

Relationship between anthropometric and biochemical profiles in children and adolescents with type 1 diabetes

Relação entre o perfil antropométrico e bioquímico em crianças e adolescentes com diabetes melito tipo 1

Relación entre perfiles antropométrico y bioquímico en niños y adolescentes con diabetes mellitus tipo 1

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ABSTRACT

Objective: To evaluate the relationship between anthropometric and biochemical variables in children and adolescents with type 1 diabetes mellitus (DM1).

Methods: This was a cross-sectional study of 11 children and 43 adolescents with DM1. The following data were collected: socioeconomic and demographic (age, sex, education, income), clinical (insulin therapy), anthropometric (weight, height, skinfolds, waist circumference – WC) and biochemical variables (glycated hemoglobin – HbA, casual blood glucose – CBG, post-prandial blood glucose – PPBG, and lipid profile). Statistical analysis included Student's *t* test ($p < 0.05$) and Pearson's correlation ($p < 0.05$).

Results: The average income *per capita* was 0.58 ± 0.39 times the monthly minimum wage and 72.2% of the sample were on insulin therapy consisting of three doses per day. Most individuals had adequate height (92.6%) and BMI (87.0%) for their ages. Subjects with an adequate HbA index (inHbA) had lower CBG ($p = 0.002$) and PPBG ($p < 0.001$). There were positive correlations between inHbA and WC ($p = 0.013$), CBG ($p = 0.014$), PPBG ($p < 0.001$), triglycerides and VLDL-cholesterol ($p < 0.001$).

Conclusions: Poorer glycemic control is related to higher serum lipids levels and larger WC.

Key-words: adolescent; anthropometry; waist circumference; child; diabetes mellitus, type 1; blood glucose.

RESUMO

Objetivo: Avaliar a relação entre o perfil antropométrico e bioquímico de crianças e adolescentes com diabetes melito tipo 1 (DM1).

Métodos: Estudo transversal com 11 crianças e 43 adolescentes com DM1. Coletaram-se dados socioeconômicos e demográficos (idade, sexo, escolaridade, renda), clínicos (insulinoterapia), antropométricos (peso, estatura, dobras cutâneas, circunferência da cintura – CC) e bioquímicos (hemoglobina glicada – HbA, glicemias casual – GLC, pós-prandial – GLPP, e perfil lipídico). Foram utilizados o teste *t* de Student ($p < 0,05$) e a correlação de Pearson ($p < 0,05$).

Resultados: A renda média *per capita* foi de $0,58 \pm 0,39$ salário-mínimo e predominou o esquema de três aplicações de insulina/dia em 72,2% da amostra. A maioria apresentou estatura (92,6%) e IMC (87%) adequados para a idade. Aqueles com índice da HbA (inHbA) adequado apresentaram menores GLC ($p = 0,002$) e GLPP ($p < 0,001$). O inHbA correlacionou-se positivamente com CC ($p = 0,013$), GLC ($p = 0,014$), GLPP ($p < 0,001$), TG e VLDL ($p < 0,001$).

Conclusões: O pior controle glicêmico relaciona-se a maiores níveis de lipídeos séricos e CC mais elevada.

Palavras-chave: adolescente; antropometria; circunferência da cintura; criança; diabetes mellitus tipo 1; glicemia.

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RESUMEN

Objetivo: Evaluar la relación entre perfil antropométrico y bioquímico de niños y adolescentes con diabetes mellitus tipo 1 (DM1).

Métodos: Estudio transversal con 11 niños y 43 adolescentes con DM1. Se recogieron datos socioeconómicos y demográficos (edad, sexo, escolaridad, ingresos), clínicos (insulinoterapia), antropométricos (peso, estatura, pliegues cutáneos, circunferencia de la cintura-CC) y bioquímicos (hemoglobina glicada – HbA, glucemias casual – GLC, postprandial – GLPP y perfil lipídico). Se utilizaron la prueba *t* de Student y la correlación de Pearson ($p < 0,05$).

