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Research Article

PLASMA AND ERYTHROCYTE CHOLINESTERASE ACTIVITIES IN CHILDREN FROM YUCATAN, MEXICO: RELATIONSHIP WITH ANTHROPOMETRY AND OBESITY

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ABSTRACT

Objective: To examine cholinesterase activities in children from three towns in Yucatan, Mexico and their relationship with anthropometry.

Methods: Plasma and erythrocyte cholinesterase activities were measured in 104 children from Ticul, Merida and Progreso. Differences between gender, sampling sites and body mass index (BMI) group were evaluated. Weight, height, BMI, hip and waist circumferences were correlated with cholinesterase activities.

Results: Significant differences in the waist circumference and butyrylcholinesterase (BChE) activity were found among sites. Children from Ticul presented higher BChE activity compared to children from the other towns. Children from Progreso had a smaller hip circumference compared with children from the other two locations. There was a high prevalence of overweight and obese children (40.3%). The results indicated that obese children had higher BChE activity respect to healthy weight children. As expected, there were also significant waist and hip circumference differences for BMI groups. The results demonstrated a positive significant correlation between BChE activity and weight, waist and hip circumference.

Conclusions: These results support the hypothesized role of BChE in lipid metabolism. Because of the high prevalence of obese children in Mexico, BChE activity may be used as a biomarker in combination with anthropometry to monitor obesity.

Keywords: Cholinesterase, Children, Anthropometry, Obesity.

INTRODUCTION

The state of Yucatan is located in southeastern Mexico on the Yucatan Peninsula. Yucatan has a population of approximately 2,000,000 [1]. Yucatan's primary economic activities are cattle ranching, intensive pig and poultry production, deep-sea fishing, honey production, tourism, and shifting agricultural production, or swidden. The population sampled in this study was from three towns in Yucatan, Merida, Progreso and Ticul. Merida is the capital of the state and its largest city, with approximately 830,000 habitants, or 780,000 excluding the rural areas of the municipality [1]. Residents of Merida engage primarily in political administration, academic activities, and services. Manufacturing is present, but plays a secondary role in the city's economy. Progreso, with a population of 47,000, excluding rural areas of the municipality [1], is located north of Merida on the Gulf Coast and is the state's primary port town. The most important economic activities are deep-sea fishing and import/export activities. Finally, Ticul, with a population of approximately 33,000, excluding rural areas of the municipality [1], is the most important town in the southern part of the state, a largely agricultural district. The residents of Ticul primarily offer services to the surrounding towns and villages, and also engage in small-scale manufacturing, particularly shoes.

Similar to much of southern Mexico, the state of Yucatan has a largely indigenous population (Maya) that is socially, politically, and economically marginalized by the dominant "mestizo" culture from central and northern Mexico. This population was relatively isolated from major globalization forces throughout much of the 20th century and continued to live in "idyllic Indian villages," noted for their oval shaped wattle-and-daub houses with thatched roofs [2-4]. However, during the last 30 years, this situation has changed dramatically as Mexico has increasingly embraced a Neoliberal economic policy [5-7]. Over this period, global markets have penetrated deep into the Yucatan countryside bringing new products and a new consumerism to many inhabitants. These changes have brought the most profound dietary and health transitions to the region since the Spanish conquest in the 1540's. Specifically, there has been an enormous increase in the consumption of soft drinks and industrially processed food in a population that had only limited access prior to 1990. After 30 years of intense globalization, the population of Yucatan is facing a diabetes-obesity-malnutrition epidemic [8-11]. Currently, 7 of every 10 adult Yucatecans is overweight, and 73% of these individuals present with abdominal obesity [12,13]. Sadly, children are quickly becoming as obese as their parents. Approximately 30-40% of children and adolescents living in Yucatan are overweight or obese [12-14].

