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# Cardiovascular Changes in Children with Acute Lower Respiratory Tract Infection

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**Abstract**

***Background:*** *Acute Lower Respiratory Tract Infections (ALRI), particularly Pneumonia and Bronchiolitis, are important causes of death in childhood in Bangladesh. The cardiovascular and respiratory systems function as a single unit and alteration in cardiorespiratory interactions, can cause significant changes in cardiac function. The objective of this study was to find out any electrical and functional changes, myocardial injury, frequency of heart failure and the outcomes in these patients with ALRIs.*

***Methodology:*** *It was a prospective observational study carried out at DMCH from January to June 2012 on 35 consecutive children admitted with ALRI, which were further diagnosed as pneumonia or bronchiolitis using operational definitions. Heart failure cases were identified and all the cases were then evaluated for any cardiovascular changes.*

***Results:*** *Most of the patients were male. ECG changes occurred in the form of tachycardia. Abnormal echocardiographic findings were noted in the form of pulmonary hypertension, left ventricular systolic (LV) dysfunction and tricuspid regurgitation. 82.9% had raised CK-MB and was significantly higher in patients with tachycardia and having abnormal echocardiographic changes. Nine patients developed heart failure, 3 of them had pulmonary hypertension along with LV systolic dysfunction and one of pulmonary hypertension and LV systolic dysfunction each. CK-MB was raised significantly in all the patients with heart failure.*

***Conclusion:*** *Raised CK-MB, tachycardia out of proportion on ECG and pulmonary hypertension with left ventricular systolic dysfunction were common findings in patients with ALRI.*

***Keywords:*** *Cardiovascular, CK-MB, Pneumonia, Bronchiolitis.*

## Introduction:

Acute lower respiratory tract infection (ALRI) particularly pneumonia is an important cause of death in childhood.[1] Acute respiratory tract infection (ARI) can be classified into upper and lower respiratory tract infection. Structures inferior to the vocal cord are accounted as lower respiratory tract. Among many, Pneumonia and Bronchiolitis remain the most important cause of respiratory illness in Bangladesh. In Bangladesh about 21% and 11.5% of under five children attending hospital are diagnosed as bronchiolitis and bronchopneumonia respectively.[2] The cardiovascular and respiratory systems function as a single unit and alteration in cardiorespiratory interactions, can cause significant changes in cardiac function.[1,3] Pneumonia can cause myocarditis by direct invasion of the microorganism, can lead to cardiac failure by myocardial depressant effect of hypoxia, and may further deteriorate cardiac function by altering preload and after load.[1,3,4] The main cause

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of acute pulmonary hypertension is hypoxia that leads to pulmonary vasoconstriction, causing right ventricular dysfunction.[5] Pulmonary hypertension increases the wall stress of right ventricle, results is a greater demand for coronary blood flow which is generally reduced because of inadequate diastole. Pulmonary hypertension causes right ventricular pressure over load and hypertrophy. The enlarged right ventricle eventually shifts the interventricular septum towards the left and limits left ventricular filling and output causing left ventricular dysfunction.[6,7,8] Since myocarditis can be a fatal disease, its detection is important by non-invasive techniques like ECG, Echocardiography and cardiac enzyme measurements.[1,9] although the gold standard of its detection remains by cardiac muscle biopsy nevertheless avoided due its invasive nature[1]. The different cardiac enzymes available for detecting myocarditis are CK-MB, Troponin I and $\alpha$–HBDH.[1,10,11] CK-MB is considered as a strong marker for myocardial damage and its rise may be the only sign of subclinical myocarditis.[12] Although Troponin I is much more accurate and specific in detecting myocarditis in acute coronary syndrome, its rise is also detected in non-cardiac causes. [13,14] A rise of pro-BNP is also highly significant for pediatric heart failure[15], which along with áHBDH measurement was not available in this hospital setting. So the remaining choice was measurement of CK-MB which is a specific cardiac enzymes for the detection of myocardial injury[1].Cardiac failure is a serious complication of pneumonia in developing countries, like Bangladesh, and may also contribute to mortality, but its role has not been clearly defined by studies in this country.[1,9,16] The objective of the study was to find out if there was any electrical, functional changes, myocardial injury, the frequency of heart failure and the outcomes in these patients with ALRIs.