Resultados: El ingreso mediano *per capita* fue de $0,58 \pm 0,39$ salario mínimo y predominó el esquema de tres aplicaciones de insulina/día en el 72,2% de la muestra. La mayoría presentó estatura (92,6%) e IMC (87%) adecuados a la edad. Aquellos con índice de HbA (inHbA) adecuado presentaron menores GLC ($p = 0,002$) y GLPP ($p < 0,001$). El inHbA se correlacionó positivamente con CC ($p = 0,013$), GLC ($p = 0,014$), GLPP ($p < 0,001$), TG y VLDL ($p < 0,001$).

Conclusiones: El peor control glucémico se relaciona a mayores niveles de lípidos séricos y CC más elevada.

Palabras clave: adolescente; antropometría; circunferencia de la cintura; niño; diabetes mellitus tipo 1; glucemia.

Introduction

Diabetes mellitus type 1 (DM1) is the most common childhood endocrine disease and is associated with increased cardiovascular risk⁽¹⁾. Hyperglycemia, hypertension and dyslipidemia are all involved in the development of the complications of DM1⁽¹⁾, accelerating different phases of atherogenesis⁽²⁾. The early manifestations of vascular dysfunction in people with DM1 are hardening and thickening of the artery walls^(3,4).

Brazil is one of the ten countries with the greatest numbers of DM cases worldwide⁽⁵⁾. No population based studies have been conducted in Brazil that have specifically identified DM1 cases. It is estimated that the prevalence and incidence of the disease in the under-14s are 4/10,000 and 8/100,000 inhabitants respectively⁽⁶⁾.

Intensive glycemic control helps prevent complications because it acts directly on serum concentrations of total cholesterol (TC), low density lipoproteins (LDL) and

triglycerides (TG)⁽⁷⁾. However, it also tends to lead to greater weight gain and increases in percentage body fat (BF) than conventional treatment⁽⁸⁾. Ineffective glycemic control, manifest in elevated glycated hemoglobin (HbA) levels, is associated with an increased tendency towards overweight. Furthermore, number of insulin doses has been identified as the most important independent predictor of body mass index (BMI) in subjects aged from 12 to 17⁽⁹⁾.

On the basis of this evidence of a link between metabolic control and nutritional status in people with diabetes type 1, the objective of this study was to investigate the relationship between the anthropometric and biochemical profiles of children and adolescents with DM1.

Method

This was a cross-sectional study of children and adolescents with DM1 seen at the endocrinology clinic of the Hospital das Clínicas, Universidade Federal de Goiás (UFG). When the study was conducted the total population with DM1 registered at the clinic comprised 240 people, 31 of whom were children (12.0%), with 79 adolescents (32.2%) and 135 adults (55.8%). The sample of 54 volunteers equated to 49% of the children and adolescents registered.

For the purposes of this study, participants aged 4 to 9 years were defined as “children” and those aged 10 to 18 were termed “adolescents”⁽¹⁰⁾. The criteria for inclusion in the study were as follows: diagnosis of DM1 confirmed at least 5 months previously and insulin treatment. The exclusion criteria were: amputation of limbs, diagnosis of dyslipidemia, celiac disease, nephropathy, thyroid diseases or cardiovascular diseases.

Data were collected during the period between January and August of 2009. Inclusion and exclusion criteria were checked by consulting patients’ medical records. All eligible patients and their carers were invited to take part. Data collection was conducted using a structured form covering the following information: a) Socioeconomic and demographic data – age, occupation, educational level of volunteer, income and lifestyle; b) Anthropometric assessment – weight, height, BMI, waist circumference (WC), tricipital skin folds (TSF) and subscapular skin folds (SSF); and c) Laboratory tests – glycated hemoglobin (HbA), casual glycemia (CGL) and post prandial glycemia (PPGL), lipid profile including TG, TC, high density lipoprotein

(HDL), very low density lipoprotein (VLDL) and LDL. Anthropometric data were measured cyclically by a single examiner; i.e. each measurement was taken once before replicate measurements were taken in the same order. Weight, height and WC were each measured twice and the skin folds were measured three times and then means were calculated.

Height was measured using a 200cm portable stadiometer (Sanny®) with divisions in millimeters. Patients were weighed using a stand-on balance (Kratos®), with maximum capacity of 150kg and sensitivity of 50 grams. Waist circumference was measured with an inextensible tape measure. Skin folds were measured with an adipometer (Lange®).

