

# Risk factors associated with carotid intima media thickness in adolescents with type 2 diabetes mellitus

## Abstract

**Objetives:** The aim of this study was to evaluate associated factors with carotid intima media thickness in type 2 diabetes mellitus adolescents treated at endocrinology department of Hospital Infantil de Mexico Dr. Federico Gómez, to evaluate carotid intima media thickness in these patients and identify risk factors associated with the increase of carotid intima media thickness in these patients.

**Material and Methods:** This is a comparative cross-sectional study that analyzed patients with type 2 diabetes mellitus treated at endocrinology department who checked neck ultrasonography at 1 cm distance to the carotid bulb, at distal and proximal complex, to evaluate carotid intima media thickness. In addition the following data was collected: age, gender, body mass index, systolic blood pressure and diastolic blood pressure, glycated hemoglobin, glucose level, cholesterol fractions.

**Results:** The number of patients included was 48 adolescents with type 2 diabetes mellitus diagnosis, aged between 12 and 17 years old. 66.6% (n=32) females and 33.4% (n=16) males. 58.3% was at pubertal stage IV/V. There was no significant differences between females and males at body mass index ( $p=0.811$ ), waist circumference ( $p=0.351$ ), and weight ( $p=0.312$ ). Average time of disease evolution was 2.42 years (0.16-10.83). 58.3% treated with insulin scheme and 75% with metformin. We found significant difference between females and males in SBP ( $p=0.019$ ) and DBP ( $p=0.008$ ). Average glycated hemoglobin was  $9.27\pm3.27\%$  and no significant differences were founded between sexes. There were no significant differences in cholesterol and fractions. Average carotid intima media thickness was  $0.531\pm0.07\text{mm}$ .

**Conclusion:** Our study showed association between glycated hemoglobin and systolic blood pressure with carotid intima media thickness. These results encourage the importance to achieve glucose good control from very early stages of the disease to prevent atherosclerosis and cardiovascular disease at adulthood.

**Keywords:** carotid intima media thickness, type 2 diabetes mellitus, adolescents, patients, disease

Volume 6 Issue 4 - 2018

Marrodan Garcia Hanna Gisela Laura Isabel,<sup>1</sup> Medina Bravo Patricia,<sup>1</sup> Garcia Morales Leticia,<sup>1</sup> Hill de Titto Ana Carolina,<sup>1</sup> Klunder Klunder Miguel,<sup>2</sup> Valadez Reyes Maria Teresa,<sup>3</sup>

<sup>1</sup>Department of Endocrinology, Hospital Infantil de Mexico Federico Gomez, Mexico

<sup>2</sup>Department of Community Health Research, Hospital Infantil de Mexico Federico Gomez, Mexico

<sup>3</sup>Department of Radiology, Hospital Infantil de Mexico Federico Gomez, Mexico

**Correspondence:** Marrodan Garcia Hanna Gisela Laura Isabel, Endocrinology Department Hospital Infantil de Mexico Dr Federico Gomez, Puebla, Mexico, Tel +052-1222-1132803, Email dramarrodan@gmail.com

**Received:** July 13, 2017 | **Published:** July 03, 2018

## Introduction

Diabetes Mellitus global prevalence has been rapidly increasing as a result of associated factors related to change in life style, urbanization and feeding. Indicators show that the total number of diabetic patients at global scale have doubled with clear indications that this increment has occurred during the last three decades, which is translated into 53% increment for the year 2030, equivalent to 285 million persons from year 2010 to 439 million to year 2030, a highly representative part of the economically active population.<sup>1</sup>

The development of this disease in pediatric and adolescent patients has been progressively incrementing in an exponential way in western countries.<sup>2</sup> It is up to recent 10 years ago that the estimations indicated that the incidence of type 2 Diabetes Mellitus in adolescents was only of 3% but actually, there has been an increment of 45% at this mentioned age.<sup>1,2</sup>

The cardiovascular diseases are the main causes of morbimortality for patients with DM as well as the most expensive; therefore these are a problem for public health care.<sup>3</sup> The commonest existent conditions in DM are hypertension and dyslipidemia.

