Prognostic value of homocysteine and highly sensitive cardiac troponin T in children with acute heart failure

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Objective: **Heart failure (HF) is a progressive disorder in children. Many HF biomarkers have been identified to assess its severity and predict its course. The aim of this study was to evaluate the prognostic value of plasma levels of homocysteine (HCY) and highly sensitive cardiac troponin T (hs-cTnT) in children with HF.**

Materials and Methods: **Eighty children with acute HF were enrolled in this study as the patient group and 80 healthy children of matched age and sex served as the control group. HCY and hs-cTnT serum levels were measured before and after HF treatment; additionally, echocardiographic examinations were performed before and after therapy. All patients were followed up for 3 months.**

Results: **Plasma levels of HCY and hs-cTnT were significantly higher in children with HF before treatment, compared with their levels in children with HF after treatment and with the control group. This increase in serum levels of both biomarkers was associated with increased severity of HF according to the Ross classification of HF. HCY had higher specificity, positive predictive value, and accuracy than hs-cTnT. Serum levels of both biomarkers had a significant positive correlation with cardiomegaly and a significant negative correlation with left ventricular ejection fraction and fraction shortening. Marked elevation of both serum biomarkers was significantly associated with poor outcome with mortality rate of 10%.**

Conclusion: **Plasma HCY and serum hs-cTnT levels have a good prognostic value in children with congestive heart failure (CHF) and their levels significantly correlated with clinical and echocardiographic data, severity of HF, and adverse outcome in children with CHF.**

Keywords: Acute heart failure, Children, Highly sensitive cardiac troponin T, Homocysteine, Prognostic

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Introduction

Heart failure (HF) is defined as the failure of the heart to pump blood at a rate commensurate with the requirements of the metabolizing tissues. HF in children may arise from structural or nonstructural heart diseases, which may be congenital or acquired [1]. It has a high morbidity and mortality in children [2].

It is very crucial that intensivists can use simple biomarkers to aid in the early diagnosis and predicting of adverse outcomes to optimize the treatment strategy. Recently, many HF biomarkers have been identified that aid in assessing the severity of HF and in predicting the course of the disease. The mechanism for the release of these markers seems to be from ventricular remodeling, myocyte injury, and reduced coronary reserve [3,4].

Cardiac troponin T is considered to be a highly sensitive and specific biomarker for myocardial injury as in ischemic heart disease. It is also reported to be increased in HF and this increase is correlated with severity and bad prognosis of HF. Highly sensitive assays for cardiac troponin T detect it in blood even at concentrations much lower than could be detected by standard methods of assay [5].

Homocysteine (HCY) is an amino acid that is derived from the conversion of methionine to cysteine. Several recent studies have reported that elevated plasma HCY level in patients with congestive heart failure (CHF) was associated with increased incidence and severity of the disease [6,7].

Hyperhomocysteinemia causes adverse cardiac remodeling, through direct effect on the myocardium or independent vascular effect leading to myocardial fibrosis, stiffness, and systolic dysfunction [8]. The prognostic value of serum HCY and highly sensitive cardiac troponin T (hs-cTnT) levels in children with acute HF is still under evaluation.

In this study, we aimed to assess the prognostic value of HCY and hs-cTnT plasma levels in children with acute HF and to correlate their levels with the severity of HF. To the best of our knowledge, this is the first study investigating the prognostic value of these two markers in children with HF.

Abbreviations

CHF	congestive heart failure
CTR	cardiothoracic ratio
EF	ejection fraction
FS	fraction shortening
HCY	homocysteine
Hs-cTnT	highly sensitive cardiac troponin T
HF	heart failure
LV	left ventricle
ROC	receiver operating characteristic

Materials and methods

This study was conducted in the Pediatric Cardiology Unit, Pediatric Department, Tanta University Hospital (Tanta, Egypt) from April 2016 to August 2017. Eighty children with acute CHF were enrolled in this study (age range, 2 months to 6 years; 44 males and 36 females). Patients were classified according to the Ross classification of HF in infants and children as Class I, II, III, and IV [9]. Eighty healthy children matched for age and sex served as the control group (age range, 2 months to 6 years; 40 males and 40 females). The study has been approved by the local ethics committee of the Faculty of Medicine, Tanta University. Consent was signed by parents of all patients.

We included infants and children with manifestations of acute HF either due to acquired or congenital heart disease. We excluded those with hypertension, active myocarditis, ischemia, pericarditis, renal diseases, acute or chronic infection, metabolic diseases, any chronic illness, neoplastic disease, or those receiving drugs (e.g., methotrexate) that would increase the serum level of HCY.

All children included in the study were subjected to the following:

- Complete history taking.
- Thorough clinical examination including body weight, heart rate, respiratory rate, and complete cardiac examination.
- Electrocardiography: Performed using a three-channel α 1000 apparatus (Chandigarh, India) to diagnose any associated arrhythmias.
- Plain X-ray (chest): Chest X-ray was obtained and cardiothoracic ratio (CTR) was measured for assessment of cardiomegaly.
- Conventional echocardiography: Performed using Vivid 7 ultrasound machine (GE Medical System, Horten, Norway, with 4S and 3.5-MHz multifrequency transducers) to evaluate cardiac function. We also evaluated fraction shortening (FS), ejection fraction (EF), and Tei index of the left ventricle (LV). Tei index is defined as the sum of isometric relaxation time and isovolumic contraction time divided by the LV ejection time obtained from LV inflow and outflow. This index is used for assessing global systolic and diastolic functions of the LV. The echocardiographic examinations were performed by two different pediatric cardiologists for all included children to assess interobserver reliability.
- Plasma HCY level: Venous blood samples (2 mL) were obtained by venipuncture from patients and controls after

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