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ORIGINAL ARTICLE

N-Terminal Pro Brain Natriuretic Peptide and Speckle Tracking Echocardiography Assessment of Cardiac Functions in Children with Juvenile Idiopathic Arthritis

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Abstract

Background: Patients with juvenile idiopathic arthritis (JIA) have a higher risk of cardiac problems, such as left heart failure. Clinical prognostic significance can be found in the examination of the left ventricle utilising conventional two-dimensional echocardiography, tissue doppler and two-dimensional speckle-tracking echocardiography along with monitoring NT-proBNP level.

Objectives: This study aimed to accurately evaluate of cardiac functions in children with JIA compared to matched healthy controls.

Subjects and methods: This case control study was conducted at Department of Pediatrics, Cardiology Unit, Rheumatology clinic and Clinical Pathology Department at Zagazig University Hospital on forty children who were allocated into two groups: control group: Twenty apparently normal, healthy children matched to case regarding to age and sex and case group: Twenty children with Juvenile rheumatoid arthritis and on regular follow-up once/month. NT-proBNP and echocardiography were assessed for all children.

Results: There was significant variations were detected between case and control groups for TAPSE and TAPSE/RVSP ratio, which were lower in the case group, and RVSV, LVEDD, LVESD, LVEDV, and LVESV, which was higher in the case group. No remarkable variations were observed for TR. There was no marked variations between both groups concerning LV longitudinal strain, LV size, right and left ventricle free wall longitudinal axes strain velocities using 2D speckle tracking except Rv4csl that was significant higher in cases than control ($p<0.0001$).

Conclusion: Regular cardiac monitoring is crucial in the early detection and management of heart disease in JIA cases, findings from an echocardiogram can help justify aggressive treatment for young cases diagnosed with juvenile rheumatoid arthritis and assess the progression of the disease in these patients.

Keywords: Juvenile Idiopathic Arthritis, Speckle Tracking Echocardiography, NT-proBNP.

Introduction

The term "juvenile idiopathic arthritis" (JIA) refers to a variety of physiologically unique and poorly understood forms of chronic inflammatory arthritis that appear in childhood **[1,2].**

Juvenile Idiopathic Arthritis (JIA) is a term that refers to all types of arthritis that start before the patient is 16 years old and last for more than six weeks. It is one of the most frequent chronic diseases of children. Idiopathic juvenile arthritis is recognized as a significant contributor to both short- and long-term impairment. In developed nations, incidence ranges between 2 and 20 cases per 100,000 people, and prevalence between 16 and 150 cases per 100,000 people. More than one-third of people continue to have an active disease as adults **[3].**Juvenile Idiopathic Arthritis is a diverse set of conditions that can cause persistent arthritis and a variety of extraarticular symptoms, such as problems with the cardiovascular system (CV). Long-term cardiovascular outcomes in people with chronic inflammatory arthritis have drawn a lot of attention in recent decades in Rheumatoid arthritis (RA) **[4].**

The well-known entities of pericardial, myocardial, or endocardial involvements are observed in JIA patients. Pericarditis, which affects around 35% of patients, is the most frequent and benign type of heart involvement, but it can also cause significant morbidity and mortality when it affects other cardiac layers (myocardium, endocardium) **[5].**

Juvenile Idiopathic Arthritis has a varied clinical course and prognosis. Modern methods are progressively achieving disease remission, but for many cases, this is a chronic condition requiring long-term immunomodulatory therapy, and there is little doubt that this has a significant influence on quality of life. According to previous research, at least one-third of individuals with JIA have an ongoing active condition, especially those who have a polyarticular course [1].

