.59		16.33 ± 2.31		2.897#	0.005**
	Range	8.9- 20		12.1- 19.9			

#Independent t- test χ^2: chi- square test, P> 0.05: Non significant,
*P <0.05: Significant **P <0.001: Highly significan, Data were expressed as a number (%) or mean±SD

1. There is highly statistically significant increase in the use of the mechanical ventilation in patients than control group (p= 0.002).

2. Frequency of surfactant use was increased in patients than control group (p= 0.002).
3. Eleven patients having congestive heart failure all of them using inotropic agents, brufen or indomethacin but only 6 receiving diuretics. The patients group showed significant increase in the frequency of using inotropics and prostagland in antagonists than in control group (p= 0.001, 0.0001 respectively).
4. Enteral feeding was highly significantly less frequent in patients group (36.6%) than control group (83.3%) at time of initial evaluation (p= 0.0001).
5. There was no statistically significant difference as regard pulse or blood pressure changes and intravenous fluids or parenteral feeding between two groups (p>0.05).
6. There is statistically significant decrease in hemoglobin level in patients than in control group initially (p= 0.005).

Table (4) Comparison between Echocardiographic finding and troponin T level between patients and control groups initially

		Patients Group No. = 41	Control Group No. = 36	T/X²*	P- Value
Troponin T level (ng/dl)	Mean±SD	0.31 ±0.06	0.16 ±0.03	13.474	0.000**
	Range	0.19- 0.42	0.12- 0.21		
Echocardiography					
Lvedd (Mm)	Mean±SD	14.77 ± 3.65	16.56 ± 5.67	- 1.660#	0.101
	Range	10- 28	10- 38		
Lvesd (Mm)	Mean±SD	9.00 ± 1.94	14.72 ± 1.563	- 2.323#	0.023**
	Range	6- 13	7- 78		
Fs (%)	Mean±SD	35.68 ± 4.92	36.28 ± 8.71	- 0.375#	0.709
	Range	29- 50	3- 42		
Ef (%)	Mean±SD	69.51 ± 6.18	73.28 ± 4.79	- 2.957#	0.004**
	Range	58- 85	64- 78		
Ivs (Mm)	Mean±SD	3.27 ±0.87	3.46 ±0.78	- 1.031#	0.306
	Range	0.7- 5.1	2- 4.7		
Rv Hypertrophy	Positive [N (%)]	11 (26.8%)	0 (0.0%)	11.268	0.001**
	Negative[N (%)]	30 (73.2%)	36 (100.0%)		
Mitral Valve Regurgitation	Positive [N (%)]	8 (19.5%)	0 (0.0%)	7.839	0.005**
	Negative[N (%)]	33 (80.5%)	36 (100.0%)		
Aortic valve regurgitation (trivial)	Positive [N (%)]	3 (7.3%)	0 (0.0%)	2.741	0.098
	Negative[N (%)]	38 (92.7%)	36 (100.0%)		
Tricuspid Valve Regurgitation	Positive [N (%)]	17 (41.5%)	2 (5.6%)	13.298	0.000**
	Negative[N (%)]	24 (58.5%)	34 (94.4%)		
Pulmonary Stenosis	Positive [N (%)]	5 (12.2%)	0 (0.0%)	4.695	0.030**
	Negative[N (%)]	36 (87.8%)	36 (100.0%)		
Pda Diameter (Mm)	Mean±SD	2.49±0.89	0.96 ±0.28	9.93#	0.0001**
	Range	1.70- 5	0.00- 1.30		

#Independent t- test χ^2: chi- square test, P> 0.05: Non significant,
*P <0.05: Significant **P <0.001: Highly significant
Data were expressed as a number (%) or mean±SD, LVEDD: Left Ventricular End-diastolic Diameter, LVESD: Left Ventricular End- Systolic Diameter, FS: Fraction shortening, ES: Ejection fraction, IVS: Interventricular septum, RV: Right Ventricular hypertrophy, PDA: Patent Ductus Arteriosus diameter