In humans, two cholinesterases are present, acetylcholinesterase (AChE, 3.1.1.7) also known as true cholinesterase, red blood cell (RBC) cholinesterase or erythrocyte cholinesterase, and butyrylcholinesterase (BChE, 3.1.1.8), also known as pseudocholinesterase or plasma cholinesterase. AChE is a key enzyme in the nervous system that hydrolyzes acetylcholine in synaptic junctions. It is also present in non-cholinergic neurons and in hematopoietic, osteogenic and various neoplastic cells where it is involved in neuritogenesis, cell adhesion, synaptogenesis, hematopoiesis, and thrombopoiesis [15]. BChE has a wide tissue distribution. Previous studies suggest that BChE may be involved in detoxification processes, lipid metabolism, cell regeneration, neurogenesis, regulation of cell proliferation, and at the onset of differentiation during early neuronal development [16].

Cholinesterases have traditionally been used to assess the toxic effects of pesticides, mainly organophosphate and carbamates [17,18]. However, they have also been used as biomarkers of nutritional status [19], hypothyroidism [20], cancer [21,22], Alzheimer's disease [23,24], inflammation [25] and other conditions [26,27].

Because of the importance of cholinesterase levels as biomarkers of human health, the objective of this study was to evaluate the plasma and erythrocyte cholinesterase activities to determine the enzyme levels in children from the state of Yucatan and to identify any relationship with anthropometric values.

METHODS

This project was evaluated and approved by the institutional ethics committee of UNAM. At the beginning of the project, a sensitization campaign was performed to inform parents, teachers, and school principals of the objective of the study, as well as the benefits and risks associated with participation. Informed consent was obtained from each participating child's legal guardian before any sample or measurement was obtained, and before any medical, psychological, and social interviews were performed. Furthermore, all personal information regarding the participants was maintained in the strictest confidence.

A total of 104 participants were recruited during 2011 in Merida (n=33), Progreso (n=35) and Ticul (n=36) following a multistage stratified sampling strategy. First, the study population was stratified by geographic entity (town). Then, the largest two towns, Merida and Progreso, were stratified by the school districts established by the Secretary of Public Education. Merida and Progreso were divided into three districts, to allow for straightforward sampling. After the eligible schools were identified in each school district, one school was randomly selected from each district using a random table of numbers for Merida and Progreso, and three schools were selected using a random table of numbers for Ticul, which is organized into a single district by the Secretary of Education. Therefore, three schools were selected in each town for sampling. After the particular schools were selected, a minimum of 5 boys and 5 girls aged 6-9 years old were recruited for participation in the study at each school. The minimum sample number for this study was 90. However, in each school, more than 5 children of each gender wished to participate, resulting in a sample size of 104 individuals. Eligible participants fulfilled the following criteria: (1) 6 and 9 years old; (2) no evidence of disease; (3) at least a 3-year residency at the site and (4) informed consent from their parents.

Blood samples were collected at their elementary schools in a fasting state, and their clinical histories and health state were obtained. Age, weight, hip and waist circumferences were measured 1-day prior to blood samples collection. The blood samples were drawn from the cubital vein using "Vacutainers" into 10 ml tubes containing heparin. The blood was centrifuged at 3000 rpm for 10 minutes. The plasma was separated from the cells and the samples were frozen at −80°C until analysis. The body mass index (BMI) was calculated using the formula BMI=(weight in Kg)/(height in m)^2. The BMI-for-age percentiles were determined using tables developed by the National Center for Health Statistics with the National Center for Chronic Disease Prevention and Health Promotion (http://www.cdc.gov/growthcharts). Children were considered underweight if their BMI was less than the 5th percentile, healthy weight children were between the 5th and 85th percentiles, overweight children were between the 85th and 95th percentiles, and obese children were those with a BMI higher than the 95th percentile.