Using echocardiography, Bharti et al. assessed the left ventricle's systolic and diastolic performance in 35 children with JIA; these cases exhibited remarkably lower ejection fractions (EF) and higher systolic and diastolic blood pressures (SBP and DBP) **[**6]. There was variation between subtypes and a link with the length of the disease; polyarticular JIA patients had stronger evidence of diastolic dysfunction than oligoarticular and systemic JIA subtypes did [7**]**. In cases with prolonged disease duration, larger left ventricular systolic and diastolic dimensions were observed. The fact that all blood pressure readings and EF were within the normal range must be emphasized **[8].**

Cardiac biomarkers such as natriuretic peptides, notably N-terminal prohormone brain-type natriuretic peptide (NT-proBNP), might be raised prior to the development of symptoms related to cardiac stress **[9,10].**Cardiomyocytes produce brain natriuretic peptide (NT-proBNP) primarily in reaction to stretching caused by volume or pressure overload **[11].**Circulating NT-proBNP levels, as well as diastolic dysfunction, have been found to be higher in autoimmune arthritis cases without heart failure compared to controls without autoimmune arthritis or other inflammatory disorders **[12].**

This study aimed to accurate assessment of cardiac functions in children with JIA compared to matched healthy cases.

Methods

This case control study was carried out at Department of Pediatrics, Cardiology Unit, Rheumatology clinic and Clinical Pathology Department at Zagazig University Hospital on forty children who were allocated into two groups: control group: Twenty apparently normal, healthy children matched to case regarding to age and sex and case group: Twenty children with Juvenile rheumatoid arthritis and on regular follow-up once / month.

Children aged from 5 to 16 years with at least two consecutive visits to the outpatient Rheumatology Clinic, both gender and patients attending with juvenile rheumatoid arthritis who fulfills the American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) 2010 classification criteria for JIA were included in the study.

Children with age up to 5 years old, patients with previous atherosclerotic cardiovascular disease (CVD), chronic obstructive pulmonary disease, overlap syndrome, interstitial lung disease, incomplete clinical and catheter pressure recording data, cardiomyopathy, moderate or severe mitral or

aortic valvular disease, atrial fibrillation, echocardiography images of poor quality, congenital heart disease and other immunological diseases were excluded from the study.

All cases were subjected to thorough history taking included demographic characteristic data (Age, sex, education), family history, duration of the disease and protocol of treatment. **Detailed general clinical examination including: a**ll body systems examination, BP, body weight, body mass index (BMI), and height. **Cardiac examination:** was performed with special comment on: pallor, jaundice, cyanosis, bounding pulse and cardiac murmurs. **Investigations including c**omplete blood picture (CBC) by automated cell counter sysmex 330, C-reactive protein (CRP) by automated COBAS 6000, ESR by westergren method, rheumatoid factor, anti CCP, ANA by Immunofluorescent and NT-proBNP marker using enzyme-linked immunosorbent assay (ELISA) (Inova Diagnostics, San Diego, CA, USA). **Radiologic investigations including** Plain x-ray of the affected joints.

Echocardiographic evaluation: At first Standard transthoracic 2D echocardiographic examination: was performed using a Philips EPIC CVx cardiovascular ultrasound with 8 & 5 MHz sector phased array transducer and will be prospectively analyzed using an EchoPAC software (Healthcare, WI, USA**)** [13]. In line with the recommendations of the American Society of Echocardiography, M-mode, 2D, TDI, as well as pulsed and continuous Doppler flow across the various heart valves, were performed [14], and it was performed by an expert pediatric cardiologist with the patient in supine position.

The following measurements were focused on and recorded LV systolic function by M mode, LA dimension measurement, wall motion abnormality and LV diastolic function. **Then Speckle tracking echocardiography of the left ventricle:** performed from the parasternal long and short axis views at the apical 4, 3, and 2 chambers, loops of numerous ECG-gated complete cardiac cycles of the LV were recorded. The offline-workstation programme EchoPAC Dimension [12.0, Philips Medical Systems GmbH, Germany] was used to store the collected data and analyze it afterwards.

Ethical approval:

Written informed consent was obtained from all participants parents. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical Analysis:

SPSS (version 20.0, IBM Corp., Armonk, New York) was used to analyze the data. The parametric data shown as mean standard deviation. Unpaired Student's t-tests for parametric data were used to conduct statistical comparisons between several groups. Frequency and percentage were used to describe categorical data, which were then compared using the chi square test or fisher exact test. Using the Mann-Whitney test, non-parametric data are analyzed. The association between various parameters was evaluated using Pearson correlation. $P<0.05$ will be used to determine the level of significance.

