

Brachial Flow Mediated Dilatation and Osteoprotegerin in Type 1 Diabetes Mellitus

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Background

Type 1 diabetes is a risk factor for cardiovascular disease. Osteoprotegerin is a predictor of cardiovascular disease. Endothelial dysfunction is the earliest event in atherosclerosis and subsequent cardiovascular disease. Flow mediated dilation of brachial artery can be used to detect endothelial dysfunction.^{1,2}

Aim: To assess flow mediated dilation of brachial artery in type 1 diabetes and its relation to serum osteoprotegerin level.

Subjects and Methods

- **Setting:** Children's Diabetes Clinic, Ain-Shams University Hospital, Cairo, Egypt
- **Study duration:** 03/2014 – 01/2015
- **Type of study:** Case control study
- **Subjects:** 40 patients with type 1 diabetes mellitus
- **Inclusion criteria:**
 1. Type 1 diabetes mellitus
 2. Age: 5 -18 years
 3. Diabetes duration > 3 years
 4. Regularly following up and adherent to their insulin doses and self monitoring of blood glucose
- **Exclusion criteria:**
 1. Patients on any medication other than insulin, especially anti-hypertensive, anti-platelet or lipid lowering medications
 2. Patients with cardiovascular disease or any chronic disease other than diabetes
- **Control group:** 40 healthy, age, sex, and puberty matched children. None were hypertensive or smokers, nor on any medication, nor had any chronic illness. All had negative family history of diabetes and dyslipidaemia.
- **Ethical approval:** local ethics committee of Ain-Shams University. All patients and controls or their legal guardians signed an informed consent prior to the study.
- **Clinical evaluation:**
 1. Detailed medical history
 2. Anthropometric evaluation including
 - Height, weight, and body mass index (BMI) standard deviation scores^{3,4}
 - Waist (WC) and hip circumferences (HC) standard deviation scores^{5,6}
 - Waist to hip ratio (WHR)^{5,6}
 - Tanner staging³
 3. Mean standing and lying blood pressure. The measurement was repeated twice in the same visit if the blood pressure was greater than 90th percentile for age and sex.⁷
- **Biochemical evaluation:**
 1. Fasting lipid profile: serum triglycerides (TG) and total cholesterol (TC), HDL cholesterol (HDL-C), and LDL cholesterol (LDL-C)⁸
 2. Urinary albumin/creatinine ratio (ACR). Microalbuminuria was defined as 30-299 mg/g in at least two out of three spot morning urine samples, taken two months apart, and over a total period of six months.⁹
 3. Glycosylated Hb (Hb A1c): Mean of eight readings over the last 2 years
 4. Serum osteoprotegerin (ELISA)
- **Flow mediated dilation of brachial artery:**

A single experienced radiologist without prior knowledge of the studied subjects performed all imaging studies. The images were obtained using a single standard 10 MHz linear array transducer (GE Logiq 9 ultrasound machine) with the subject in the supine position. The right brachial artery images were obtained above the antecubital fossa using B-mode imaging in the longitudinal plane of the artery. A baseline image was acquired using a resolution box function to magnify this part of the artery. A sphygmomanometer cuff was placed on the proximal right forearm. The cuff was inflated to 100 mmHg above the systolic pressure to occlude arterial flow for 2 minutes. Endothelium-dependent, flow-mediated dilation (FMD) was determined by measurement of the brachial artery diameter one minute after release of the cuff.¹⁰

Flow mediated dilation (FMD) of brachial artery was assessed by measuring

 - Brachial artery diameter at baseline (A)
 - Brachial artery diameter at one minute after release of pressure (B)
 - The absolute change in brachial artery diameter in mm [FMD (B – A)]
 - The Delta change (Δ FMD) = (B – A)/ A
- **Statistical analysis:**
 - IBM SPSS statistics (V. 22.0, IBM Corp., USA, 2013)
 - Data expression: mean (SD) for quantitative parametric measures, median (25th- 75th percentiles) for quantitative non-parametric measures, and number and percentage for categorized data
 - Tests: Student *t* test for comparison between two independent mean groups for parametric data, Wilcoxon Rank Sum test for non-parametric data, and Chi-square test for categorized data. Ranked Spearman correlation test for the possible association between variables.
 - The probability of error at 0.05 was considered significant.

