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Comparison of serum Cardiac Troponin I and Creatine Kinase MB concentrations in Perinatal Asphyxia

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Abstract

Background: *Perinatal asphyxia considered one of the most important causes of neonatal morbidity and mortality. Perinatal asphyxia results in hypoxic and/or ischemic injuries to various organs of the newborn mainly kidneys, heart, lungs, liver and brain. Myocardial dysfunction is relatively common in asphyxiated neonates. Creatine Kinase MB had been the marker protein of choice for diagnosis of acute myocardial injury for many years. Recently, cardiac troponin I has been an area of interest in the assessment of the magnitude of myocardial injury in asphyxiated neonates.*

Aim of the work: *This study aimed to compare serum Creatine Kinase MB (CK-MB) concentrations and cardiac troponin I(cTnI) concentrations among asphyxiated neonates in relation to other clinical and laboratory findings as useful markers of myocardial injury caused by perinatal asphyxia.*

Patients and Methods: *This study included 40 asphyxiated neonates according to AAP & ACOG,(2006)and 20 healthy full term neonates as controls. Both asphyxiated and healthy neonates subjected to Umbilical cord blood gases, cardiac troponin I and CK-MB. During first 24 hrs was done, After 24 hrs CRP, serum electrolytes (Na, K, and Ca), renal and liver function tests.*

The results: *The asphyxiated neonates had lower Apgar scores at 1,5,10 minutes than control neonates. Also asphyxiated neonates had moderate to severe metabolic or mixed acidosis, elevated both renal and liver*

function tests and hyperkalemia. Also they had thrombocytopenia, hyponatreamia and hypocalcaemia. These laboratory changes were severe in those who died than those who recovered. Asphyxiated neonates had significantly higher concentrations of cTnI and CK-MB than controls. There were a highly significant negative correlation between cTn I and Apgar scores in the asphyxiated groups at 1 min, 5 min and 10 min. There were a highly significant negative correlation between serum creatinine kinase and Apgar score at 5 min and 10 min. There were significant negative correlation between cTnI, and pH, PO2 and HCO3 in asphyxiated neonates. There were a significant positive correlation between cTnI and PaCO2. Also there was a highly significant negative correlation between CK.MB and both pH and HCO3. There were a significant negative correlation between cTnI and both hemoglobin & platelet count. Also, there were significant positive correlation between cTnI, CK-MB and WBCS count. There were a positive correlation between cTnI and CK.MB. Serum CK.MB had a significant positive correlation with serum creatinine. Serum cTnI concentrations were significantly higher in asphyxiated who died than those who survived. The serum cTnI had a sensitivity of 97% and specificity of 95%. While serum CK.MB had a sensitivity of 85% and specificity of 89% in prediction of perinatal asphyxia.

Conclusion: *CK MB was elevated in some healthy neonates, so it is not distinguish infants with and without asphyxia. Cardiac troponin I was more sensitive and specific than CK-MB in prediction of morbidity and mortality of perinatal asphyxia and can be used as a useful proxy marker for the anticipated severity of myocardial dysfunction.*

Key words: *Cardiac troponin I; CK-MB enzyme; myocardial damage; perinatal asphyxia.*

Introduction

Perinatal asphyxia defined as an impairment of exchange of respiratory gases during the perinatal period results in hypoxic and/or ischemic injuries to various organs of the newborn as kidneys, heart, lungs, liver and brain [(1)]. Myocardial dysfunction is relatively common with reported incidence of 26 to 78% [(2)]. 75% of severely asphyxiated & 15% of moderately asphyxiated newborns was found in shock. Pansystolic murmur was present in 20% of newborns with severe asphyxia & congestive cardiac failure in 15% newborns with severe asphyxia [(3)]. Arrhythmias secondary to focal cardiac lesion are also common [(4)]. Laboratory usage of Cardiac markers help in diagnosis of myocardial dysfunction, Creatine Kinase had been the marker protein of choice for diagnosis of acute myocardial injury for many years [(5)]. However, CK MB also increased in patient with acute or chronic muscle disease in absence of detectable cardiac injury [(6)]. Recently, cardiac treponin (T, I, C) has been an area of interest. Cardiac treponin I is an inhibitory protein complex located on the actin filament in all striated muscles [(7)]. Cardiac troponin represents a sensitive and specific marker in the assessment of the magnitude of myocardial injury in neonatal populations [(8)].

Aim of the work

This study aimed to compare serum Creatine Kinase MB (CK-MB) concentrations and cardiac troponin I (cTnI) concentrations among asphyxiated neonates in relation to other clinical and laboratory findings as useful markers of myocardial injury caused by perinatal asphyxia.

Patients and Methods:

This study was carried out from April 2014 to January 2015 at Menoufiya University Hospital on 60 neonates arranged in 2 groups:

Group 1: Included forty neonates (20 males and 20 females) suffered from periatal asphyxia and admitted to neonatal intensive care unit. 13 neonates were preterms and 27 neonates were full terms. Their gestational ages ranged between 35-40 weeks. Ten neonates were delivered vaginally and 30 neonates by cesarean section.