Results

This mean age was 11.6 and 12.4 years for control and cases, respectively. For the cases group, 55% were males, while for control group 45% were males. There was no notable variation between groups concerning demographic and anthropometric data **(Table 1).**

Table 1. Comparison of demographic and anthropometric data between JIA cases and control

Variables		Control (N=20)	Cases (N=20)	t	P
Age (y)		11.6 ± 2.7	12.4 ± 1.9	-0.99	0.32
Sex	**Female**	9 (45%)	11 (55%)	X^2= 0.45	0.75
	Male	11 (55%)	9 (45%)		
Weight (kg)		40.2 ± 9.9	44.9 ± 10.7	-1.4	0.15
Height (cm)		139.6 ± 6.5	142.2 ± 9.9	-0.97	0.33
BMI (kg/m^2)		20.3 ± 4.8	22.2 ± 4.2	-1.2	0.21

Data are represented as mean ± SD or Number (%). Data are analyzed using independent t test and chi square test.

Regarding vital signs and laboratory data, there was remarkable variation between both groups regarding SBP, DBP, temperature, ESR, CRP, RF, anti-CCP, and NT-proBNP (P<0.05) **(Table 2).**

Table 2. Comparison of Vital sign, Laboratory Data, and BNP between JIA Cases and Control.

Variables	Control (N=20)	Cases (N=20)	t	P
SBP (mm Hg)	107.5 ± 5.2	113.7 ± 5.8	-3.5	**0.001***
DBP (mm Hg)	65.7 ± 5.2	71.7 ± 6.3	-3.2	**0.002***
Temperature (°C)	36.5 ± 1.4	38.9 ± 2.5	5.4	**<0.0001***
ESR (mm/hr)	5.4 ± 2.1	26.3 ± 11.6	-7.9	**<0.0001***
CRP (mg/L)	4.3 ± 0.77	9.4 ± 6.7	-3.2	**0.002***
RF(Negative)	20 (100%)	20 (100%)	-	-
Anti CCP (EU/mL) **(Positive)**	4.2 ± 1.1 0 (0%)	17.2 ± 3.3 5 (25%)	16.7 F	**<0.0001*** **0.04**
BNP (pg/mL) **Median** **Range**	22 (20-27)	40.5 (21-120)	18	**<0.0001***

***** P-value < 0.05 (significant), ESR: erythrocyte sedimentation rate, CRP: C reactive protein, RF: rheumatoid factor, Anti-CCP: anti Anti–cyclic citrullinated peptide, SBP: systolic blood pressure, DBP: diastolic blood pressure, BNP, brain natriuretic peptide.
Data are represented as mean ± SD. Data are analyzed using independent t test and fisher exact test.

Table (3) showed that there was significant differences were observed between the case and control groups for TAPSE and TAPSE/RVSP ratio, which were lower in the case group, and RVSV, LVEDD, LVESD, LVEDV, and LVESV, which was higher in the case group. No notable variance were noticed for TR.

Table 3. Comparison of 2- D Echocardiographic parameters between JIA Cases and Control

Variables		Control (N=20)	Cases (N=20)	t	P
LVEDD (mm)		3.9 ± 0.16	4.3 ± 0.19	-6.6	**<0.0001***
LVESD (mm)		2.5 ± 0.13	2.7 ± 0.08	-4.2	**<0.0001***
LVEDV(ml)		76.5 ± 3.4	91.6 ± 5.1	-10.8	**<0.0001***
LVESV (ml)		30.6 ± 1.42	33.3 ± 2.1	-4.7	**<0.0001***
FS(%)		32.8 ± 2.3	32.8 ± 2.6	0.06	0.95
EF (%)		65.6 ± 2.23	65.7 ± 4.9	-0.15	0.88
LA (mm)		27±6.49	29.2 ± 4.74	1.49	0.149
AO (mm)		22.2±3.94	25.1±3.86	1.62	0.116
LA/AO		1.15±0.15	1.18±0.15	0.68	0.505
MR/mmHg		22.05 ± 5.6	23.1 ± 11.1	U= 176	0.56
RV	**TR/mmHg**	29.1 ± 2.9	27.2 ± 5.3	1.35	0.18
	TAPSE (mm)	26 ± 1.6	21.3 ± 4.9	4.02	**<0.0001***
	RVSP mmHg	33.20 ± 4.38	37.90 ± 6.63	2.60	**0.013***
	TAPSE/RVSP ratio	0.783 ± 0.000	0.562 ± 0.196	-7.097	**<0.001***