Results

Table 1: Background data of patients and controls

	Patients (n = 40)	Controls (n = 40)	p value
Male : Female n (%)	20 (50): 20 (50)	20 (50): 20 (50)	1
Age (years)	13.6 (9.3 - 15.4)	10.8 (7.7 - 13.4)	0.06
Height (SDS)	-1.3 (-2.6 - -0.2)	-1.3 (-2.3 - 0.1)	0.4
Weight (SDS)	-0.2 (-1.1 - 0.5)	-0.6 (-1.1 - 0.5)	0.6
BMI (SDS)	0.9 (-0.2 - 2.01)	0.4 (-0.7 - 1.9)	0.2
WC (SDS)	-0.4 (-0.9 - 0.4)	-0.4(-1.04 - 0.1)	0.5
HC (SDS)	-1.5 (-2.2- -0.4)	-1.7 (-1.9 - -1.1)	0.7
WHR (SDS)	1.6 (0.8 – 2)	1.9 (0.8 - 2.3)	0.1
SBP (mmHg)	112.6 (11.3)	110.3 (15.5)	0.4
DBP (mmHg)	75.3 (11.5)	70.8 (12.4)	0.1

BMI: body mass index, WC: waist circumference, HC: hip circumference, WHR: waist to hip ratio, SBP: systolic blood pressure, DBP: diastolic blood pressure
All data are expressed as median (25th - 75th percentile) except sex ratio (number and percentage) and blood pressure (mean and SD)

