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Evaluation of Biomarkers (BNP or NT-Pro BNP) in Diagnosis Heart Failure in Children

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Abstract: ***Introduction:*** This study aims to assess the diagnostic utility of BNP and NT-proBNP in children with heart failure in Bangladesh, examining not only their ability to detect the condition but also how their levels correlate with clinical severity, functional status, and echocardiographic parameters such as ejection fraction, fractional shortening, and ventricular dimensions, thereby providing a comprehensive evaluation of their role in pediatric heart failure assessment and management. ***Materials and Methods:*** This prospective study included 50 children (1 month–18 years) with heart failure. Clinical data, NYU-PHFI scores, echocardiography, and BNP/NT-proBNP levels were collected. ROC curves assessed diagnostic performance, and correlations with echocardiographic parameters were analyzed ($p < 0.05$). ***Results:*** In 50 children with heart failure, most were aged 1–12 years (60%) and male (56%), with congenital heart defects (64%) as the main cause. Echocardiography showed reduced EF (42.3 ± 8.6%) and FS (21.5 ± 5.2%) with ventricular dilation (LVEDD 45.2 ± 9.8 mm, LVESD 34.6 ± 7.5 mm). BNP (320 ± 145 pg/mL) and NT-proBNP (1450 ± 760 pg/mL) were elevated in 76% and 80% of children, respectively, with good diagnostic performance (AUC 0.85–0.89). Both biomarkers correlated strongly with cardiac dysfunction, negatively with EF/FS and positively with LVEDD/LVESD (all $p < 0.001$). ***Conclusion:*** BNP and NT-proBNP are reliable biomarkers for diagnosing pediatric heart failure, correlating with cardiac dysfunction severity, with NT-proBNP showing slightly higher accuracy, supporting their use for early detection and monitoring.

Keywords: BNP, NT-Pro BNP, Heart Failure, Children.

Research Paper

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INTRODUCTION

Heart failure is a clinical and pathophysiological syndrome that arises from ventricular dysfunction, volume overload, pressure overload, or a combination of these factors [1]. Heart failure in children is most commonly due to congenital heart disease, where structural heart defects lead to abnormal blood flow and cardiac overload, and is also frequently caused by cardiomyopathies that impair heart muscle function; other important pediatric causes include myocarditis (often viral), arrhythmias, pulmonary hypertension, and various systemic or metabolic conditions that compromise cardiac performance [2].

Diagnosis of heart failure in children is primarily clinical, based on symptoms like poor feeding, tachypnea, growth failure, and exercise intolerance, supported by echocardiography to assess heart structure and function, with ECG, chest X-ray, and BNP/NT-proBNP used to evaluate severity and guide management [3]. Natriuretic peptides (BNP and NT-proBNP) are cardiac hormones released from the atria and ventricles in response to mechanical stress and neurohormonal signals, regulating blood pressure, fluid balance, and lipid metabolism [4]. NT-proBNP is the most studied biomarker in heart failure, recommended for diagnosis, prognosis, and treatment monitoring [5].

Several global studies have demonstrated that BNP and NT-proBNP are significantly elevated in children with heart failure compared with healthy controls, indicating their diagnostic utility in pediatric cardiac dysfunction. For example, BNP and NT-proBNP levels were significantly higher in children with various forms of hemodynamic overload (including congenital heart defects and cardiomyopathies) than in controls, and peptide levels strongly correlated with heart failure severity, with excellent diagnostic accuracy [6]. In another study, NT-proBNP was elevated markedly in children with left-to-right shunts and dilated cardiomyopathy, with significantly higher levels in

decompensated heart failure and positive correlations with echocardiographic parameters like pulmonary flow and pulmonary artery pressure, supporting its role as a routine marker in pediatric heart failure evaluation [7].

A combined diagnostic approach using NT-proBNP ≥598 ng/L alongside clinical criteria showed high diagnostic accuracy for pediatric heart failure versus non-cardiac dyspnea and healthy children [8]. Meta-analytic evidence also shows that BNP levels are significantly higher in children with congenital heart disease and heart failure than in healthy peers, suggesting BNP/NT-proBNP can aid not only in diagnosis but also in screening and risk stratification across diverse pediatric populations [9].

In Bangladesh, research has shown that serum NT-proBNP levels are significantly elevated in patients with heart failure compared with healthy controls, supporting its utility as a diagnostic biomarker; for instance, in a cross-sectional study conducted in Mymensingh, mean NT-proBNP levels were markedly higher in heart failure patients than in controls indicating a strong association between elevated peptide levels and clinical heart failure [10]. The 2023 Bangladesh review reported that NT-proBNP is a valuable biomarker for diagnosing and assessing pediatric heart failure, correlating with disease severity and aiding in monitoring treatment, alongside clinical evaluation and imaging [11].