Data for weight and height were analyzed and classified using the WHO software Antro⁽¹¹⁾ on the basis of z score for height/age (Z H/A) and z score for BMI/age (Z BMI/A). After the software had performed the classification, H/A was defined as low if $Z < -2$ and appropriate if $Z \geq -2$. For BMI/A, $Z < -2$ was defined as underweight, $-2 \geq Z < +1$ as healthy weight and $Z \geq +1$ as obesity⁽¹²⁾.

Cutoff points proposed by McCarthy, Jarrett and Crawley⁽¹³⁾ were used to classify WC data. Tricipital skin folds classified using percentiles proposed by Frisancho⁽¹⁴⁾ the Slaughter *et al*⁽¹⁵⁾ were used to calculate estimated body composition for participants aged 8 to 18. The equation could not be used for six participants because they were less than 8 years old. The sample was classified using the body fat percentage adiposity categories proposed by Lohman⁽¹⁶⁾, stratifying by sex and adiposity categories. For the boys, $<10\%$ was defined as low adiposity, from 10 to 20% as good adiposity and $>20\%$ was defined as moderately high and high adiposity; for the girls, $<15\%$ was defined as low adiposity, from 15 to 25% as good adiposity and $>25\%$ was defined as moderately high and high adiposity. In order to make data presentation clearer, the sample was stratified as “children” or “adolescents” and grouped into the categories “low”, “good” and “excessive” adiposity.

Data on lipid profiles and HbA were obtained from medical records, always taking the most recent results. New tests were requested for participants whose most recent lipid profile was more than 3 months old, as part of routine outpatients follow-up. Patients brought new HbA test results to every new consultation, so these data were less than 2 weeks old. Casual glycemia tests were conducted in the reception area using a blood glucose meter (Accu-chek Advantage).

The lipid profile was assessed on the basis of figures recommended by the American Academy of Pediatrics⁽¹⁷⁾. Since the HbA tests had been conducted using a variety of methods, a glycosylated hemoglobin index (inHbA) was used to classify glycemic control (GC) as adequate or inadequate. The inHbA is calculate by dividing the HbA test result by the upper limit of normality for the test method used, as described by Chase *et al*⁽¹⁸⁾. For the purposes of this study, $\text{inHbA} < 1.33$ was defined as adequate GC and $\text{inHbA} \geq 1.33$ as inadequate GC.

This study was approved by the Human and Animal Medical Research Ethics Committee at the UFG Hospital das Clínicas under protocol number 128/08. Free and informed consent forms were signed voluntarily by all participants and their guardians after all procedures involved had been explained in detail.

The database was constructed in a Microsoft Excel spreadsheet (version 2003) and analyzed using the Statistical Package for the Social Sciences (version 17.0). Socioeconomic and demographic data are described in frequencies and percentages for categorical variables and measure of central tendency for numerical variables. The distribution of continuous variables was analyzed using the Kolmogorov-Smirnov test and distributions with results of $p \geq 0.05$ were considered normal. Comparisons between groups with adequate GC and inadequate GC were conducted using Student's *t* test and the chi-square test. Pearson's correlation coefficient was used to analyze relationships between biochemical and anthropometric variables.

Results

Table 1 lists the socioeconomic, demographic and anthropometric characteristics of the sample. The sample comprised 11 children and 43 adolescents, totaling 54 patients, 29 (54%) of whom were female and 25 (46%) of whom were male. Note that 83.3% were over 9 years old. Mean per capita income was 0.58 ± 0.39 times the monthly minimum wage, and the majority of families comprised up to four members (68.5%).

In 66.7% of cases the insulin regime was made up of intermediate (I) and rapid (R) acting insulins, whereas 11.1% were taking long duration (LD) and ultra rapid (UR) analogues (Table 2). The majority of participants (72.2%) were on three insulin doses per day. Although 87% were healthy according to Z-BMI/age, 25.9% had

Table 1 - Socioeconomic and demographic characteristics of children and adolescents with diabetes mellitus type 1

