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RESEARCH ARTICLE

Subclinical atherosclerosis in Egyptian children with JIA: assessment of the risk factors.

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Abstract

Background and aim of work: Juvenile idiopathic arthritis (JIA), is expected to accelerate the process of atherosclerosis. The aim of the current study is to identify possible risk factors of early development of subclinical atherosclerosis in children with JIA.

Subjects and methods: This study included 42 JIA and 42 healthy controls. Traditional cardiovascular risk factors and inflammatory markers together with IMT (intima-media thickness), FMD (flow mediated dilation) of brachial arteries, and LVMi (left ventricle mass index) as surrogate markers of subclinical atherosclerosis were assessed and compared between patients and controls.

Results: Patients with JIA had increased IMT and LVMi and decreased FMD% as compared to controls. The increased IMT, LVMi and brachial artery diameter and the decreased FMD% were associated with elevated BMI, elevated systolic blood pressure, and elevated inflammatory markers and with decreased HDL. Regression analysis revealed that for the increased IMT in patients who had JIA, BMI, SBP, hsCRP and TNF-α were the best predictors. Also, in the regression model the best predictors for FMD %, were the BMI, hsCRP and TNF-α while for LVMi, SBP was the only significant predictors in the regression model.

Conclusion: Patients with JIA had impaired endothelial function, increased carotid IMT and increased LVMi which strongly confirm the evidence of presence of subclinical CV system changes that predispose to the development of atherosclerosis at this early age. This increased subclinical atherosclerosis depends mainly on increased BMI and the heightened inflammatory mediators.

INTRODUCTION

Atherosclerosis is a chronic inflammatory disease of the arteries. Clinical consequences of the atherosclerotic process, in the form of ischaemic heart disease, disorders of cerebral circulation, or circulatory disorders of peripheral arteries occur in the adult population, however, the process of atherosclerosis starts in childhood.(1) In normal children, the extent of vascular involvement is minor and the rate of progression is slow. Some chronic pediatric diseases, in particular the inflammatory conditions, are expected to accelerate the process of atherosclerosis. The rate of the progression of atherosclerosis in these children is dependent on the number of risk factors and their intensity(2) (3) . Juvenile idiopathic arthritis (JIA) is a chronic inflammatory diseases, have been considered as a high risk pediatric conditions that is associated with premature cardiovascular disease (CVD) (4).

The available data as regards subclinical atherosclerosis in children with JIA are lacking. It was previously reported that children who had JIA had increased intima media thickness (5) (6) and impaired endothelial function (7). However, children with traditional risk factors for CVD were not included in these studies. Obesity in childhood is an increasing problem almost in all populations and childhood obesity predicts adulthood obesity and CVD (8) (9).

Currently, numerous non-invasive imaging procedures can be used to detect the development of atherosclerosis in children who had CVD risk factors. Endothelial function, that is, the vasodilator response to increased blood flow (flow mediated vasodilatation (FMD)), the analysis of carotid artery intima-media thickness (IMT), and echocardiographic assessment of left ventricle mass (LVM), are currently used for identification of these children at high risk to develop CVD (10).

Therefore identify high-risk children in preclinical phase who may benefit from early intervention to prevent development of clinical disease or to slow progression to atherosclerosis is crucial for proper management and may be life-saving. The aim of the current study is to identify possible risk factors of early development of subclinical atherosclerosis in children with JIA.

Subjects and Methods:

Participants

In this study, 42 consecutive children with JIA diagnosed according to the criteria of the International League of Associations for Rheumatology (11)were recruited from the Rheumatology and Paediatric Departments, Zagazig University Hospitals, Egypt in the period from August 2014 to March 2015. The patients were 24 females and 18 males with their ages ranged from 11 to 15 years. Diseases duration of JIA ranged from 2.5 to 7 years. A group of 42 healthy children (22 females and 20 males) were also enrolled in the study to serve as a control group. Children with a history of cardiovascular disease due to any medical conditions other than the current JIA were excluded from the study.

All children included in this study and their parents were given separate full detailed written information about the study. A verbal and written consent from all JIA patients and their parents was obtained before entering the study.

Data Collection

From the Follow up clinics of Rheumatology and Paediatric Departments, we also collected data from Zagazig Hospitals computerized records for all diagnosed JIA patients. The patient's clinical notes were reviewed to gather information on his/her age, sex, the age of disease onset, disease duration, eye involvement, fever- rash- hepatomegaly- spleenomegaly- generalized lymphadenopathy- serositis and JIA onset subtype.

