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"Cardiac Functional Status in Asphyxiated Neonates: A measurement of serum Troponin-I and Echocardiographic changes"

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Abstract: *This was an observational prospective experimental study was distributed in Dhaka Shishu Hospital (DSH) from July 2015 to June 2017. Our aim was to observe cardiac functional status in Neonates by measuring of serum Troponin-I and Echocardiographic changes. A total of 75 cases were selected for the study period. The enrolled patients were grouped into HIE Stage-I, HIE Stage-II, and HIE Stage-III. For all patients in each group Level of Cardiac troponin I, ECG changes, and Echocardiographic parameters were observed and recorded.Twenty cases were found to be in HIE Stage-I, twenty-four cases in HIE stage-II and thirty-one Cases in HIE stage-III. Among the neonates with HIE Stage-I, HIE stage-II and HIE stage-III groups with respect to parameters like birth weight, sex, gestational age, crown heel length (CHL), occipital frontal circumference (OFC), maternal age, and antenatal complications.Occurrence of myocardial dysfunction in different stages of HIE. Difference between Stage-I and stage-II was not found significant statistically. Common cardiac abnormalities seen were Pulmonary hypertension, Tricuspid regurgitation, right atrial and right ventricular dilatations, left atrial and left ventricular dilatations and myocardial dysfunctional. Analysis done by Chi squire test revealed that there was significant association myocardial dysfunction with hypoxic ischemic encephalopathy (p-value < .001). Measurement of serum cardiac troponin I and determination of Myocardial performance index (Tei index), both are effective in assessment of myocardial dysfunction in asphyxiated neonates with HIE. Pearson's Correlation Coefficient (r) test was done to see whether the two methods correlate in diagnosing myocardial dysfunction.*

Key Word: *Echocardiographic, Crown Heel Length (CHL), Occipital Frontal Circumference (OFC), Myocardial, Dysfunctional, Serum, Cardiac Troponin.*

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I. Introduction

Perinatal asphyxia affects multiple organ system including myocardium. Cardiac impairment is one of the major contributing factors for neonatal morbidity and mortality from perinatal asphyxia. The more severe the neurological involvement (as evident by increasing stages of HIE) the more probability of myocardial impairment. The reduced myocardial performance following perinatal asphyxia can contribute to increased end-organ damage and thus responsible for increased mortality and morbidity. A better understanding of the cardiac status in patients with perinatal asphyxia done by assessing enzyme cardiac Troponin I level, and detailed Echocardiographic information, would be useful to manage the asphyxiated newborn more precisely and improving their survival. The reduced myocardial performance following perinatal asphyxia can contribute to increase end-organ damage and mortality. Standard methods for cardiovascular monitoring in neonates such as blood pressure, capillary refill time, urinary output, biochemical markers and ECG are of limited value. Reduced myocardial performance after perinatal asphyxia can be assessed by cardiac ultrasound[1]. Cardiac enzyme levels are changed in myocardial dysfunction in newborn with perinatal asphyxia. The enzymes are CK-MB (activity), CK-MB (mass), Cardiac troponin I (cTn I) and troponin T etc. Among them, cardiac troponin I and T are more sensitive and specific than CK-MB (activity), CK-MB (mass) [2, 3, 4]. Previous study showed that Electrocardiographic changes found in 73.3% cases. The most common findings are T-wave inversion followed by T-wave flattening[4]. In different studies, Echocardiographic evaluation of patients with perinatal asphyxia