The pro inflammatory stage associated with the insulin resistance, even at earlier disease stages and without diagnose diabetes mellitus yet, lead to the stimulation of cytokines, as well as C reactive protein, elements which have been too associated with the development of atherosclerosis.<sup>3,4</sup>

The search and measurement of the subclinical atherosclerosis is a tool of easy use, accessible and usable in the prediction of cardiovascular risk.<sup>5</sup> The intima media thickness should be ideally measured at the carotid bifurcation, at 1 cm distance from the bulbous, in proximal measurement and distal to the transducer. It represents a hypertrophic adaptive response of the smooth muscle cells in the tunica media in front of a continuous aggression.<sup>6</sup>

There is nowadays no consensus or standardized protocol as to measure the intima media thickness, which leads to an important obstacle for its application, however, it has been possible to correlate the thicknesses according to the associated risk.

## Materials and methods

A cross sectional study was conducted in 48 type 2 diabetes mellitus children and adolescents aged 12-17 years attending the outpatient

diabetic clinic in the Hospital Infantil de México Dr. Federico Gómez (Mexico City, Mexico). All patients were diagnosed according to the American Diabetes Association criteria. A physical examination on each patient was conducted in order to determine weight, size, BMI, waist circumference, systolic and diastolic blood pressure. A blood test was taken in fast in order to determine total cholesterol, triglycerides, c-HDL and c-LDL, glucose and glycosylated hemoglobin (HbA1c).

A carotid ultrasonography of neck and at 1 cm next to the carotid bifurcation at the distal complex and in proximity to the transducer was taken in order to evaluate the intima media thickness. With ACUSON SIEMENS medical equipment, lineal transducer in protocol for vascular of 5MHz decibel adjustment between the range of 20 to 25 and pre set gains without further adjustment during the time of the research.

## Statistical analysis

Descriptive statistics were performed with measures of central tendency, dispersion and frequencies. Continuous variables were compared using Student's T-test for independent samples, for dichotomous variables X2 test. To evaluate the association between carotid intima thickness and variables such as HbA1c, age, gender and blood pressure, a multiple linear regression model was conducted, considering a  $p \leq 0.05$  as significant. Statistical program STATA V.O. 9.0 was used for the analysis.

## Results and discussion

A total of 48 patients with DM2 between ages of 12 and 17 years old, who attended the Diabetes Child Care Clinic of the Hospital In-

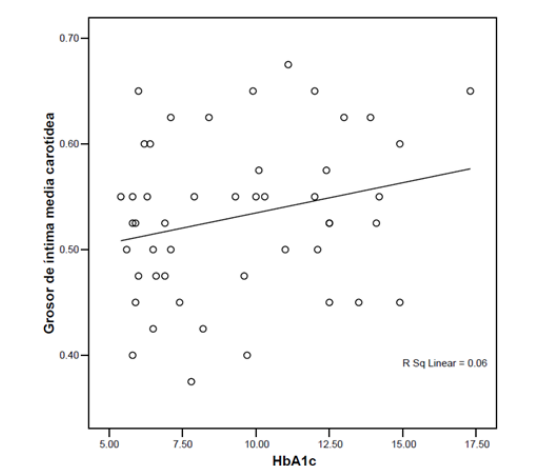
fantil de Mexico Federico Gomez, were included. Of the total number of patients included, 66.6% (n=32) were female, with a mean age of  $14.37 \pm 2.27$  years. The 58.3% were in the pubertal stage IV/V without observing a significant difference between the group of men or women. Male patients had a greater size than women ( $p=0.046$ ), with no difference in weight ( $p=0.312$ ), BMI ( $p=0.811$ ) and waist circumference ( $p=0.351$ ). Regarding the waist/height index, in both groups it was observed that it exceeded the ideal (less than 0.5) with an average of 0.54. The average time of evolution of the disease was 2.42 years (0.16-10.83). Of all patients, 58.3% were treated with insulin and 75% with metformin. A significant difference was found between male and female patients in the systolic ( $p=0.019$ ) and diastolic pressure (0.008) values. The mean HbA1c of the total patient was  $9.27 \pm 3.27\%$ , without finding significant differences between both sexes. Likewise, no difference was found in total cholesterol, triglyceride, c-HDL and c-LDL concentrations. The mean intima media thickness in the total number of patients was  $0.531 \pm 0.07$ mm. (Table 1) (Table 2)