Group 2**:** Included twenty healthy neonates. Thirteen males and 7 females. All were full terms and their gestational ages ranged between 37-40 weeks. Five Neonates were delivered vaginally and 15 neonates by cesarean section.

****Parental informed written consents and approval of local research ethics committee were obtained.

Diagnosis of perinatal asphyxia was done according to the criteria of American Academy of Pediatrics (AAP, 2006) and the American College of Obstetrics and Gynecology (ACOG, 2006). These criteriae are: Profound metabolic or mixed acidemia (pH<7.00) on an umbilical cord arterial blood sample, persistence of an apgar score of 0 to 3 at >5minutes, clinical neurologic squeals in the immediate neonatal period (e.g., seizures, hypotonia, hypertonia or coma) and evidence of multi organ system dysfunction in the immediate neonatal period [(9)].

Exclusion criteria:

- Congenital hypothyroidism.
- Congenital heart diseases.
- Inborn errors of metabolism.
- Congenital malformations
- Surgical problems.
- Neonatal sepsis.

All neonates in both groups were subjected to the following:-

1-Detailed perinatal history with special emphasis on:-

- Gestational age assisted by new ballard score.
- Maternal age in years.
- Maternal diseases as DM and Hypertension.
- Labour events: prolonged, obstructed, abnormal presentations, passage of meconium, premature rupture of membranes, drugs intake during pregnancy, maternal infections, mode and place of delivery,

2-Thorough clinical examinations including :-

- Sex: male or female.
- Birth weight in kilograms.
- Apgar score at 1,5,10 and 15 minutes after labor.
- Neurological assessment.
- Chest examination.
- Cardiovascular assessment.

3-Investigations including :-

1-From the umbilical cord:

-Arterial blood gases (ABG): Sample was taken from umbilical artery, collected into heparinized syringe and measured by Blood Gas Analyzer *"Bayer 348"* machine**.**

-Serum Creatine Kinase (CK MB): Quantitative determination by using of *Vidas®cTnI ultra* machine.

-Serum cardiac treponin I: Immunoenzymometric assay by using of *Vidas®cTnI ultra* machine.

2-During first day:

-Complete blood count (CBC): Venous blood sample was collected in tubes with EDETA (ethylene diamine tetra-acetic acid) and counted by using of Automated Cell Counter *"ABX Pentra 60"* machine**.**

3- After 24 hrs age:

-C-reactive protein (CRP): Venous sample was collected in a plain tube without additives or gel barrier. Blood was allowed to clot. Then centrifuged to separate the serum from the cells. Quantitative determination by using of full automated chemical analyzer *"Dropbox"* machine.

-Serum Electrolytes: measurement of Na, K and Ca levels. Venous sample was collected in a plain tube without additives or gel barrier. Blood was allowed to clot. Then centrifuged to separate the serum from the cells. Then test was done by using of fully automated chemical analyzer *"A 25"* machine.

-Kidney function tests: measurement of blood urea nitrogens (BUN) and creatinine levels. Venous sample was collected in a plain tube without additives or gel barrier. Blood was allowed to clot. Then centrifuged to separate the serum from the cells. Then test was done by using of fully automated chemical analyzer *"AU 480"* machine.

-Liver function tests: measurement of Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT) levels. Venous sample was collected in plain tube without additives or gel barrier. Blood was allowed to clot. Then centrifuged to separate the serum from the cells. Test was done by using of fully automated chemical analyzer *"A 25"*machine.

Statistical analysis: Data were collected, tabulated, statistically analyzed using an IBM personal computer with Statistical Package of Social Science (SPSS) version 20 [(10).]

P values of <0.05 and <0.001 were considered statistically significant and of high statistical significance respectively.

Table (1): Demographic data among studied groups (N=60):

Fetal and maternal data	Studied groups				Test of significance	P value
	Group I (n=40)		Group II (n=20)			
	No.	%	No.	%		
Gender:						
- Male	20	50	13	65	χ^2 = 1.21	0.27
- female	20	50	7	35		
Labour						
- CS	30	75	15	75	χ^2 = 0.0	1
- SVD	10	25	5	25		
Maternal associated disease:						
- Hypertension	6	15	0	0	χ^2 = 3.35	0.18
- Diabetes mellitus	2	5	1	5		
- No	32	80	19	95		
Complications:						
- Prenatal hemorrhage	7	17.5	0	0	χ^2 = 22.9	**0.001***
- PROM	9	22.5	0	0		
- Passage of meconium	10	25	0	0		
- No	14	35	20	100		
Fetal distress (showed by CTG)						
- Yes	40	100	0	0	χ^2 = 60	**0.003***
- No	0	0	20	100		
Gestational age(wks):						
- Full term ≥37wks	27	67.5	20	100	χ^2 = 8.29	**0.001***
- Pre term <37wks	13	32.5	0	0		
($\bar{X}$ ±SD)	37.7±2.16		39.1±0.96		t-test= 3.4	**0.01***
Range	(35 - 40)		(38.1-40)			
Body weight (Kg)						
($\bar{X}$ ±SD)	2.71±0.84		2.98±0.38		t-test= 1.6	0.18
Range	(1.87 - 3.55)		(2.6-3.36)			
Outcome:						
- Died	5	12.5	0	0	Fisher's exact= 2.72	0.09
- Survivors	35	87.5	20	100		

PROM: premature rupture of membranes.

