

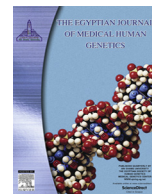
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Original article

## Left ventricle myocardial performance in Down Syndrome children with clinically and anatomically normal hearts: Relationship to oxidative stress

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## ABSTRACT

Oxidative stress is implicated in many organs pathophysiologies in Down syndrome. Scarce data exist concerning left ventricular (LV) performance in DS children with normal hearts. Tissue Doppler derived myocardial performance index (TDI-Tei index) is a reliable method for ventricular performance evaluation. Myeloperoxidase (MPO) enzyme plays a crucial role in oxidants production and is a marker of cardiovascular risk.

**Aim:** To evaluate LV myocardial performance in DS children with normal hearts using TDI-Tei index and correlate it with plasma MPO as a marker of oxidative stress.

**Patients and methods:** This cross-sectional study included 120 DS children recruited from Children's Hospital, Ain Shams University. Out patients clinic and echocardiography unit (mean age,  $8.35 \pm 4.25$  years) who were subjected to: history taking, clinical examination, laboratory investigations (Complete blood count, serum Alanine Transaminase, serum creatinine, Thyroid profile, 12 lead Electrocardiogram and conventional Doppler echocardiography). DS children with congenital or acquired heart diseases, dysrhythmias, anaemia, pulmonary hypertension, thyroid, renal disease, diabetes were excluded. The remaining 50 DS children with normal hearts (group I) were compared to 50 age. Sex matched healthy children as control (group II) Studied groups were subjected to: plasma MPO using ELISA technique and TDI LV-Tei index assessment using Vivid E9 Echocardiography machine (GE, Horton, Norway).

**Results:** LV TDI-Tei was significantly increased in group I compared to group II ( $0.46 \pm 0.02$  vs  $0.32 \pm 0.08$ ,  $p < 0.001$ ). Plasma MPO was increased in group I than group II ( $64.4831 \pm 0.6$  ng/ml vs  $50.4 \pm 30.2$  ng/ml,  $p < 0.001$ ). A significant positive correlation was found between plasma MPO and LV TDI-Tei ( $r = 0.877$ ,  $p = 0.001$ ) in group I.

**Conclusion:** Subclinical Left ventricle dysfunction evidenced by increased TDI Tei index was detected in DS children with normal hearts. This dysfunction correlated with plasma MPO level which mandates antioxidants treatment and tissue Doppler myocardial performance regular evaluation for early identification, monitoring and early intervention.

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## 1. Introduction

Down Syndrome (DS) is the most common human aneuploidy [1]. Nearly 50% of DS patients have cardiac defects [2] Right ventricular function affection resulting from pulmonary hypertension due to upper airway obstruction and abnormal vasculature growth, is a

known complication in DS patients [3]. Very scarce data exist about left ventricular (LV) performance in DS patients with clinically and anatomically normal hearts especially in the pediatric age group.

DS is a human disorder etiologically related to oxidative stress. This was found to be due to redox imbalance from overexpression of Cu, Zn-superoxide dismutase (SOD-1), encoded by trisomic chromosome 21 [4].

Oxidative stress in DS was also reported to result from genes located at chromosomes other than chromosome 21 and in transcriptional regulation of those genes. This is implicated in many of DS patients organs pathophysiologies [5].

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Myeloperoxidase (MPO) enzyme released by leukocytes plays a crucial role in inflammation and oxidative stress [6]. MPO plays a central role in oxidants production by neutrophils and uses superoxide and hydrogen peroxide to catalyse hypochlorous acid generation which is a strong oxidant produced at sites of inflammation with antibacterial effect [6].

Numerous studies showed significant elevations of the systemic MPO levels in many cardiovascular disease scenarios with acute coronary syndromes and heart failure being the most studied. The involvement of MPO in the pathogenesis of cardiovascular diseases is supported by evidence that elevated MPO concentrations are an independent risk factor for future cardiovascular events in healthy individuals [7].

Tissue Doppler derived myocardial performance index (TDI-MPI) also known as TDI-Tei index, is a simple, reproducible method for ventricular function assessment both systolic and diastolic [8]. TDI-Tei index records both systolic and diastolic velocity signals during the same cardiac cycle and has been reported to correlate well with other invasive and noninvasive measures [9,10].

The aim of the current study was to evaluate left ventricular myocardial performance in DS children with clinically and anatomically normal hearts using tissue Doppler derived myocardial performance index (TDI - Tei) and correlate it with plasma Myeloperoxidase as a marker of oxidants stress in those patients.