Data are represented as mean ± SD. Data are analyzed using independent t test. ***** P-value < 0.05 (significant).RV: Right Ventricle, TAPSE: Tricuspid Annular Plane Systolic Excursion, RVSP: Right Ventricular Systolic Pressure

Regarding 2D conventional LV diastolic function there was remarkable variation between both groups respecting E/A that was lower in cases than normal group, while there was no significant variation concerning E,A and D/T. Concerning 2D Conventional RV Diastolic Function there was no notable difference between both groups cases than control group, regarding E, A and D/T. of RV DF trans annular tricuspid velocities **(Table 4).**

Table 4. Comparison of 2D Conventional LV and RV Diastolic Function (trans-Mitral Annular Velocity) between JIA Cases and Control

Variables		Control (N=20)	Cases (N=20)	t/U	P
LV DF (Mitral inflow velocities)	**E** (m/s) Median Range	1.1 (0.58-1.19)	0.85 (0.1-1.1)	U=147	0.15
	A(m/s) Median Range	0.6 (0.5-1.9)	0.61 (0.44-0.72)	U=188	0.74
	E/A Median Range	1.9 (0-2)	1.4 (1-2)	2.7	**0.009***
	D/T(ms)	156.7 ± 28.02	164.9 ± 27.6	-0.93	0.35
RV DF (Trans annular tricuspid velocities)	**E** (m/s)	82.3 ±8.92	83.3 ±10.43 (0.1-1.1)	0.241	0.811
	A(m/s)	0.64 ±0.029	0.65 ±0.049	0.204	0.839
	E/A	1.38±0.14	1.43 ±0.20	0.66	0.512
	D/T(ms)	165 ± 9.31	160.8 ± 8.64	-0.311	0.35

Data are represented as mean ± SD. Data are analyzed using Mann whitney and independent t test. ***** P-value < 0.05 (significant) LV DF, left ventricular diastolic function, MV Mitral Annular Velocity ,D/T: Deceleration Time, E: early filling phase , A:late filing phase due to atrial contraction. RV DF, right ventricular diastolic function.

Only the early and late diastolic velocities (É and Á) of the tricuspid annular tissue had a significant difference between the cases and controls. The other parameters did not show any remarkable variation between the two groups **(Table 5).**

Table 5. Comparison of Tissue Doppler Velocities between JIA Cases and Control

	Variables	Control (N=20)	Cases (N=20)	t/MW	P
Tissue Doppler mitral annular velocities					
LV (MV)	**S cm/sec** Median Range	0.41 (0.22-0.72)	0.53 (0.1-0.96)	U= 129.5	0.05
	E cm/sec Mean± SD	0.16 ± 0.03	0.17 ± 0.03	-0.93	0.35
	Á cm/sec Median Range	0.57 (0.26-0.83)	0.53 (0.1-0.96)	U=188	0.74

	E/ é Mean± SD	4.7 ± 1.15	5.06 ± 1.06	-0.76	0.44
Tissue Doppler tricuspid annular velocities					
RV (TV)	**S cm/sec** Mean± SD	0.51± 0.16	0.51 ± 0.21	-0.01	0.99
	É cm/sec Mean± SD	0.3 ± 0.11	0.22 ± 0.08	2.3	**0.02**
	Á cm/sec Mean± SD	0.49 ± 0.12	0.6 ± 0.12	-2.7	**0.009**
	E/ é Mean± SD	5.1 ± 1.3	5.2 ± 1.27	-0.18	0.85
Tissue Doppler MPI					
LV-MPI		0.42 ± 0.07	0.44 ± 0.12	188	0.74
RV-MPI		0.35 ± 0.04	0.35 ± 0.03	-0.03	0.96