It was observed that at higher HbA1c levels, higher thickness in carotid intima media were found, although this correlation was no statistically significant ( $p=0.093$ ). (Figure 1)

A multiple linear regression analysis was performed to assess the factors associated with carotid intima-media thickness in adolescents with DM2. It was found that the positively associated variables with the carotid intima media thickness were the concentrations of HbA1c ( $p=0.033$ ) and the systolic blood pressure values ( $p=0.024$ ) regardless gender, evolution time, IMC, waist circumference, total cholesterol, c-HDL and c-LDL levels. The model explains the 36.7% of the variance (Table 3).

**Table 1** Clinical, anthropometric and biochemical characteristics of adolescents with type 2 diabetes mellitus

	Total (n=48)	Mujeres (n=32)	Hombres(n=16)	p
Age (years)	$14.37 \pm 2.27$	$14.04 \pm 2.28$	$14.99 \pm 2.18$	0.165
Time evolution (years)	$2.42(0.16-10.83)$	$2.66(0.16-9.0)$	$2.25(0.16-10.83)$	0.871
Insulin treatment (n%)	28(58.33)	19(60.61)	9(62.5)	0.571
Metformin treatment (n%)	35(75)	25(78.80)	11(68.75)	0.728
Weight (kg)	$64.34 \pm 17.60$	$62.51 \pm 67.88$	$67.88 \pm 16.39$	0.312
Height (cm)	$1.55 \pm 0.18$	$1.51 \pm 0.20$	$1.62 \pm 0.11$	0.046
BMI (kg/m <sup>2</sup> )	$26.84 \pm 11.18$	$27.70 \pm 13.49$	$25.18 \pm 3.86$	0.811
Waist circumference (cm)	$86.65 \pm 12.20$	$85.37 \pm 12.40$	$89.14 \pm 11.70$	0.351
waist/height index	$0.54 \pm 0.06$	$0.54 \pm 0.08$	$0.54 \pm 0.06$	0.931
Tanner Pubertal Stage (n%)				
I	3(6.25)	1(3.2)	2(12.5)	0.137
II/III	14(29.1)	11(38.7)	3(18.75)	
IV/V	28(58.33)	17(58.1)	11(68.75)	
Systolic Blood Pressure (mmHg)	$111.38 \pm 9.55$	$108.71 \pm 6.93$	$116.59 \pm 11.82$	0.019
Dyastolic Blood Pressure (mmHg)	$71.01 \pm 7.82$	$68.94 \pm 7.15$	$75.01 \pm 7.70$	0.008
Average HbA1c	$9.27 \pm 3.27$	$9.62 \pm 3.21$	$8.95 \pm 9.62$	0.5
Total Cholesterol (mg/dl)	$160.65 \pm 38.91$	$160.97 \pm 40.40$	$160.02 \pm 36.91$	0.936
Triglycerides (mg/dl)	$147.08 \pm 78.62$	$143.97 \pm 87.41$	$153.5 \pm 58.44$	0.695
C-HDL (mg/dl)	$44.01 \pm 12.33$	$43.58 \pm 11.77$	$44.88 \pm 13.79$	0.734
C-LDL (mg/dl)	$93.05 \pm 32.01$	$92.12 \pm 34.44$	$94.98 \pm 27.21$	0.772
Intima media thickness (mm)	$0.531 \pm 0.007$	$0.52 \pm 0.07$	$0.55 \pm 0.81$	0.226



**Figure 1** Correlation between carotid intima media thickness and HbA1c levels in type 2 diabetes mellitus adolescents.