Table (2): Clinical findings among studied groups (N=60):

Clinical examinations	Studied groups				Test of significace	P value
	Group I (n=40)		Group II (n=20)			
	No.	%	No.	%		
Parameters of Apgar Score at 1 min:						
1-Heart rate:*						
-Normal(110-160b/m)	13	32.5	20	100	χ^2	**0.004***
-Bradycardia(<100b/m)	27	67.5	0	0	23.3	
2-Respiratory rate: *						
-Normal(40-60c/m)	10	25	20	100	χ^2	**0.001***
-Bradypneia(<40c/m)	24	60	0	0	15.2	
-Apnea	6	15	0	0		
3-Color:						
-Blue or pale	10	25	0	0	χ^2	**0.001***
-Pink body & blue extremities	30	75	3	15	47.7	
-Pink	0	0	17	85		
4-Reflexes :						
-Poor	31	77.5	0	0	χ^2	**0.001***
-Absent	6	15	0	0	48.2	
-Intact	3	7.5	20	100		
5-Muscle tone:						
-Hypotonia	20	50	0	0	χ^2	**0.001***
-Flaccid	7	17.5	0	0	23.8	
-Normal	13	32.5	20	100		
Apgar score 1 min. ($\bar{X}$ ±SD) range	0.35±0.53 (0 – 2)		8.75±0.78 (8 – 10)		t-test= 30.2	**0.001***
Apgar score 5 min. ($\bar{X}$ ±SD) range	3±0.51 (2 – 4)		9.25±0.63 (9-10)		t-test= 38.1	**0.001***
Apgar score 10 min. ($\bar{X}$ ±SD) range	7.54±1.46 (6 - 9)		10.25±0.50 (9 -10)		t-test= 7.62	**0.001***
Apgar score 15 min. ($\bar{X}$ ±SD) range	9.8±0.26 (9 - 10)		10.25±0.50 (9 -10)		t-test= 1.32	0.23

***= Gomella, (2009).**

Table (3): Laboratory findings among the 2 studied groups (N=60):

Laboratory findings	Studied groups		t-test	P value
	Group I (n=40)	Group II (n=20)		
	$\bar{X}$ ±SD	$\bar{X}$ ±SD		
pH (7.35-7.45)	6.95±0.09 (7.0 – 7.18)	7.33±0.04 (7.3 -7.4)	10.3	**0.001***
PCO_2 (35-46mmHg)	83.4±10.5 (52.3 – 98)	37.7±4.2 (32.1-48)	23.7	**0.001***
PO_2 (80-100 mmHg)	33.9±9.1 (19.6-66.5)	90.4±3.2 (83.3 -97)	34.8	**0.001***
HCO_3 (17-24 mEq/L)	10.87±4.18 (6.7-15.2)	18.4±0.8 (17.8 -20.1)	8.2	**0.001***
WBCs (5.3-11.5× $10^3/mm^3$)	15.7±10.1 (3.2 -25.8)	7.26±1.1 (5.3 -10.3)	5.2	0.31
Total PMN(7.8-14.5/mm³)	*12.3-14.2*	*11.6-12.3*	*1.3*	*0.21*
Immature PMN(0.5-1.5)	*0.9-1.4*	*0.7-1.1*	*0.5*	*0.07*
I:T ratio(0.120)	*0.09*	*0.05*	*0.04*	*0.6*
I:M ratio(≥0.3)	*0.33*	*0.41*	*0.01*	*0.31*
Degenerative changes in PMN(0.3)	*0.2*	*0.1*	*0.10*	*0.2*
RBCs (3.4-5.4× $10^6/mm^3$)	3.99±2.7 (2.2 -19.9)	3.85±0.89 (0.5 -5)	0.25	0.25
HGB (16.5-19.5g/dl)	18.3±1.6 (13.4 -20.8)	18.8±1.0 (16.5 -20)	1.3	0.79
Platelets (150-350× $10^3/mm^3$)	132.9±29.7 (38.2 -182)	153.5±5.9 (145 -164)	4.1	**0.001***
BUN(22-46 mg/dl)	79.2±16.8 (49 -118)	25.3±7.8 (14-45)	16.1	**0.007***
Creatinine(0.6-1.4 mg/dl)	1.70±0.2 (2.1 -1.7)	0.72±0.3 (0.02 -1.2)	12.2	**0.001***
Aspartate amino transferase. (AST:≤45 IU/L)	81.6±21.2 (32.1 -121)	37.7±4.9 (29 -45)	11.6	**0.001***
Alanine amino transferase (ALT: 5-35 IU/L)	48.7±13.7 (23 -82)	18.1±8.1 (4 -34)	8.5**	**0.001***
CRP (≤3 mg/dl)	2.6±0.3 (2.3 - 2.9)	0.56±0.59 (0.01 -2)	1.1**	0.13
Sodium (Na:133-146 mEq/L)	130.6±3.4 (123 -136)	134.2±1.7 (132 -138)	5.1	**0.004***
Potassium (K :3.7-5.9 mEq/L)	5.58±0.45 (4.6 -6.8)	4.35±0.88 (0.90 – 5)	19**	**0.001***
Calcium(Ca:7.4-13.8 mg/dL)	7.15±0.63 (5.8 – 8.1)	8.72±0.83 (7.9 -9.4)	11.4	**0.01***
CK.MB (normal value ≤ 25 U/L)	37.7± 15.4 (22.3 -53.1)	18.36±7.7 (10.66-25.06)	7.9	**0.001***
Cardiac troponin I (cTnI:normal value <0.01ng/ml)	5.67±6.71 (0.01-20.9)	0.00±0.01 (0.00-0.01)	47.5**	**0.001***