Data are represented as mean ± SD. Data are analyzed using independent t test and Mann whitney test. ***** P-value < 0.05 (significant). **Mitra**l: S wave velocity of mitral annular tissue,É Early diastolic mitral annular velocity (Ea), Á Late diastolic mitral annular velocity (Aa), E/é Ratio of early diastolic mitral inflow velocity (E) to mitral annular early diastolic velocity (é). **Tricuspid** :S wave velocity of tricuspid annular tissue, É Early diastolic tricuspid annular velocity (Ea), Á Late diastolic tricuspid annular velocity (Aa), E/é Ratio of early diastolic tricuspid inflow velocity (E) to tricuspid annular early diastolic velocity (é). RV-MPI: Right Ventricular Myocardial Performance Index, LV-MPI: Left Ventricular Myocardial Performance Index.

The present findings showed that there was no significant variations between both groups regarding LV longitudinal strain, LV size, right and left ventricle free wall longitudinal axes strain velocities using 2D speckle tracking except Rv4csl that was significant higher in cases than control (p<0.0001) **(Table 6).**

Table 6. LV longitudinal strain, LV size, right and left ventricle free wall longitudinal axes strain velocities using 2D speckle tracking: Comparison between JIA Cases and Control

Variables	Control (N=20)	Cases (N=20)	U	P
LV longitudinal strain				
Basal septal segment % Median Range	-14.4 (-34.1-30.1)	-13 (-34.2-31.2)	192.5	0.83
Mid septal segment % Median Range	-19.6 (-35.8-34.7)	-17.7 (-33.7-35.4)	178.5	0.56
Apical septal segment % Median Range	-10.6 (-35.2-30.4)	-6.7 (-34.7-33.9)	175	0.49
Basal posterior segment % Median Range	-22.3 (-52.6-29.4)	-10.3 (-49.7-33.4)	142	0.11
Mid posterior segment % Median Range	5.05 (-31.8-36.7)	3.09 (-29.6-33.7)	171	0.59
Apical posterior segment %			184	0.87

Median Range	-0.2 (-32.4-20.9)	5.5 (-32.4- 20.4)		
Average Global LV strain % Median Range	-0.55 (-31.2-25.4)	16.2 (-30.4-25.8)	179	0.56
LV size				
Diastolic major axis A4c (mm) Mean± SD	69.4 ± 8.2	70.6 ± 9.6	-0.44	0.66
Systolic major axis A4c (mm) Mean± SD	55.4 ± 7.9	56.3 ± 9.3	-0.33	0.74
Diastolic major axis A2c(mm) Mean± SD	70.1 ± 8.2	71.3 ± 8.6	-0.46	0.64
Systolic Major Axis A2C(mm) Mean± SD	54.5 ± 8.8	56.8 ± 8.7	-0.82	0.41
right ventricle free wall longitudinal axes strain velocities				
Rvfwsl % Median Range	-14.1 (34.1-35.6)	-9.2 (-23.4-16.3)	164	0.83
Rv4csl % Median Range	-10.4 (-27.9-16.3)	-19.8 (-29.2-1.1)	16	<0.0001*
Basal RV free wall % Median Range	-28.1 (-45.7-30.7)	-27.6 (-45.7-33.2)	162.5	0.59
Mid RV free wall % Median Range	-23.6 (-38.2-27.8)	-11.8 (-37.2-33.5)	161	0.56
Apical RV free % Median Range	-23.1 (-27-12.8)	-23 (-25.1-33.1)	152	0.4
Left Atrial Free Wall Longitudinal Axes Strain Velocities				
LASr_ AC % Median Range	35.2 (-46.4-55.9)	28.1 (-52.6-52.1)	144.5	0.29
LAScd_ AC % Median Range	-26.6 (-46.7-32.6)	-22.3 (-43.2-39.6)	150	0.37
LASct_ AC % Median Range	-6.9 (-14.4-16.3)	5.4 (-12.1-16.5)	149	0.35
LASr_ ED % Median Range	40.3 (-37.2-63.2)	37.1 (-52.6-60.5)	152.5	0.41
LAScd_ ED % Median Range	30.9 (-51.5-55.9)	27.1 (-49.1-56.1)	163.5	0.61
LASct_ ED % Median Range	-10.1 (-16.6-7.9)	-8.9 (-12.4-8.8)	172.5	0.81

Data are represented as mean ± SD . Data are analyzed using Mann whitney test; GLS-endo_peak_A4C, GLS-endo_peak_A2C, and GLS-endo_peak_A3C represent the peak global longitudinal strain of the endocardial layer of the heart muscle, measured from the apical 4-chamber, 2-chamber, and 3-chamber views, respectively.