**Materials and Method**

An observational case series comprised of 35 consecutive children admitted with acute lower respiratory infection at Department of Paediatrics was carried out at Dhaka Medical College and Hospital from January to June in the year 2012. Children aged less than 2 months and more than 5 years, or having severe acute malnutrition, or having congenital heart disease or previously diagnosed with bronchial asthma were excluded from the study. Initially 50 consecutive patients fulfilling the inclusion criteria were taken into the study. Out of these, six were taken out of the study as they deteriorated and became too sick to be evaluated, ultimately 35 were fully assessed. Written consents were taken from all the parents. Detailed history was taken and noted in the pre-tested questionnaire. Thorough examination of the respiratory, cardiovascular and other related systems was carried out and diagnosed as either pneumonia or bronchiolitis according to the case definition. Blood samples were taken on admission for complete blood count, serum electrolytes, C - reactive protein and CK-MB. Cardiovascular workup such as X-ray chest, ECG and Echocardiography were carried out. Patients were managed according to the institutional protocol with oxygen inhalation as per requirement, proper antibiotics in cases of pneumonia, Digoxin to those who developed heart failure. The cardiovascular workups were compared in the pneumonia and bronchiolitis group. Patients who developed heart failure were identified and their results were compared with patients who did not. Statistical analyses related were performed by using of SPSS 17.0 package program.

**Results**

Out of the 35 patients, 82.5% were between the age of 2 months to 6 months and 80.1% were male. Depending on clinical features, auscultatory findings and chest x-ray findings, 15 (42.9 %) children was diagnosed as Bronchopneumonia and 20 (57.1%) as Bronchiolitis. They were further evaluated by ECG, Echocardiography and CK-MB for cardiovascular changes.

The ECGs showed tachycardia in 10 (66.7%) patients with Bronchopneumonia and 9(45%) with Bronchiolitis although the difference was not statistically significant. None of them had arrhythmia (Table-I).

**Table I**

*Distribution of patients by ECG findings (n=35)*

| ECG findings | Pneumonia (n %) | Bronchiolitis (n %) | P value |
|---|---|---|---|
| Normal | 5 (33.3) | 11 (55.0) | |
| Tachycardia | 10 (66.7) | 9 (45.0) | 0.202$^{ns}$ |
| Arrhythmia | 0.0 | 0.0 | |

ns= not significant

P value reached from chi-square test

At echocardiographic evaluation (Table-II), it was seen 15 (75%) from the Bronchiolitis group had normal findings whereas 4 (26.7%) patients from pneumonia group had normal findings, the rest of the patients from the Pneumonia group, 11 (73.3%), had abnormal findings, i.e there were more echocardiographic changes in the pneumonia group. However, Pulmonary hypertension was noted in 5 (33.3 %) and 3 (15%), LV systolic dysfunction in 6 (40%) and 6 (30%) in Bronchopneumonia and Bronchiolitis group respectively, Tricuspid Regurgitation was found in 2 (13.3%) children with Bronchopneumonia and 1(5%) with Bronchiolitis.

**Table II**

*Distribution of the study patients by echocardiographic findings (n=35)*

| Echocardiographic findings | Pneumonia (n=15) n (%) | Bronchiolitis *(n=20) n (%) | P value |
|---|---|---|---|
| Normal | 4 (26.7) | 15 (75.0) | [a]0.004[s] |
| Pulmonary hypertension | 5 (33.3) | 3 (15.0) | [a]0.191[ns] |
| LV systolic dysfunction | 6 (40.0) | 6 (30.0) | [b]0.357[ns] |
| Tricuspid regurgitation | 2 (13.3) | 1 (5.0) | [a]0.390[ns] |

* A single patient may exhibit multiple findings

CK-MB values are marked normal upto 25U/L. 82.9% patients were found to have raised CK-MB levels (Figure-1). Mean CK-MB difference was not statistically significant (P>0.05) between broncho-pneumonia and bronchiolitis, i.e CK-MB was raised irrespective of the diagnosis (Table-III).