with HIE found abnormalities in 56.7% cases. These include pulmonary hypertension, Tricuspid Regurgitation (TR), Mitral Regurgitation (MR), myocardial ischemia in the form of Right and Left ventricular hypokinesia. Echocardiographic changes due to myocardial impairment was also reflected by Left ventricular enddiastolic (LVED) diameter and Left ventricular end systolic (LVES) diameter which are expected to be increased. Significant changes also occur in Ejection fraction (EF%) and Fractional shortening (FS%)[5,] Reduced myocardial performance after perinatal asphyxia can be assessed by cardiac ultrasound. Traditionally it is based on left ventricle cavity measures such as fractional shortening and ejection fraction. Some studies have shown a reduction in these indices after perinatal asphyxia[6]. Doppler tissue imaging (DTI) is a relatively new echocardiographic technique that provides quantitative information about myocardium and records systolic and diastolic times and velocities within the myocardium. The myocardial performance index or Tei index is a powerful index that provides evaluation of systolic and diastolic functions at the same time[7]. The diastolic functional parameter of left ventricle is the E-wave and A-wave ratio (E/A ratio) of mitral valves, and that of the tricuspid valves for the right ventricle[8]. Tricuspid annular plane systolic excursion (TAPSE) is an additional echocardiographic tool to analyze right ventricular (RV) systolic function[9]. echocardiographic evaluation of the neonates having perinatal asphyxia with HIE will be useful for proper evaluation and appropriate management, thereby reducing mortality and morbidity. There are very few studies aimed to observe the cardiac status in different stages of HIE among asphyxiated neonates and none with special emphasis on systolic and / or diastolic myocardial dysfunction in our context.

II. Objectives

General objective:
To observe the cardiac function of the cases by measuring serum Troponin-I and Echocardiographic changes.
Specific objectives:
To observe the immediate outcome of the asphyxiated neonates with myocardial impairment.

III. Methodology And Materials

It was an observational prospective study with a sample size 75 carried out at Dhaka Shishu Hospital (DSH) over a period of 2 years from July'2015 to June2017. The aim wasto observe cardiac functional status in Neonates by measuring of serum Troponin-I and Echocardiographic changesTerm neonates with definite history of perinatal asphyxia having no congenital heart disease, congenital infection or other major congenital anomalies were selected purposively for the study. Selected neonates were divided into three groups according to Sarnat&Sarnat staging system of HIE as Group—I (HIE Stage-I), Group—II (HIE stage-II) and Group—III (HIE stage-III). Numbers of cases were 20 in Group-I, 24 in group-II and 31 in group-III. Thorough clinical examination was done at admission and during hospital stay and followed up till discharge or death. Necessary laboratory tests were done to evaluate each patient including assessment of serum troponin- I and Echocardiography. All investigations were done within 72 hours of age of the neonates. Cardiac impairments were evaluated by raised S. troponin I and echocardiographic information. Mortality and duration of hospital stay were recorded. Data was entered into SPSS software and Analysis done to see the association between variables by Chi squire test

IV. Results

Total 75 term neonates diagnosed as perinatal asphyxia with different grades of HIE were selected to evaluate the cardiac status. The enrolled patients were grouped into HIE Stage-I, HIE Stage-II, and HIE Stage-III. For all patients in each group Level of Cardiac troponin I, ECG changes, and Echocardiographic parameters were observed and recorded. The significance of raised Cardiac Troponin I level and Echocardiographic parameters for diagnosis of myocardial dysfunctions were compared among the groups to see whether these two methods correlate in diagnosing myocardial dysfunction. Immediate outcomes were monitored in terms of mortality and prolonged hospital stay. The results of this study are as follows: Table I: Demographic data according to various stages of HIE is presented in table I. No significant difference was seen among the neonates with HIE Stage-I, HIE stage-II and HIE stage-III groups with respect to parameters like birth weight, sex, gestational age, crown heel length (CHL), occipital frontal circumference (OFC), maternal age, and antenatal complications. Table II: Biochemical parameters (cardiac troponin I) in different stages of HIE with perinatal asphyxia shown in table-II**.** Itis seen from the above table that cardiac troponin I level raises as the stages of HIE increases. Comparison of Values in different groups were assessed by applying ANOVA with Post hoc multiple comparison test showing statistically significant difference in values between stage-II and stage-III and stage-III and Stage-I. Difference between Stage-I and stage-II was not found significant statistically. Table III: showing various cardiac changes determined by echocardiography. Common cardiac abnormalities seen were Pulmonary hypertension, Tricuspid regurgitation, right atrial and right ventricular dilatations, left atrial and left ventricular dilatations and myocardial dysfunctional. Figure I: Shows