1. There is highly statistically significant increase in troponin T concentration (cTnT) in patients group than in control group initially (p= 0.0001).
2. There is statistically significant decrease in left ventricular end systolic diameter and ejection fraction in patients than in control group initially (p= 0.023, 0.004 respectively).
3. There is also highly statistically significant increase in frequency of patients with right ventricular hypertrophy compared to control group (p= 0.001).
4. There is highly statistically increase in frequency of mitral valve regurgitation in patients group (only 8% of patients group having trivial regurgitation while none of control group having this change) (p= 0.005).
5. There is highly statistically significant increase in frequency of patients with physiological trivial tricuspid regurgitation (41.5%) compared to control group (5.6%) (p= 0.0001).
6. Significant increase in pulmonary stenosis observed in patients group (12.2%) having pulmonary stenosis while none of the control group having pulmonary stenosis (p= 0.03).
7. There is highly significant increase in diameter of patent ductus arteriosus in patients compared to control group (p= 0.001).

Table (5) Comparison of troponin T (cTnT) concentration and echocardiographic finding of patients group initially and follow up studies

Patients Group		Initially No. = 41	Follow Up No. = 41	T/X²	P- Value
Troponin T level (ng/dl)	Mean±SD	0.31 ±0.06	0.27 ±0.07	6.042#	0.000
	Range	0.19- 0.42	0.13- 0.4		
Lvedd (Mm)	Mean±SD	14.77 ± 3.65	16.45 ± 3.10	- 3.366#	0.002
	Range	10- 28	8- 22		
Lvesd (Mm)	Mean±SD	9.00 ± 1.94	10.80 ± 1.67	- 6.908#	0.000
	Range	6- 13	6- 14		
Fs (%)	Mean±SD	35.68 ± 4.92	38.08 ± 4.06	- 6.961#	0.000
	Range	29- 50	30- 46		
Ef (%)	Mean±SD	69.51 ± 6.18	72.40 ± 5.15	- 8.149#	0.000
	Range	58- 85	60- 85		
Ivs (Mm)	Mean±SD	3.27 ±0.87	3.62 ±0.70	- 2.867#	0.007
	Range	0.7- 5.1	2- 5.2		
Right Ventricular Hypertrophy	Positive [N, %]	11 (26.8%)	4 (9.8%)	3.998	0.046
	Negative [N, %]	30 (73.2%)	37 (90.2%)		
Mitral Valve Regurgitation	Positive [N, %]	8 (19.5%)	1 (2.4%)	6.116	0.013
	Negative [N, %]	33 (80.5%)	40 (97.6%)		
Aortic Value Regurgitation	Positive [N, %]	3 (7.3%)	0 (0.0%)	3.114	0.078
	Negative [N, %]	38 (92.7%)	41 (100.0%)		
Tricuspid Valve Regurgitation	Positive [N, %]	17 (41.5%)	7 (17.1%)	5.891	0.015
	Negative [N, %]	24 (58.5%)	34 (82.9%)		
Pulmonary Valve Stenosis	Positive [N, %]	5 (12.2%)	0 (0.0%)	5.325	0.021
	Negative [N, %]	36 (87.8%)	41 (100.0%)		
PDA Diameter (Mm)	Mean±SD	2.49±0.89	0.17±0.38	17.94	0.0001
	Range	1.7- 5	0.0- 1.0		

#Independent t- test χ^2: chi- square test, P> 0.05: Non significant *P <0.05: Significant **P <0.001: Highly significant, Data were expressed as a number (%) or mean±SD, LVEDD: Left Ventricular End- diastolic Diameter, LVESD: Left Ventricular End-Systolic Diameter, FS: Fraction shortening ES: Ejection fraction, IVS: Interventricular septum RV: Right Ventricular hypertrophy, PDA: Patent Ductus Arteriosus diameter

1. There is statistically significant decrease in the troponin T (cTnT) concentration by the end of the first week in patient group (p= 0.0001).
2. There is statistically significant increase in left ventricular end systolic and diastolic diameter, ejection fraction and fraction shortening by the end of the first week of life in patient group (p= 0.0001, 0.0002,

0.0001, 0.0001 respectively).