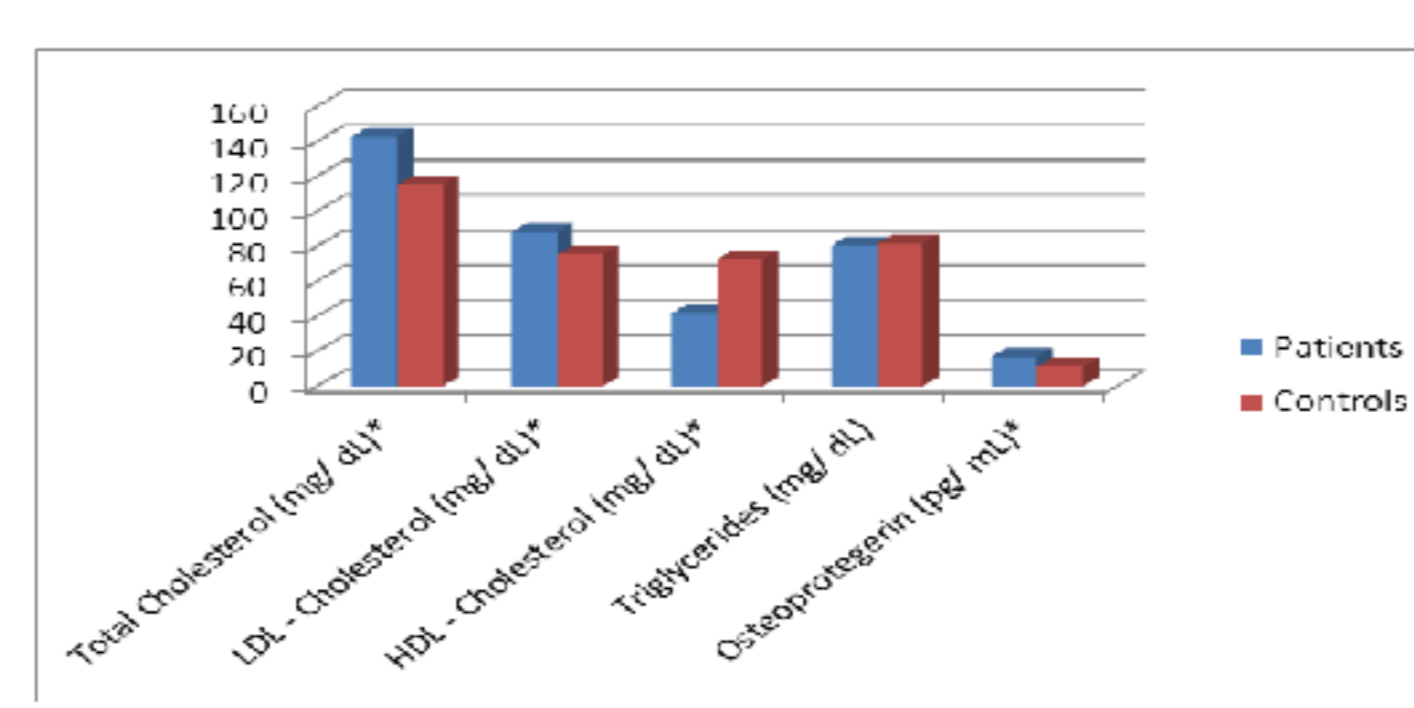


Figure 1: Lipid profile and osteoprotegerin level in patients and controls

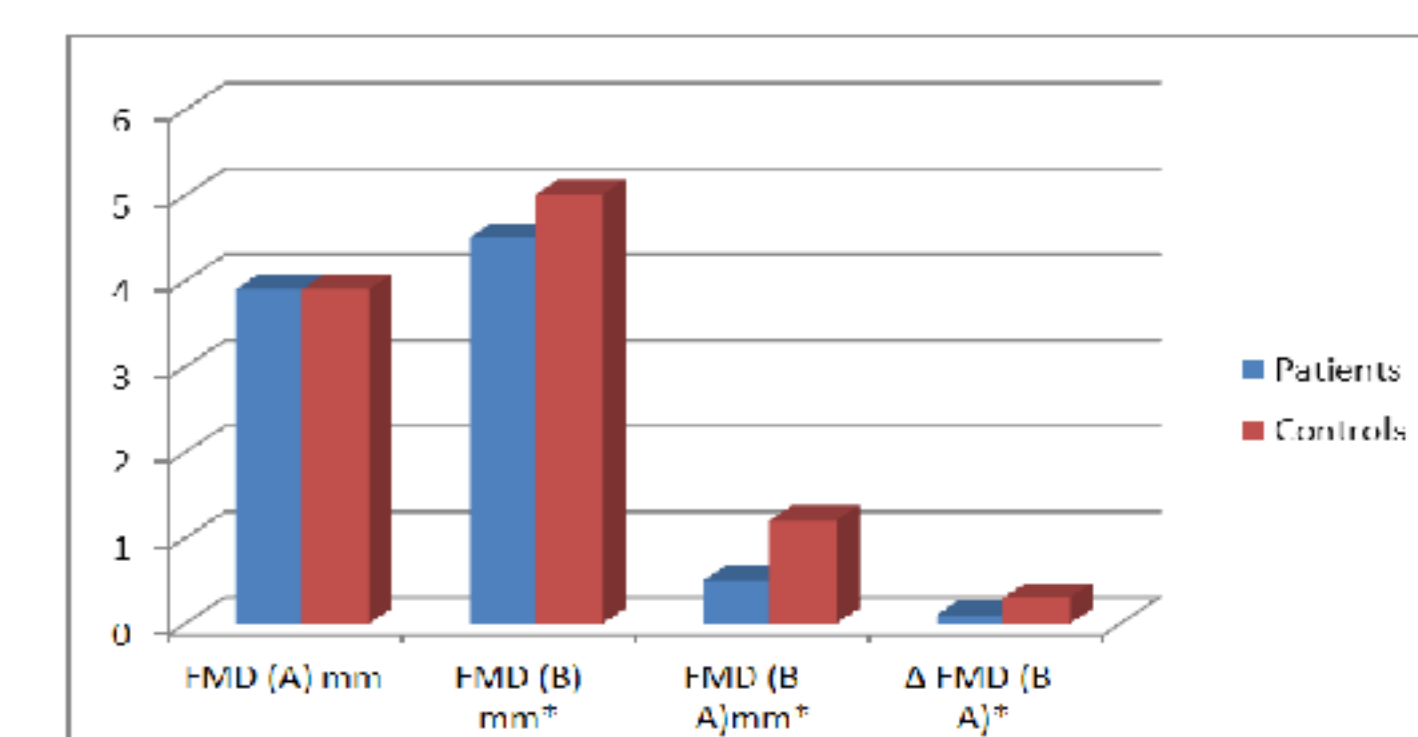


Figure 2: Flow mediated dilation