	Categories	Children (n=11)		Adolescents (n=43)		Total (n=54)	
		n	%	n	%	n	%
Sex	F	6	54.5	23	53.5	29	53.7
	M	5	45.5	20	46.5	25	46.3
Age (years) ^a	4-9	11	100.0	–	–	11	20.4
	10-13	–	–	19	44.2	19	35.2
	14-18	–	–	24	55.8	24	44.4
Educational level (years) ^b		2.1±1.2		7.3±2.2		–	
Per capita income (as proportion of monthly minimum wage) ^b		0.54±0.32		0.58±0.41		0.58±0.39	
	2-3	2	18.2	8	18.6	10	18.5
Number of members in family	4	6	54.5	21	48.8	27	50.0
	5-6	3	27.3	14	32.6	17	31.5
Physical activity	yes	4	36.4	31	72.1	35	64.8
	no	7	63.6	12	27.9	19	35.2

^aMean age±standard deviation: 12.6±3.7; ^bmean±standard deviation

Table 2 - Clinical and anthropometric characteristics of children and adolescents with diabetes mellitus type 1

	Categories	Children (n=11)		Adolescents (n=43)		Total (n=54)	
		n	%	n	%	n	%
Insulin regime ^a	I/R	5	45.5	31	72.1	36	66.7
	I/UR	4	36.4	4	9.3	8	14.8
	LD/UR	1	9.1	5	11.6	6	11.1
	LD or I	1	9.1	3	7.0	4	7.4
Number of times insulin administered per day	1-2	3	27.3	6	14.0	9	16.7
	3	8	72.7	31	72.1	39	72.2
	4	–	–	6	14.0	6	11.1
Z H/A	Low	–	–	4	9.3	4	7.4
	Appropriate	11	100	39	90.7	50	92.6
Z BMI/A	Underweight	1	9.1	2	4.7	3	5.6
	Healthy weight	8	72.7	39	90.7	47	87.0
	Obese	2	18.2	2	4.7	4	7.4
WC	p10-p90	8	72.7	32	74.4	40	74.1
	>p90	3	27.3	11	25.6	14	25.9
TSF	<p10	1	9.1	–	–	1	1.9
	p10-p90	8	72.7	39	90.7	47	87.0
	>p90	2	18.2	4	9.3	6	11.1
BF	Low	1	9.1	1	2.3	2	3.7
	Good	3	27.3	22	51.2	25	46.3
	Excessive ^b	1	9.1	20	46.5	21	38.9
	<8 years ^c	6	54.5	–	–	6	11.1

I: intermediate; R: rapid; UR: ultra rapid; LD: long duration. Z H/A: standard deviation score for height for age. Z BMI/A: standard deviation score for body mass index for age. WC: waist circumference (in percentiles) TSF: triceps skinfold; BF: body fat, classified as per Lohman⁽¹⁶⁾. ^amean insulin dose of 0.8 U/kg; ^bexcessive includes the categories moderately high and high; ^cpercentage BF could not be estimated for these children

WC over the 90th percentile. With regard to adiposity, approximately half of the participants (46.3%) had good BF percentage, but 38.9% had higher than recommended adiposity.

Table 3 contains the anthropometric and biochemical data stratified by GC, which was inadequate in 35% of cases, the majority males (58%). The group with inadequate GC had significantly higher CGL levels ($p < 0.05$), although both groups had maximum values over 500mg/dL; and the inadequate group also had significantly higher PPGL ($p < 0.001$) with the lowest result in the group being 150mg/dL. Triglycerides were significantly higher in the group of 10 to 19-year-olds with inadequate GC ($p < 0.05$). Children under ten in the adequate GC group had higher HDL levels, but the difference was on the threshold of significance ($p = 0.057$).

The results for the analysis of relationships between variables are shown in Table 4. There were significant correlations between inHbA and the following variables: WC ($r = 0.336$; $p = 0.013$), CGL ($r = 0.332$; $p = 0.014$), PPGL ($r = 0.49$; $p < 0.001$), TG ($r = 0.422$; $p = 0.001$) and VLDL ($r = 0.443$; $p = 0.001$). There was a significant correlation between LDL and TC ($r = 0.85$; $p < 0.001$). Triglycerides correlated with WC ($r = 0.313$; $p = 0.021$) and with VLDL ($r = 0.97$; $p < 0.001$).

Discussion

There were significant correlations between inHbA and WC, CGL, PPGL, TG and VLDL, indicating that glycemia and the lipid profile affect metabolic control in DM1 patients. The relationship between hyperglycemia and development of cardiovascular complications has been shown in an experimental study with diabetic mice. A group of mice fed a cholesterol free diet had significantly larger atherosclerotic lesions than non diabetic mice⁽²⁾.