BUN: Blood urea nitrogen. - CRP: C reactive protein. - CK MB :Creatine kinase myocardial bound.

Table (4): Laboratory findings among survivors and died neonates of asphyxiated group (n=40).

Laboratory findings	Studied group		Man-Whitney test	P value
	Survivors (n=35)	Died* (n=5)		
	$\overline{X}$ ±SD	$\overline{X}$ ±SD		
pH (7.35-7.45)	7.09±0.09	6.95±0.09	6.1	**0.001***
PCO_2 (35-46mmHg)	82.5±10.1	89.7±12.2	1.46	0.15
PO_2 (80-100 mmHg)	34.8±9.29	28.3±6.3	1.51	0.14
HCO_3 (17-24 mEq/L)	12.2±5.89	9.6±4.7	28**	**0.01***
WBCs ($5.3-11.5\times 10^3/mm^3$)	14.1±5.7	24.3±3.1	21.5	0.14
RBCs ($3.4-5.4\times 10^6/mm^3$)	3.68±0.77	6.14±7.71	53.5	0.16
HGB (16.5-19.5g/dl)	18.6±1.29	15.6±2.42	4.04**	**0.001***
Platelets ($150-350\times 10^3/mm^3$)	139.1±23.1	78.3±27.5	2	**0.002***
CK.MB (IU/L) (normal value ≤ 25 U/L)	37.7± 15.4	39.7±22.6	54.1	0.14
cTnI (ng/ml) (normal value <0.01ng/ml)	4.66±5.62	19.6±1.5	8	**0.001***

****t-test**

*Died neonates was died during first day of life, so other investigations were not done.

Table (5): Pearson correlation between serum cardiac troponin I & CK-MB and gestational age, body weight and Apgar scores of asphyxiated group (N=40):

	cTn I		CK.MB	
	r	P value	r	P value
Apgar score 1min	-0.34	**0.04***	-0.23	0.14
Apgar score 5min	-0.55	**0.003***	-0.33	**0.03***
Apgar score 10min	-0.64	**0.001***	-0.47	**0.002***

Table (6): Pearson correlation between serum cardiac troponin I & CK-MB and laboratory findings of asphyxiated group (N=40):

Laboratory findings	cTn I		CK.MB	
	r	P value	r	P value
pH (7.35-7.45)	-0.87	**0.001***	-0.57	**0.001***
PCO_2(35-46mmHg)	0.32	**0.04***	0.27	0.08
PO_2(80-100 mmHg)	-0.33	**0.04***	-0.17	0.27
HCO_3(17-24mEq/L)	-0.51	**0.001***	-0.43	0.006*
WBCs (5.3-11.5× $10^3/mm^3$)	0.36	**0.02***	0.35	**0.03***
RBCs(3.4-5.4× $10^6/mm^3$)	-0.29	0.07	-0.28	0.08
HGB(16.5-19.5g/dl)	-0.32	**0.04***	-0.16	0.56
Platelets(150-350× $10^3/mm^3$)	-0.40	**0.01***	-0.26	0.11
BUN (22-46 mg/dl)	0.02	0.89	0.08	0.61
Creatinine(0.6-1.4 mg/dl)	0.28	0.10	0.37	**0.02***
AST (≤45 IU/L)	0.05	0.74	-0.03	0.82
ALT (5-35 IU/L)	0.17	0.32	-0.19	0.26
CRP (≤3 mg/dl)	0.23	0.18	0.17	0.31
Na (133-146 mEq/L)	-0.05	0.76	-0.08	0.63
K (3.7-5.9 mEq/L)	-0.12	0.13	-0.06	0.71
Ca (7.4-13.8 mg/dL)	-0.14	0.42	-0.18	0.28
CK.MB(normal value ≤ 25 U/L)	0.65	**0.001***		
cTn I (normal value <0.01ng/ml)			0.65	**0.001***