Echocardiographic Abnormalities among the cases with different stages of HIE. Table IV: Showing association of myocardial dysfunction among the cases with different stages of HIE. Analysis done by Chi squire test revealed that there was significant association myocardial dysfunction with hypoxic ischemic encephalopathy (p-value < .001). Table V: Measurement of serum cardiac troponin I and determination of Myocardial performance index (Tei index), both are effective in assessment of myocardial dysfunction in asphyxiated neonates with HIE. Pearson's Correlation Coefficient (r) test was done to see whether the two methods correlate in diagnosing myocardial dysfunction. Table VI: Risk estimation of myocardial dysfunction for mortality assessed by using odds ratio showed (Table VI) that there was significantly increased risk of mortality in cases with myocardial dysfunction.

Table I: Demographic data according to HIE stages (n=75).

Demographic parameters		HIE stages			Chi Value	F-Value	P-value
		Stage-I	Stage-II	Stage-III			
Sex	Male	9	15	21	.93		.62
	Female	11	9	10			
Gestational age (weeks)		38.40±1.09	38.35± .67	38.15± 2.11		.172	.84
Maternal age	≤ 20yrs	12	14	21	.41		.81
	>20 yrs.	8	10	10			
Parity	Prime	11	9	11	1.77		.41
	Multi	9	15	20			
Birth Weight (Kg)		2.85± .17	2.89± .16	2.97± .17		2.50	.09
Length (cm)		47.98± .56	47.88± .52	47.81± .52		.469	.62
OFC (cm)		33.87± .35	33.96± .31	33.92±.29		.471	.62
Antenatal checkup	Regular	10	8	17	.44		.80
	Irregular	10	17	14			
Mode of delivery	Vaginal delivery	11	15	21	.53		.76
	Caesarian section	9	9	10			

Table II: Comparison of cardiac troponin levels between different stages of HIE(n=75)

	Stage-I (m±SD) (n=20)	Stage-II (m±SD) (n=24)	Stage-III(m±SD) (n=31)	F-Value	P- Value
cTn I (ngm/ml)	.66±.21	.99±.52	1.47±.50	20.33	P = < .001 P1= .058 P2= .001 P3= < .001

$P_{1=}$ Comparison between Stage -I and Stage -II, $P_{2=}$ Comparison between Stage -II and Stage -III, $P_{3=}$ Comparison between Stage -III and Stage -I.

Figure I: Echocardiographic Abnormalities among the cases with different stages of HIE.(n=75).

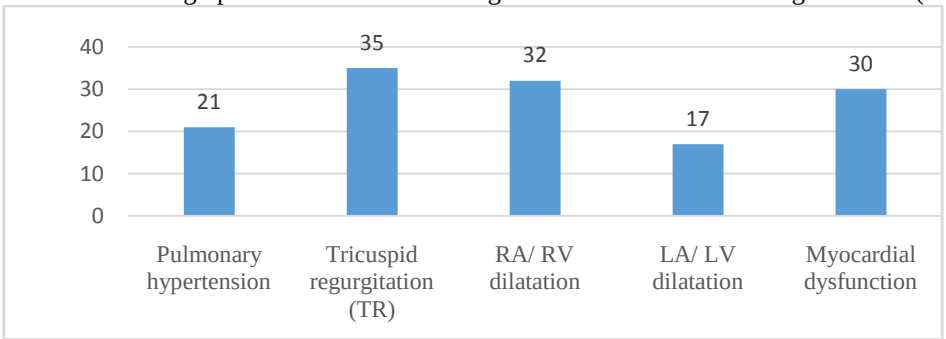

Table IV: Association between myocardial dysfunction and the cases with different stages of HIE (n=75).