After stratification by glycemic control, the group of patients with inHbA ≥ 1.33 exhibit greater cardiovascular risk, expressed by the significant correlation with CGL, PPGL and TG levels, in subjects 10 to 19 years old, and with HDL, at the threshold of significance, in subjects under 10 years old. Although the relationship between inadequate glycemic control and dyslipidemia is a consistent finding in the literature, the mechanism by which hyperglycemia is related to atherosclerosis has not yet been fully understood. The recommendation is therefore that, in addition to glycemic control, DM1 patients' blood pressure and serum lipids should also be rigorously monitored in order to avoid the development of cardiovascular complications⁽¹⁹⁾.

Table 3 - Means and standard deviations for anthropometric and biochemical characteristics against glycemic control

	Reference values	adequate GC inHbA <1.33	inadequate GC inHbA ≥ 1.33	p-value
Participants (n/%)	–	35/65	19/35	–
Sex M/F (n)	–	14/21	11/08	0.208
Age \pm SD (years)	–	12.3 \pm 3.9	13.2 \pm 3.4	0.400
Z H/A	Z ≥ -2	-0.5 \pm 1.3	0.0 \pm 1.0	0.197
Z BMI/A	-2 \geq Z \leq +1	-0.4 \pm 1.2	0.0 \pm 0.7	0.179
BF (%)	♂: ≥ 10 and ≤ 20 ♀: ≥ 15 and ≤ 25	15.8 \pm 6.2 25.7 \pm 8.7	18.4 \pm 3.4 28.4 \pm 4.9	0.250 0.441
CGL (mg/dL)	<200	227.8 \pm 117.3	342.9 \pm 133.1	0.002
PPGL (mg/dL)	<140	207.2 \pm 98.5	338.0 \pm 111.5	<0.001
TG (mg/dL)	<10 years: ≤ 100 10-19 years: ≤ 130	78.6 \pm 26.9 83.5 \pm 33.9	62.0 \pm 10.5 120.1 \pm 55.7	0.326 0.028
TC (mg/dL)	<200	156.6 \pm 28.4	163.4 \pm 29.5	0.418
HDL (mg/dL)	<10 years: ≥ 40 10-19 years: ≥ 35	54.8 \pm 12.9 49.5 \pm 11.1	38.0 \pm 8.1 44.9 \pm 7.9	0.057 0.163
VLDL (mg/dL)	–	16.1 \pm 6.4	21.7 \pm 11.2	0.054
LDL (mg/dL)	<130	89.7 \pm 25.0	98.0 \pm 24.6	0.251

Z H/A: standard deviation score for height for age. Z BMI/A: standard deviation score for body mass index for age; BF: body fat. ♂: males. ♀: females. CGL: casual glycemia. PPGL: postprandial glycemia. TG: triglycerides. TC: total serum cholesterol. HDL: high density lipoprotein. VLDL: very low density lipoprotein. LDL: low density lipoprotein

Table 4 - Correlations between anthropometric and biochemical variables in children and adolescents with DM1

	inHbA		LDL		TC		TG	
	r	p-value	r	p-value	r	p-value	r	p-value
inHbA	1.000	–	0.160	0.249	–	–	–	–
WC (cm)	0.336	0.013*	0.030	0.830	0.134	0.335	0.313	0.021*
TSF (mm)	-0.061	0.664	0.066	0.633	0.114	0.413	0.017	0.902
SSF (mm)	0.175	0.206	0.061	0.661	0.153	0.271	0.239	0.082
BF (%)	-0.029	0.844	0.069	0.639	0.124	0.403	0.046	0.754
CGL (mg/dL) ^k	0.332	0.014*	0.075	0.587	-0.003	0.982	0.128	0.356
PPGL (mg/dL)	0.490	<0.001***	0.092	0.507	0.009	0.949	0.196	0.155
TG (mg/dL)	0.422	0.001**	0.149	0.283	0.478	<0.001***	1.000	–
TC (mg/dL)	0.201	0.146	0.854	<0.001***	1.000	–	–	–
HDL (mg/dL)	-0.196	0.155	-0.091	0.513	0.344	0.011*	0.142	0.307
VLDL (mg/dL)	0.443	0.001**	0.093	0.503	0.431	0.001**	0.975	<0.001***