Table (7): Diagnostic validity of serum cardic troponin I and CK-MB in diagnosis of perinatal asphyxia (ROC curve)

	Cut off point	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Diagnostic accuracy
cTnI	0.013	97	95	93	90	96
CK.MB	12.8	85	89	94	74	86

Discussion

Our study showed that, there was no significant difference between both groups regarding to their sex and body weights.

As regard to gestational age, Mean gestational age of asphyxiated group was lower than control group (37.7±2.16 and 39.1±0.96 respectively) as we had 13 preterm asphyxiated neonates while all controls were full terms. This agrees with Nicoletta et al., [11] who found that the incidence of perinatal asphyxia is higher in preterm neonates. Also Lee et al., [12] described the prematurity as one of the risk factors of perinatal asphyxia.

As regard to mode of delivery, CS deliveries were more than vaginal deliveries in both studied groups. This agreed with Szymankiemicz et al., [13] who found that perinatal asphyxia were common in CS deliveries than vaginal deliveries. Also both Palsdottir et al., [14] and Gomella et al., [15] described that the indications for CS delivery are the risk factors of perinatal asphyxia. But not agreed with Kosika et al., [16] who found that perinatal asphyxia was common in vaginal deliveries rather than CS.

As regard to perinatal history, there was a highly significant difference between both studied groups. Maternal diseases (HTN, DM), PROM, prenatal hemorrhage, passage of meconium and fetal distress were significantly high in asphyxiated neonates (P<0.001). This agrees with Adcock et al., [17] who described maternal diseases (HTN, DM), PROM, prenatal hemorrhage, passage of meconium and fetal distress as risk factors of birth asphyxia.

In our study, There was a high significant difference between both groups as regarding neonatal deaths, which were (12.5%) in asphyxiated neonates and (0%) in healthy neonates. This was agreed with Chnayna et al., [18] who considered perinatal asphyxia one of the most important causes of neonatal morbidity and mortality.

There was a high significant difference between both groups regarding Apgar scores at 1, 5 and 10 minutes. It was lower in asphyxiated group than normal neonates (P <0.001). This agrees with Mahmud et al [19] which found the same result in their study.

As regard to neonatal reflexes, asphyxiated neonates had a highly significant difference

between them and control group. This agreed with Volpe et al., [20] who found that the CNS (accompanied by hypotonia, abnormal reflexes, absent /weak suck) was the most affected organ in asphyxiated neonates

As regard to cardio-respiratory affection, incidence of bradycardia (67.5%) and bradyapneia (60%) were higher in asphyxiated neonates compared to that in control group (0%).This agrees with Levene and DeVries [21] who found that severe asphyxia cause myocardial ischemia that typically presents as impaired myocardial contractility, decreased cardiac output, bradypneia, bradycardia and hypotension.

Mean number of WBCs is higher in asphyxiated neonates than control neonates, but it was within normal range in both groups. Its normal elevation in asphyxiated neonates may be attributed to asphyxia or to presence of 13 preterms who normally had WBCs count up to 30000 in the first day of life. But its normal elevation do not due to sepsis as I:T ratio were within normal with other hematological sepsis score.

There were mild thrombocytopenia in asphyxiated neonates and normal platelets count in control neonates. This agrees with Castle V et al., [22] who considered perinatal asphyxia an associated risk factor for thrombocytopenia.

Mean of hemoglobin and platelets of died neonates were significantly lower than that of survivor asphyxiated neonates ($P<0.001$). Gomella et al., [23] agreed with the present results and said that the severe asphyxia may leads to anemia and thrombocytopenia caused by prenatal bleeding (as rupture uterus, placental separation or cord prolapsed), neonatal intracranial hemorrhage or disseminated intravascular coagulopathy.

Asphyxiated neonates had moderate to severe metabolic or mixed acidosis while control neonates had mild metabolic acidosis which is compensated in a big number of them. This agrees with the criteria of American Academy of Pediatrics and the American College of Obstetrics and Gynecology (AAP and ACOG) [24] to confirm the occurrence of perinatal asphyxia and predict the possibility for resultant neurologic deficit, from which, profound metabolic or mixed acidemia ($pH<7.00$) on the umbilical arterial blood sample.

The acidosis was severe in those who died than recovered. Ambalavanan, [25] agrees with the present results and stated that the mortality was enhanced by severity of metabolic acidosis.

