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Original article

Level of Cardiac Troponin T in Relation to Disease Severity and Outcomes in Neonates with Respiratory Distress

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Abstract:

Background: Cardiac troponin T (cTnT) has been proposed as specific biochemical marker for myocardial infarction in adults. Cardiac function in neonates could be influenced by the severity of respiratory distress (RD) and its ventilatory management. Aim of the study was to investigate cTnT levels in neonates with respiratory distress as a marker of myocardial dysfunction **Methods:** Total sample size 100 neonate, 50 neonates with RD and 50 healthy neonates (without RD). Concentrations of cTnT were compared between sick and healthy infants, Age at sampling, need for ventilation, duration of respiratory support, and inotropic use in addition to neonatal and maternal characteristics. **Results:** CTnT levels were significantly higher ($p<0.001$) in study group (RD cases) (0.200±0.156 ng/ml) than in control group (healthy neonates) (0.034±0.019 ng/ml). Area under the ROC curve was 0.962 with best cutoff value (>0.056), sensitivity was 90%, specificity was 90%. Also, cTnT levels were significantly higher in neonates who required inotropic support when compared to those without inotropes. We found CTnT levels were significantly higher in cases who died than in cases who survived ($p<0.001$). **Conclusion:** Cardiac troponin T could be used as a useful marker for myocardial dysfunction in neonates with respiratory distress.

Keywords: Cardiac troponin T; respiratory distress; neonates.

Introduction

Respiratory distress is one of the most common causes for neonatal intensive care unit (NICU) admission. The most frequently diagnosed causes for it are respiratory distress syndrome, transient tachypnea of newborn, meconium aspiration syndrome and neonatal pneumonia [(1)]. Management and outcomes of such cases depends mainly on severity of RD. The more severe is RD, The more duration of ventilator support and the more incidence of complications. Cardiovascular compromise is common in cases of RD. Impaired myocardial contractility and low cardiac output are common complications of severe RD and its ventillatory management [(2)]. This reduced cardiovascular reserve may present clinically with hypotension, which is associated with increased mortality and adverse neurological outcomes [(3)] This associated myocardial dysfunction has been attributed to myocardial ischemia and/or necrosis [(4)] The troponin complex involves three subunits: (cTnT), which binds to tropomyosin and helps contraction; troponin I (cTnI), which binds to actin and restricts actin-myosin interactions; and troponin C (cTnC), which binds to calcium ions[(5)]Cardiac troponin I (cTnI) and cardiac troponin T (cTnT) are released as a result of myocardial cell injury and are highly sensitive and specific biomarkers of myocardial damage. Because cTnI is cleared more rapidly from the circulation than cTnT, its utility as a monitor of ongoing cardiac injury is limited. [(6)] The aim of our study was to investigate cTnT levels in neonates with respiratory distress as a marker of myocardial dysfunction.

Patients and Methods:

Study design and participant:

Case –control prospective study was carried out in NICU of Benha University Hospital and outpatient neonatology clinic department in Benha University Hospital during the period from January 2022 to January 2023. The study was under the following inclusion and exclusion criteria:

Inclusion criteria: Study group: All neonates admitted to NICU for respiratory distress during first 48 hours postnatal, males and females, full term and preterm.

Exclusion criteria: Neonates with congenital heart diseases and birth asphyxia were excluded.

Ethical consideration:

An informed consent was obtained from the parents before enrollment in the study.

An approval from Research Ethics Committee in Benha Faculty of Medicine was obtained {M.S.41.3.2019}.

Methods: A standardized data sheet was utilized to record patient's history

Full history taking with special emphasis on sex, gestational age, mode of delivery, history of disease or medication during pregnancy, history of premature rupture of membrane (PROM), history of bleeding, history of any maternal risk factor, history of resuscitation, history of lethargy, delayed cry, poor feeding and low Apgar score 3 for 5min.history of birth weight and age at sample taking.

Clinical examination: General examination: Vital signs and anthropometric measurements (weight, length & head circumference). Neurological examination and neonatal reflexes. Chest examination: signs of respiratory distress**;** Grade 1: tachypnea (more than 60 breaths/mi) and nasal flaring**,** Grade 2: subcostal and intercostal

retraction**,** Grade 3: grunting**,** Grade 4: cyanosis**.** Heart examination and abdominal examination.