Myocardial dysfunction	HIE Stage-I	HIE Stage-II	HIE Stage-III	Total	Chi Value	P- Value
Present	01	08	22	31	22.74	< .001
Absent	19	16	09	44		

Table V: Correlations of Cardiac Troponin I (cTn I) with LV and RV Tei Index among cases with different stages of HIE (n=75).

	Mean ± SD	Pearson's correlation coefficient (r)	P Value
cTn I	1.10±.56		
LV Tei Index	.43±.05	.30	.012
RV Tei Index	.36±.09	.33	.004

Table VI: Risk measurement of myocardial dysfunction with mortality (n=75)

Factors	Death	No death	OR (95% Confidence Interval)
Myocardial dysfunction	21	9	22.66
No myocardial dysfunction	7	38	

V. Discussion

The ideal characteristics of a cardiac marker should fulfill the following characteristics: High concentrations of the marker in the myocardium, with relatively low concentrations in non-cardiac tissue. It is important to consider the tissue distribution of a potential marker in pathological states as well as in normal physiological conditions. Cardiac troponins I and T are well-established markers of myocardial ischemia and cardiac failure in adults and children, Creatine kinase (CK) exists as a dimer of two subunits: B and M, and three isoenzymes: CK-MM, CK-BB and CK-MB[10]. The 3-unit troponin complex (troponin I, T and C) along with tropomyosin is located on the actin filament. It is essential for the calcium-mediated regulation of skeletal and cardiac muscle contraction[11]. It has been seen that early cTnI concentrations may provide a useful marker for the assessment of severity of myocardial dysfunction in asphyxiated neonates**.** Cardiac troponins are very sensitive markers for the detection of myocardial damage. The ability to assay their serum levels accurately and quickly has revolutionized the concepts of minor myocardial injury and infarction. Cardiac troponin also serves as a useful adjunct in the assessment of the magnitude of myocardial injury in respiratory distress syndrome and asphyxia**.** One of the cTnI Isoform has been shown to be 100% specific for the heart. While one to four cTnT isoforms are expressed in diseased and regenerating human skeletal muscle, these isoforms are not the same as the cTnT isoforms expressed in the human heart. Cardiac TnI has the highest specificity and positive predictive value (99% and 98%) as compared with cardiac troponin T (96% and 93%), Creatine kinase-mass (92% and 86%) and Creatine kinase activity (89% and 80%) [12]. There are two major patterns of myocardial dysfunction. The first pattern is depression of left ventricular (LV) function that can be assessed by measuring contractility (fractional shortening, ejection fraction) and reduced cardiac output. The second pattern is moderate to severe pulmonary hypertension causing tricuspid regurgitation, reduced right ventricular (RV) output, and RV dysfunction[13]. Left ventricular systolic function can be evaluated by using M Mode echocardiography to measure ejection fraction (EF) and shortening fraction (SF). Barberi*et al* found that SF decreased in severely versus mildly asphyxiated newborns[14]. Comparison of Values in different groups were assessed by applying ANOVA with Post hoc multiple comparison test showing statistically significant difference in values between stage-II and stage-III and stage-III and Stage-I. Difference between Stage-I and stage-II was not found significant statistically. Table III: showing various cardiac changes determined by echocardiography. Under these circumstances this study was aimed observe the cardiac function of the cases by measuring serum Troponin-I and Echocardiographic changes.

Limitations Of The Study

It was an observational prospective experimental study with small sample size, which doesn't reflect the scenario of the whole country.

VI. Conclusion And Recommendations

Echocardiography is a noninvasive procedure that can be used for early and accurate evaluation of cardiac functional status. Along with other management, echocardiographic evaluation of the neonates having perinatal asphyxia with HIE will be useful for proper evaluation and appropriate management, thereby reducing mortality and morbidity. Cardiac dysfunction is a common consequence that develops secondary to perinatal asphyxia and its frequency rises with increased severity of HIE. Cardiac abnormality in asphyxiated neonates

with HIE is a risk factor that adversely affects the immediate outcome and thus increases the mortality and duration of hospital stay.

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