3. There is decrease in the number of patients having right ventricular hypertrophy, mild tricuspid regurgitation and pulmonary stenosis by the end of the first week (p= 0.046, 0.013, 0.015, 0.021 respectively).
4. There is positive correlation between the troponin T level initially and the diameter of the patent ductus arteriosus (p= 0.046).
5. There is significant decrease in the diameter of patent ductus arteriosus in patient group by the end of the first week (p= 0.0001).
6. There is no significant correlation between troponin T level and other clinical, laboratory and echocardiographic findings on initial evaluation.

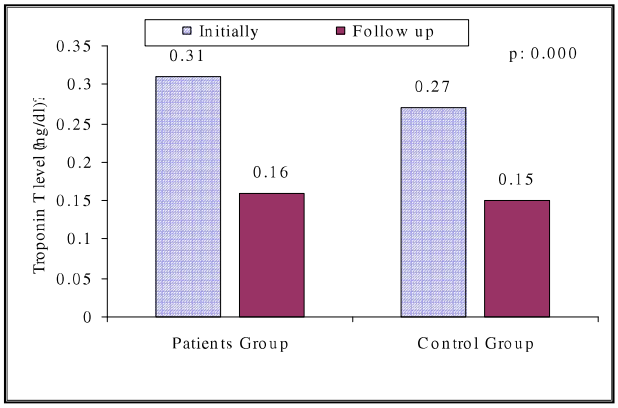

Figure (1) Troponin T concentration on initial and follow up in patients and control groups

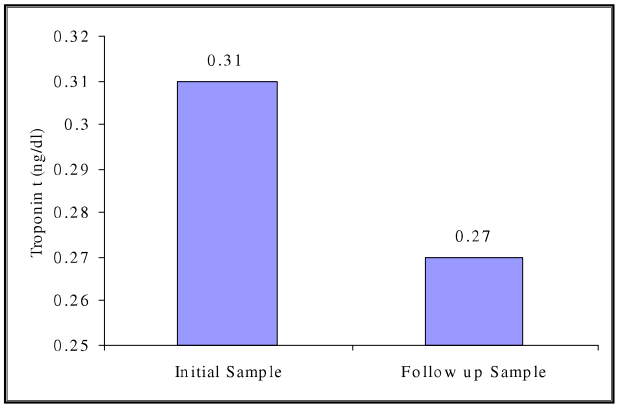

Figure (2) Initial and follow up troponin T levels in patients group

There is negative correlation between cTnT concentration and Apgar score at one and five minutes initially (p= 0.030.0.014 respectively), as shown in figures (3& 4):

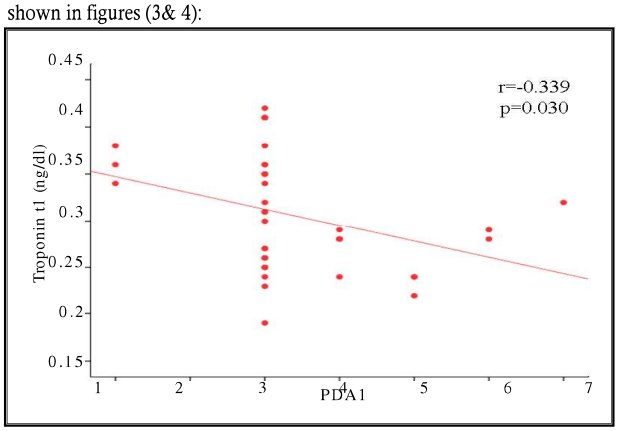

Figure (3) Correlation between the troponin T level initially and Apgar score at one minute in the patients group

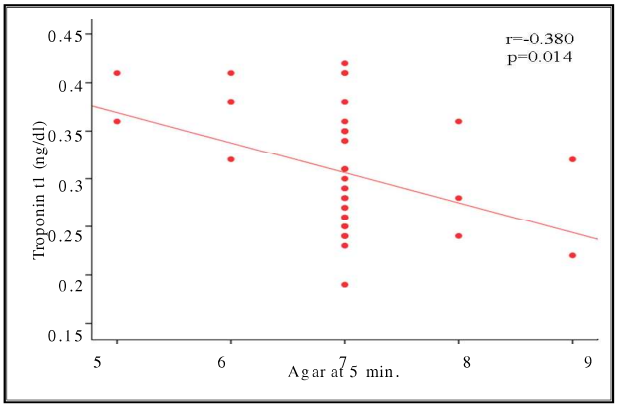

Figure (4) Correlation between the troponin T level initially and Apgar score at five minutes in the patients group