of brachial artery in patients and controls

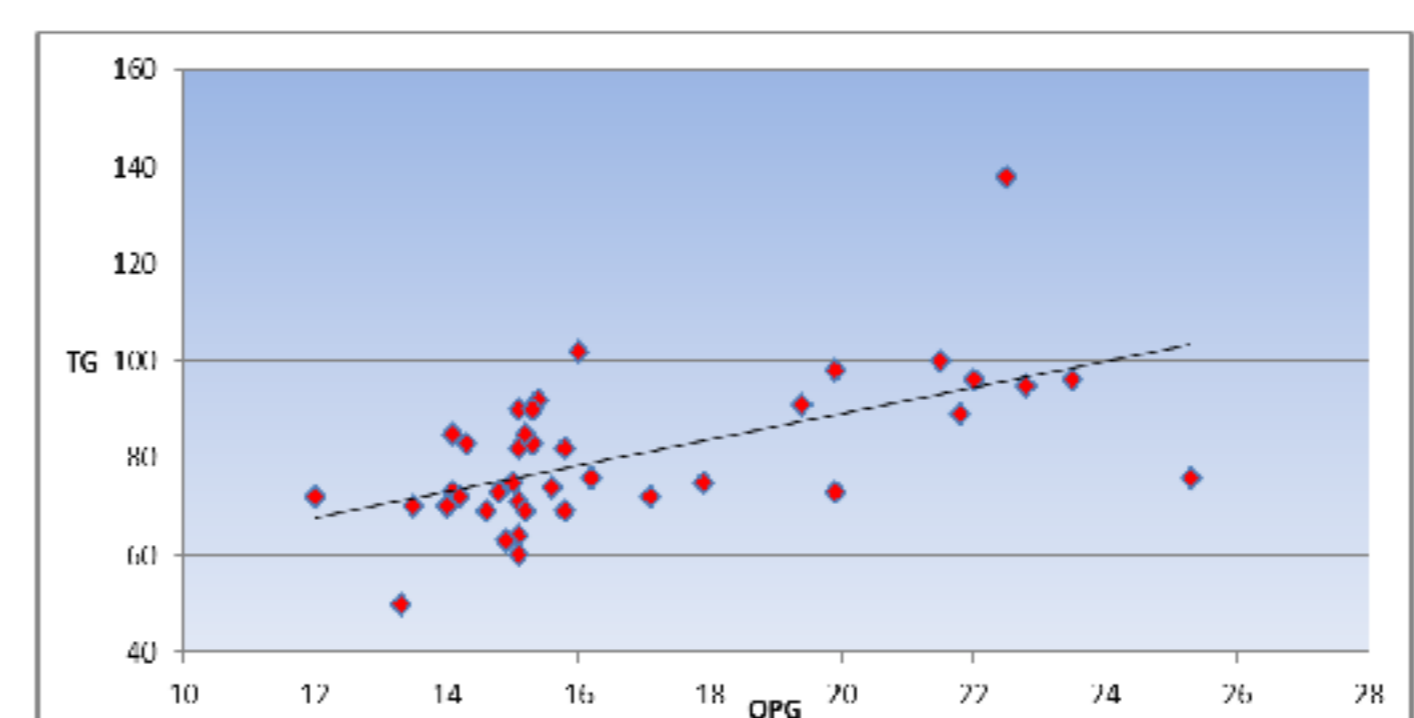


Figure 3: Correlation between serum OPG (pg/mL) and TG (mg/dL) in patients. $r = 0.6$, $p < 0.001$