All unitless parameters measured in percentage (%).LASr_AC: Left atrial free wall longitudinal strain at atrial contraction .LAScd_AC: Left atrial free wall longitudinal strain at atrial contraction peak deflection ,LASct_AC: Left atrial free wall longitudinal strain at atrial contraction termination - ,LASr_ED: Left atrial free wall longitudinal strain at end-diastole - ,LAScd_ED: Left atrial free wall longitudinal strain at end-diastole peak deflection ,LASct_ED: Left atrial free wall longitudinal strain at end-diastole termination

There was positive correlation between NT-proBNP and each of LVEDD, LVESD, LVEDV, LVESV, IVSD, and MR. There was there was negative correlation between NT-proBNP and Tricuspedv É, GLS-endo_peak_Avg, Mid septal segment, mid posterior segment, apical posterior segment, mid septal segment, mid posterior segment, Rv4csl, and basal RV free wall(cm/sec) **(Table 7).**

Table 7. Correlation between BNP with study data

Variables	BNP	
	r	p
SBP	0.28	0.06
DBP	0.195	0.228
Temp	0.135	0.46
ESR	0.293	0.066
CRP	0.451	0.451
Anti-CCP	0.078	0.078
LVEDD	**0.458****	**0.003**
LVEDS	**0.475****	**0.002**
LVEDV	**0.639****	**0**
LVESV	**0.450****	**0.004**
IVSD	**0.349***	**0.027**
MR	**0.403****	**0.01**
Tricuspid É	**-0.371***	**0.018**
GLS-endo_peak_A4C	-0.286	0.073
GLS-endo_peak_A2C	-0.302	0.058
GLS-endo_peak_A3C	-0.222	0.168
GLS-endo_peak_Avg	-0.362*	**0.024**
Basal septal segment	-0.214	0.184
Mid septal segment	-0.340*	0.032
Apical septal segment	-0.303	0.057
Basal posterior segment	-0.214	0.186
Mid posterior segment	-0.439**	0.005
Apical posterior segment	-0.345*	0.031
Average Global LV strain	-0.245	0.128
Systolic major axis A4c	**0.22**	**0.177**
Diastolic major axis A2c	**0.023**	**0.89**
Systolic Major Axis A2C	**0.008**	**0.96**
Basal septal seg	**-0.284**	**0.076**
Mid septal seg	**-0.370***	**0.019**
Apical septal seg	**-0.241**	**0.134**
Basal posterior seg	**-0.248**	**0.123**
Mid posterior seg	**-0.335***	**0.034**
Apical posterior seg	**-0.223**	**0.167**
Rvfwsl	-0.155	0.358
Rv4csl	**-0.504****	**0.005**

Basal RV free wall(cm/sec)	**-0.338***	**0.038**
Mid RV free wall (cm/sec)	-0.211	0.204
Apical RV free(cm/sec)	-0.122	0.466
LASR_AC	0.255	0.122
LASCD_AC	-0.283	0.085
LASCT_AC	-0.17	0.308
LASR_ED	0.196	0.237
LASCD_ED	-0.216	0.192
LASCT_ED	-0.081	0.629

Discussion

Our study reported that there was no remarkable variation between both groups concerning demographic data. These data agreeing with **Cavallo et al., Alkady et al.,** and **Azpiri et al.** [15–17]. While our results were in disagreement with studies by **Duffy et al., and Martini et al.,** which showed a higher prevalence of JIA in females [18,19].