There is positive correlation between the troponin T level initially and the diameter of the patent ductus arteriosus (p= 0.046), as shown in figure (5):

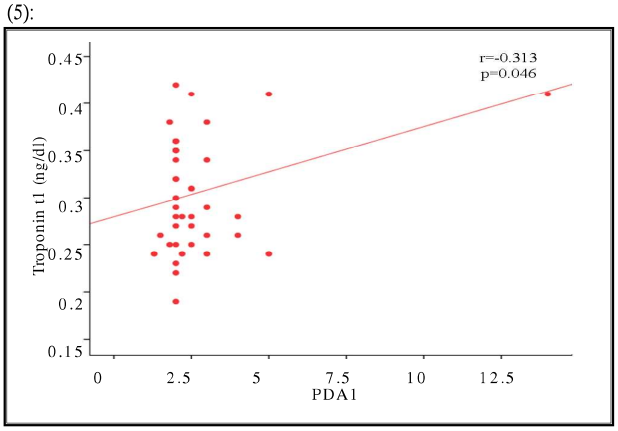

Figure (5) Correlation between the troponin T levels initially and the dimeter of patent ductus arteriosus in the patients group

There was only one neonate died at the 7th day. He was male, 34 weeks gestation, para one mother, single pregnancy, delivered by caesarian section, intra uterine growth retardation, oligohydramnios, 1.340 kg, Apgar 4 at 1 minute and 7 at 5 minutes, RDS II, mechanically ventilated for 7 days, hypotension, gallop rhythm and congestive heart failure.

His laboratory investigations (Hb= 10.9 gm/dl, CRP +ve, troponin T level initially 0.38ng/ dl). Echogradiographic finding (LVEDD= 16, LVESD= 18, EF= 8 0%, FS= 50%, IVS= 0.7, RV hypertrophy, mitral and tricuspid valve regurgitation, PDA diameter= 4mm).

He was on inotropics agents and diuretics and he died from pulmonary hemorrhage and congestive heart failure.

Discussion:

PDA is the most common cardiovascular abnormality in preterm neonates occurring in a bout 33% of infants less than 30 weeks gestation and up to 60% of infants less than 28 weeks gestation. Left to right shunting across the PDA is associated with congestive heart failure, increased ventilatory dependence and pulmonary hemorrhage (Van and Chemtobs, 2005).

In premature infants, the ductus arteriosus remains open for a longer time and the frequency of PDA increases in proportion to the degree of immaturity.

Symptomatic PDA is defined by the presence of heart murmur, tachycardia, hyperactive precordium and increase in the amplitude of the pulse, so echocardiography the primary role in diagnosis and management of PDA in preterm newborn (Miyague NI, 2005).

Serum cTnT is a marker of cardiac injury and mortality and is a good determinant of myocardial injury in prenatally asphyxiated neonates (Costa et.al., 2007). The main aim of this study was to assess the ability of cTnT to predict outcome in the group of infants with clinically significant PDA.

Echocardiography alone can not identify the high risk PDA patients. We demonstrated the association between elevated cTnT and poor outcome in infants with clinically significant large PDA, but not causing higher mortality only morbidity. The cTnT level were unaffected by gender, gestational age, weight, maternal complications and mode of delivery in patients group. Our study agreed with ElKhuffash et.al., 2008, that found cTnT unaffected by the delivery mode. In agreement with the data reported by Karadeniz et.al. (2010) in preterm neonates with/ without RDS, the cTnT concentration was independent of gestational age, in addition Clark et.al., (2006) reported the same for sex, gestation age, birth weight and mode of delivery.

Our study disagreed with the study done by Sadoh and Ergie (2012), they found significant decrease in cTnT level in patients delivered by cesarean sections. These lower levels might be because the procedure itself is an intervention, which might have limited the degree of perinatal asphyxia.