Investigations: laboratory investigation include (complete blood count (CBC) ,C reactive protein (CRP) ,arterial blood gases (ABG) and radiographic assessment.as regard C TnT level , 2ml venous blood was collected by venipuncture during the first 48 hours post natally. Samples were separated and frozen at -20 until batch analysis be performed. We performed biochemical analysis with an Elecsys 2010 analyzer using the third generation Elecsys Troponin T STAT Immunoassay (Roche Diagnostics Mannheim, Germany). This electrochemiluminescent sandwich enzyme-linked immunosorbent assay has a lower limit of detection of 0.01 mg/l, with minimal cross-reactivity with cardiac troponin I (0.002%) and skeletal troponin T (0.001%) and maximal upper limit of detection of 25 mg/l.

Statistical Analysis:

Descriptive statistics were used, including percentage for categorical variables and median with interquartile range (IQR) for continuous variables, because data were not normally distributed. Demographic and clinical characteristics were compared between survival and morbidity groups. x^2tests for categorical variables (with Fisher's exact correction for expected cell counts, 10) and Mann-Whitney *U* tests for continuous variables were used. A level of 5% was considered significant. Data were analyzed using Statistical analysis, by using the SPSS V.21 program (statistical package for the social sciences) (SPSS Inc., Chicago, Illinois, USA) program data The following tests were used to test differences for significance; difference and association of qualitative variable by Chi square test (X2). For differences between quantitative independent groups, t test was used. P value <0.05 was set for significant results & <0.001 for highly significant results.

Results:

Study group included 50 RD cases, their mean gestational age was 34.2 weeks (range 24-40), and their mean age at sample collection was 15.6 hours. Mean birth weight was 2.5 kg (range 0.8-3.9). They were 36% males and 64% females, they were delivered by caesarian section (CS) in 36% and 64% by normal vaginal delivery(NVD) Maternal demographic characteristics and obstetrical outcomes were compared between neonates with normal and elevated cTnT concentrations (Table 1).

Table (1) Sociodemographic characteristics and maternal data for both studied groups.

			Control n=50		RD n=50		*test*	*p*
Gestational age (weeks)		mean±SD	38.1	1.3	34.2	4.3	T=6.209	<0.001
		Median, range	38	36-40	36	24-40		
Neonatal age (hours)		mean±SD	30.1	10.8	15.6	7.6	T=7.785	<0.001
		Median, range	24	20-48	15	4-40		
Birth weight (kg)		mean±SD	3.1	0.4	2.5	0.8	F=5.396	<0.001
		Median, range	3	2.5-3.9	2.6	0.8-3.9		
Gender	**Male**	N (%)	16	32.0%	18	36.0%	X^2=0.178	0.673
	Female	N (%)	34	68.0%	32	64.0%		
Mode of	**CS**	N (%)	16	32.0%	18	36.0%	X^2=0.178	0.673
delivary	**NVD**	N (%)	34	68.0%	32	64.0%		
maternal	chorioaminitis	N, %	0	0%	0	0%	-	-
diseases	**pre eclamsia**	N, %	3	6.0%	8	16.0%	X^2=2.554	0.110
Maternal age (years)		mean±SD	27.7	2.6	27.4	3.7	T=0.138	0.879
		Median, range	26	21-33	27	22-35		
Parity		mean±SD	2	1	2	1	U=12.211	0.856
maternal	chorioaminitis	N, %	0	0%	0	0%	-	-
diseases	**pre eclamsia**	N, %	3	6.0%	8	16.0%	X^2=2.554	0.110

In this study, 100 neonates were included, 50 healthy neonates (control group) and 50 sick neonates suffering from RD and admitted to NICU (study group). However, some neonates of the control group (7 neonates) were admitted to NICU for nutritional support or hyperbilirubinemia without any signs of respiratory distress or need for respiratory support.

From our 50 RD cases 40% required mechanical ventilation, 32% required inotropes, mean Duration of respiratory support was 6.4 days. Mean Length of ICU stay was 8 days as shown in Table (2). Among all studied cases, 28 %(14cases) died, while 72% (36cases) discharged Table (3).

Table (2). Required treatment and duration among all studied cases.

		RD n=50	
Length of ICU stay (days)	mean±SD	8.0	3.4
	Median, range	7	3-20
Need for mechanical ventilation	N, %	20	40.0%
Inotropes	N, %	16	32.0%
Duration of respiratory support (days)	mean±SD	6.4	3.1
	Median, range	5	2-12

Table (3). Comparison of Troponin T level according to requirement of Mechanical ventillation and inotrops.