inHbA: glycated hemoglobin index. LDL: low density lipoprotein. TC: total cholesterol. TG: triglycerides. WC: waist circumference. TSF: triceps skinfold. SSF: subscapular skinfold. BF: body fat. CGL: casual glycemia. PPGL: postprandial glycemia. TG: triglycerides. TC: total serum cholesterol. HDL: high density lipoprotein. VLDL: very low density lipoprotein. Student's *t* test: **p*<0.05; ***p*<0.01; ****p*<0.001

This study did not analyze short stature, but it is known that DM1 is associated with a reduction in the final height of patients, compromising growth in children and adolescents^(20,21). The anthropometric profile identified in this study is satisfactory, since the majority were at a healthy weight, with appropriate height for age, at the time of assessment.

With regard to BF, it is considered worrying that 38.9% of the sample had undesirably high adiposity. However, it should be remembered that fat mass percentages can be overestimated using skin folds when compared with dual-emission X-ray (DEXA), especially in diabetics with high fat percentages. Collagen glycation in subcutaneous tissues can contribute to these tissues hardening and, in common with early findings of reduced joint mobility, may be an early consequence of DM1, preceding other long term complications⁽²²⁾. On the other hand, one study that compared diabetic children, aged 1 to 11 years, with non-diabetic children found no difference in body fat percentage or lean mass⁽²¹⁾. Therefore, in this study it has not been possible to determine whether the number of subjects with undesirably high adiposity is a consequence of DM1 or an inherent feature of childhood and adolescence.

Waist circumference is a measure of central obesity and reflects visceral fat that is metabolically active⁽²³⁾. The inHbA correlated significantly with WC, which is in line with the findings of the Diabetes Control and Complications Trial⁽²⁴⁾. Several studies have demonstrated the relationship between WC and vascular rigidity, early stages of atherosclerosis⁽²⁵⁾, cardiovascular mortality⁽²⁶⁾, the development of microalbuminuria⁽²⁴⁾

and emergence of the metabolic syndrome in DM1⁽²⁷⁾. There is evidence for the relationship between insulin treatment, increase in WC and weight gain, especially among patients on intensive GC, suggesting that the increase in WC is influenced by the insulin treatment⁽⁸⁾.

Elevated inHbA indicates ineffective metabolic control and has been correlated with increased PPGL. An in vitro study showed that one of the consequences of chronic hyperglycemia is increased LDL glycation, making it more susceptible to the oxidative process⁽²⁸⁾. These results provide more evidence that inadequate GC increases cardiovascular risk in DM1. Data from Epidemiology of Diabetes Complications indicate a relationship between HbA and weight gain, where people with worse GC had greater weight gain⁽²⁹⁾. In this study, there was a correlation between Z BMI/A and inHbA, but this was not significant, possibly because of the restricted sample size.

It was found that increases in BMI, WC, TSF, SSF and BF all increased insulin resistance proportionally among DM1 patients aged 8 to 18. Higher HbA levels were also associated with insulin resistance. The consequent incapacity to take up glucose has been linked with increased TC, LDL and TG concentrations and reduced HDL levels⁽³⁰⁾.

The cross-sectional study design means that causality in the relationships between biochemical and anthropometric parameters cannot be determined. Notwithstanding, the results confirm the importance of glycemic control to reducing cardiovascular risk in DM1. The number of people in the sample was a limiting factor, but this was a consequence of the decision to attempt to understand the

relationship between the anthropometric and biochemical profiles of DM1 patients who were still free from the disease's complications. Including people with associated diseases could have affected the results, particularly with relation to serum lipids.

In summary, this study has shown that inadequate GC is correlated with higher serum lipid concentrations, specifically TG and VLDL, which indicates increased cardiovascular risk. The correlation between WC and inHbA shows the importance of including WC measurement in routine outpatients follow-up of young people with DM1, thereby

screening for patients at cardiovascular risk. In order to achieve this, it is necessary to define specific WC cutoff points for this group. Furthermore, it is essential that serum lipids be monitored if adequate metabolic control is to be achieved and maintained.

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