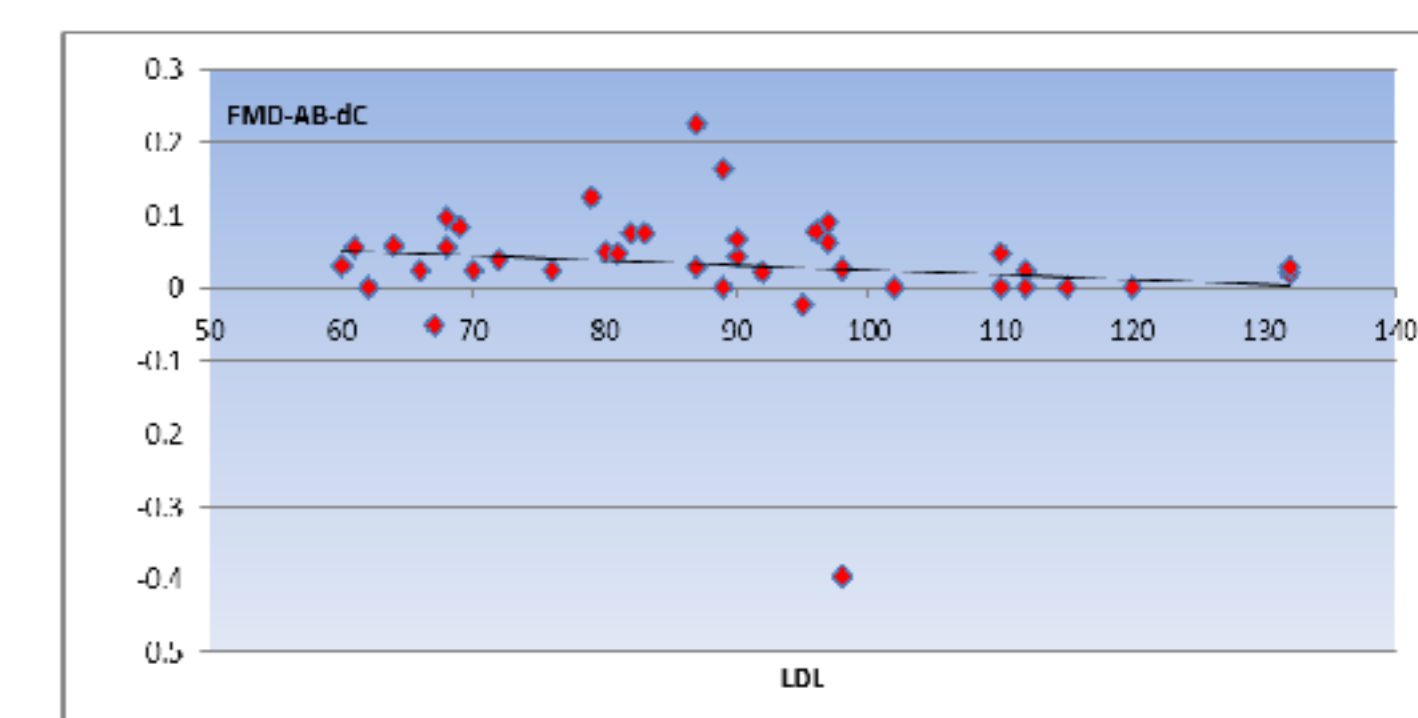


Figure 4a: Correlation between LDL-Cholesterol (mg/dL) and delta change in FMD of brachial artery. $r = -0.5$, $p = 0.001$