Clinical Assessment including:

1- General examination

Weight - height and body mass index (BMI);BMI was calculated for each child to determine childhood overweight and obesity. BMI was measured as follow Weight in Kg ÷ Stature in cm ÷ stature in cm * 10000 .(12) (13).

Systolic (SBP) and diastolic(DBP) blood pressures were measured twice at the right arm after a 10-minute rest using calibrated sphygmomanometer with appropriate cuff size and were averaged.

2-Local joint examination

Stiffness- tender joints- swollen joints- limited range of motion- deformities

3-Disease activity

Disease activity was measured by different ways: tender joint count, swollen joint count, juvenile arthritis disease activity score (JADAS 27) (14) ,100-mm pain visual analogue scale (VAS) [15] and serological markers of inflammation such as ESR (Westergren method) and/or CRP for all participating patients.

4- Assessment of the cardiovascular parameters

Brachial artery flow mediated dilatation

The FMD was measured to assess the vascular endothelial function.

Subject should be fasting for 8 hours, no caffeine or tobacco, no drugs that can affect Cardiovascular system for 4 half lifes, No vitamins for 72 hours, No exercise for 12 hours ,If menstruating female she is instructed to come at day 1 to day 7 of the cycle. Subject should be seated or lie down for 10 minutes to rest and avoid orthostatic changes in blood pressure effects before examination (16)

To create a flow stimulus in the brachial artery, a sphygmomanometric (blood pressure) cuff is first placed either above the ante-cubital fossa or on the forearm. A baseline rest image is acquired using Toshiba Nemio 20 with linear multi-frequency transducer 6 – 11 Mhz .Blood flow is estimated by time-averaging the pulsed Doppler velocity signal obtained from a mid-artery sample volume. Thereafter, arterial occlusion is created by cuff inflation to supra-systolic pressure. Typically, the cuff is inflated to at least 50 mm Hg above systolic pressure to occlude arterial inflow for 5 minutes . This causes ischemia and consequent dilation of downstream resistance vessels via auto-regulatory mechanisms. Subsequent cuff deflation induces a brief high-flow state through the brachial artery (reactive hyperemia) to accommodate the dilated resistance vessels. A longitudinal image of the artery is recorded continuously from 30 s before to 2 min after cuff deflation. A mid-artery pulsed Doppler signal is obtained upon cuff deflation to assess hyperemic velocity. Measurement of arteries was performed during the diastolic phase as determined by ECG gating (R wave identifies end diatole), measuring the distance between innermost limit of one side of the artery to the other. The FMD% was calculated according to the following formula; FMD% = [(maximum diameter−baseline diameter)/baseline diameter] × 100(17).

Carotid Ultrasound Scanning

JIA patients were examined in the supine position with their neck in extension and head turned contra-laterally 45° with a high resolution B-mode ultrasonography equipped with a 6-11 MHz linear array transducer using a Toshiba Nemio 20 Ultrasound device. All the ultrasound examinations were performed by the same operator who was blinded to clinical and laboratory findings of the participants. The right and left common carotid arteries were evaluated. Measurements included end-diastolic (minimum diameter) IMT of the far walls (the distance from the leading edge of the first echogenic line to the leading edge of the second echogenic line of the two anatomic boundaries ; lumen-intima and media-adventitia interface)(18). Average IMT calculation in millimeters was obtained from 3 measurements performed 1 cm below the common carotid bifurcation.

Echocardiographic Doppler examination

All participants underwent a complete 2D echocardiogram with M-mode and Doppler study demonstrating structurally normal heart. Measurements were done using GE Vivid 7 ultrasound machine using sector probes 3S, 5S .Measurements of the left ventricle (LV) internal dimension, interventricular septal thickness, and posterior wall thickness were made during diastole according to practice guidelines of the American Society of Echocardiography.

LV mass was calculated from m-mode measurement using ASE convention leading edge to leading edge by the following formula (19)

LV mass (ASE): 0.8 (1.04 ([LVIDD + PWTD + IVSTD]3- [LVIDD]3))+ 0,6 g

LVIDD = Left Ventricular Internal Diameter in Diastole

PWTD = Posterior Wall Thickness in Diastole

IVSTD = Interventricular Septum Thickness in Diastole

LV mass index was calculated by dividing LV mass by the height in meters raised to power 2.7 to minimize effect of age and gender (20)

All the examinations were carried out and analyzed by one experienced Pediatric Cardiology physician, who was blinded to the participants' cardiovascular risk factor status.