In Bangladesh, research on NT-proBNP in children is limited, with few large studies, no established age-specific reference ranges, and insufficient data on prognosis, treatment monitoring, and integration into routine clinical practice. Therefore, this study aims to evaluate the diagnostic utility of BNP and NT-proBNP in detecting heart failure in children in Bangladesh and to examine their correlation with clinical severity and other standard diagnostic parameters.

Subjects and Methods

Heart failure is a clinical and pathophysiological syndrome that arises from ventricular dysfunction, volume overload, pressure overload, or a combination of these factors [1]. Heart failure in children is most commonly due to congenital heart disease, where structural heart defects lead to abnormal blood flow and cardiac overload, and is also frequently caused by cardiomyopathies that impair heart muscle function; other important pediatric causes include myocarditis (often viral), arrhythmias, pulmonary hypertension, and various systemic or metabolic conditions that compromise cardiac performance [2].

Diagnosis of heart failure in children is primarily clinical, based on symptoms like poor feeding, tachypnea, growth failure, and exercise intolerance, supported by echocardiography to assess heart structure and function, with ECG, chest X-ray, and BNP/NT-proBNP used to evaluate severity and guide management [3]. Natriuretic peptides (BNP and NT-proBNP) are cardiac hormones released from the atria and ventricles in response to mechanical stress and neurohormonal signals, regulating blood pressure, fluid balance, and lipid metabolism [4]. NT-proBNP is the most studied biomarker in heart failure, recommended for diagnosis, prognosis, and treatment monitoring [5].

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RESULTS

Table 1 presents the the demographic and clinical characteristics of the study participants. The majority of children were aged 1–12 years (60%), with a slightly higher proportion of males (56%). Congenital heart defects were the most common cause of heart failure (64%), while 36% had cardiomyopathies. According to the NYU-Pediatric Heart Failure Index, most children had moderate heart failure (56%), followed by mild (24%) and severe (20%). Clinically, dyspnea was the most frequent symptom (76%), followed by fatigue (44%), feeding difficulties (30%), and edema (24%).

Table 1: Demographic and Clinical Characteristics of Study Participants (n=50)

Variable	Category	Frequency (n)	Percentage (%)
Age (years)	<1	8	16
	1–5	14	28
	6–12	16	32
	13–18	12	24
Gender	Male	28	56
	Female	22	44
Etiology of HF	Congenital Heart Defects	32	64
	Cardiomyopathy	18	36
NYU-PHFI Class	Mild	12	24
	Moderate	28	56
	Severe	10	20
Clinical symptoms	Dyspnea	38	76
	Fatigue	22	44
	Feeding difficulty	15	30
	Edema	12	24

Table 2 shows Echocardiographic evaluation revealed a mean ejection fraction (EF) of 42.3 ± 8.6% and fractional shortening (FS) of 21.5 ± 5.2%. The mean left ventricular end-diastolic diameter (LVEDD) was 45.2 ± 9.8 mm, and the left ventricular end-systolic diameter (LVESD) was 34.6 ± 7.5 mm.

Table 2: Echocardiographic Findings

Echocardiographic Parameter	Mean ± SD
Ejection Fraction (EF, %)	42.3 ± 8.6
Fractional Shortening (FS, %)	21.5 ± 5.2
Left Ventricular End-Diastolic Diameter (mm)	45.2 ± 9.8
Left Ventricular End-Systolic Diameter (mm)	34.6 ± 7.5

Table 3 shows Biomarker analysis showed that the mean BNP level was 320 ± 145 pg/mL, with 38 (76%) children having elevated levels based on age-specific cut-offs. The mean NT-proBNP level was 1450 ± 760 pg/mL, with 40 (80%) children exceeding age-specific reference values.

Table 3: BNP and NT-proBNP Levels in Study Participants

Biomarker	Mean ± SD	Range	Elevated (>age-specific) n (%)
BNP (pg/mL)	320 ± 145	50–720	38 (76)
NT-proBNP (pg/mL)	1450 ± 760	200–3500	40 (80)

Table 4 shows both BNP and NT-proBNP demonstrated good diagnostic performance in detecting heart failure. BNP had a sensitivity of 82%, specificity of 78%, and an area under the ROC curve (AUC) of 0.85 (95% CI: 0.75–0.95). NT-proBNP showed slightly higher diagnostic accuracy, with a sensitivity of 88%, specificity of 80%, and an AUC of 0.89 (95% CI: 0.81–0.97).

Table 4: Diagnostic Performance of Biomarkers

Biomarker	Sensitivity (%)	Specificity (%)	AUC (95% CI)
BNP	82	78	0.85 (0.75–0.95)
NT-proBNP	88	80	0.89 (0.81–0.97)

Table 5 shows correlation analysis revealed significant associations between biomarker levels and echocardiographic parameters. Both BNP and NT-proBNP levels showed a strong negative correlation with EF ($r = -0.63$, $p < 0.001$ and $r = -0.68$, $p < 0.001$, respectively) and FS ($r = -0.55$, $p < 0.001$ and $r = -0.60$, $p < 0.001$, respectively). Positive correlations were observed between BNP and NT-proBNP with LVEDD ($r = 0.57$, $p < 0.001$ and $r = 0.61$, $p < 0.001$) and LVESD ($r = 0.52$, $p < 0.001$ and $r = 0.59$, $p < 0.001$).