Anthropometric data, such as height, weight, and BMI, have been found not associated with the incidence and severity of JIA **[20].**

There is some evidence to suggest that there may be a difference in temperature in patients with JIA, with increases in joint temperature possibly indicating active disease **[21].** Our study found a significant difference in temperature between the cases and control group, with higher temperatures observed in the cases group. This finding agreed with **Hardal et al.,** which revealed that cases with systemic JIA, may present with fever of unknown origin **[22].**

Our study also found significantly higher SBP and DBP in the JIA group compared to the control group, although all readings remained within the normal range. This was consistent with **Bharti et al.,** who also found higher blood pressures in JIA patients, along with reduced EF **[6]. Arsenaki et al.** and **Alkady et al.** also noted a link between JIA subtypes and blood pressure, with polyarticular JIA patients showing stronger evidence of diastolic dysfunction and higher SBP, DBP, and heart rate than other subtypes or control groups **[16,23].**

ESR and CRP levels are commonly used biomarkers to detect and monitor inflammation in the body in all types of JIA. Higher ESR and CRP levels indicate the presence of inflammation in the body (active synovitis) **[24],** while elevated levels of anti-CCP antibodies are more commonly correlated with adult-onset RA and may not be present in children with JIA **[25].** Therefore, these tests are useful in evaluating the extent and severity of inflammation in JIA patients **[26,27].** In own study reported that there was a notable variation between both JIA and control groups concerning ESR, CRP, and anti-CCP levels, with higher levels in the JIA group.

According to our study, there was a remarkable variation in NT-proBNP levels between individuals with JIA and normal, with the JIA group displaying higher levels. This finding aligns with previous research conducted by **Holovko et al.** which also reported elevated levels of NT- NT-proBNP in JIA cases compared to normal cases **[28].** This study suggest that NT-proBNP could serve as a valuable biomarker for identifying JIA patients who may be at an elevated risk of CVD and for monitoring disease progression and treatment response. The authors also recommend that NT-proBNP testing may aid in identifying JIA patients who could benefit from additional cardiovascular screening and intervention.

We observed that patients with JIA had significantly larger LVEDD, LVESD, LVEDV, and LVESV compared to the normal cases. These results are consistent with **Bharti et al.,** which also reported significant variations between JIA and normal groups concerning LVEDV and LVESV**[6].**

In our study, we observed that there were no marked variations between the JIA and control groups concerning fractional shortening (FS) and EF in agreeing with **Lianza et al [1].**

However, **Bharti et al.** reported that both FS and EF were lower in JIA cases than controls **[6].**

In addition, **Alkady et al.** showed that LVEDV and LVEDD were considerably greater in JIA cases compared to controls, although LVESV and LVESD were insignificantly larger, and FS and EF

were insignificantly lower. These differences were seen for left ventricular systolic function metrics **[16].**

In our study, we found that the TAPSE values differed significantly between the case and control groups, with lower values seen in the case group. In **Lianza et. al.** study, a remarkable variation in TAPSE values was detected in the JIA group (23.2 ± 3.7 mm) compared to the control group (25.3 ± 3.2 mm), indicating impaired right ventricular (RV) function **[1].**

Our study found that RVSP was higher in the case group (37.9 mmHg vs. 33.2 mmHg, $p < 0.013$) and TAPSE/RVSP ratio was low. However, a study by **Azpiri-Lopez et al.** found that RVSP levels were comparable in RA cases and non-RA normal cases, but the TAPSE/RVSP ratio in RA patients was substantially lower than in controls [17], similar to our study, this shows that RA patients, particularly those with mild echocardiographic pulmonary hypertension (ePH), have impaired RV-pulmonary arterial coupling.

In our study, we found no significant variation between the cases of JIA and control in all parameters of mitral TDV, including S', E', A', E/e', and DT. However, a study by **Koca et al,** reported that JIA cases had lower mitral annular early diastolic velocity (E) and E/A ratio on TDI analysis, indicating impaired LV diastolic functions **[4].**

In the current study, our data for MPI indices were detected by pulsed wave tissue Doppler. Regarding to both the LV- MPI and RV- MPI we found no significant variations in LV MPI and RV MPI between the case and control groups ($P>0.05$). These findings match those of **Mavrogeni et al.** who also found no notable variation in LV and RV-MPI between JIA and control groups, suggesting similar LV global systolic and diastolic function in both groups **[29]** .