5-Laboratory investigations

- Complete blood picture (CBC)
- Rheumatoid factor (RF)
- Acute phase reactant (ESR, CRP)
- Concentrations of (IL-6, and TNF- α) were determined by ELISA
- Lipid profile

Statistical analysis

Continuous data were expressed as mean ±standard deviation (SD) while the categorical data were expressed as number and percent. All continuous data were tested for the skewness and kurtosis prior to any analyses. Comparisons between continuous data were performed using the independent sample Student's t test meanwhile the comparisons between the categorical data were performed using the chi square test. One way ANOVA test was used for the comparison of FMD%, IMT and LVMi among the patients with different types of the JIA. Correlations between the studied variables were assessed by correlation co-efficient test. The multiple regression analysis models was used to reveal the predictive value of the traditional risk factors and the inflammatory markers for the increased IMT, reduced FMD% and increased LVMi in patients who had JIA. Statistical significance was determined at $p < 0.05$. All calculations were made using SPSS version 20.0.

Results :

This study included 42 JIA and 42 healthy controls. The patients were 57.1% (n=24) females and 42.9% (n=18) males with their average age of 13 ±1.4 years (ranged from 11 to 15 years). The controls were 52.4% (n=22) females and 47.1% (n=20) males with an average of 13.1 ±1.3 years (ranged from 11 to 15). The two groups were similar as regards the age and gender (Table 1). The JIA features of the patients were also demonstrated in Table 1. The average duration of JIA among the patients was 4.6 ±1.3 years. The criteria of an inactive disease were met by 22 children (52.4%) and those of an active disease by 20 children (47.6%).Of these patients, 50% (n=21) had oligoarthicular type, 40.5% (n=17) had polyarticular type and 9.5% (n=4) had systemic type of JIA. Among the patients participated in the study 64.3% (n=27) were currently using corticosteroids, 47.6% (n=20) were on methotrexate and 7.1% (n=6) were on biological therapy.

Table 1. Demographic and clinical data of the participants

	JIA (n=42)	Controls (n=42)	p
Age (years)	13 ±1.4	13.1 ±1.3	0.812
Sex (n, %)			
Girls	24, 57.1%	22, 52.4%	0.661
Boys	18, 42.9%	20, 47.1%	
JIA related features			
Age at onset of JIA (years)	8.4 ±2.7		
Duration of JIA (years)	4.6 ±1.3		
Disease activity (n, %)			
Active	20, 47.6%		
Inactive	22, 52.4%		
Type of JIA (n, %)			
Oligoarticular	21, 50%		
Polyarticular	17, 40.5%		
Systemic	4, 9.5%		

Current treatment (n, %)	
Corticosteroids	27, 64.3%
Methotrexate	20, 47.6%
Biologics	6, 7.1%

The cardiovascular risk factors were compared between the JIA patients and the controls (Table 2). JIA patients had a significantly higher DBP and SBP than the controls (p=0.032 and p=0.015 respectively).However, the BMI and serum lipids did not differ significantly between the patients and the controls. Comparing the inflammatory markers between the two groups showed that hsCRP, IL-6 and TNF-α were significantly higher in the JIA patients as compared to the controls (p<0.001).

Prior to the induction of ischemia, ultrasonographic examination of the brachial artery revealed that the brachial artery diameter did not differ significantly between the JIA patients and the controls, however, FMD% was 6.7 ±1.1 versus 10 ±1.1 in the JIA patients and controls respectively. This difference was significant (95% CI: -3.308; -2.848, p<0.001). The carotid IMT of the JIA patients was 0.49 ±0.03 mm compared to 0.42 ±0.02 mm in the controls. This difference was significant (95% CI: 0.053; 0.075, p<0.001). The echocardiographic examination showed that LVMi of the JIA patients was 26 ±1.6 compared to 23.2 ±3.2 of the controls. This difference was significant (95% CI: 1.718; 3.891, p<0.001) (Table 2).