		Respiratory distress group serum troponin T **Mean**					
Need for mechanical ventilation		**No**	**SD**	**Median**	**Minimum**	**Maximum**	**p**
Need for mechanical ventilation.	yes	0.085	0.032	0.082	0.040	0.170	<0.001
	No	0.372	0.097	0.403	0.160	0.480	
Inotropes							
Inotropes	yes	0.112	0.088	0.084	0.040	0.450	<0.001
RD group		0.387	0.088	0.415	0.170	0.480	
RD group fate							
	Discharge	0.114	0.077	0.088	0.040	0.360	<0.001
	Death	0.420	0.056	0.420	0.260	0.480	

As regard the cardiac troponin T (CTnT) levels among our studied groups, We found CTnT levels were significantly higher (p<0.001) in study group (RD cases)(0.200±0.156 ng/ml) than in control group (healthy neonates) (0.034±0.019 ng/ml) Fig (1) .Area under the ROC curve was 0.962 with best cutoff value(>0.056), sensitivity was 90%, specificity was 90% Fig (2). Higher Troponin T level was significantly associated with Need for mechanical ventilation and inotropes Table (2). CTnT level was significantly higher in cases who died than in survived cases Table (3) CTnT concentrations were positively correlated to duration of ventilatory support in the ventilated subgroup (+0.5) with p value !0.05. Eleven (50%) infants were ventilated for 3 day or less and 11 infants (50%) were ventilated for more than 3 days. with p value = <0.001(Table 4).

Table (4) . Correlations of troponin T with other parameters among all studied subjects.

	Troponin T **correlation coefficient**	***p***
gestational age	-0.845	<0.001
Neonatal age	-0.326	0.001
birth weight	-0.836	<0.001
Duration of respiratory support	0.862	<0.001
Length of ICU stay	0.743	<0.001

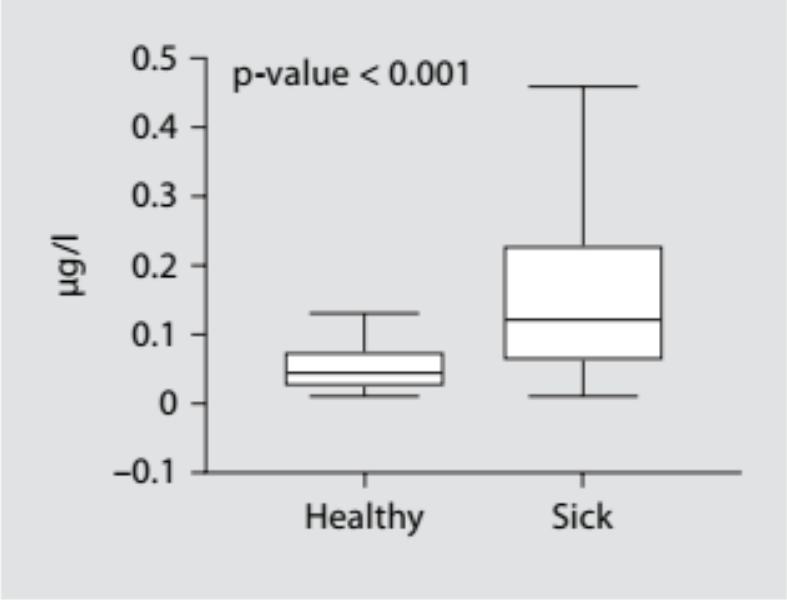

Figure (1). Troponin T level among studied groups.