Cholinesterase activities were determined as described previously [28] with modifications adapted to a microplate reader. For the plasma BChE activities, 2 µl plasma were assayed in 188 µl 0.5 mM, 5-dithiobis (2-nitrobenzoic acid) (DTNB, Sigma, St. Louis, MO, USA) in 0.05 M Tris Buffer pH 7.4. The reaction was initiated with the addition of 10 µl 20 mM butyrylthiocholine iodide (Sigma, St. Louis, MO, USA). For the erythrocyte AChE activities, the cells were diluted 1:700 in Tris buffer pH 7.4. Each well contained 20 µl diluted erythrocytes and 180 µl 0.5 DTNB in 0.05 M Tris buffer pH 7.4. The reaction was initiated with the addition of 10 µl 20 mM acetylthiocholine iodide (Sigma, St. Louis, MO, USA). All enzyme activities were measured at 26°C.

For both AChE and BChE activities, the rate of product formation was measured for 120 seconds in a microplate reader at 405 nm. Triplicate analysis was performed for each sample. The enzyme activities were calculated and expressed as U/ml plasma or U/ml RBC.

Basic statistics were performed with Statistica v 7.0. or Graph Pad Prism v 6.0. Height, weight, waist circumference, hip circumference, AChE, and BChE activity differences between sampling sites and BMI were determined using the Kruskal–Wallis test, followed by Dunn's *post-hoc* test. Gender differences were evaluated using a Mann–Whitney test. Correlations of ChE activities with height, weight, waist, and hip circumference were determined using Spearman rank order test.

RESULTS

The age and anthropometric medians of the participants are presented in Table 1. The cholinesterase activities are reported in Table 2. The results indicated that there were no significant gender differences in age, height, weight, BMI, waist, or hip circumference. This was also observed for the AChE and BChE activities. When comparing the sampling sites, significant differences within towns were observed for hip circumference and BChE activity. *Post-hoc* tests indicated that the children from Ticul presented with higher BChE activity compared to the children from Merida or Progreso. Children from Progreso also had a smaller hip circumference compared to the children from the other two towns. No differences were observed for AChE activity within the towns.

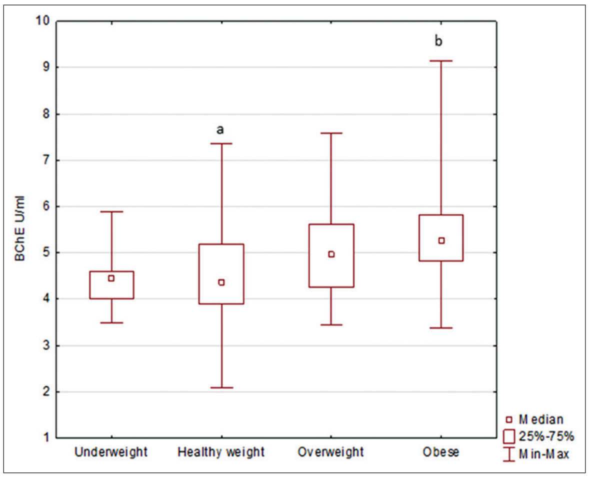

Fig. 1: Butyrylcholinesterase activity in children from Yucatan, Mexico grouped according to their body mass index. The different letters indicate paired differences at p≤0.05

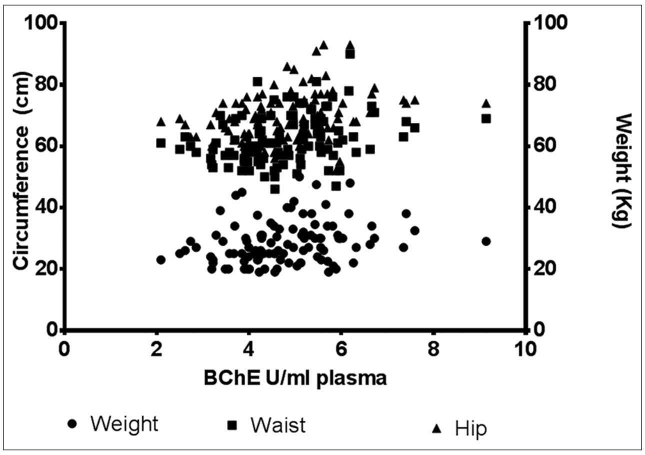

Fig. 2: Butyrylcholinesterase activities and its relationship with weight, hip and waist circumference