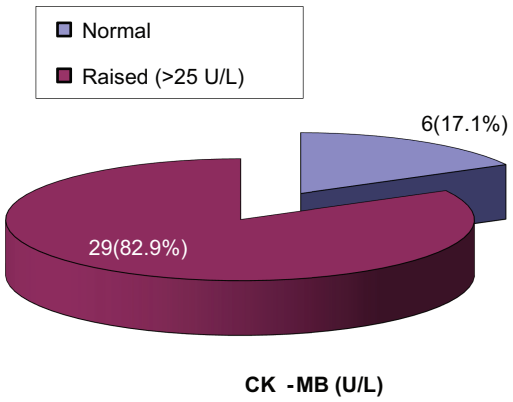


**Fig 1:** *Distribution of patients by CK-MB findings (n=35)*

**Table III**

*Distribution of study patients with mean CKMB value by diagnosis (n=35)*

| | | CKMB (U/L) | | P value |
|---|---|---|---|---|
| Diagnosis | No. | Mean±SD | (Min-max) | |
| Bronchopneumonia | 15 | 41.46±17.42 | (17-66) | 0.801[ns] |
| Bronchiolitis | 20 | 40.1±14.26 | (10-71) | |

Figure-2 showed 9 (25%) patients, among all 35 developed heart failure, 6 of which had Bronchiolitis and 3 pneumonia. Table-IV showed the cardio-vascular workup of the heart failure group. All of them had tachycardia on ECG. In echo-cardiography among the 9 patients, 4(44.4%) had normal findings and the rest 5(56%) had findings. 3 (33.3%) of them had Pulmonary hypertension along with LV Systolic Dysfunction, 1 of pulmonary hypertension and LV systolic dysfunction each. All of them had raised CK-MB levels.

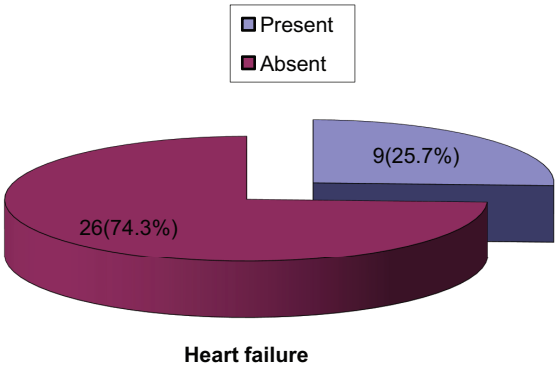


**Fig 2:** *Distribution of the study patients by presence and absence of heart failure (n=35)*

(81%). Pulmonary hypertension and LV systolic dysfunction findings by Echocardiography was also found to be significantly different (P<0.05) between the normal and tachycardic groups signifying that patients with tachycardia on ECG had more Pulmonary hypertension and LV systolic dysfunction than those with normal ECG.

Patients with normal Echo findings had more normal ECG findings (Table-V). All the patients with Pulmonary hypertension had tachycardia on ECG and LV systolic dysfunction was significantly more in patients with tachycardia (p<0.5).

Mean CK-MB was found to be higher in tachycardic group than those with normal heart rate and the

difference was statistically significant (P<0.05). Mean CK-MB was also raised significantly more in patients with pulmonary hypertension, LV systolic dysfunction and in patients with Tricuspid regurgitation than patients with normal echo findings (Table-VI). They were also statistically significant. Table-VII showed association of heart failure with CK-MB value. Mean CKMB was found to be 50.33±11.6 U/L in with heart failure and 36.72±14.9 U/L in without heart failure. The difference was statistically significant (P<0.05) between two groups. This means CK-MB value was significantly raised in heart failure group. All the patients survived, the patients who developed heart failure stayed around 9 to days and those did not were discharged with an average of 5 days.