**Table 2** Correlation analysis of factors associated with carotid intima media thickness in adolescents with type 2 diabetes mellitus

Carotid intima media thickness		
	r	P
HbA1c (%)	0.245	0.093
Age (years)	0.192	0.192
BMI (kg/m <sup>2</sup> )	-0.012	0.421
waist circumference (cm)	0.015	0.918
SBP (mmHg)	0.303	0.036
DBP (mmHg)	0.147	0.318
Total Cholesterol (mg/dl)	-0.031	0.841
Triglycerides (mg/dl)	-0.054	0.715
C-HDL (mg/dl)	-0.004	0.979
C-LDL (mg/dl)	-0.041	0.787

**Table 3** Association between carotid intima media thickness and cardiovascular risk factors in type 2 diabetes mellitus adolescents

	Coefficiente $\beta$	IC 95%	P	R <sup>2</sup>
HbA1c (%)	0.008	0.007 0.0168	0.033	0.367
Age	0.006	-0.006 0.0189	0.355	
Gender	-0.006	-0.0579 0.0458	0.815	
BMI (kg/m <sup>2</sup> )	-0.002	-0.0044 0.0003	0.087	
Waist circumference	0	-0.003 0.0025	0.862	
Time evolution	-0.004	-0.017 0.0076	0.446	
SBP (mmHg)	0.004	0.0005 0.0069	0.024	
DBP (mmHg)	-0.001	-0.0045 0.0027	0.614	
Total Cholesterol (mg/dl)	0	-0.0021 0.0015	0.702	
Triglycerides (mg/dl)	0	-0.0006 0.0001	0.199	
C-HDL (mg/dl)	0	-0.0026 0.0023	0.906	
C-LDL (mg/dl)	0	-0.0016 0.0023	0.731	

## Discussion

It was found in our search a direct association among the systolic blood pressure values and HbA1c levels with the carotid intima media thickness, regardless age and gender, time of evolution and lipid profile.

It is important to mention that most of our patients were overweight and/or obese but we didn't find a significant correlation between this factor and the carotid media thickness, nevertheless, in multiple researches it has been demonstrated the relationship between obesity with metabolic syndrome and insulin resistance, being in turn the most important contributing factors to develop cardio and cerebrovascular disease. In the research conducted by Nesreen A, Kotb, et al.,<sup>7</sup> 27 DM2 patients between 12 and 19 years were included and were compared with a control group of healthy patients. It was also observed association between the carotid intima media thickness with the systolic blood pressure levels. At the same time, the positive association with the triglyceride levels, HOMA-IR and reactive C protein was also documented. Although no patient in this research exceeded the thickness of carotid intima media thickness, it could be established an association of these variables with higher thickness, being the most important element the poor glycemic control.

It has been observed that type 2 diabetes mellitus patients diagnosed at pediatric age and during the adolescence are at major risk to develop cardio and cerebrovascular complication at earlier age as opposed to those patients diagnosed at adult stages.

## Conclusion

There are a number of different studies which have been conducted to evaluate the associations of different variables with the development of microvascular complications in type 2 diabetes mellitus patients, nonetheless, the current available information regarding pediatric population is scarce due to the fact that type 2 diabetes mellitus is a fairly recently developed disease in last decades. Our research is not far from the previously reported results of other groups, in which the association of HbA1c concentrations and the systolic blood pressure values has been documented as a subrogated atherosclerosis variable for carotid intima media thickness.

These results reinforce the importance to achieve a suitable glycemic control in these patients, yet at early stages of the disease in order to prevent the development of cardio and cerebrovascular disease in adulthood. In view of the progressive incidence and prevalence of type 2 diabetes mellitus in pediatric population, it is important to emphasize primary prevention measures as mentioned above. It is important to promote healthy lifestyle to avoid progression to obesity, metabolic syndrome and type 2 diabetes mellitus thereafter. In individuals who already have type 2 diabetes mellitus, the healthy lifestyle, exercise and pharmacological treatment are fundamental to treat and prevent the develop of complications in the medium and long term.