Liver and renal function tests were normal in control neonates and were impaired in asphyxiated neonates. This agrees with Durkan and Alexander, [26] who found that acute kidney injury (AKI) is a common consequence of perinatal asphyxia, occurring in up to 56% of these infants. Also Gupta et al., [27] found that asphyxiated neonates had elevated urinary excretion of protein and uric acid, and may correlate with disease severity. Shah and Perlman, [28] found increased levels of AST and ALT during the first 72 hours after birth in asphyxiated newborns.

There was hyponatremia in asphyxiated neonates and normal serum Na^+ level in controls.

This agrees with Kliegman, [29] who described syndrome of Inappropriate ADH secretion (SIADH) with resulting hyponatreamia as one of metabolic complications of perinatal asphyxia.

There was hypocalcaemia in asphyxiated neonates and normal serum ca^{++} level in controls. This agrees with Gomella et al., [30] who found that hypocalcaemia was secondary to impaired renal function and transient reduction in parathyroid hormone secretion in asphyxiated newborns.

There was hyperkalemia in asphyxiated neonates and normal serum K^{+} level in control. This agrees with study of Shah et al., [31] who found elevated serum k in asphyxiated neonates reflecting effects of asphyxia on kidney function. El Naggar [32] explained that severe metabolic acidosis is associated with hyperkalemia.

Mean CK MB and cTnI in asphyxiated neonates were significantly higher than that of healthy control neonates. This agrees with Rajakumar et al., [33] which found elevation of both CK MB and cTn I in asphyxiated newborns.

There were a highly significant negative correlation between both (CK MB and cTnI) and Apgar scores (P<0.001). Also there was no significant correlation between both (CK MB and cTnI) and gestational age and weight in the asphyxiated group. This agrees with Turker et al., [34] who found that both (CK MB and cTnI) in the cord blood are not affected by gestation, birth weight, sex, or mode of delivery but are significantly high in the critically ill with low Apgar scores.

Our results showed a highly significant negative correlation between CK MB and both pH and HCO_3 (P<0.001). This agrees with Boo et al., [35] who found that CK MB was elevated in asphyxiated neonates with metabolic acidosis.

Also, there was a significant positive correlation between CK MB and serum creatinine in asphyxiated neonates (P<0.05).This agrees with Asknazi et al.,[36] who found that CK-MB may be elevated not only when there is myocardial injury but also when there is associated renal injury or when only renal injury occurs.

There was also, a significant negative correlation between cTn I and both Hgb & platelets count. This agrees with Caliskan et al., [37] who found that some asphyxiated newborns had anemia. Also agrees with Castle V et al., [38] who considered perinatal asphyxia an associated risk factor for thrombocytopenia.

There was a significant negative correlation between both (CK MB & cTnI) and pH, PaO_2 and HCO_3. There was a significant positive correlation between cTnI and $PaCO_2$.This reflects the effect of asphyxia in developing acidosis and CO_2 retention that lead to increased risk of myocardial injury and release of its markers. This agrees with Turker et al., [39] who found that cTnI was significaly correlated with pH, PaO_2 and HCO_3 in asphyxiated neonates. Also agrees with Gomella et al., [40] who described metabolic acidosis and hypoxia as complications of perinatal asphyxia.

Both CK MB and cTnI showed increased levels in died neonates, but the elevation of serum

cTn I was significant. This agrees with Rajakumar et al., [41] who found that all died asphyxiated neonates had cardiac involvement and elevated serum levels of both CK MB and cTn I. Boo NY.et al., [42] who concluded that unlike CK-MB, serum cardiac troponoin I concentrations are significantly higher in died asphyxiated infants. Also Roopa et al., [43] found that died cases of their study had significantly high mean cTnI value compared to improved cases, So they considered cTnI a good predictor of the outcome of the asphyxiated neonates.

In our study, we found that CK MB elevated in some healthy control cases. This denotes that CK MB was not specific only for myocardial injury in asphyxiated neonates. This agrees with Mollar et al., [44] who found that cord blood levels of creatinine kinase and its MB fraction do not distinguish infants with and without asphyxia. Also Adams et al., [45] found that CK MB increased in patient with acute or chronic muscle disease in absence of detectable cardiac injury.

Our study showed that the sensitivity of CK MB=85% and its specificity=89%, while the sensitivity of cTnI=97% and its specificity =95%. This means that cTnI is more sensitive and specific than CK MB in prediction of mortality and morbidity of perinatal asphyxia. This agrees with Shastri et al., [46] and Aleksandra et al., [47] who found that cTnI concentrations correlated strongly with severity of asphyxia and considered that early cTnI concentrations may provide a useful proxy marker for the anticipated severity of myocardial dysfunction.

Conclusion

CK MB was elevated in some healthy neonates, so it is not distinguish infants with and without asphyxia. Cardiac troponin I was more sensitive and specific than CK-MB in prediction of morbidity and mortality of perinatal asphyxia and can be used as a useful proxy marker for the anticipated severity of myocardial dysfunction.