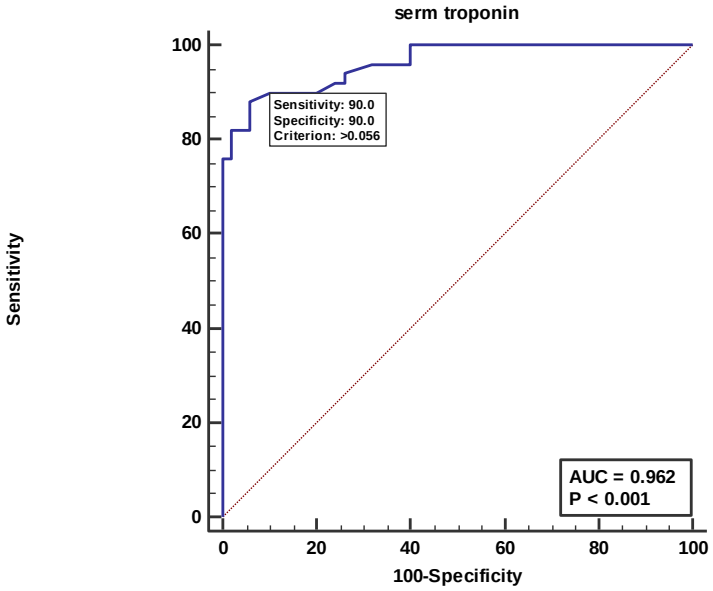

Figure (2). ROC curve of troponinT for discrimination between RD cases and control**.** groups

Discussion:

Measurements of cardiac troponins represent a definite advance in the biochemical diagnostics of myocardial damage in adult population. Efforts have been made to highlight the clinical utility of troponins in neonatal population with cardiovascular compromise [(7).]

The cardiac troponin T levels were significantly higher (p<0.001) in study group (RD cases) (0.200±0.156 ng/ml) than in control group. they agree with Trevisanuto et al [(8)] these illustrated by increased cardiac troponin T (CTnT) concentrations could be related to the fact

that primary respiratory disease may lead to myocardial injury [9].

On studying CTnT levels among our study group, there was significant negative correlations with gestational age and birth weight ($p<0.001$) these results corroborate with those Trevisanuto et al [8] we also found significant positive correlations with duration of respiratory support, Length of NICU stay. These results corroborate with previous studies [9].

Cardiac troponin T (CTnT) levels were significantly higher in cases who needed mechanical ventilator (MV) than non-ventilated cases. Also positive significant correlation was found between CTnT and duration needed on MV. As we measured troponin T level in the 1st 48 hours of life, this result suggests that CTnT level can be used as a predictor of the clinical course of the ventilated neonates. This might raise several questions about the need of early medical cardiac or respiratory support for those who are expected to require long periods of intubation, this agree with Awada et al who had 22 cases on MV, out of 48 RD cases [10.].

In our study, 16 % cases of the ventilated cases required use of inotropes (mainly dopamine) for hypotension and hypoperfusion. Cardiac troponin T(CTnT) levels were significantly higher in cases received inotropes than cases who did not receive inotropes ($p<0.001$). Troponin was measured before starting inotropes to exclude their possible effect on cTnT concentrations. The elevated levels suggest the presence of cardiac injury that led to impaired contractility and low cardiac output, either due to the primary pulmonary disease or the mechanical ventilation itself, our findings agreed with others [9- 11].

However the study of Trevisanuto et al [8] who studied CTnT in preterm neonates with RDS compared to preterm without RDS. They found no significant relation between troponin T level and hypotension in RDS cases or the use of inotropes. [8]

In our study, 14 % cases died, while 36 cases survived and were discharged from NICU. We found CTnT levels were significantly higher in cases who died than in cases who survived ($p<0.001$) (mean was 0.420 and 0.1 14 respectively). This result support the possibility to use CTnT level as a predictor or an early marker for clinical course of ventilated neonates.

These results were in keeping with Awada et al. ***[10]***, who found cTnT concentrations in ventilated, hypotensive infants who died were higher than others of the sick group. Also, was agreed with us in finding the sick hypotensive infants who died had higher cardiac troponin T concentrations than the sick hypotensive infants who survived [10].

In contrast to our results, Fahmey et al. found no significant difference in CTnT levels between RD cases who died and those who survived ***[11].*** Unlike healthy adults- where cardiac troponin T is undetectable- our study revealed that CTnT was in detectable concentrations in healthy neonate ranging from 0.010 to 0.072 ng/ml with mean value 0.034±0.019, however CTnT was undetectable in 14 healthy neonates.

Conclusion:

Cardiac troponin T level was found significantly higher in RD cases than in healthy neonates and was associatd with the severity of disease in the cases .As higher levels of CTnT were detected in cases needed mechanical ventilation and was significantly higher than those who

were not ventilated and also was associated with longer duration on MV . Among ventilated cases CTnT was higher in hypotensive cases who required the use of inotropes .Also, it was higher in cases who died than survived cases .These results support the possibility to use CTnT level as a predictor of cardiac compromise in RD cases and as an early predictor of clinical course and disease severity in those cases.

Study limitations

We aware that our study may have some limitations. The first is the small sample size. The second is that we did not perform echocardiogram to assess myocardial function.

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