**Table IV**

*Distribution of heart failure patients by cardiovascular workup (n=9)*

| Cardiovascular Workup | n (%) |
|---|---|
| ECG: Tachycardia | 9 (100%) |
| ECHO: | |
| Pulmonary Hypertension with LV Systolic Dysfunction | 3 (33.3%) |
| Pulmonary Hypertension | 1 (11.1%) |
| LV Systolic Dysfunction | 1 (11.1%) |
| Normal | 4 (44.4%) |
| Mean CK-MB | 50.33 |

**Table V**

*Distribution of the patients with ECG findings by Echocardiographic changes (n=35)*

| Echocardiographic changes | ECG Findings | | | | P value |
|---|---|---|---|---|---|
| | Normal (n=16) | | Tachycardia (n=19) | | |
| | N | % | N | % | |
| Normal | 13 | 81.2 | 6 | 31.6 | 0.003[s] |
| Pulmonary hypertension | 0 | 0.0 | 8 | 42.1 | 0.003[s] |
| LV systolic dysfunction | 2 | 12.5 | 10 | 52.5 | 0.012 |
| Tricuspid regurgitation | 1 | 6.25 | 2 | 10.5 | 0.556[ns] |

* A single patient may exhibit multiple findings

**Table VI**

*Distribution of study patients with mean CK-MB value by ECG and Echocardiographic findings (n=35)*

| | | | CKMB (U/L) | | P value |
|---|---|---|---|---|---|
| | No. | Mean±SD | (Min-max) | | |
| ECG findings | Normal | 16 | 34.5±15.24 | (10-71) | 0.043[s] |
| | Tachycardia | 19 | 44.61±13.22 | (20-66) | |
| Echocardiographic findings | Normal | 19 | 34±12.4 | (10-60) | 0.036[s] |
| | Pulmonary hypertension | 8 | 45±16.28 | (20-62) | |
| | LV Systolic dysfunction | 12 | 49.33±12.22 | (29-62) | |
| | Tricuspid regurgitation | 3 | 41.67±26.35 | (20-71) | |

**Table VII**

*Distribution of study patients with and without heart failure by CK-MB findings (n=35)*

| | With heart failure(n=9) | | Without heart failure(n=25) | | P value |
|---|---|---|---|---|---|
| | Mean | ±SD | Mean | ±SD | |
| CKMB (U/L) | 50.33 | ±11.6 | 36.72 | ±14.9 | 0.018[s] |
| Range (min-max) | (30 | -66) | (10 | -71) | |

## Discussion

ALRI is an important cause of death in childhood in Bangladesh. The functioning of the cardiovascular and the respiratory systems are dependent on each other in various ways and alteration in their interactions, can cause significant changes in cardiac function[1]. This study was carried out on 35 children with ALRI aging from 2 to 59 months and was diagnosed as Bronchiolitis in 20 (57.1%) patients and Bronchopneumonia in 15 (42.9%) patients.

Tachycardia was observed in 66.7% and 45% in the Pneumonia and Bronchiolitis group respectively by ECG in the current study and the results were not significantly different from each other. No arrhythmia was observed in the study patients (Table-I). Similar findings were seen by Fine et al[17] in 26% of the study population, and 64.5% by Kocak et al.[18] Fine et al stated that the most significant single sign of myocarditis was a tachycardia out of proportion to temperature. Another study by Esposito et al found an association with sinoatrial block and RSV load implementing RSV could play a direct role in inducing arrhythmia.[10]

The Echocardiographic findings in this study revealed Pulmonary hypertension in 33.3% in Pneumonia and 15% in Bronchiolitis group, Left ventricular systolic dysfunction in 40% and 30% in Pneumonia and Bronchiolitis group respectively (Table-II). It is to be noted that abnormal findings were more common in the pneumonia group, although difference in findings between the two groups were not stastically significant. Bardi-Peti[19] et al found Pulmonary hypertension in 18 patients with acute respiratory disease; they however interestingly described the mechanical effect of hyperinflation of the lung parenchyma on pulmonary vessels to be the probable cause of increased pulmonary arterial pressure during these broncho-obstructive diseases. Tricuspid regurgitation is a common finding along with pulmonary hypertension, although it can be found isolated in normal patients. Isolated TR was found in a study by Senocak et al[1,20] as a part of normal cardiac anatomy and Neubauer et al[21], Mahmoud et al[22] along with reduction of ejection fraction and Sreeram et al[19] found 11 patients with Bronchiolitis having TR in an otherwise normal cardiac finding.This current study, however, did not find right ventricular systolic dysfunction as a result of pulmonary hypertension, but rather left ventricular/r dysfunction which correlates with the study of Kumar[6], Hopkins[7] and Bates[8], where they signify that the enlarged right ventricle shifts the interventricular septum towards the left and causes left ventricular systolic dysfunction.