## 2. Patients and methods

The current cross-sectional study included 120 DS children recruited from Children s Hospital, Ain Shams University Out patients clinic and echocardiography unit (mean age,  $8.35 \pm 4.25$  years) in the period from January 2014 till April 2016. DS children were subjected to: Thorough history taking, clinical general and cardiac examination, laboratory investigations [Complete blood Count (CBC), serum Alanine Transaminase (ALT), serum creatinine, Thyroid stimulating hormone (TSH), thyroid hormones (FT3 and T4)], 12 lead ECG as well as Two dimension (2D), Motio (M) mode, color, pulsed and continuous wave Doppler echocardiography using (Vivid E9, Vingmed, GE, Horten, Norway). Left ventricle (LV) end-diastolic and end-systolic dimensions (LVEDD, LVESD), posterior wall thickness (LVPWT), interventricular septal thickness (IVSd), and LV ejection fraction (EF%) were evaluated by M-mode. The pulmonary artery systolic pressure was measured via tricuspid regurgitation jet using the Bernoulli equation [11].

DS children with congenital or acquired heart diseases, dysrhythmias, anaemia, pulmonary hypertension (mean pulmonary artery pressure more than 25 mmHg) thyroid, renal disease, diabetes were excluded from the study.

### 2.1. The remaining 50 DS children

with anatomically and clinically normal hearts (group I) were compared to 50 age and sex matched healthy children as control (group II).

Studied groups were subjected to: plasma Myeloperoxidase (MPO) level assessment by ELISA technique and TDI derived LV Tei index evaluation using echocardiographic machine equipped with 5-M HZ transducer and simultaneous electrocardiogram. Three consecutive cardiac cycles were measured and averaged. Heart rate was determined from ECG tracings obtained during echocardiographic studies [12].

### 2.2. Assessment of TDI derived LV Tei index

Tissue Doppler imaging waveforms of the mitral annulus were recorded and analyzed. Early diastolic waves ( $E'$ ), late diastolic

waves ( $A'$ ), systolic waves ( $S'$ ). The time interval from the end to the onset of the mitral annular velocity pattern during diastole (**A**) was measured from the TDI recordings. The duration of wave (**B**) was measured from the onset to the end of  $S'$  wave. LV- TDI Tei index was calculated as  $(A-B)/B$ , Fig. 1.

The isovolumic contraction time (ICT) was measured from the end of the  $A'$  wave to the beginning of the  $S'$  wave. The isovolumic relaxation time (IRT) was measured from the end of the  $S'$  wave to the beginning of the  $E'$  wave. The average of septal and lateral mitral annular values were estimated for measured waves and intervals. Waves mean values were obtained by averaging five consecutive beats [13]. An informed written consent was obtained from all parents/caregivers before the start of clinical, laboratory and radiological studies. The study was accepted by the ethical committee of Ain Shams University. The work has been carried out in accordance with the Code of Ethics of World Medical association of Helsinki for experiments in humans.

Statistical analysis: were performed using SPSS version 15.0 (SPSS, Inc. Chicago IL) software. Data were presented as mean (standard deviation) values. Pearson's product-moment correlation coefficient analysis, the Chi-square analysis, unpaired Student's *t* test for comparison of mean values of groups. P value < 0.05 was statistically significant (see Fig. 2).

## 3. Results

The demographic and clinical characteristics of studied groups are shown in Table 1.

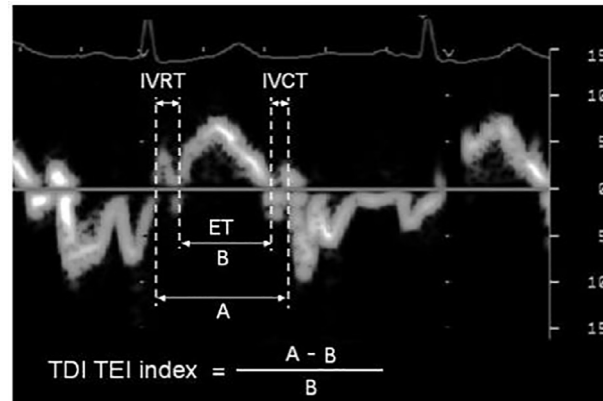


Fig. 1. TDI derived Tei index (A-B/B) [12]. IVRT: isovolumic relaxation time, ICT: isovolumic contraction time. ET: ejection time.

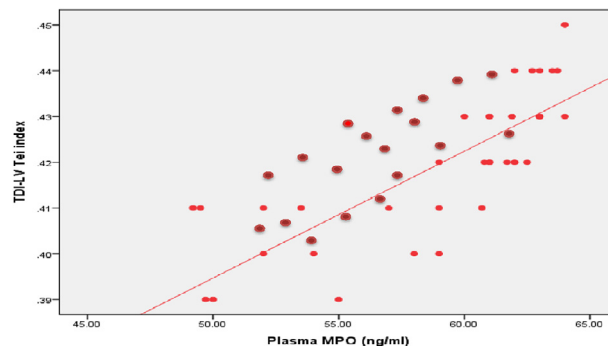


Fig. 2. Correlation between LV TDI-Tei index and plasma MPO in DS children.

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