Table 1: Age and anthropometric parameters of children from Merida, Progreso and Ticul, Yucatan, Mexico

Parameters	Age (years)	Height (cm)	Weight (Kg)	BMI (Kg/m²)	Waist circumference (cm)	Hip circumference (cm)*
General						
Total n=104	8.0	125.0	27.0	17.2	61.0	69.0
	(8.0-8.0)	(122.0-129.0)	(23.0-31.5)	(15.5-19.8)	(57.0-68.5)	(64.0-74.0)
	(6.0, 9.0)	(112.0, 139.0)	(19.0, 50.0)	(12.5, 28.8)	(52.0, 90.0)	(52.0, 93.0)
Boys n=51	8.0	126.0	27.0	18.3	61.0	70.0
	(8.0-8.0)	(123.0-129.0)	(24.0-34.5)	(15.5-21.0)	(56.0-70.0)	(64.0-74.0)
	(6.0, 9.0)	(113, 137)	(20.0, 50.0)	(13.0, 28.0)	(50.0, 90.0)	(56.0, 93.0)
Girls n=53	8.0	124.0	27.0	17.0	61.0	68.0
	(8.0-8.0)	(121.0-129.0)	(23.0-30.0)	(15.5-18.9)	(57.0-64.0)	(63.0-74.0)
	(7.0, 9.0)	(112.0, 139.0)	(19.0, 42.0)	(12.5, 22.8)	(46.0, 76.0)	(52.0, 93.0)
Merida						
Total n=33	8.0	125.0	27.0	17.1	61.0	70.0[a]
	(8.0-9.0)	(122.0-129.0)	(23.0-33.0)	(15.4-19.7)	(58.0-70.0)	(65.0-76.0)
	(6.0, 9.0)	(114.0, 139.0)	(20.0, 47.5)	(14.4, 25.3)	(53.0, 81.0)	(60.0, 91.0)
Boys n=16	8.0	127.3	28.5	16.8	61.0	70.5
	(8.0, 8.0)	(122.5, 129.3)	(20.0, 47.5)	(15.3, 21.0)	(57.0, 71.5)	(67.0, 75.0)
	(6.0, 9.0)	(115.0, 137.0)	(23.5, 34.5)	(14.4, 25.3)	(54.0, 81.0)	(60.0, 91.0)
Girls n=17	8.0	124.0	27.0	17.1	61.0	69.0
	(8.0, 8.0)	(121.0, 129.0)	(23.0, 31.0)	(15.4, 18.7)	(58.0, 66.0)	(65.0, 76.0)
	(7.0, 9.0)	(114.0, 139.0)	(20.0, 42.0)	(14.6, 22.8)	(53.0, 76.0)	(60.0, 85.0)
Progreso						
Total n=35	8.0	126.0	29.0	18.1	60.0	65.0[b]
	(8.0, 8.0)	(123.0-131.0)	(25.0-32.0)	(16.0-20.5)	(54.0-67.0)	(61.0, 72.0)
	(7.0, 9.0)	(115.0, 137.0)	(20.0, 50.0)	(13.2, 28.7)	(47.0, 74.0)	(52.0, 81.0)
Boys n=17	8.0	126.0	30.0	19.2	65.0	67.0
	(8.0, 8.0)	(125.0, 131.0)	(25.0, 39.0)	(16.0, 22.8)	(54.0, 69.0)	(60.0, 74.0)
	(7.0, 9.0)	(118.0, 137.0)	(20.0, 50.0)	(13.7, 28.7)	(50.0, 74.0)	(56.0, 78.0)
Girls n=18	8.0	125.0	28.5	17.6	59.5	64.0
	(8.0, 8.0)	(123.0, 131.0)	(25.0, 31.0)	(16.0, 19.6)	(54.0, 62.0)	(62.0, 69.0)
	(7.0, 9.0)	(115.0, 136.0)	(20.0, 38.0)	(13.2, 22.8)	(47.0, 74.0)	(52.0, 81.0)
Ticul						
Total n=36	8.0	124.5	26.0	16.5	62.5	69.5[a]
	(8.0, 8.0)	(121.0, 129.0)	(22.0, 30.3)	(15.2-19.2)	(57.0-69.0)	(66.0-76.0)
	(7.0, 9.0)	(112.0, 136.0)	(19.0, 48.0)	(12.5, 28.8)	(46.0, 90.0)	(46.0, 90.0)
Boys n=18	8.0	126.5	26.5	16.3	60.5	69.5
	(8.0, 8.0)	(122.0, 129.0)	(22.5, 34.0)	(15.3, 20.7)	(58.0, 72.0)	(66.0, 77.0)
	(7.0, 9.0)	(113.0, 133.0)	(20.0, 48.0)	(13.0, 28.8)	(53.0, 90.0)	(62.0, 93.0)
Girls n=18	8.0	122.5	26.0	16.9	63.0	70.0
	(8.0, 8.0)	(119.0, 128.0)	(20.0, 30.0)	(15.1, 17.8)	(57.0, 68.0)	(67.0, 75.0)
	(7.0, 9.0)	(112.0, 136.0)	(19.0, 40)	(12.5, 22.2)	(46.0, 76.0)	(58.0, 93.0)