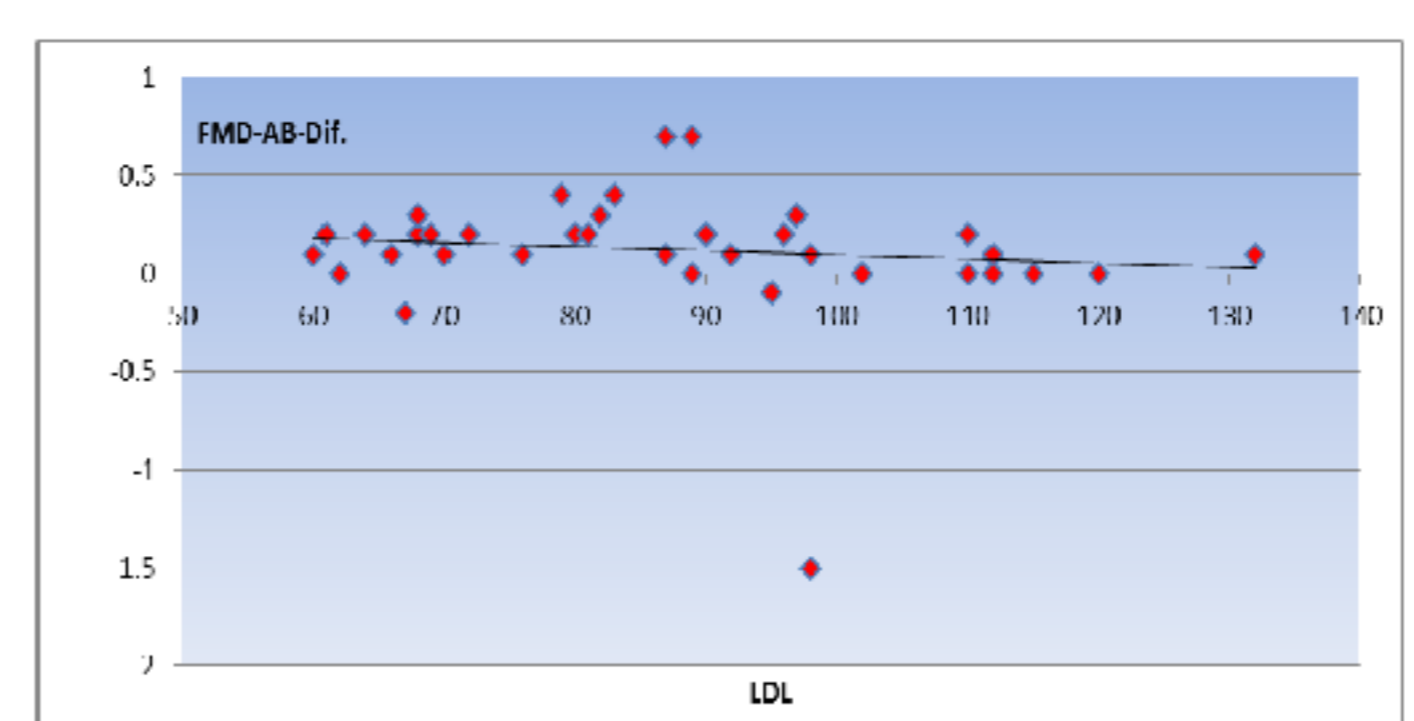


Figure 4b: Correlation between LDL-Cholesterol (mg/dL) and absolute change in FMD of brachial artery. $r = -0.5$, $p = 0.002$

- Mean (SD) diabetes duration was 4.5 (3.7) years [range:3-15].
- Eighteen patients (45%) were microalbuminuric while 22 (55%) had normal ACR.
- Mean (SD) HbA1c % was 8.6 (2).
- There was no relation between serum osteoprotegerin level and Tanner stage ($p > 0.05$).
- No significant difference was found in osteoprotegerin level between patients with and without microalbuminuria ($p > 0.05$).
- Serum osteoprotegerin neither correlated with HbA1c nor with disease duration ($p > 0.05$).
- No significant correlation was found between osteoprotegerin and brachial artery FMD in our studied population.

Conclusion

Endothelial dysfunction and risk of atherosclerosis exist early in children with type 1 diabetes as shown by reduced brachial artery flow mediated dilation and higher osteoprotegerin level respectively. Dyslipidaemia is a contributing factor in such events. Early recognition of these events and adequate control of lipid profile is recommended to prevent progression of atherosclerosis and cardiovascular disease at an early age.

Disclosure of interest: The authors declare no conflict of interest.

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