## Limitations

The size of the sample is small, so it may have not been possible to find a greater correlation with other variables. Because of the cross-sectional nature of the research, no causal associations can be established, only correlations. The transducer used for the measurement was of 5Hz, as opposed to those reported units in other researches which use higher resolution equipment up to 7.5Hz.<sup>8-16</sup>

## Acknowledgments

None.

## Conflict of interest

The author declares there is no conflict of interest.

## References

1. Lei Chen, Dianna Magliano J, Paul Zimmet Z. The worldwide epidemiology of Type 2 Diabetes Mellitus—Present and future perspectives. *Nature*. 2012;228–236.
2. Ebe Dádamo MD, Sonia Caprio MD. Type 2 Diabetes in youth: epidemiology and pathophysiology. *Diabetes Care*. 2011;34(Supplement 2):S161–S165.
3. Arthur Zieske W, Gray T Malcom. Natural History and Risk Factors of Atherosclerosis in children and youth: The PDAY study. *Pediatr Pathol Mol Med*. 2002;21(2):213–237.
4. Nancy West A, Richard Hamman F, Elizabeth Mayer Davis J, et al. Cardiovascular Risk Factors among young with and without type 2 diabetes. *Diabetes Care*. 2009;32(1):175–180.
5. Herder M, Johnsen SH, Arntzen KA, et al. Risk factors for progression of Carotid Intima Media Thickness and Total Plaque Area. A 13 year follow up study. *Stroke*. 2012;1–6.
6. Devine PJ, Carlson DW, Taylor AJ. Clinical value of carotid intima media thickness testing. *J Nucl Cardiol*. 2006;13(5):710–718.
7. Kotb NA, Gaber R, Salama M, et al. Clinical and biochemical predictors of increased carotid intima media thickness in overweight and obese adolescents with type 2 diabetes. *Diab Vasc Dis Res*. 2012;9(1):35–41.
8. Colagiuri S. Diabetesity: Therapeutic options. *Diabetes Obes Metab*. 2010;12(6):463–473.
9. Zafar H, Israilli, et al. Advances in the treatment of type 2 Diabetes Mellitus. *Am J Ther*. 2011;18(2):117–152.
10. Kristi M Cowell. Focus on diagnosis Type 2 Diabetes Mellitus. *Pediatr Rev*. 2008;29(8):289–292.
11. Eppens MC, Craig ME, Cusumano J, et al. Prevalence of diabetes complications in adolescents with type 2 compared with type 1 diabetes. *Diabetes Care*. 2006;29(6):1300–1306.
12. Jennifer Couper J, Timothy Jones W. The Diabetes Control and Complications Trial. A Follow Up Study. *National Diabetes Information Clearinghouse*. NIH Publication. 2008.
13. Saul Genuth, Richard Eastman, Richard Khan. Implications of the United Kingdom Prospective Diabetes Study. American Diabetes Association. *Diabetes Care*. 2012;25 (supl 1):528–532.
14. Zachary Bloomgarden T. Cardiovascular diseases in diabetes. *Diabetes Care*. 2010;33(4):e49–e54.
15. Amy Shah S, Lawrence Dolan M, Thomas Kimball R, et al. Influence of duration of diabetes, glycemic control, and traditional cardiovascular risk factors in adolescents and young adults with type 2 diabetes mellitus. *J Clin Endocrinol Metab*. 2009;94(10):3740–3745.
16. Elaine Urbina M, Thomas Kimball R, Connie McCoy E, et al. Youth with Obesity and Obesity Related Type 2 Diabetes Mellitus Demonstrate Abnormalities in Carotid Structure and Function. *Circulation*. 2009;119:2913–2919.