The medians, interquartile range, minimum and maximum, separated by a comma, are reported. *Variables with significant differences for location at p≤0.05.
The different letters indicate variables that are significantly different

Notably, when the children were classified according to their BMI (Table 3), there was a high prevalence of overweight and obese children, particularly boys (48.9%). When the data were analyzed using the BMI group as the grouping factor, the results indicated that there were significant differences in the BChE activities, but not AChE activities (Fig. 1). As expected, there were also significant waist and hip circumference differences based on the BMI. The results demonstrated a positive significant correlation between BChE activity and weight (r=0.2724, p=0.0051), waist (r=0.32, p=0.0008) or hip circumference (r=0.35, p=0.0002, Fig. 2). No significant correlations were found for the AChE activities and these same variables.

DISCUSSION

Obesity is an emerging health problem in Mexico. This condition is not exclusive to adults, but is present at all ages, including children [29]. In this study, overweight or obese children represented 40.3% of the sampled population. This number is higher than that of the Mexican National Nutrition Survey, in which the prevalence of overweight or obese children was 27.2% [13]. However, it is consistent with another study conducted in Mexico City (48.5%) [30] and a recent study conducted in rural Yucatan (38%) [12].

Changes in BChE activity are related to nutritional status. Several studies found that lower activities occur during malnutrition. By contrast, increased activity levels are related to obesity and metabolic syndrome [19]. Although the role of BChE has not been completely elucidated, it has an important role in lipid metabolism, via the hydrolysis of choline esters, which are products of free fatty acid metabolism and liver lipogenesis [31].

In this study, the results indicate that there are significant differences in BChE activity when children are grouped by BMI. Other reports have also found a relationship between BChE activity and BMI [32-34]. Interestingly, a positive correlation is present between BChE activity and weight. This relationship has also been observed in previous studies [35,36] Currently, BMI is the standard for classifying the nutritional status of children and adults; however, BMI does not measure fat distribution. Therefore, waist circumference has been proposed as an estimate of the amount of abdominal fat [37]. In this study, a positive correlation was found between BChE activities and waist circumference, providing additional information to support the hypothesis of the role of BChE in fat metabolism.