Serum CK-MB was found to be elevated in 82.9% subjects in this study in the absence of severe hypoxia, acidosis or sepsis (Figure-1). The finding was consonant with the 68% in the study by Ilten et al[1] and with 60% of Mahmoud et al[21] and significant increase by Ma et al[38]. Also, to be noted is the finding that CK-MB was raised unequivocally in both the bronchopneumonia and bronchiolitis groups (Table-III).

9 (25%) children developed heart failure (Figure-2). This was akin to the incidence (14%) in the study by Ilten et al[1] and 8.5% to that of Navarro et al[23]. All the patients had tachycardia on ECG (Table-IV). On Echocardiogram four patients had Pulmonary Hypertension out of which 3 were along with LV systolic dysfunction. One patient had only LV systolic dysfunction. All the patients had raised CK-MB level. Seedat et al[16] found tachycardia to be a poor prognostic feature among the patients with pneumonia who had ECG changes, especially those with a raised CK-MB level whereas Douglas et al[24] concluded that uncontrolled tachycardia may result in significant LV dysfunction. Nerheim et al[25] found that tachycardia-induced cardiomyopathy develops slowly and appears reversible by left ventricular ejection fraction improvement, but recurrent tachycardia causes rapid decline in left ventricular function and development of heart failure. Both these studies points out to the fact that tachycardia is associated with left ventricular dysfunction which is a prominent finding among the heart failure patients of the current study.

The most prominent echocardiographic finding of the heart failure patients in the prevailing study were Pulmonary hypertension along with LV systolic dysfunction (Table-IV). Although right heart involvement is a more common finding in patients with pulmonary hypertension, especially with respiratory tract infections as found by Shann et al[5] where 26% of the subjects developed right ventricular failure secondary to pulmonary hypertension, but this current study interestingly found left ventricular involvement. These findings can be related to the study carried out by Shah et al[26], who stated that Pulmonary hypertension is found secondary to left

ventricular systolic dysfunction in 68% to 78% of patients with heart failure patients along with right heart involvement[27,28,29]. A different study was carried out to find out the determinants of pulmonary hypertension in left ventricular dysfunction by Enriques-Sarano et al[30] and they concluded that pulmonary hypertension is associated with congestive heart failure. They discussed the probable causes to be an increase in left atrial pressure[31] and pulmonary resistance[32] and, possibly, from the loss of endothelium-dependent vasodilation of the pulmonary arterial bed[33]. Pulmonary hypertension is also associated with neurohumoral activation[34, 35] in particular of endothelin-1[36], a potent vasoconstrictor that is increased markedly in heart failure[37]. The probable cause of the left ventricular involvement can be attributed to myocarditis. [38]

All the children who developed heart failure probably had myocarditis as CK-MB is considered as a strong marker for myocardial damage and its rise may be the only sign of subclinical myocarditis as found by Heikkila et al[37]. In this current study CK-MB was also found to be significantly raised in children who had tachycardia on ECG ( p=0.43) ( Table-VI). Similar finding of 26.1% of study group with tachycardia was associated with clinical myocarditis as found by Fine et al[17]. When seen the association between the CK-MB values with the Echocardiographic findings in the prevailing study, it was found to be more raised in those with Pulmonary hypertension, LV systolic dysfunction and Tricuspid regurgitation (p=0.03) (Table-VI). This means that CK-MB values were much higher in children with abnormal echocardiographic findings than with children with normal findings (P value 0.036). Similar findings can be related to the study by Mahmoud et al.[22]

The most remarkable finding in this study found when the CK-MB values were compared between the heart failure and non-heart failure group. (Table-VII). Serum CK-MB values were significantly high in those with heart failure than those without (p= 0.018), suggesting that children who developed heart failure also had myocarditis as depicted by the very high values of serum CK-MB in them.

**Conclusion**

Cardiovascular changes, along with heart failure were found in children with acute lower respiratory tract infections. Raised CK-MB, tachycardia out of proportion on ECG and pulmonary hypertension with left ventricular systolic dysfunction were common findings. Serum CK-MB, was raised in those with ECG and Echo changes. raised significantly more in the heart failure group. Cardiovascular changes in ALRI are associated with increased hospital stay and thus bed occupancy.

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