Table 2. Traditional cardiovascular risk factors, inflammatory markers, and cardiovascular system parameters of JIA patients and the controls

	JIA (n=42)	Controls (n=42)	p
Traditional risk factors			
BMI (kg/m2)	19.6 ±1.7	20 ±1.8	0.372
DBP (mmHg)	67.3 ±4.6	65.3 ±3.4	0.032
SBP (mmHg)	112.7 ±7.4	109.1 ±5.7	0.015
Cholesterol (mg/dl)	160.7 ±11	157.9 ±12.5	0.290
LDL (mg/dl)	82.6 ±8.9	83.2 ±7.6	0.750
HDL (mg/dl)	52.7 ±3.5	52.2 ±3.6	0.474
Triglycerides (mg/dl)	130.6 ±4.5	131 ±4.1	0.709
Inflammatory markers			
hsCRP (mg/L)	1.8 ±1	0.11 ±0.06	<0.001
IL-6 (pg/ml)	2.02 ±1	0.24 ±0.1	<0.001
TNF-α (pg/ml)	2.3 ±0.6	0.82 ±0.07	<0.001
Cardiovascular system parameters			

Brachial artery diameter (mm)	3.8 ±0.3	3.7 ±0.3	0.206
FMD%	6.7 ±1.1	10 ±1.1	<0.001
IMT (mm)	0.49 ±0.03	0.42 ±0.02	<0.001
LVMi ($g/m^{2.7}$)	26 ±1.6	23.2 ±3.2	<0.001

JIA patients who had active disease had significantly higher hsCRP (p=0.025), higher IL-6 (p=0.024) and higher TNF-α (p=0.038) than patients who had no active disease. Also, IMT and LVMi were significantly higher in patients with active JIA than patients with inactive JIA (p= 0.025 and p=0.040 respectively) while FMD% was significantly lower in the patients with active JIA than those with inactive JIA. The current use of corticosteroids is more frequent in the JIA patients with active than those with inactive disease (p=0.013). On the other hand age, gender and the traditional cardiovascular risk factors did not differ significantly between the patients with active than with inactive JIA (Table 3).

Table 3. Comparison of the traditional cardiovascular risk factors, inflammatory markers, and cardiovascular system parameters of JIA patients with clinically active and inactive disease

	JIA patients with		
	inactive disease	active disease	p
N	20	22	
Age (years)	12.7 ±1.6	13.3 ±1.3	0.204
Sex (n, %)			
Girls	10, 50%	14, 63.6%	0.372
Boys	10, 50%	8, 36.4%	
Traditional risk factors			
BMI (kg/m2)	19.60 ±1.6	19.63 ±1.8	0.845
DBP (mmHg)	66.1 ±4.3	68.3 ±4.7	0.120
SBP (mmHg)	110.1 ±6.4	115.1 ±7.7	0.029
Cholesterol (mg/dl)	159.8 ±12	161.5 ±10.3	0.635
LDL (mg/dl)	81.7 ±8.9	83.3 ±8.9	0.547
HDL (mg/dl)	52.3 ±3.7	53.1 ±3.5	0.476
Triglycerides (mg/dl)	130.5 ±4.6	130.7 ±4.4	0.845
Use of corticosteroids	9, 45%	18, 81.8%	0.013
Inflammatory markers			
hsCRP (mg/L)	1.5 ±0.9	2.2 ±1	0.025

IL-6 (pg/ml)	1.7 ±1	2.3 ±0.8	0.024
TNF-α	2.1 ±0.6	2.5 ±0.5	0.038
Ultrasonographic evaluation of cardiovascular system			
Brachial artery diameter (mm)	3.7 ±0.3	3.8 ±0.3	0.305
FMD%	7.1 ±1.1	6.4 ±1	0.041
IMT (mm)	0.48 ±0.03	0.50 ±0.03	0.025
LVMi	25.5 ±1.5	26.5 ±1.6	0.040

Brachial artery was significantly correlated with BMI (p=0.003), SBP (p=0.010), hsCRP (0.036), IL-6 (p=0.010) and with TNF-α (0.024) and was inversely correlated with HDL (0.008). FMD% was inversely correlated with BMI (p=0.039), SBP (p=0.008), hsCRP (0.005), IL-6 (p=0.009) and with TNF-α (0.005) but directly correlated with HDL (p=0.031). IMT was significantly correlated with BMI (p=0.015), SBP (p=0.008), hsCRP (0.002), IL-6 (p=0.005) and with TNF-α (0.006) and was inversely correlated with HDL (0.019). LVMi was significantly correlated with BMI (p=0.003), SBP (p=0.007), hsCRP (0.004), IL-6 (p=0.004) and with TNF-α (0.047) and was inversely correlated with HDL (0.016) (Table 4).