No correlations were found between erythrocyte AChE activities and anthropometric measurements. Previous reports indicated that

Table 2: AChE and BChE activities in children from Merida, Progreso and Ticul, Yucatan, Mexico

General	AChE (U/ml RBC)	BChE* (U/ml plasma)
General		
Total n=104	74.3	4.7
	(64.1-83.3)	(4.0-5.5)
	(44.063, 117.57)	(2.1, 9.1)
Boys n=51	75.01	4.9
	(67.6-84.5)	(4.2-5.5)
	(44.1, 96.5)	(3.2-7.4)
Girls n=53	71.3	4.7
	(63.4-82.2)	(3.8-5.6)
	(44.7, 117.6)	(2.1, 9.1)
Merida		
Total n=33	74.85	4.3[a]
	(64.0-82.5)	(3.9-5.4)
	(49.4, 117.57)	(2.1, 7.6)
Boys n=16	76.6	4.7
	(68.8-86.9)	(4.0-5.6)
	(57.74, 88.24)	(3.2, 6.3)
Girls n=17	66.0	4.2
	(62.6-79.5)	(4.0-5.0)
	(49.5, 117.6)	(2.1, 7.6)
Progreso		
Total n=35	71.6	4.4[a]
	(64.1-81.2)	(3.7-5.2)
	(46.0, 99.4)	(2.6, 7.4)
Boys n=17	71.56	4.6
	(67.6-80.5)	(4.3, 5.1)
	(50.2, 89.4)	(3.4, 7.4)
Girls n=18	71.3	4.1
	(62.2-81.2)	(3.3-5.2)
	(46.0, 99.4)	(2.6, 60)
Ticul		
Total n=36	76.25	5.3[b]
	(64.9-84.9)	(4.6-5.8)
	(44.1, 103.1)	(3.5, 9.1)
Boys n=18	76.4	5.2
	(67.3-85.9)	(4.6-5.7)
	(44.1, 96.5)	(3.8-6.2)
Girls n=18	75.9	5.4
	(62.6, 83.5)	(4.6-6.3)
	(44.7-103.1)	(3.5, 9.1)

The median, interquartile range, minimum and maximum, separated by a comma are reported. *Variables with significant differences for location p≤0.05. The different letters indicate variables that are significantly different, RBC: Red blood cell, AChe: Acetylcholinesterase, BChE: Butyrylcholinesterase

a significantly lower AChE activity is found in overweight people compared to normal weight individuals, indicating that AChE may result in impaired physicochemical properties of the erythrocyte membrane in overweight and obese people because of higher levels of cholesterol [38]. However, this was not present in the children sampled in this study.

Obesity is related to other conditions, such as cardiovascular disease, Type 2 diabetes, and metabolic syndrome. Because of the high prevalence of overweight and obese children in Mexico, including Yucatan, BChE activity may be used as a fast and inexpensive biomarker, in combination with hip and weight circumference, to help monitor health in children. The importance of constant surveillance of at risk populations using cost-effective tools may help to elucidate the prevalence of obesity.

Table 3: BMI group percentage in children from Merida, Progreso and Ticul, Yucatan, Mexico

BMI condition	Underweight (%)	Healthy weight (%)	Overweight (%)	Obese (%)
General				
Total	5.8	53.9	16.3	24.0
Boys	3.9	47.0	13.7	35.2
Girls	7.5	60.4	18.9	13.2
Merida				
Total	0	63.6	9.1	27.2
Boys	0.0	56.2	6.2	37.5
Girls	0.0	70.58	11.8	17.6
Progreso				
Total	5.7	42.9	25.7	25.7
Boys	5.9	35.3	17.6	41.17
Girls	5.6	50.0	33.3	11.1
Ticul				
Total	11.1	55.6	13.9	19.4
Boys	5.6	50.0	16.7	27.8
Girls	16.7	61.1	11.1	11.1

BMI: Body mass index

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