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References

1. Herrera M, Morales P, Leyton L, et al. Perinatal asphyxia: current status and approaches towards neuroprotective strategies, with focus on sentinel proteins. Neurotox Res. 2011; 19:603–27.
2. Shah P, Ohlsson A, Perlman M. Hypothermia to treat neonatal hypoxic ischemic

encephalopathy: A systemic review. Arch. Pediatr. Adolesc. Med.2012; 161:951–58.

3. Rowe R, Hoffman T. Transient myocardial ischemia of the newborn infant: a form of severe cardio respiratory distress in full tern infants. J Paediatr 1972; 81:243-50.
4. Palmer J. Perienatal Hypoxic-Ischemic Disease URL: Therapeutic approaches against micro vascular injury, and role of neutrophils, PAF, and free redicals. CliniPerinatol 2004; 22: 481- 517.
5. Toyota N, Shimada Y. Differentiation of troponin in cardiac and skeletal muscles in chicken embryos as studied by immune fluorescence microscopy. J cell Biol.1981; 91:497-504.
6. Adams J, Bodor G, Davila V, et al. Cardiac troponin I. A marker with high specificity for cardiac injury. Circulation 1993; 88:101–106.
7. Trevissanuto D, Picco G, Golin R, et al. Cardiac Troponin I in Asphyxiated Neonates. Biol Neonate 2006; 89:190-93.
8. Correale M, NunnoL, Lava R, et al. Troponin in newborn and pediatric patints. Cardiovascular & Hematological agents in Medical Chemistry 2009 October4, 7; 270-78.
9. American Academy of Pediatrics and American College of Obstetrics and Gynecology. Committee on fetus and newborn, and Committee on obstetric practice. Pediatr: 2006; 117:1444-47.
10. Roster, Band G. Use of the Mann-Whitney-test for clustered data. Statistics in Medicine 1999; 18:1387 –1400.
11. Nicoletta I, Maria B, Demetrios G, et al. Perinatal changes of cardiac troponin I in normal and intrauterine growth restricted pregnancies. Hindawi Publishing Corporation 2007; 53921: 1-5.
12. Lee C, Mullany C, Tielsch M, et al. Risk factors for neonatal mortality due to birth asphyxia in Southern Nepal. Pediatric 2007, Vol. 121 No. 5, pp. 1381-1390.
13. Szymankiewicz M, Matuszczak M, Hodgman J, et al. Usefulness of cardiac troponin T and echocardiography in the diagnosis of hypoxic myocardial injury of full-term neonates. Biol Neonate 2005; 88:19-23.
14. Palsdottir K, Thorkelsson T, Hardardottir H, et al. Birth asphyxia neonatal riskfactors for hypoxia ischemic encephalopathy. Laeknabladid 2007; 93:669-73.
15. GomellaTl, Cunningham MD. Perinatal asphyxia. In: Gomella TL, Cunningham MD, Eyal FG and Zenk KE.(Eds). Neonatology; Management, procedures, On-call problems, Diseases and Drugs. (6th edition), Lange 2009; pp. 624-35.
16. Koscica K, Bebbington M, Bernstein P, et al. Are neonatal serum cTn levels affected by vaginal or caesarean delivery? Am J Perinatol 2004; 21:31-34.
17. Adcock LM, Stark AR. Systemic effects of pe rinatal asphyxia. Up-To Date version 18.3. Internet 2010 [updated 2010 August 23; cited 2010 Dec 15].
18. Chnayna J, Truttmann A. Perinatal asphyxia and neonatal hydroephrosis. Rev Med Suisse 2010 Jan 13; 6:63-6.