Table 4. Correlations between IMT, FMD and LVMi with traditional cardiovascular risk factors and inflammatory markers in patients with JIA

		Brachial artery	FMD%	IMT	LVMi
Age	r	0.026	0.034	-0.242	0.193
	p	0.870	0.829	0.123	0.220
BMI	r	0.445	-0.320	0.373	0.442
	p	0.003	0.039	0.015	0.003
SBP	r	0.391	-0.406	0.401	0.411
	p	0.010	0.008	0.008	0.007
DBP	r	0.032	0.088	0.055	0.043
	p	0.840	0.578	0.729	0.786
Cholesterol	r	0.049	-0.115	0.104	0.143
	p	0.758	0.470	0.514	0.366
LDL	r	0.098	-0.046	0.038	0.065
	p	0.535	0.771	0.812	0.683
HDL	r	-0.401	0.333	-0.361	-0.371

	p	0.008	0.031	0.019	0.016
Triglycerides	r	0.093	-0.105	0.095	0.079
	p	0.559	0.508	0.549	0.621
hsCRP	r	0.324	-0.426	0.458	0.435
	p	0.036	0.005	0.002	0.004
IL-6	r	0.394	-0.398	0.429	0.438
	p	0.010	0.009	0.005	0.004
TNF-α	r	0.348	-0.427	0.418	0.309
	p	0.024	0.005	0.006	0.047

The Table 5 showed that the FMD%, IMT and LVMi did not differ significantly among the JIA patients who had oligoarticular, polyarticular and systemic types of the JIA.

Table 5. Difference between the IMT, FMD and LVMi in different types of JIA

	Type of JIA			
	Oligoarticular	Polyarticular	systemic	p
FMD%	6.8 ±1.1	6.4 ±1.1	7.5 ±0.7	0.187
IMT	0.48 ±0.03	0.49 ±0.03	0.47 ±0.03	0.273
LVMi	25.9 ±1.5	26.5 ±1.7	24.9 ±0.8	0.179

In the multiple regression analysis model to reveal the predictive value of the traditional risk factors and the inflammatory markers for the increased IMT in patients who had JIA, BMI, SBP, hsCRP and TNF-α were the best predictors. In the regression model with FMD%, the BMI, hsCRP and TNF-α were the best predictors appeared to be the best predictors for decreased FMD%. For LVMi, SBP was the only significant predictors in the regression model (Table 6).

Table 6. Multiple linear regression analyses for IMT, FMD, and LVMi as dependent variables with traditional cardiovascular risk factors and inflammatory markers

	Dependant variable					
	IMT		FMD%		LVMi	
	B	p	β	p	β	p
Independent variable						

BMI	0.371	0.015	-0.320	0.039	0.178	0.162
SBP	0.401	0.008	-0.264	0.070	0.296	0.034
HDL	0.146	0.273	-0.076	0.588	0.148	0.267
hsCRP	0.303	0.028	-0.297	0.040	0.046	0.612
IL-6	0.206	0.136	-0.176	0.223	0.208	0.133
TNF-α	0.418	0.006	-0.427	0.005	0.064	0.638
Current corticosteroids	0.003	0.997	-0.199	0.126	0.083	0.515

Discussion:

The major finding of the current study is that patients with JIA had increased IMT and LVMi and impaired endothelial function, measured as FMD of brachial arteries as compared to matched controls. These findings strongly confirm the evidence of presence of subclinical CV system changes that predispose to the development of atherosclerosis at this early age. Another major finding in our study is that increased IMT, LVMi and brachial artery diameter and the decreased FMD% were associated with elevated BMI, elevated systolic blood pressure, and elevated inflammatory markers and with decreased HDL. Our findings are in agreement with that of ***Głowińska-Olszewska B et al.*** (21). Besides, several studies had shown that subclinical atherosclerosis, vascular stiffness, and endothelial dysfunction were more frequent among RA patients than controls ***(22) (23) (24)***.

Obesity and elevated BMI is commonly recognized as cardiovascular risk factor. Childhood obesity has been found to be associated with increased risk for development of accelerated atherosclerosis. Several studies found that obesity is more prevalent among the JIA patients compared to healthy children and also reported that obesity is associated with increased IMT, LVMi and brachial artery diameter and the decreased FMD%. In our finding, BMI was found to be significantly correlated with increased IMT, LVMi and brachial artery diameter and the decreased FMD%.***(25) (26)(21)***

However, in patients with RA, cachexia (characterized by low BMI) was found to be also associated with increased occurrence of CV risk ***(27)***. Cachexia is characterized by the loss of body mass, but fat mass tends to be maintained or increased ***(28)*** which may account for the increased CV risk despite low BMI. In two studies that used whole body dual X-ray absorptiometry scans the percentage of total body fat was significantly higher whereas the total lean body mass was significantly lower in children with JIA compared to healthy children***(29) (30)***.