The present study reported that there was no remarkable variation between groups concerning speckle tracking data. There are several studies that have evaluated speckle tracking data in JIA patients, but some of them have reported conflicting results. One study by **Mavrogeni et al.** did not show remarkable variance in LV strain and strain rate between JIA patients and controls **[29].** However, a study by **Koca et al.** assumed that JIA cases had notably lower LV longitudinal strain compared to controls **[4].**

Similarly to the LA 2-D speckle tracking studies, several studies that have reported no significant variation between JIA and control groups in this regard. For example, a study by **Mavrogeni et al.** found no significant variation in left atrial strain rate between JIA cases and normal cases**[29].**

In relation to RV 2-D speckle tracking finding, our study reported that there was no notable variation between the JIA and normal groups regarding the RV free wall longitudinal axes strain velocities by speckle tracking, except for the longitudinal strain of the RV in the four-chamber view (Rv4csl), which was notably higher in JIA cases than in the normal group. While the study conducted by **Lianza et al.** is in line with previous reports found that JIA patients had reduced right ventricular Global Circumferential Strain (GCS) compared to healthy cases that have reported subclinical cardiac involvement in JIA patients using speckle tracking 2D, there is still some conflicting evidence **[1].**

Regarding correlations our study, there was no remarkable association between NT-proBNP and vital signs and laboratory data. There are a few studies that specifically investigated the correlation between NT-proBNP and vital signs, CRP, ESR, and anti-CCP in JIA compared to controls.

Provan et al. showed that the multivariate linear regression analyses that took into account the association between age and gender as an impact modifier also maintained a significant correlation. Demographic data, creatinine, CRP, and duration of disease were all substantially correlated with levels of NT-proBNP at the 10-year follow-up test. NT-proBNP and CRP levels were substantially correlated, supporting baseline analyses. The strong correlation between NT-proBNP levels and disease duration was also preserved **[30].**

Provan et al. conducted a study using a repeated mixed model analysis to evaluate the relationship between various markers of disease activity and NT-proBNP levels in JIA cases. They reported that CRP was the only notable predictor of NT-proBNP levels after adjusting for time of follow-up. Additionally, they observed that NT-proBNP levels increased over time and that the effects of age and gender on these levels were significant **[30].**

This study found that there was positive relationship between NT-proBNP and each of LVEDD, LVESD, LVEDV, LVESV, and MR. There was no correlation between NT-PROBNP and each of right ventricle parameters. There was there was negative correlation between NT-proBNP and É.

Also, in agreement with our study, there was no correlation between NT-PROBNP levels and right ventricular parameters as noted by **Gong et al.,** who found that there was no notable relationship between NT-proBNP levels and any of the RV parameters studied, including RVEF, RV end-diastolic volume, and RV end-systolic volume, they also found a negative association between NT-proBNP levels and É, which is a measure of early diastolic mitral annular velocity **[31].**

This study showed that there was negative relationship between NT-proBNP and each of GLS-endo_peak_Avg, Mid septal segment, mid posterior segment and apical posterior segment. There was negative correlation between NT-proBNP and each of mid septal segment and mid posterior segment. There was no remarkable variation between both groups concerning Left atrial free wall longitudinal axes strain velocities by speckle tracking. Also, a previous study reported a negative association between NT-proBNP levels and global longitudinal strain (GLS) assessed at the endocardial peak in the average of all segments (GLS-endo_peak_Avg), as well as the mid-septal and mid-posterior segments. Additionally, the study found no significant difference in left atrial free wall longitudinal axes strain velocities by speckle tracking between patients with higher and lower NT-proBNP levels **[32].**

Conclusion

Regular cardiac monitoring is crucial in the early detection and management of heart disease in JIA patients, findings from an echocardiogram can help justify aggressive treatment for young cases diagnosed with juvenile rheumatoid arthritis and assess the progression of the disease in these patients.

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