19. Mahmud T.A., El Basiony M.E., Al Azab S.A. Cardiac troponin I as early predictor of perinatal asphyxia. Menoufiya Medical Journal, 2014, Volume 2013, Vol 26, Issue 2 p. 145-150.
20. Volpe JJ. Hypoxic –ischemic encephalopathy: biochemical and physiological aspects In: volpe JJ, ed. Neuology of the Newborn. Philadelphia, PA: Elsevier Saunders 2008; 331- 94.
21. Levene MI, deVries LS. Hypoxic-ischemic encephalopathy. In: Fanaroff & Martin's Neonatal-Perinatal Medicine: Diseases of the Fetus and Infant, 9th ed, Martin RJ, Fanaroff AA, Walsh MC (Eds), Elsevier, St.Louis 2011. p.952.
22. Castle V, Andrew M, Kelton J, et al. Frequency and mechanism of neonatal thrombocytopenia. J Pediatr 1986; 108: 49.
23. GomellaTl, Cunningham MD. Perinatal asphyxia. In: Gomella TL, Cunningham MD, Eyal FG and Zenk KE.(Eds). Neonatology; Management, procedures, On-call problems, Diseases and Drugs. (6th edition), Lange 2009; pp. 624-35.
24. American Academy of Pediatrics and American College of Obstetrics and Gynecology: Committee on fetus and newborn, and Committee on obstetric practice. Pediatr. 2006; 117:1444-47.
25. Ambalavanan N. Predicting outcomes of neonates diagnosed with hypoxic ischemic encephalopathy. Pediatrics 2006; 118:2084-2039.
26. Durkan A, Alexander R. Acute kidney injury post neonatal asphyxia. The Journal of 20 Pediatr.2011; 158:29-33.
27. Gupta B, Sharma P, Bagla J, et al. Renal failure in asphyxiated neonates. Indian Pediatr 2005; 942: 28.
28. Shah P, Perlman M. Birth Asphyxia and Multi organ dysfunction. In: David TJ, editor. Recent Advances in Paediatrics23.RSM press. 2006; 113-26.
29. Kliegman RM, Stoll BJ. Fetus and neonatal infant. Nelson Text Book of Pediatric, Philadelphia, 16th edition, WB Saunders Co., 2008; 451.
30. GomellaTl, Cunningham MD. Perinatal asphyxia. In: Gomella TL, Cunningham MD, Eyal FG and Zenk KE.(Eds). Neonatology; Management, procedures, On-call problems, Diseases and Drugs. (6th edition), Lange 2009; pp. 624-635.
31. Shah G, Agrawal J, Mishra O, et al. Clinical profile of birth asphyxia in Rajshahi Medical College Hospital. TAJ 2012; 18(2):106-108.
32. El Naggar M. Electrolyte disorder, hyperkalemia in: Pediatric critical care. (^{2nd} edition) Egypt, Cairo 2006; pp 168.
33. Rajakumar P, Bhat B, Sridhar M, et al. Cardiac enzyme levels in myocardial dysfunction in newborns with perinatal asphyxia. Indian J Pediatr. 2008 Dec; 75(12):1223-5.
34. Turker G, Sarper N, Gokalp A, et al. Early prognostic significance of umbilical cord troponin I in critically ill newborns. J Perinat. Med.2005; 33(1):54-59.

35. Boo N, Hafidz H, Nzwawi H, et al. comparison of serum cardiac troponin T and creatine kinase MB isoenzyme mass concentrations in asphyxiated term infants during the first 48 hrs of life. J pediatr. heal; 41(7): 331-7.
36. Askenazi D, Ambalavanan N and Goldstein S. Acute kidney injury in critically ill newborns: What do we know? What do we need to learn? Pediatr Nephrol 2009; 24:265-74.
37. Caliskan E, Doger E, Cakiroglu Y, et al. Cord blood cTnI and CK MB levels in poor neonatal outcome. J Turkish-German Gynecol Assoc 2006; 7(2)98-102.
38. Castle V, Andrew M, Kelton J, et al. Frequency and mechanism of neonatal thrombocytopenia. J Pediatr 1986; 108:749.
39. Turker G, Sarper N, Gokalp A, et al. Early prognostic significance of umbilical cord troponin I in critically ill newborns. J Perinat. Med.2005; 33(1):54-59.
40. GomellaTl, Cunningham MD. Perinatal asphyxia. In: Gomella TL, Cunningham MD, Eyal FG and Zenk KE.(Eds). Neonatology; Management, procedures, On-call problems, Diseases and Drugs. (6th edition), Lange 2009; pp. 624-35.
41. Rajakumar P, Bhat B, Sridhar M, et al. Cardiac enzyme levels in myocardial dysfunction in newborns with perinatal asphyxia. Indian J Pediatr. 2008 Dec; 75(12):1223-5.
42. Boo N, Hafidz H, Nawawi H, et al. Comparison of serum cardiac troponin I and creatine kinase MB isoenzyme mass concentrations in asphyxiated term infants during the first 48 h of life. J Pediatric Child Health 2008; 41: 331-37.
43. Roopa B, Mangshetty E, Iraganteppa T, et al. Cardiac Troponin-I as marker of myocardial damage in Newborns with Hypoxic Ischemic Encephalopathy. Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 74, December 29; Page: 15482-86.
44. Möller J, Thielsen B, Schaible T, et al. Value of myocardial hypoxia markers (creatine kinase and its MB-fraction, troponin I, QT-intervals) and serum creatinine for the retrospective diagnosis of perinatal asphyxia. Biol Neonate 1998; 73:367.
45. Adams J, Bodor G, Davila V, et al. Cardiac troponin I. A marker with high specificity for cardiac injury. Circulation 1993; 88:101–106.
46. Shastri A, Samasekara S, Muniraman H, et al. Cardiac troponin I concentrations in neonates with hypoxic-ischemic encephalopathy. ActaPaediatr.2012; 1651-2227.
47. Aleksandra M, Jovan L, Sergej M, et al. Prognostic significance of umbilical cord troponin I in critically ill newborns. Prospective study with a control group. Vojnosanit Pregl 2014; 71(2):149–55.