Another possibility that can explain the elevated CV risk among patients with RA despite the decreased BMI can be attributed to heightened inflammatory mediators in these patients. In our study, patients with JIA had significantly higher hsCRP, TNF-α and IL-6 than the healthy controls. The elevated levels of pro-inflammatory cytokines are observed in RA ***(31)***, and in children with JIA***(1)***. Another important finding in the current study is that JIA who had an active disease had significantly higher IMT and LVMi but lower FMD% than JIA patients who had no active disease. This finding seems reasonable since disease activity is associated with elevated inflammatory markers which are itself a risk factor for the accelerated atherosclerosis.

Currently, FMD assessment is progressively used for juvenile CV risk evaluation ***(21)***. Interestingly, it was observed that endothelial dysfunction in obese children was significantly higher in comparison to the non-obese children although that IMT did not differ significantly between the two groups ***(32)***. The authors, hence, concluded that endothelial dysfunction seems to be the earliest marker of subclinical atherosclerosis. The pro-inflammatory cytokines, in particular IL-6, are involved in the process of endothelial dysfunction and these cytokines increase the ICAM-1 expression and CRP synthesis ***(33)***. IL-6 was found to play a vital role in the vascular endothelial activation ***(34)***. It was Demonstrated significantly higher IL-6 levels in children with JIA compared to the control group, this finding is consistent to our findings ***(35)***.

The IMT is a factor predicting the stage of atherosclerosis and it may help to assess the cardiovascular risk in asymptomatic patients with a moderate cardiovascular risk . In the current study, IMT was significantly higher among patients with JIA as compared to controls and IMT was elevated with increased BMI, elevated systolic blood pressure, and elevated inflammatory markers and with decreased HDL. This finding is in agreement with that of ***Undas A et al*** (36). The increased IMT in children with JIA compared to healthy children was also demonstrated by the study of ***Breda L et al.*** (37).However, the study of ***Jednacz and Rutkowska-Sak (2015)*** did not demonstrate differences in IMT between healthy children and children with JIA. The study of ***Jednacz E et al. (35)*** did not include children with a systemic disease where the intensity of inflammatory process is particularly high.In the study by ***Vlahos AP et al.*** (7) that assessed CV risk in children with JIA, increased IMT was observed only in children with a systemic disease, and this difference was not observed for oligoarticular or polyarticular form.

In our study, children with JIA had increased LVMi, and the difference in LVMi between JIA obese and non-obese was also significant. Increased LVM is a recognized predictor of cardiovascular morbidity and mortality. Obesity in childhood and adolescence has also been associated with significant alterations in cardiac parameters geometry ***(38)***. A previous study had shown that change in weight and blood pressure during childhood is predictive of excess LVM in young adults ***(39)***. ***Crowley et al.*** reported that higher LVMi tend to be associated with increasing BMI, consistently with our findings ***(40)***.

In our study the multiple regression analysis model revealed that for the increased IMT in patients who had JIA, BMI, SBP, hsCRP and TNF-α were the best predictors. Also, in the regression model the best predictors for FMD%, were the BMI, hsCRP and TNF-α while for LVMi, SBP was the only significant predictors in the regression model. In agreement with our findings, in addition to elevated BMI, the clustered factors that is elevated SBP, inflammatory markers, dyslipidemia and its association with increased prevalence of subclinical atherosclerosis among obese JIA patients as compared to the non-obese JIA patients and to the control sand even in obese compared to the non-obese children had been reported by many studies ***(25) (26)(21)*** . ***Głowińska-Olszewska B et al. (41)***, in agreement with our findings, reported that the impaired endothelium function, diminished FMD, and increased IMT were more frequent among obese hypertensive adolescents. Also in agreement with our findings, ***Głowińska-Olszewska B et al. (21)***found that the obese JIA patients had many factors that are associated with increased cardiovascular including increased SBP, alongside with increased inflammatory markers such as hsCRP and IL-6 in comparison to non-obese patients and controls. They also reported that these alterations were associated with increased evidence for early atherosclerosis.

Conclusion:

Patients with JIA had impaired endothelial function and increased carotid intima-media thickness accompanied by increased left ventricle mass index which strongly confirm the evidence of presence of subclinical CV system changes that predispose to the development of atherosclerosis at this early age. This increased subclinical atherosclerosis depends mainly on increased BMI and the heightened inflammatory mediators.

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