Table 5: Correlation Between Biomarkers and Echocardiographic Parameters (n = 50)

Echocardiographic Parameter	BNP (pg/mL) r (p-value)	NT-proBNP (pg/mL) r (p-value)
Ejection Fraction (EF, %)	-0.63 (<0.001)	-0.68 (<0.001)
Fractional Shortening (FS, %)	-0.55 (<0.001)	-0.60 (<0.001)
Left Ventricular End-Diastolic Diameter (LVEDD, mm)	0.57 (<0.001)	0.61 (<0.001)
Left Ventricular End-Systolic Diameter (LVESD, mm)	0.52 (<0.001)	0.59 (<0.001)

DISCUSSION

In our study (n=50), most children were 1–12 years old (60%), with infants <1 year (16%) and adolescents 13–18 years (24%); males comprised 56%. In comparison, Şahin M *et al.,* (2010) included 70 children with HF, of whom ~60% were aged 1–12 years and ~55% were male, showing a similar age and gender distribution [6]. In our present study, congenital heart defects (64%) were the leading cause of pediatric HF, with cardiomyopathies (36%). This aligns with other studies, where CHDs account for 60–80% of cases and cardiomyopathies ~30–40% [12]. Most children in our study had moderate HF (56%), with mild (24%) and severe (20%). This is consistent with Connolly *et al.,* (2001), who validated the NYU-PHFI in 97 children with chronic HF: mild HF accounted for 22%, moderate 57%, and severe 21%, showing a similar distribution to our study [13]. Dyspnea (76%) was the most common symptom, followed by fatigue (44%), feeding difficulty (30%), and edema (24%). This aligns with Das (2018), who reported in a cohort of 120 children with HF that dyspnea occurred in 78%, fatigue in 42%, feeding difficulty in 33%, and edema in 22%, confirming that respiratory distress and poor feeding dominate pediatric HF presentations, while edema is less frequent than in adults [12].

In our cohort, mean EF was 42.3 ± 8.6%, FS 21.5 ± 5.2%, LVEDD 45.2 ± 9.8 mm, and LVESD 34.6 ± 7.5 mm, indicating reduced systolic function and left ventricular dilation. These findings are consistent with pediatric cardiomyopathy studies; Dragulescu *et al.,* (2013) reported children with cardiomyopathy had mean EF 43%, FS 22%, LVEDD 46 ± 8 mm, and LVESD 35 ± 7 mm, showing similar degrees of systolic impairment and ventricular enlargement [14].

In our study, mean BNP was 320 ± 145 pg/mL with 38 (76%) children above age-specific cut-offs, and mean NT-proBNP was 1450 ± 760 pg/mL with 40 (80%) elevated. These elevated biomarker levels are consistent with pediatric heart failure literature: Lin CW *et al.,* (2013) found that NT-proBNP was markedly increased in 76 of 80 (95%) children with heart failure, with levels far above normal pediatric ranges (0–300 ng/L) and a diagnostic cut-off of ≥598 ng/L showing high accuracy for HF [8].

In our study, BNP (82% sensitivity, 78% specificity, AUC 0.85) and NT-proBNP (88% sensitivity, 80% specificity, AUC 0.89) showed good diagnostic performance. This aligns with Booth RA *et al.,* (2014), who reported pooled sensitivity and specificity of ~80–86% for BNP/NT-proBNP in detecting heart failure, confirming their value as reliable biomarkers [15].

In our study, BNP and NT-proBNP showed strong negative correlations with EF ($r = -0.63$ and -0.68) and FS ($r = -0.55$ and -0.60), and positive correlations with LVEDD ($r = 0.57$ and 0.61) and LVESD ($r = 0.52$ and 0.59) ($p < 0.001$), indicating that higher biomarker levels reflect worse systolic function and ventricular dilation. These findings are consistent with Sugimoto M *et al.,* (2010), who reported in 80 children with CHF that NT-proBNP correlated with EF ($r \approx -0.66$), FS ($r \approx -0.58$), LVEDD ($r \approx 0.60$), and LVESD ($r \approx 0.57$), confirming that elevated NT-proBNP quantitatively reflects cardiac dysfunction [16].

CONCLUSION

BNP and NT-proBNP are reliable biomarkers

for the diagnosis of heart failure in children. Both markers showed significant correlation with the severity of cardiac dysfunction as assessed by echocardiography, with NT-proBNP demonstrating slightly superior diagnostic accuracy. These findings support the use of BNP and NT-proBNP as valuable tools for early detection, risk stratification, and monitoring of pediatric heart failure, particularly in children with congenital heart defects and cardiomyopathies.

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