There is significant decrease in Apgar score at 1 and 5 minutes between patients and control group. The median of patients at 1 and 5 minutes (3 and 7 respectively), while in control was (4 and 7 respectively).

Uzodimma C et.al. (2012) agreed with our results, the reported that Apgar at 1 and 5 minutes as well as PH significantly correlated with high risk serum troponin T levels, which may be explained by persistent hypoxia. Moreover, Cruz et.al. (2006) agreed with our results. Our study, the number of the patients with RDS, needing surfactant using mechanical ventilation were significantly higher than the controls. Inspite of there was no significant correlation between troponin level initially and follow up with RDS and using mechanical ventilation. This result might be due to early management of the patients with PDA and RDS in NICU by using of surfactant and mechanical ventilation that leads to decrease the myocardial injury on follow up study, so preserving the cTnT at not at higher levels.

Elkhuffash et.al. (2000) and Trevisanuto et.al. (2000) disagreed with our results, they found significantly higher cTnT in VLBW infants with acute RDS, which might be due to more damage to immature myocardium from hypoxia and acidosis secondary to the respiratory diseases. Our study revealed no significant correlation between the cTnT initially in the study and the blood pressure of the patients, while positive significant correlation between the cTnT in patients and increase the blood pressure on follow up study, might be due to the use of positive inotropic drugs that improve the early ischemia occurred to the myocardial muscles. These results coincident with the results of Elkhuffash et.al. 2008.

Our study reported no significant correlation between the cTnT and the use of inotropics and troponin levels of the patients initially. These results were disagreed with the results with Perugu et.al (2014) and Clark et.al. 2001, the found cTnT was greatest in babies receiving dopamine with clinically significant PDA, these finding might be due to high risk of VLBW for hypotension damaged myocardium and early ischemic insult.

Cruz et.al. (2006), also found highest levels of cTnT in babies requiring pressor support and there was no relationship with the diameter of PDA.

In the current study, we observed significant correlation between congestive heart failure and troponin T concentration in patients group initially. These results coincident with the result of Cruz et.al., (2006), the manifestation of congestive heart failure and the cardiac output inversely related to cTnT, these findings suggests that early neonatal myocardial ischemia in VLBW infants manifests primarily during the first 48 hours after birth and associated with clinically apparent hemodynamic instability independent of the presence of large PDA.

Our results disagreed with the results of Tarkowska A and Furmaga W (2012) they found higher cTnT did not correlate with clinical symptoms of heart failure or with echocardiographic markers of left ventricular functions.

Our study revealed no significant correlation between the patient receiving treatment with brufen, indomethacin or inotropic agents and those not receiving as regard cTnT level inspite of more patients receiving treatment than controls. Abdel Hady et.al. 2013 supported our results, our study found no significant correlation between LVEDD, LVESD and troponin level initially a, these results supported with Perugu et.al 2014 and Cruz et.al. 2006.

Our current study revealed significant increase in the level of cTnT in patients receiving diuretics than others not receiving, these results agreed with the result of Sung SI et.al. (2016).

Our study showed that the cTnT was significantly higher in patients than control group with positive correlation with the diameter of PDA. McNamara and Sehgal 2007 and Asrani et.al. 2016 agreed with our findings, on the contrary Elkhuffash reported that no relationship between cTnT level and PDA diameter.

Our study showed nonsignificant increase in mortality between the patients and control group, only one male patient died at the the 7th day.

The result of Boo NY et.al., (2005), the mean of cTnT level was higher in infants who died, who had severe birth asphyxia, more severe myocardial injury than survivors. ElKhuffash et.al. (2008) demonstrated an association between high cTnT and death in infants with PDA.

Conclusion:

In the current study, we concluded that cTnT in conjunction with echocardiography may provide the basis for early diagnosis of neonatal myocardial ischemia in VLBW infants (in the first 48 hours) after birth

and it is association with clinically apparent hemodynamically significant PDA and early detection of complication for trials of targeted medical treatment. We can use cTnT as plasma biomarker for detection of stability of cardiac condition by the end of the first week (through decreased the elevated level cTnT).

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